Review of Global Medicine and Healthcare Research

Editors:
Forouzan Bayat Nejad
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Review of Global Medicine and Healthcare Research

Vol. 1 No. 1

Proceedings of the 3rd International Online Medical Conference (IOMC 2010)

Editors:
Forouzan Bayat Nejad
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Editorial

Review of Global Medicine and Healthcare Research

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On behalf of IOMC 2010 Conference secretariat and the International Online Medical Council (IOMC), we would like to thank everyone who contributed to the conference and made it another success, specially the Conference Advisory & Committee Board Members, Reviewers, Panelists & Judges, and the conference participants & presenters.

Having said that, we are glad to inform you about launching of this new periodical publication entitled “Review of Global Medicine and Healthcare Research”. It will mainly cover the papers from IOMC Conferences.

The IOMC secretariat has already tarted to index this publication and its papers in renowned databases, whcich we will later update you on it accordingly.

Thank you once again and we wlook forward to seeing you in IOMC 2011.

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Optimum number of antenatal visits among antenatal mothers to reduce low birth weight babies as an outcome

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Abstract

Introduction: In Malaysia, the antenatal care services are provided by both public and the private sectors. This study aims to determine the optimum number of antenatal visits required for low-risk mother taking the low birth weight as the outcome indicator.

Materials and methods: It is a cross sectional study, conducted in the Kuala Muda District of Kedah in Malaysia. Antenatal records of each mother were reviewed according to the selection criteria. Face to face interview was also done to collect other data.

Results: The average age of the pregnant mothers was 28.5 years, and the majority of them were Malays (62.5%), married (96.5 %), with 70.1% having at least secondary education level. The mean gestation week at delivery was 38.45 weeks, while mean birth weight of baby at birth was 2.97 kg. The prevalence of low birth weight among low risk mothers in the district was 9.7%. The odds of having low birth weight babies among mothers with ten antenatal visits reduced by 91%, compared to mothers with visits less than eights, when other variables held constant.

Discussion: Majority of the mothers had at least secondary education, married; non-smokers and majority of them (83%) of them were between the ages of 18 to 34 years. This study shows that mothers with less than eight visits had twice the risk of having low birth weight babies as compared to mothers with eight visits and more. Using the low birth weight as an outcome indicator it is proposed that the low risk mother need to have only 10 visits as the benefits are the same after 10 visits.

Conclusion: Mothers with less than 8 antenatal visits had twice the risk of having low birth weight than the normal birth weight babies. This study showed that the minimum number of antenatal visits required for low risk mothers to reduce the low birth weight incidence was 10 antenatal visits although the mothers wanted to have about 7 visits.
Key words: antenatal care, antenatal visits, low birth weight, maternal and child health, Malaysia

Introduction

Traditionally, the schedule of antenatal visits is not ordered by a set of clearly defined maternal or foetal requirements, but by a routine established in United Kingdom in 1920s. The rationale of this schedule is based on the theory that regular visits with predefined content enable midwives and doctors to detect conditions in the mother and the baby that may threaten their health. Conditions are then monitored or treated to ensure a safe delivery and better outcomes. According to this routine, antenatal visits were scheduled as; monthly until 28 or 32 weeks' gestation, then fortnightly until 36 weeks, and weekly thereafter until delivery, resulting in up to 16 visits during pregnancy with little or no distinction between high and low-risk mothers.

The assessment done during the antenatal visits depend on various factors such as the health status of the pregnant women, the category of staff providing the service, the services available at the health centre, and various other factors. In Malaysia, the antenatal care services are provided by both public and the private sectors. Even at the public sectors, different set of services are provided based on the site of care namely; community health clinics, health clinics with or without Family Medicine Specialist, and also hospital with or without an Obstetrician. However, the basic services provided are similar, i.e. monitoring of maternal and fetal conditions to look for any complication which needs referral for further management if at the peripheries.

In the developing world, the traditional model of antenatal care has become the recommended standard, with little adaptation made for differing local circumstances. However, in many of these developing countries where resources for reproductive health care are sparse or used inefficiently, the care often consist of irregularly spaced visits with long waiting time and poor feedback to mothers.

In 1989, the National Institutes of Health Expert Panel on Prenatal Care, had proposed to reduce the number of prenatal visits for low-risk nulliparous women to 10 visits and for low-risk, parous women to 8 visits, from their traditional 14 visits. Various studies had noted no significant difference in the obstetric outcomes of low risk pregnancies when comparing the new model, which advocate less antenatal visits, with the traditional model.

In 1998, Mathai had suggested a reduced number of antenatal visits for low-risk pregnancy in under-resourced settings. Based on the report, the minimum number of goal-oriented antenatal visits in the low risk women should be at least four. The suggested visits include; first visit during first trimester with the purpose of eliciting details of previous pregnancy outcomes and maternal diseases, identify and treat women with anemia and syphilis, and accurate determination of gestational age using available tools. Subsequent visits include: at 22 to 28 weeks to record blood pressure and symphysis-fundus height measurements, at 32 weeks to identify pregnancy-induced hypertension, pre-eclampsia and altered fetal growth, and at 36 weeks to
identify malpresentations and initiate appropriate action such as referral for external cephalic version for breech presentation. From 1996 to 1998, a multicentre randomized controlled trial\textsuperscript{10} was conducted by WHO in 53 clinics in Argentina, Cuba, Saudi Arabia, and Thailand to compare the standard model of antenatal care with a new model. The result showed that women in the new model had a median of five visits compared with the eight visits in the standard model. The study revealed that the provision of routine antenatal care by the new model seemed not to affect both the maternal and perinatal outcomes, and so it can be implemented without major resistance from women and providers of health care at reduce cost.

In 1999 Cochrane review\textsuperscript{11} had concluded that based on various trials evaluating the number of visits, four antenatal visits appeared to be the minimum that should be offered to a low risk pregnant women. A study in Perak, Malaysia in 2000,\textsuperscript{12} noted that there is no association between number of visits and maternal intrapartum complication or birth weight of the babies. In Malaysia, based on the Model of Good Care, antenatal visits of eight or more are considered as adequate care.\textsuperscript{13}

Over the years, the average number of antenatal visits per pregnant mother had improved tremendously from an average of 4.4 visits per mother in 1975 to 8.9 visits in 2001.\textsuperscript{14} However in order to assess whether it is necessary to reduce the number of visits for low risk pregnancy locally, the exact optimum number of antenatal visits for low-risk pregnancies should be identified. The Report of the National Research Priorities in Reproductive Health for Malaysia during the Sixth Meeting of the Regional Advisory Panel (RAP) for Asia and Pacific in 2002 had identified several areas for research purposes. The frequency of antenatal visit had been identified as the Priority One, i.e. to be done within one year.\textsuperscript{15}

This study aims to determine the optimum number of antenatal visits required for low-risk mother taking the low birth weight as the outcome indicator. The mothers’ preference of number of antenatal visits for low risk pregnancies will be also determined.

**Materials and Methods**

This study is a cross-sectional study, conducted in the Kuala Muda District, Kedah, Malaysia. The study population consists of all low risk mothers; who were coded white or green during last antenatal check-up based on the colour coding system for Risk Approach Strategy currently used in Ministry of Health. The white and green code is an identification of low risk pregnant women. An antenatal visit is defined as an intentional encounter between pregnant women and a midwife or doctor to assess and improve maternal and fetal well being through out pregnancy and prior to labour\textsuperscript{16}

The required sample size was calculated based on the prevalence of low birth weight in Malaysia (9.7% in 2000). Using EPI INFO 6 for a cross sectional study with 10% prevalence of low birth weight, Odds Ratio was set at 2.0, which meant a different of twice the risk of having low birth weight was considered as significant. Based on significance level which was set at 0.05 with 95% confidence interval and 80% power of study, the estimated sample size was 737 subjects. Based on the sample size
required, 737 mothers were selected using systematic random sampling during the period of the study. There were 87 non-responders due to defaulted follow-up resulting in 88.2% response rate. Inclusion criteria of the subjects included low risk mothers based on the colour code given during last antenatal check-up, mothers who gave birth after 1st August 2003 and before 31st March 2004, those mothers who received postnatal care (at one month postpartum) in all the health centres in the district. The exclusion criteria included high risk mothers (coded either yellow or red during last check-up), mothers who gave birth before 22 weeks, multiple pregnancies, transferred cases, either in or out, and those who received antenatal and/or postnatal care at private clinics.

Antenatal records of each mother, who were under postnatal care by the clinic staff, were checked by the researcher and the assistants according to the selection criteria, and consent forms were attached to eligible records. Before the implementation of the study, the researcher briefed the assistants about the objective of the study and trained them in conducting the interview. Systematic random sampling from the sampling frame was done. The first case was selected randomly, followed by every second case. The socio demographic profile of the non-participate mothers including mothers who defaulted follow-up were taken to compare with the profile of the participating mothers to avoid any bias in the study. Written consent of every selected mother was sought before the interview. Among the independent variables studied included; socio economic status (education levels, family income), social problem (marital status, smoking), body mass index in the first trimester (as a proxy of pre-pregnancy BMI), parity, inter pregnancy interval, and the number of comprehensive antenatal visits.

Data was collected using the Data Collection Form which consist of two sections; first section which required face-to-face interview and the second section which required extracting data from the identified records. Consent from the mothers was taken at the registration at the clinics for postnatal check-up at one month postpartum. The raw data was stored as both hard copies and in software using Statistical Package for Social Science, SPSS Version 11.5. Data was analysed using summary statistics, followed by bivariate analysis using Chi-square test. The significance level of the statistical test was set at 95% Confidence Interval and α was set at 0.05. The Odds Ratio was calculated followed by Logistic Regression to look for interaction or confounding, and also adjusted odds ratio.

Results

The average the age of the mothers was 28.5 years, and the majority of them were Malays (62.5%), married (96.5 %), with 70.1% having at least secondary education level. (table 1)
Table 1: Socio demographic profile of the mothers, n=650

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>28.47 (0.21)</td>
<td></td>
</tr>
<tr>
<td>Ethnic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>360 (55.4%)</td>
<td></td>
</tr>
<tr>
<td>Chinese</td>
<td>120 (18.5%)</td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>153 (23.5%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>17 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Education level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>12 (1.9%)</td>
<td></td>
</tr>
<tr>
<td>Primary school</td>
<td>80 (12.3%)</td>
<td></td>
</tr>
<tr>
<td>Secondary school</td>
<td>494 (76.0%)</td>
<td></td>
</tr>
<tr>
<td>Tertiary level</td>
<td>64 (9.8%)</td>
<td></td>
</tr>
<tr>
<td>Household income</td>
<td>RM 542.61</td>
<td>(44.71)</td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>627 (96.5%)</td>
<td></td>
</tr>
<tr>
<td>Unmarried/widow/divorsee</td>
<td>23 (3.5%)</td>
<td></td>
</tr>
<tr>
<td>Ever smoke during pregnancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>621 (95.5%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>29 (4.5%)</td>
<td></td>
</tr>
</tbody>
</table>

SD: standard deviation

Table 2: Obstetric Profiles of the low risk mothers, n=650.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parity</td>
<td>1.53 (0.06)</td>
<td></td>
</tr>
<tr>
<td>Inter pregnancy interval (in month)</td>
<td>23.81 (0.08)</td>
<td></td>
</tr>
<tr>
<td>Colour Code</td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>172 (26.5%)</td>
<td></td>
</tr>
<tr>
<td>Green</td>
<td>478 (73.5%)</td>
<td></td>
</tr>
<tr>
<td>Gestation week at first check-up (in week)</td>
<td>12.66 (0.21)</td>
<td></td>
</tr>
<tr>
<td>BMI in first trimester (kg/m²)</td>
<td>22.09 (0.19)</td>
<td></td>
</tr>
<tr>
<td>Number of antenatal visit</td>
<td>9.58 (0.09)</td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard Deviation
BMI: Body Mass Index

Table 2 shows the first check of these mothers was about 12.66 weeks (about three months) and the average BMI was around 22. This study also revealed that the mean gestation week at delivery was 38.45 weeks, while mean birth weight of baby at birth was 2.97 kg. The prevalence of low birth weight among low risk mothers in the district was 9.7% (63 mothers), and 38 mothers (5.8%) had pre-term deliveries.

Bivariate analyses was done, to look for association between independent variables and low birth weight among low risk mothers and it showed that there was a significant association between the number of antenatal visit, age, parity, inter pregnancy interval, with the dependent variable of low birth weight. Low risk
mothers with less than eight visits were noted as having twice the risk of low birth weight compared to mothers with more than eight visits (p=0.006, Crude Odds Ratio: 2.28, 95% Confidence interval: 1.24 – 4.10).

This study also shows that ethnic Indian mothers are having a higher prevalence of low birth weight (p=0.000) compared to the Malay and Chinese mothers. Low risk mothers who had ever smoked during the pregnancy were noted to have about three times higher risk of having low birth weight infants compared to mothers who were non- smokers (p=0.041, Crude OR: 2.58, 95% CI: 1.01 – 6.60). A significantly higher prevalence of low birth weight was also noticed among mothers who initiated antenatal care during first trimester, compared to those after the first trimester (p=0.008, Crude OR: 2.08, 95% CI: 1.20 – 3.63). Among the low risk mother who had antenatal care in first trimester, body mass index at booking of less than 18.5 kg/m² had significantly higher percentage of low birth weight infants (p=0.027).

Logistic Regression was done with low birth weight as the dependent variable. To find the minimum number of visit that had the lowest percentage of low birth weight, antenatal visit which is a continuous variable was changed to a categorical variable. Antenatal visits were recoded into eight groups namely; < 8 visits, 8 visits, 9 visits, 10 visits, 11 visits, 12 visits, 13 visits, and > 13 visits. Other covariates included were ethnicity, interpregnancy interval, age, and parity, Body Mass Index (BMI) at first trimester, pre-term delivery, and smoking status. Analysis was done only for mothers, who initiated care during first trimester, and result of the logistic regression had noted no significant interaction or confounders, and all the significant variables were independent variables. Result of the analysis had noted that R² was 0.18, which showed an average ‘percent of variance explained’ of 18%. Result also noted that the Hosmer and Lemeshow test was not significant (p=0.844, df =8) while, classification table showed an overall percentage of 88.0%, which indicate a well-fitting models.

Table 3 shows the result of logistic regression, the odds of having low birth weight babies among mothers with ten antenatal visits reduced by 91%, compared to mothers with visits less than eights, when other variables held constant. In addition, the odds of having low birth weight infants among mothers with 11 antenatal visits reduced by 86%, compared mothers with visits less than 8, with other variables being held constant. Among mothers with 12 visits, the odds of having low birth weight reduced by 94%, compared mothers with visits less than 8, when other variables held constant. Logistic regression analysis had also noted that the odds of having low birth weight infants among Indian mothers were six times of Malay mothers, when other variables held constant. Furthermore, the odds of having low birth weight infants among ever smokers were 15 times of non-smokers, when other variables held constant. Other variables were found to be not significantly contributed to the occurrence of low birth weight infants.

Table 3: Logistic regression analysis of the number of visit and low birth weight

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted OR* (95% CI*)</th>
<th>LR² Statistic (df²)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antenatal visit</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than 8 visits</td>
<td>1</td>
<td>17.788 (7)</td>
<td>0.013</td>
</tr>
<tr>
<td>8 visits</td>
<td>0.238 (0.049 – 1.163)</td>
<td>3.146 (1)</td>
<td>0.076</td>
</tr>
<tr>
<td>9 visits</td>
<td>0.499 (0.141 – 1.771)</td>
<td>1.157 (1)</td>
<td>0.282</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Visits</th>
<th>Odds Ratio (CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 visits</td>
<td>0.091 (0.018 - 0.468)</td>
<td>0.004a</td>
</tr>
<tr>
<td>11 visits</td>
<td>0.145 (0.033 - 0.635)</td>
<td>0.010c</td>
</tr>
<tr>
<td>12 visits</td>
<td>0.059 (0.009 - 0.375)</td>
<td>0.003e</td>
</tr>
<tr>
<td>13 visits</td>
<td>0.103 (0.009 - 1.159)</td>
<td>0.066</td>
</tr>
<tr>
<td>More than 13 visits</td>
<td>0.124 (0.011 - 1.400)</td>
<td>0.091</td>
</tr>
</tbody>
</table>

**Ethnic**
- Malay: 1, 17.512 (3), 0.001
- Chinese: 0.770 (0.154 – 3.835), 0.102 (1), 0.749
- Indian: 6.015 (2.448 – 14.776), 15.308 (1), 0.000e
- Others: 0

**Smoking Status**
- Smokers: 15.179 (2.953 – 78.023), 10.603 (1), 0.001e
- Non smokers: 1

**Pre-pregnancy BMI**
- < 18.5 kg/m²: 1, 2.972 (2), 0.226
- 18.5 – 24.9 kg/m²: 0.542 (0.210 – 1.400), 1.600 (1), 0.206
- 25 kg/m² and >: 0.352 (0.103 – 1.204), 2.769 (1), 0.096

**Age**
- < 18 yrs: 1, 0.520 (2), 0.771
- 18 – 34 yrs: 0.00, 0.00, 0.999
- 35 yrs and >: 0.00, 0.00, 0.999

**Parity**
- Primip: 1, 0.288 (2), 0.866
- Para 1-4: 1.489 (0.348 – 6.373), 0.288 (1), 0.592
- Para 5 and >: 0.000, 0.00 (1), 0.999

**Inter pregnancy interval**
- Primip: 1, 2.511 (2), 0.285
- < 2 years: 2.862 (0.595 – 13.763), 1.721 (1), 0.190
- 2-5 years: 1.370 (0.320 – 5.866), 0.180 (1), 0.671
- 5 years and >: 0.00

**Pre-term delivery**
- Pre-term: 1, 0.840 (0.205 – 3.439), 0.059 (1), 0.809

Odds Ratio (OR), Log Likelihood Ratio (LR), Confidence Interval (CI), Degree of Freedom (df), and r² values are reported.

Result of the face-to-face interview of the mothers in this study noted that 92.2% of the mothers were satisfied with the current schedule of antenatal visits. The mean number of visits preferred by the mothers in the study population for low risk pregnancies was 7.23 visits.

**Discussion**

Majority of the mothers had at least secondary school education, they were married, were non-smokers and their household income was between RM500 to RM1, 500. Eighty three percent of the mothers in this study were between the ages of 18 to 34 years. Based on the status at the initiation of antenatal care, 95.8% of the mothers were either primigravidas, or para one to four, and 49.6% had inter pregnancy interval of more than two years but less than five years. Fifty three percent of the low risk mothers initiated care during first trimester, and 61.7% of them had ideal Body Mass Index (BMI), at booking of antenatal care.
Low birth weight was taken as the obstetric outcome for this study. Out of 650 babies, 63 (9.7%) of them were low birth weight babies. Prevalence of low birth weight during the study period was similar to the national level, which was generally below 10% (7% in 1999). A recent study on the effectiveness of reducing numbers of antenatal visits for low risk mothers in Kuantan in 2002, (n=240) revealed a low birth weight prevalence of 2.9%\textsuperscript{16} which was much lower than the national figure. This study shows that the prevalence of low birth weight is higher among Indian mothers and mothers who had low BMI at the first trimester.

The mean number of antenatal visits for the study population was 9.58 visits and the majority of them (84.2%) had eight visits or more. This study shows that mothers with less than eight visits had twice the risk of having low birth weight babies as compared to mothers with eight visits and more (Crude OR: 2.28, 95%CI: 1.25 – 4.10, p=0.006). Being an Indian mother, history of ever smoked during pregnancy, and low BMI at booking in the first trimester, were significantly associated with higher prevalence of low birth weight babies.

Logistic regression analysis to look for the minimum number of antenatal visits required for low risk mothers had noted that mothers with antenatal visits of 10, 11, and 12 were associated with significantly lower chance of having low birth weight infants compared to mothers with less than eight visits when other variables held constant. Based on low birth weight alone as the outcome indicator, 10 antenatal visits can be considered as an optimum number of visits. It must be noted however that reduction in antenatal visit need not necessarily reduce the incidence of low birth weight. For instance McDuffie\textsuperscript{4} noted that a reduction of antenatal visits for low risk mothers from 15 visits to 12 visits did not resulting in any adverse obstetric outcome significantly (pre-term delivery, low birth weight, and Caesarean section). Another study by Binstock\textsuperscript{3} which reduced the number of visits from 11 to eight had also noted similar findings. Sikorski\textsuperscript{5} had also noted no significant different in the obstetric outcomes (Caesarean section for hypertensive disorders, maternal and fetal morbidity), with the reduction of visits from 11 to 9 visit.

Presently, Ministry of Health suggests a minimum of seven visits during antenatal, which is once during first trimester, twice during second trimester, three times during third trimester, and once at term. The maximum number of visits now is around 12 to 13 visits per mother. Using the low birth weight as an outcome we propose that the low risk mother need to have only 10 visits as the benefits are the same after 10 visits. However the mean number of visits preferred by the mothers in the study population for low risk pregnancies was 7.23 visits.

**Conclusion**

This study shows that the low birth weight is high in the ethnic Indian mothers as compared to the Chinese and Malay mothers in the study area. It also shows that the mother with less than 8 antenatal visits had twice the risk of having low birth weight than the normal birth weight babies. The minimum number of antenatal visits required for low risk mothers to reduce the incidence was 10 visits. Reduction in the number of visits may reduce the cost and improve quality of each visit. When the mothers were asked the number of antenatal visits the mothers wanted about 7 visits. However that
the number of visits may not only be important but the quality to detect the risk factors and to reduce bad outcome of the mother is equally important.

References

Ventricular arrhythmia risk in elderly heart failure patients

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Abstract

**Background:** Post-infarction heart failure is associated with electrical instability and sudden cardiac death risk due to structural inhomogeneities.

**Aim:** We hypothesized that aging increases electrical instability in post-infarction heart failure patients.

**Methods:** 27 post-infarction heart failure patients underwent: Signal Averaged ECG, 64-lead body surface mapping and 12-lead ECG. They were included in two groups considering their age: 15 adults, aged 52±5 (mean±SD) years and 12 elderly patients, aged 72±5 years.

**Results:** In the elderly patients group: 92% had late ventricular potentials (vs. 47% of the adult patients), 33% multipolar isointegral QRST maps (vs. 20%), 25% ventricular arrhythmias (vs. 20%). There were significant higher values in the elderly group for: SA-QRS duration (138±10 ms vs.118±11 ms, p=0.000151), LAS40 (Low Amplitude Signal) (73±19 ms vs.38±12 ms, p<0.01), maximal QT interval (QTmax: 450±49 ms vs. 438±34 ms, p=0.038), heart rate corrected QT interval (QTc: 543±37 ms vs. 528±65 ms, p<0.01), mean QT interval (QTm: 449±37 ms vs. 413±54 ms, p=0.042), Tpeak-Tend interval and significant lower values for RMS40 (Root Mean Square) (10±2 μV vs. 22±9 μV, p=0.000547).

**Study Limitations:** The main limitations were: the small number of patients, difficulties in delineating the end of T wave and no clear consensus about normal values for Tpe.

**Conclusion:** Ventricular arrhythmia risk is increased in elderly post-infarction heart failure patients compared to adult patients.

**Keywords:** heart failure, aging, QT interval, Tpeak-Tend interval, late ventricular potentials, body surface mapping
Background

Electrical instability in post-infarction heart failure patients is due to the structural
inhomogeneities: fibrosis (fibroid tissue replaces the necrotic infarction area) and
ventricular remodeling. Structural inhomogeneities cause repolarisation
heterogeneities, reentry, ventricular arrhythmias and sudden cardiac death.

Sudden cardiac death, one of the leading causes of mortality, remains a health
problem of epidemic proportions (Kunavarapu & Bloomfield, 2004), and is caused
mainly by fatal ventricular arrhythmias. Identifying patients at risk for these
arrhythmias remains a major challenge in preventive epidemiology.

Aging is considered a cardiovascular risk factor and is usually associated with
increased cardiovascular pathology, the use of multiple drugs, some structural,
functional and vascular changes (Beers, Jones, Berkwits, 2005). The changes of the
senescent heart result from the general process of senescence, the senescence of the
endocrine system and the senescence of the vessels (Swynghedauw, 1999). The most
important age-associated cardiovascular changes are: increased left ventricular wall
thickness, focal collagen deposition and increased vascular stiffness (Beers et al,
2005). Fibrosis renders the myocardium stiffer and mechanically and electrically
heterogeneous, and this plays a crucial role in the genesis of arrhythmias and
impairment of systolic and diastolic function. Senescence is, also, considered an
interfering factor for cardiac remodeling (Diez &, Ertl, 2009). The senescent heart is
comparable to left ventricular overload, myocyte number is decreased (due to necrosis
and apoptosis in the left ventricle), but their size is increased, the action potential
duration and relaxation are prolonged and there are degenerative changes of the
conducting system. The senescent heart, even in the absence of coronary
insufficiency, is potentially a diseased heart (Swynghedauw, 1999).

Cardiac failure is mainly a disease of the elderly (Swynghedauw, 1999) and
ventricular arrhythmias are common in elderly, and their prevalence increases in the
presence of structural heart disease, especially coronary heart disease.

Electrical instability is assessed using noninvasive methods like: signal averaged
electrocardiography (SAECG), body surface mapping (BSM) and 12-lead ECG
(Mozos, Hancu & Cristescu, 2008).

SAECG is used to detect ventricular late potentials (LVP), markers of an
electrophysiological substrate for reentrant ventricular tachyarrhythmia and sudden
cardiac death. LVP are thought to originate from slow-conducting areas of the
myocardium and are low-amplitude, high frequency waveforms in the terminal part of
the QRS complex (Cain, Arthur & Trobaugh, 2003; Mozos, Hancu, Chiulan, Gorun,
2007; Zipes, Camm & Borggrefe, 2006).

The long QT interval was associated with all-cause mortality and cardiovascular
mortality (Sohaib, Papacosta, Morris, Macfarlane & Whincup, 2008). A prolonged
QT interval predisposes to the development of ventricular tachyarrhythmia such as
torsades de pointes and ventricular fibrillation, which could cause syncope, cardiac
arrest, or sudden cardiac death (Sohaib et al, 2008; Zareba, 2007). The Tpeak-Tend
interval (Tpe) has been reported to predict life-threatening arrhythmias in the long QT
syndrome, and is considered a measure of transmural dispersion of repolarization (Fish, Di Diego, Nesterenko & Antzelevitch, 2004; Hevia et al, 2006).

BSM has multiple advantages compared to conventional electrocardiogram in providing diagnostic informations to detect electrical activity changes and allows the most complete visualization of the heart activity mapped on the body surface. Isointegral QRST maps (De Ambroggi, Aime, Cerotti, Rovida & Negroni, 1997) have, in normal persons, only two extremes: a maximum and a minimum, a dipolar character. A complex, multipolar QRST map, with more maxima and minima reflect the regional heterogeneity of the repolarisation process and arrhythmia vulnerability (Gardner, Montague, Armstrong, Horacek & Smith, 1986).

**Aim**

Considering the high prevalence of cardiovascular disorders in elderly patients and the age-associated cardiovascular changes, we hypothesized that aging influences electrical instability in post-infarction heart failure patients and ventricular arrhythmia risk is increased.

**Methods**

**Patients:** 27 post-infarction heart failure patients, stage B and C, from the ASCAR clinic from Timisoara, underwent: SAECG (time-domain analysis), 64-leads body surface mapping and 12-lead ECG in the Functional Exploration Laboratory of the Pathophysiology department of the “Victor Babes” University of Medicine and Pharmacy. They were included in two groups considering their age: the first group was made of 15 adults, aged 52±5 years; the second group of 12 elderly patients, aged 72±5 years. The clinical characteristics of the patients are included in table 1. There were no significant differences between the two groups considering their main characteristics, except the age.

The inclusion criteria were: old myocardial infarction diagnosed according to the ESC /ACCF /AHA /WHF Universal Definition Criteria (Thygesen, Alpert, White, 2007), heart failure diagnosed according to the ESC Guidelines 2008 (Dickstein et al, 2008) and a written consent of the patient. The exclusion criteria were: bundle branch block, atrial fibrillation or flutter at the moment of investigation, electrolyte imbalances, systemic inflammatory processes, active infections and trauma, any symptoms of an inflammatory process.

The investigations conform to the principles outlined in the Declaration of Helsinki (Cardiovascular Research 1997; 35:2-4) and were approved by the Ethics Committee of the University.
Table 1: The characteristics of the study population

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adult patients (15)</th>
<th>Elderly patients (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (means±SD)</td>
<td>52±5</td>
<td>72±5</td>
</tr>
<tr>
<td>Sex M:W</td>
<td>3:2</td>
<td>3:1</td>
</tr>
<tr>
<td>MI survival (years)</td>
<td>1-6</td>
<td>2-9</td>
</tr>
<tr>
<td>MI location: Anterior/inferior/anterior and inferior</td>
<td>9/5/1</td>
<td>8/3/1</td>
</tr>
<tr>
<td>CV risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>smokers 20% (3), HT 33% (5), obesity 20% (3)</td>
<td></td>
<td>smokers 42% (5), HT 42% (5), obesity 25% (3)</td>
</tr>
<tr>
<td>PC: 20% atrial (3), 13% junctional (2),</td>
<td></td>
<td>PC: 17% atrial (2), 17% ventricular (2),</td>
</tr>
<tr>
<td>Sinus tachycardia: 53% (8), Atrial flutter: 20% (3), Atrial fibrillation: 13% (2)</td>
<td></td>
<td>Atrial fibrillation: 8% (1)</td>
</tr>
<tr>
<td>LV Ejection fraction</td>
<td>44±8%</td>
<td>53±6%</td>
</tr>
<tr>
<td>Associated diseases</td>
<td>RVH: 13% (2), Unstable angina: 13% (2), COPD: 20% (3), chronic kidney disease (20%)</td>
<td>Ventricular aneurism: 8% (1), Unstable angina: 8% (1), COPD: 8% (1), 3 chronic kidney disease 4 (33%)</td>
</tr>
<tr>
<td>Therapy:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACEI</td>
<td>80% (12),</td>
<td>50% (6),</td>
</tr>
<tr>
<td>Calcium blockers</td>
<td>40% (6),</td>
<td>42% (5),</td>
</tr>
<tr>
<td>Beta blockers</td>
<td>-</td>
<td>8% (1),</td>
</tr>
<tr>
<td>Class III</td>
<td>33% (5),</td>
<td>33% (4),</td>
</tr>
<tr>
<td>antiarrhythmics</td>
<td>40% (6)</td>
<td>33% (4)</td>
</tr>
</tbody>
</table>

M=men, W=women, MI= myocardial infarction, CV=cardiovascular, HT=hypertension, PC=premature contractions, RVH=right ventricular hypertrophy, COPD=chronic obstructive pulmonary disease, LV= left ventricular, ACEI=angiotensin conversion enzyme inhibitors

SAECG

SAECG, was performed using a Siemens-Megacart electrocardiograph. The single use electrodes were applied as follows: R – on the right arm, L – on the left arm, F – on the left leg, N- on the right leg, C1- on the right midaxillary line, in the V intercostal space, C2 – on the left midaxillary line, in the V intercostal space, C3 – at
the bottom of the sternum, C4 – on the left iliac crest, C5 – posterior, in the IV intercostal space, on the right side of the spinal column, C6 – in the IV intercostal space, on the left side of the sternum (the normal position for V2). Three orthogonal bipolar leads resulted: x (connecting the leads C1 and C2), y (connecting leads C3 and C4) and z (connecting leads C5 and C6) (Mozos et al, 2008).

A correlation coefficient between 0.90 and 0.98 was selected. The signal derived from the 300 beats was amplified, processed and mediated, and filtrated with a bidirectional filter. The noise level was: 0.3-0.6 μV.

The following parameters are essential for the existence of LVP: SAECG QRS duration (SA-QRS), LAS40 (the duration of the signal at the end of the QRS complex with an amplitude below 40 μV - „Low Amplitude Signal”) and RMS40 („Root Mean Square”- the square root of the last 40 ms of the signal). We considered a patient having LVP, if two of the following criteria were positive: QRS duration >120 ms, LAS40>38 ms and RMS40<20 μV (Mozos, 2006; Mozos et al, 2007, Mozos et al 2008).

**Body surface mapping**

The 64 electrodes vest was applied to each patient. The ECG signal recording electrodes were placed around the thorax on 7 rows (placed at a fixed distance of 5 cm) and 13 columns, as an incorporated network in the electrodes vest. 9 columns were placed in the antero-lateral part of the thorax between the right mid-axillary line and the left mid-axillary line, and 4 columns on the posterior part of the thorax, on the mid-scapullary and paravertebral lines, as previously described (Mozos et al, 2008).

The ECG signals from the 64 thorax leads, were recorded using the central Wilson electrode as a reference, were amplified using adjustable amplifiers, multiplexed with a sampling rate of 5 ms and digital converted with a 10 bits resolution. The data were processed using a Pentium computer with a 400 Mhz frequency, 36MB RAM memory, coloured monitor and printer. The maps were displayed in a rectangular format, which corresponds to the surface of the thorax, as a section on the right mid-axillary line.

Isointegral maps provide a distribution of the sum of potentials over a specified time interval. QRST isointegral maps represent the QRST areas for each lead, from the start of the QRS complex through the end of the T wave. The start of the Q wave and the end of the T wave were marked using a cursor. The time integral of the QRST intervals were calculated.

Isointegral maps were then analyzed, by two independent observers, who weren’t informed about the clinical data, to assess the number of extreme positive values (maxima) and extreme negative values (minima).
12-lead ECG

12-lead ECG was assessed using the same Siemens-Megacart electrocardiograph at a paper speed of 25 mm/sec.

The QT interval duration was manually measured from the earliest Q wave onset over all 12 leads. The end of the T wave was defined as the intersection of a tangent to the steepest slope of the last limb of the T wave and the baseline (Postema, De Jong, Van der Bilt, Wilde, 2008). The leads in which the end of the T wave couldn’t be determined exactly, or in which the T wave had low amplitude or was isoelectric, were eliminated.

QTmax (the maximal QT interval duration in all 12 ECG leads) (Rautaharju, Surawicz, Gettes, 2009), QTc (heart rate corrected QT interval) and QTm (mean QT interval duration in all 12 leads) (Mozos, Hancu, Costea & Cristescu, 2009) were assessed.

The QT interval was corrected for rate using using the Bazett formula (Bazett, 1920):

$$\text{QTc} = \frac{\text{QT}}{\sqrt{\text{RR}}}$$

where QTc is the heart rate corrected QT interval and RR, the R-R distance. The Bazett’s formula is the most popular heart rate correction used in clinical practice.

A QT threshold of 450 ms was used to differentiate normal from prolonged QT intervals (Postema et al, 2008; Rautaharju et al, 2009).

The Tpeak-Tend interval (Tpe) is the interval from the T wave peak to the end of the T wave (Hevia et al, 2006). The Tpe was measured in each lead and obtained from the difference between QT interval and QTpeak interval (from the beginning of the QRS until the peak of the T-wave). The Tpe value reported was the maximum obtained by two observers in all leads.

The measurement of each parameter in each lead was obtained by averaging two consecutive beats. Two independent observers, who weren’t informed about the clinical data, obtained the measurements and in case of a difference of >20 ms in each measurement, an agreement was obtained.

Left ventricular hypertrophy

Left ventricular hypertrophy was diagnosed considering at least one of the five following ECG criteria: The Romhilt-Estes scoring system (a score of 5 diagnoses LVH and a score of 4 diagnoses probable LVH) (Romhilt & Estes, 1968), Sokolow-Lyon voltage criteria (SV1 + RV5/R V6 >35 mm) (Sokolov & Lyon,1949), Cornell voltage criteria (R in a VL + S in V3: >28 mm in men, >20 mm in women) (Casale et al,1985) the diagnostic criteria based on the Framingham Heart Study data (Levy, et al, 1990) , Perugia score (Schillaci et al, 1994).
Statistics

Statistical analysis was performed using the t Student test, the Bravais-Pearson linear correlation coefficient (r) and the relative risk (RR).

Results

Late ventricular potentials were present in 47% of the adult post-infarction heart failure patients and 92% of the elderly patients. All SAECG parameters were significant different in the two groups (table 2): SA-QRS duration and LAS40 were significant increased in the elderly patients group and RMS40 was significant increase in the adult post-infarction heart failure group.

The mean QT interval duration (QTm), QTmax and QTc were significant prolonged in the elderly group. 27% of the adult patients and 42% of the elderly had a QTm longer than 450 ms.

Table 2: Parameters in the two post-infarction heart failure patients groups: the adult group and the elderly

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adult group (n=15)</th>
<th>Elderly group (n=12)</th>
<th>Significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVP</td>
<td>7 (47%)</td>
<td>11 (92%)</td>
<td>p=0.000151</td>
</tr>
<tr>
<td>SA-QRS</td>
<td>118±11 ms</td>
<td>138±10 ms</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>LAS40</td>
<td>38±12 ms</td>
<td>73±19 ms</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>RMS40</td>
<td>22±9 μV</td>
<td>10±2 μV</td>
<td>p=0.000547</td>
</tr>
<tr>
<td>QTm</td>
<td>413±54 ms</td>
<td>449±37 ms</td>
<td>p=0.042</td>
</tr>
<tr>
<td>QTmax</td>
<td>438±34 ms</td>
<td>450±49 ms</td>
<td>p=0.038</td>
</tr>
<tr>
<td>QTc</td>
<td>528±65 ms</td>
<td>543±37 ms</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>QTm&gt;450 ms</td>
<td>4 (27%)</td>
<td>5 (42%)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Tpe</td>
<td>150±16 ms</td>
<td>150±20 ms</td>
<td></td>
</tr>
<tr>
<td>LVH (ECG)</td>
<td>6 (40%)</td>
<td>6 (50%)</td>
<td></td>
</tr>
<tr>
<td>Ventricular arrhythmias</td>
<td>3 (20%) PVC</td>
<td>3 (25%) PVC and VF (SCD)</td>
<td></td>
</tr>
<tr>
<td>Multipolar maps</td>
<td>3 (20%)</td>
<td>4 (33%)</td>
<td></td>
</tr>
</tbody>
</table>

LVP=late ventricular potentials, SA-QRS=SAECG QRS duration, LAS40=the duration of the signal at the end of the QRS complex with an amplitude below 40 μV - „Low Amplitude Signal”, RMS40=„Root Mean Square”- the square root of the last 40 ms of the signal , QTm=the mean, heart rate corrected QT interval duration in the 12 ECG leads, QTmax= maximal QT interval, QTc=heart rate corrected QT interval, LVH=left ventricular hypertrophy, PVC=premature ventricular contractions, SCD=sudden cardiac death, VF=ventricular fibrillation

The values are expressed as means±SD for: SA-QRS, LAS40, RMS40, QTm, QTmax, QTc and Tpe.
3 (20%) of the adult post-infarction heart failure patients and 2 (17%) of the elderly had a history of premature ventricular contractions, and 1 (8%) of the elderly died suddenly (ventricular fibrillation). Considering all 27 patients, the best predictor for ventricular arrhythmias was the appearance of multipolar isointegral maps. The presence of LVP, a QTm>450 ms and left ventricular hypertrophy (according to ECG criteria) also predicted ventricular arrhythmias (table 3).

Table 3: The relative risk for ventricular arrhythmias

<table>
<thead>
<tr>
<th>RR for ventricular arrhythmias</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVP</td>
</tr>
<tr>
<td>Multipolar isointegral QRST maps</td>
</tr>
<tr>
<td>QTm&gt;450 ms</td>
</tr>
<tr>
<td>LVH</td>
</tr>
</tbody>
</table>

RR=relative risk, LVP=late ventricular potentials, QTm=mean QT interval duration, LVH=left ventricular hypertrophy

Table 4: The correlation between: LVP criteria (SA-QRS, LAS40 and RMS40), QTm and age of the patients;

<table>
<thead>
<tr>
<th>Parameter</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>SA-QRS</td>
<td>0.76</td>
</tr>
<tr>
<td>LAS40</td>
<td>0.78</td>
</tr>
<tr>
<td>RMS40</td>
<td>-0.66</td>
</tr>
<tr>
<td>QTm</td>
<td>0.62</td>
</tr>
</tbody>
</table>

r=the Bravais-Pearson correlation coefficient

Study Limitations

The QT interval is considered a practical measure of repolarization duration that could be obtained from routine ECG recordings. Despite this presumed simplicity, QT measurement remains a challenge both for clinicians and for specialized ECG labs and the most frequent difficulties consist of delineating the end of T wave, when the T wave is flat, bifid, biphasic or overlapping on a U wave (Zareba, 2007). This is the reason why, leads in which the end of the T wave could not be assessed, were eliminated.

Significant differences exist in the duration of the QT interval when measured in the individual leads. When the QT interval is measured in individual leads, the lead showing the longest QT should be used (Rautaharju et al, 2009). This is the reason why we used QTmax.
Because of lack of studies involving large populations, there is no clear consensus about the normal values for Tpe (Hevia et al, 2006).

Some of the drugs could have influenced the results: amiodarone, diuretics, calcium channel blockers and beta blockers produce QT lengthening (Sohaib et al, 2008; Riera et al, 2008; Zareba, 2007). Other causes of QT interval elongation are: heart failure, hypertension, left ventricular hypertrophy and obesity (Crouch, Limon & Cassano, 2003; Sohaib et al, 2008; Zareba, 2007). A shorter QT interval was observed in diabetics and current smokers (Sohaib et al, 2008). There were significant differences only considering age, between the two groups (p<0.005).

The ECG is still considered a standard method for the detection of left ventricular hypertrophy in epidemiological studies, and remains widely used because of its availability and low cost. However, it has limited value because different rating criteria are used to diagnose LVH. We used multiple ECG-LVH criteria to increase sensitivity and specificity of LVH diagnosis.

Only two patients had an EF<30% (from the elderly group); but the differences were not statistical significant between the two groups, considering EF. Sudden cardiac death occurs most frequent in patients with an EF below 40% (Zipes et al, 2006). But there were some studies considering that the prognosis of patients with heart failure with preserved ejection fraction was similar or worse compared to that of patients with reduced ejection fraction (Bhatia et al, 2006; Tribouilloy et al, 2008).

Some patients were taking antiarrhythmic drugs at the time of BSM, SAECG and 12-lead ECG recordings, including drugs that affect repolarization. Despite therapy, we found that multipolar maps, late ventricular potentials and QTm>450ms were significant associated with ventricular arrhythmias.

Another limitation of our study is the low number of patients; therefore the results need to be confirmed in larger groups.

The results of our study, if confirmed in larger groups, can be valuable in current clinical management of post-infarction patients and might support the selection of post-infarction patients at high risk of life threatening ventricular arrhythmias.

**Conclusion**

Electrical instability and ventricular arrhythmia risk are increased in elderly post-infarction heart failure patients compared to adult patients. Late ventricular potentials, multipolar isointegral QRST maps, QTm>450 ms and ECG-LVH are good predictors of ventricular arrhythmia in post-infarction heart failure patients. QT prolonging drugs should be avoided in elderly patients with post-infarction heart failure.

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Abstract

**Background:** The problem of alcohol use is a major public health problem in the general students’ population in Belarus.

**Aims & Objectives:** We therefore screen and compare the prevalence of alcohol use and related problems among juniors and seniors in Belarusian universities.

**Methods / Study Design:** A total of 2460 university students from four different campuses in Minsk (Belarus) were explained the study aims and objectives. 1599 respondents enrolled for the study. Participants were administered questionnaire, containing the AUDIT, MAST, CAGE and other alcohol related questions. Of them, 100 students could not complete the questionnaire satisfactorily. A total of 1499 (average age = 21) students were considered for analysis. The cut-off point on the AUDIT was set at 8.

**Results / Findings:** The screening results confirm a high level of alcohol use (87.66%) and related problems in the students’ population. The level of alcohol problems increases with increase in the year of study. The use of strong strength alcoholic beverages is related to a high risk of alcohol related problems, than the use of weak alcoholic beverages in the students’ population.

**Conclusion:** The level of alcohol use and related problems in the general Belarusian students’ population are high and show increase in order of increase in the year of study.

**Keywords:** Trajectory, alcohol use, alcohol problems, university students, Belarus
Introduction

Alcohol use is a factor of risk for health and reduces life expectancy by 15-20 years (Babor et al, 2000; Catherine 2004; Jernigan 2001; Welcome et al, 2008). According to leading scientific data approximately 4% of global burden of disease is associated with alcohol misuse (Babor et al, 2000; Catherine 2004; Jernigan 2001). In the global scale alcohol causes approximately 1.8 million deaths yearly (Babor et al, 2000; Catherine 2004; Jernigan 2001; Welcome et al, 2008). According to some researchers one of the major risks for health is associated with heavy alcohol use (Babor et al, 2000; Brewster 1991; Brown 2004; Caetano et al, 1998; Catherine 2004; Hays et al, 1995; Jernigan 2001; Wechsler et al, 1994; Welcome et al, 2008).

Alcohol abuse is a major problem in the general students’ population in many countries (Adewuya 2005; Elissa et al, 2004; Emmanuel et al, 2005; Federico et al, 2007; Kypri et al, 2003; Mangus et al, 1998; Manuel et al, 2005; Wechsler et al, 1994 & 2002). Alcohol abuse by students is associated with a complex range of problems – asocial behavior, injuries, low academic performance, alcohol dependence (Wechsler et al, 1994 & 2002). It was reported in a screening survey involving 548 graduate students in Oregon that 18% of them use alcohol often (3 or more times per week), 21% were bingers (5 or more drinks per session). 18% of women and 11% males reported alcohol use only in the university years (Mangus et al. 1998). Analogical screening exercise performed in Spain showed that out of a total of 545 students that participated over 70% use alcoholic beverages. Their average alcohol use by one student per year was 8.4 liters of absolute ethanol (Carmen et al, 1989).

Many researchers have noted that the level of alcohol use and related problems is higher among seniors compared to freshmen (Flaherty et al, 1993; Brown 2004; do Amaral et al, 2006; O'Brien et al, 1999). This problem might be related to many factors, one of which might be the increase in stress that is experienced by students in course of their study in the university (Weitzman et al. 2004; Wechsler et al. 1994 & 2002; Frone 1999).


In Belarus, there is a dearth of scientific data addressing the problem of students’ alcohol use. This has contributed partly to the increase in the prevalence of alcohol use and related problems, as no intervention program is carried out and since no data show any problem. The cases of alcohol related liver cirrhosis, psychoses, alcoholic intoxication etc have been shown to increase in middle adulthood, and this is a major problem that border the general public (Razvodovsky 2008; Welcome et al. 2008).

A screening result that will address the prevalence of alcohol use and related problems, including the rate in which alcohol use and related problems increase with
both age and year of study in the university will be of great importance (Flaherty et al., 1993; Helen et al., 2005; Joseph et al., 2006; Kypri et al., 2003; Mangus et al., 1998; Manuel et al., 2005; O'Brien et al., 1999; Thomas et al., 2004). Besides, the students’ population is easily accessible, and since every data suggest that screening for the prevalence of alcohol use in the student’s population is of great benefit to public health (Kypri et al., 2003; Mangus et al., 1998; Manuel et al., 2005; Weitzman et al., 2004), we therefore, screen for the prevalence of alcohol use and related problems in the general Belarusian students’ population and trace the rate of rise of alcohol use and related problems in course of their study in major universities in Minsk, Belarus.

The commonly used psychometric instruments recommended by WHO, which are used in epidemiological research aimed at early detection of problems related with alcohol use are the AUDIT (The Alcohol Use Disorders Identification Test), MAST (Michigan Alcohol Screening Test), and CAGE (the Cut, Annoyed, Guilty and Eye questionnaire) (Babor et al., 2000; Catherine 2004; Jernigan 2001; Welcome et al., 2008). The MAST is used for express diagnosis of alcoholism in expertise condition (Welcome et al. 2008). The Michigan Alcohol Screening Test is one of the most used tests for analysis of alcohol related problems. The sensitivity and specificity of the MAST is 90% and 80% respectively (Welcome et al., 2008). According to research MAST sometimes gives a lot of false-positive results (Bohn et al., 1995; Katharine et al., 1998; Welcome et al., 2008). The CAGE as an instrument of screening has a sensitivity of 85-94% and specificity of 79-88% (Bohn et al., 1995; Jernigan 2001; Katharine et al., 1998; Welcome et al., 2008). A score of 2-4 on the CAGE test is considered clinically significant. Even at a single positive answer the sensitivity of the CAGE test equals 62% (for comparison with the sensitivity of laboratory tests: GGT, Average Corpuscular Volume of erythrocytes, liver transaminase – 30-36%). The CAGE test is aimed at disclosing dissimulative symptoms of alcoholism, initial signs of alcoholism, and its anamnesis (Welcome et al., 2008). The AUDIT is a validated and superior screening instrument and corresponds with the DSM-IV and ICD-10 definition of alcohol dependence and abuse (Janca et al., 1993; Jernigan 2001; Katharine et al., 1998; Welcome et al., 2008). The AUDIT is a structured interview of 10 questions with a sensitivity of 92% and specificity of 93%. It correlates with both the MAST and CAGE (Gache et al., 2005; Katharine et al., 1998; Welcome et al., 2008; Saunders et al., 1993; Claussen et al., 1993; Bohn et al., 1995). The AUDIT gives a more accurate result in comparison with the CAGE and MAST (Welcome et al. 2008). A total score of ≥8 defines the presence of alcohol related problems and a necessary referral to a specialist (Katharine et al., 1998; Saunders et al., 1993; Bohn et al., 1995).

Materials and methods

Study population: Minsk is the capital city of Belarus, with the highest number of students from all over the country. There are four major universities (Belarusian State Medical University, Belarusian National Technical University, Belarusian State University, and Belarusian State Agrarian Technical University) in this city, where students from all over the country study. Some proportion (5-8%) of foreign students from Iran, Pakistan, Jordan, Syria, Nigeria, Ghana etc also study in these universities. Students in these universities are both Christians (95%) and Muslims (4%), other are
non-religious – 1%. In these universities the population of female students is about
trice that of the male students.

**Sampling size and technique:** The interview was carried out in four consecutive
days in the different universities. A total of 2460 students at random were explained
the study aim, only those who agreed to participate were considered for interview in
their various universities. Students who disagreed to participate were 207 students
from the Belarusian State Medical University, 255 from Belarusian National
Technical University, 237 from Belarusian State University, and 162 from Belarusian
State Agrarian Technical University. Questionnaires were distributed equally among
students of all universities and in all courses. In total, only 1599 students (average age
21yrs) agreed to participate in the study. Out of the 1599 respondents that participated
in the study, 100 (26 from the Belarusian State Medical University, 23 from
Belarusian National Technical University, 29 from Belarusian State University, and
22 from Belarusian State Agrarian Technical University) could not complete the
questionnaire satisfactorily, so only 1499 students were considered for analysis. 7.5%
of the participants were Muslims and 92.5% Christians; 68.71% (n=1030) females
and 31.29% (n=469) males.

**Procedure:** The Ethics and Research Committee of the various universities approved
the study protocol and informed consents were obtained from the respondents after
the aims and objectives of the survey had been explained. All 1499 students were
administered questionnaire, containing the AUDIT, CAGE, MAST and other alcohol
related questions. The MAST (Michigan Alcohol Screening Test), AUDIT (Alcohol
Use Disorders Identification Test) and CAGE (the Cut, Annoyed, Guilty and Eye
questionnaire) were used simultaneously as a measure for problems related with
alcohol use because of their high sensitivity and specificity (Claussen et al, 1993;

**Measures:** A total score of 3 or more on the MAST was considered problematic
alcohol use, while 2 to 4 score on the CAGE is considered clinically significant.
Scores of ≥8 on the AUDIT define problematic alcohol use (Welcome et al, 2008).
The students with scores of 8-40 on the AUDIT were classified in group № 1 (the
problem group). Students with 1-7 score on the AUDIT were classified as the non-
problem group (group № 2).

**Data analysis:** Statistical calculations were performed using the SPSS (The Statistical
Package for the Social Sciences) 16.0 version for Windows and the Chi square, $\chi^2$
(Bland 2000). The probability value for significance was set at $p < .05$. All volumes of
alcohol used are given in values of absolute ethanol. A standard drink was set at 8g of
absolute ethanol. Results were calculated as means and standard error of means,
M±m, as well as in percentages, %.

**Results**

From the screening results shown in table 1, the proportion of alcohol users are
significantly higher among seniors. Statistically, a tendency to increase was noted in
the male population ($\chi^2 =5.48$, $p >.05$), but there was a significant increase among
females ($\chi^2=22.8$, $p < .001$).
Table 1: The proportion of alcohol users in various courses and their average scores on the AUDIT, CAGE and MAST

<table>
<thead>
<tr>
<th>Course</th>
<th>Sex</th>
<th>Average age</th>
<th>Average score</th>
<th>% alcohol users</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>AUDIT</td>
<td>CAGE</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M (n=150)</td>
<td>19.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F (n=415)</td>
<td>18.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M (n=201)</td>
<td>21.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F (n=336)</td>
<td>20.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>M (n=118)</td>
<td>23.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>F (n=279)</td>
<td>22.5</td>
</tr>
</tbody>
</table>

The average scores on the AUDIT, CAGE and MAST among the males tend to increase in respect to the increase in the year of study. The differences between students of I-II and V-VI courses were statistically significant according to the results in all three tests. The number of male problem students increases according to the order of increase in the year of study (Table 2). So, in comparison with students of I-II courses, the number of problem drinkers on the V-VI courses on the AUDIT increased from 28.67% to 47.46%, on the CAGE from 26.67% to 31.4%, and from 17.3% to 33.9% on the MAST (Table 2).

Table 2: Proportion of problem drinkers in various courses on AUDIT, CAGE and MAST

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Sex</th>
<th>AUDIT</th>
<th>CAGE</th>
<th>MAST</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M (n=150)</td>
<td>28.67% (n=43)</td>
<td>26.67% (n=40)</td>
<td>17.33% (n=26)</td>
</tr>
<tr>
<td></td>
<td>F (n=415)</td>
<td>9.40% (n=39)</td>
<td>11.08% (n=46)</td>
<td>6.75% (n=28)</td>
</tr>
<tr>
<td></td>
<td>M (n=201)</td>
<td>29.35% (n=59)</td>
<td>28.36% (n=57)</td>
<td>19.40% (n=39)</td>
</tr>
<tr>
<td></td>
<td>F (n=336)</td>
<td>11.01% (n=37)</td>
<td>13.10% (n=44)</td>
<td>4.46% (n=15)</td>
</tr>
<tr>
<td></td>
<td>M (n=118)</td>
<td>47.46% (n=56)</td>
<td>31.36% (n=37)</td>
<td>33.90% (n=40)</td>
</tr>
<tr>
<td></td>
<td>F (n=279)</td>
<td>9.68% (n=27)</td>
<td>8.96% (n=25)</td>
<td>6.09% (n=17)</td>
</tr>
</tbody>
</table>

As a distinction from the males, among the females the average scores, as well as the proportion of problem alcohol users did not change in relation to the increase in the year of study. In general, the average scores on the tests, as well as the proportion of problem alcohol users among the females was lower. In this case, the gender differences in the level of alcohol related problems increases according to the increase in the year of study. For example, the male to female ratio of the problem drinkers on the AUDIT increased from 3.1 in the I-II courses to 4.9 in the V-VI courses (Table 2).

The frequency-quantity block (frequency of alcohol use, dose per session and monthly dose), as well as different problems related with alcohol use (loss of control, hangover, blackouts, injuries, feeling of guilt) are shown in table 3. The data shown in the table indicate that the frequency-quantity of alcohol use are significantly higher...
among the males of the problem group (group № 1), compared to the moderate male drinkers (group № 1). On the average, the dose per session of alcohol use by males of the group № 1 (51 ml) was more than the dose per session of males in the group № 2 (26.7 ml) by 1.9 times. The average monthly dose of alcohol use by the males of the problem group (223 ml) was more than analogical parameter for the moderate male alcohol users (39.5 ml) by 5.7 times. Among the males of the problem group there is a tendency of rise of the proportion of alcohol related problems, precisely loss of control, and injuries with increase in the year of study. Among the females of the problem group, the frequency, dose per session as well as the monthly dose of alcohol use, alcohol related problems such as loss of control, hangover, blackouts and injuries increase according to the increase in the year of study. At the same time, among the moderate female alcohol users such tendencies were not recorded. The problem female drinkers had significantly greater frequency-quantity of alcohol use, compared to the moderate drinkers. On the average, the dose per session of alcohol use by the females of group № 1 (42.4 ml) exceeded the dose per session of the females of group № 2 (23.7 ml) by 1.8 times. The average monthly dose of alcohol use by the females of the problem group (170.4 ml) exceeds analogical parameter for the moderate female drinkers (31.4 ml) by 5.4 times.

Table 3: Dose and frequency of alcohol used by the problem (group № 1) and non-problem drinkers (group № 2) and the proportion of alcohol related problems according to the AUDIT

<table>
<thead>
<tr>
<th>Course</th>
<th>Sex</th>
<th>Groups</th>
<th>Frequency/session (ml)</th>
<th>Dose/month (ml)</th>
<th>Dose/month (ml)</th>
<th>Loss of control, %</th>
<th>Hango over, %</th>
<th>Guilt, %</th>
<th>Blackouts, %</th>
<th>Injuries, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-II</td>
<td>M</td>
<td>№ 1</td>
<td>4.5</td>
<td>53.0</td>
<td>238.0</td>
<td>37.78</td>
<td>48.64</td>
<td>47.63</td>
<td>62.22</td>
<td>42.76</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.4</td>
<td>25.9</td>
<td>35.8</td>
<td>6.04</td>
<td>1.19</td>
<td>26.74</td>
<td>9.71</td>
<td>9.62</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>№ 1</td>
<td>3.0</td>
<td>38.3</td>
<td>115.1</td>
<td>22.92</td>
<td>25.00</td>
<td>66.67</td>
<td>45.84</td>
<td>37.50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.3</td>
<td>23.9</td>
<td>30.8</td>
<td>1.95</td>
<td>1.29</td>
<td>18.93</td>
<td>5.16</td>
<td>2.55</td>
</tr>
<tr>
<td>III-IV</td>
<td>M</td>
<td>№ 1</td>
<td>4.4</td>
<td>50.5</td>
<td>221.8</td>
<td>45.00</td>
<td>34.47</td>
<td>62.15</td>
<td>56.97</td>
<td>65.42</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.5</td>
<td>27.6</td>
<td>41.4</td>
<td>4.51</td>
<td>0.00</td>
<td>16.45</td>
<td>8.75</td>
<td>4.78</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>№ 1</td>
<td>4.2</td>
<td>36.9</td>
<td>155.9</td>
<td>40.61</td>
<td>18.03</td>
<td>63.03</td>
<td>56.21</td>
<td>38.34</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.3</td>
<td>23.6</td>
<td>30.9</td>
<td>1.04</td>
<td>1.84</td>
<td>15.63</td>
<td>4.57</td>
<td>2.63</td>
</tr>
<tr>
<td>V-VI</td>
<td>M</td>
<td>№ 1</td>
<td>4.2</td>
<td>49.6</td>
<td>209.3</td>
<td>65.26</td>
<td>44.23</td>
<td>66.03</td>
<td>67.18</td>
<td>69.36</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.6</td>
<td>26.5</td>
<td>41.3</td>
<td>7.89</td>
<td>1.57</td>
<td>33.12</td>
<td>7.07</td>
<td>4.69</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>№ 1</td>
<td>4.6</td>
<td>52.1</td>
<td>240.2</td>
<td>58.53</td>
<td>57.65</td>
<td>69.41</td>
<td>67.65</td>
<td>61.47</td>
</tr>
<tr>
<td></td>
<td></td>
<td>№ 2</td>
<td>1.4</td>
<td>23.6</td>
<td>32.6</td>
<td>3.28</td>
<td>2.07</td>
<td>13.09</td>
<td>3.60</td>
<td>2.07</td>
</tr>
</tbody>
</table>
The data in table 4 confirm that the level of alcohol related problems among students is determined not only by the frequency and dose of alcohol use, but also the types of alcoholic beverages. A total of 37.3% problem male drinkers and 25% problem female drinkers use mainly vodka. Among the moderate drinkers vodka (as well as weak strength alcoholic beverages) use accounted for only 10.7% males and 1% females. This data show that the use of strong strength alcoholic beverages leads to a high level of alcohol related problems.

Table 4: Alcoholic beverages used by the problem and non-problem alcohol users

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Males (n=469)</th>
<th>Females (n=1030)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>group 1 (n=158)</td>
<td>group 2 (n=244)</td>
</tr>
<tr>
<td>beer/dry wine</td>
<td>43.04% (n=68)</td>
<td>55.32% (n=135)</td>
</tr>
<tr>
<td>beer/fortified wine</td>
<td>8.23% (n=13)</td>
<td>9.02% (n=22)</td>
</tr>
<tr>
<td>vodka</td>
<td>37.34% (n=59)</td>
<td>10.66% (n=26)</td>
</tr>
<tr>
<td>*beer/wine/vodka</td>
<td>11.39% (n=18)</td>
<td>25.00% (n=61)</td>
</tr>
</tbody>
</table>

*Composition of alcohol in the various alcoholic beverages: beer/dry wine (<7%); fortified wine (7-17%); vodka (~40%) (Welcome et al, 2008)

It is interesting to state the motives of alcohol use that were reported by the students. For more than 90% of the respondents, the main motive of alcohol use was reported as the tradition to use alcohol on different social occasions. A total of 32% respondents use alcohol as a result of its sweet qualities. A total of 15% of the respondents use alcohol to get drunk.

Discussion

The present screening results show a high level of alcohol related problems in the general students' population in Minsk, Belarus. The highest level of alcohol related problems was experienced by the male students of V-VI courses and showed increase in order of increase in their ages (Table 1). Among the female students such peculiarities in the age linked increase in alcohol related problems were not recorded (Table 1). These differences allow us to assume that the increase in alcohol related problems among males is not likely conditioned by age, but by the peculiarities of socialization. Many students leaving in hostels, where they are not subjected to the control of their parents, may organize their leisure according to their discretion (Thomas et al, 2004; Welcome et al. 2008). One main ways by which students may pass time under those conditions is to use alcohol (Wechsler et al, 1994 & 2002; Weitzman et al, 2004; Welcome et al, 2008). Many researchers have acknowledged the fact that males are more disposed to alcohol abuse than females, since females have alternative ways of socialization (Jernigan 2001; Joseph et al, 2006). It is also necessary not to forget the fact that risk factors like stress which are linked to academic activities may play important role in the pattern of alcohol use among students (Frone 1999; Wechsler et al, 1994 & 2002). Scientific data have suggested
that young males may use alcohol more frequently (than the females) as ways of reducing stress (Caetano et al, 1998; Frone 1999; Jernigan 2001; Joseph et al, 2006). The increase in the level of alcohol related problems with increase in the year of study in the university may be evidence of the fact that alcohol use is a tradition in the students’ subculture. As a result of this many students at the end of their studied is likely to have instead of the diploma, alcohol problems. Another probable explanation for the increase in the level of alcohol related problems with increase in the year of study is the dose-time dependent effect of alcohol – the negative effect of alcohol use increases with increase in “time” and dose of alcoholic drinks (Welcome et al, 2008). The increase in the level of alcohol related problems among problem male drinkers according to the increase in the year of study allows us to talk about the possibilities that the increase in alcohol related problems is determined by not only the dose, but also the duration of alcohol use (the time dependent effect of alcohol use). Among the moderate male drinkers alcohol related problems such as loss of control, and hangover was extremely minimal.

Worthy of attention is the fact that problem students (relatively high proportion of both males and females) prefer both weak and strong strength alcoholic drinks, compared to the non-problem drinkers who use mainly weak strength alcoholic beverages (Table 4). Thus, alcohol related problems are largely related to the use of strong strength alcoholic drinks than the use of weak strength alcoholic drinks by students.

Overall, 17.5% (33.7% males and 10.1% females: Table 2 and 4) of all students need the intervention of a specialist (psychiatrist) according to WHO recommendation (Babor et al, 2000; Catherine 2004; Jernigan 2001).

The recommended cut-off point of 8 for problematic alcohol use in this study is in agreement with the recommended cut-off for the AUDIT in Belarus (Welcome et al, 2008), although lower and higher cut-off points have been suggested in other studies (Adewuya 2005; Babor et al, 2000; Jernigan 2001).

It is important to note some differences concerning the results of the various screening instruments. For example, the proportion of problem alcohol users of I-II and III-IV courses on the AUDIT and CAGE was significantly higher than the data on the MAST. At the same time, the proportion of students of V-VI courses in the problem group according to the AUDIT was more than analogical value on the CAGE and MAST. Probably, these discrepancies are conditioned by different sensitivities of the various screening instruments. It can also be assumed that the AUDIT may give false-positive results in a number of cases.

**Study Limitations:** The limitations of this study include the fact that some respondents with alcohol related problems may have under-reported them in the AUDIT, MAST and CAGE. This may have affected the significance value of the results. Another limitation of this study is that the questionnaire was administered ones and so the reliability indices of the various tests were not assessed.
Conclusion

The level of alcohol use and related problems in Belarusian universities is high. The proportion of male and female alcohol users were approximately the same and showed an increase in order of increase in the year of study. The average score on the AUDIT, CAGE and MAST, as well as the proportion of problem drinkers were significantly higher among the male students. There was also an increase in the number of problem drinkers according to the increase in the year of study in the male population, but showed only a slight increase in the female population. The use of strong, as well as weak strength alcoholic beverages is associated with a high risk of alcohol related problems.

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Study of Anthropometry in Individuals Having Parental Hypertension

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Abstract

The adverse association of cardiovascular risk factors in both children and adults with parental history of disease is seen. A family history of hypertension has been shown to be a risk factor for the subsequent development of disease. This study is aimed to compare any observed differences in the mean BPs, BMI, Hip waist ratio in children of hypertensive and normotensive parents. A cross sectional study was conducted among the 100 students of a University. Anthropometric measurements were taken. Among the participants studied, 63% were male and the average age was 19.76 years (SD ±2.01) with a median of 20 years, varying from 18 to 25 years. Males with BMI of 25 or more were 35.4% from the Study group and 12.5% from the control group. Females with BMI of 25 or more were 26.3% from the study and only 5.5% from the control group. 58% males and 52.6% females from the study group had their waist-hip ratio equal or more than the Standard cut-off. Triceps fat distribution was more in females of study group. To conclude, the study shows a positive relation of increasing BMI, WHR and Triceps Skin fold Thickness with the development of Hypertension in future. The findings of present study suggest need of monitoring the anthropometry of children of hypertensive parents. Health care providers have an important role to play in educating families and children about approaches that are useful in preventing hypertension.

Keywords: Waist-hip Ratio, BMI, Hypertension, hypertensive parents, Triceps Skin fold Thickness

Introduction

Hypertension is estimated to cause 4.5% of current global disease burden and is as prevalent in many developing countries, as in the developed world. Blood pressure-induced cardiovascular risk rises continuously across the whole blood pressure range. Indeed, hypertension accounts for more than 5.8% of total deaths, 1.9% of years of life lost and 1.4% disability adjusted life years all over the world. These figures are more dramatic in the formerly socialist economies countries. Hypertension is a chronic condition of concern due to its role in the causation of Coronary Heart Disease, stroke and other vascular complications. Increasing trend of hypertension is a
worldwide phenomenon\textsuperscript{2}. Essential hypertension, a major risk factor for cardiovascular disease (CVD), is prevalent in the adult population\textsuperscript{3,4}. Hypertension is the most often prevalent atherosclerosis risk factor in families\textsuperscript{5}. It is the commonest cardiovascular disorder, posing a major public health challenge to population and socio-economic and epidemiological transition. It is one of the major risk factors for cardiovascular mortality, which accounts for 20-50 percent of adult deaths. The adverse association of cardiovascular risk factors in both children and adults with parental history of disease is well recognized\textsuperscript{6,7}. A family history of cardiovascular disease (CVD) has been shown to be a risk factor for the subsequent development of disease. Familial aggregation has been shown to occur for hypertension\textsuperscript{8}, myocardial infarction\textsuperscript{9}, diabetes\textsuperscript{10}, and obesity\textsuperscript{11}. In fact hypertension in adults may be preceded by high blood pressure values in childhood\textsuperscript{12}. Children with positive family history of cardiovascular diseases have significantly higher body mass index\textsuperscript{13}. Obesity is a common phenomenon occurring in the young adults of today. Obese persons are approximately 6 times as likely to develop heart disease as normal weighted persons. Overweight and obesity is known to be a significant risk factor for hypertension. The World Health Report, 2002 “Reducing Risks, Promoting Healthy Life” has identified obesity as one of the ten leading risk factors, globally\textsuperscript{14}. Essential Hypertension is much more common in obese individuals. George Smith has also confirmed positive association of weight and Blood Pressure\textsuperscript{15}. Further, it is confirmed that change in the Body Mass Index (BMI) from higher range to lower side is associated with decreased cardiovascular risk\textsuperscript{16}. The waist-hip ratio is used as an indicator of body-fat distribution. The waist–hip ratio is the preferred measure of obesity for predicting cardiovascular disease, with more universal application in individuals and population groups of different body builds. Benchmark studies of waist–hip ratio as dominant cardiovascular risk factors were reported in Swedish men and women in 1984\textsuperscript{17}.

Glowinska B et al. (2002)\textsuperscript{5} studied the obesity and coexisting hypertension. Positive family history of cardiovascular diseases was found in 28% families, and in 8% families it was premature cardiovascular disease. In 48% children we found hypertension in family. Children with positive family history had significantly higher body mass index (25.4 v/s 23.8 kg/m\textsuperscript{2}).

Maria C et al\textsuperscript{18} (2007) in the study investigated the risk factors associated with essential arterial hypertension in adolescents. Nutritional status was assessed by means of body mass index. Data were also obtained on waist circumference, height, family history of arterial hypertension, birth weight and pubertal development. Body mass index was associated with hypertension. Height had a positive association with hypertension only among the girls. In contrast, family history, particularly when both parents had hypertension, exhibited a robust association, both among the boys (OR = 13.32; 95\textsuperscript{th}CI 2.25-78.94), and the girls (OR = 11.35; 95\textsuperscript{th}CI 1.42-90.21). The study concluded that overweight, obesity and family history of hypertension (father and mother with hypertension) were the principal risk factors for arterial hypertension in adolescents.

Deshmukh PR et al (2005)\textsuperscript{14} studied that higher abdominal fat is known to be a significant risk factor for hypertension and other related metabolic disorders. 11.3\% of hypertensive’s had BMI of 25 or more while 38.5\% of hypertensive’s had a waist-hip ratio equal to or more than the cut-off point, i.e. 0.8 for females and 0.9 for males. In all the strata of BMI, hypertension was significantly higher in individuals having a
waist-hip ratio higher than the cut-off point. The study emphasized the need for using the waist-hip ratio for assessing the risk of hypertension in populations where majority of the population is thin as traditionally measured by BMI.

Chhatwal J et al\textsuperscript{19} (2004) mentioned in their study that there are very few reports from the developing world on the prevalence of obesity among children even though in developed countries it has reached epidemic proportions. Significantly more children from higher socio-economic status were obese and overweight than those from lower socio-economic status groups. No significant gender difference for obesity prevalence was seen among children from a less privileged background, however, amongst children from affluent families, significantly more boys were obese as compared to girls.

Aim & Objectives

1. To measure the anthropometric parameters of young healthy adults having parental history of Hypertension.

2. To correlate the anthropometric parameters of these individuals with those of the young healthy individuals who do not have parental history of Hypertension.

Methodology

This is a study conducted in Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital (A.V.B.R.H.), a 900 bedded tertiary teaching hospital of Datta Meghe Institute of Medical Sciences, Deemed University. This study has been approved from the Institutional Ethical Committee of Datta Meghe Institute of Medical Sciences, Deemed University. The participants were the students from Jawaharlal Nehru Medical College of Datta Meghe Institute of Medical Sciences, Deemed University. 100 Students were contacted for the study. A group of 50 students having parental History of Hypertension constituted the Study group. Another 50 students having no parental history of Hypertension constituted the control group. The participants were matched across age (18-25) and sex. Participants were evaluated according to pre-designed protocol. All the participants were examined only once on a single meeting. The participants were examined for various anthropometric parameters.

Any past history of Hypertension, past admissions for cardiovascular diseases and past or current treatment with cardio active drugs like antihypertensive, antilipidemic, etc and steroid was noted. A personal history of smoking or other addictions and diet habits was also noted in all cases. Parental history of hypertension was recorded. The anthropometric parameters measured in the study were height in cm, Weight in kg, skin fold thickness, body mass index, waist hip ratio.
1. **Body Weight** - Body weight was measured (to the nearest 0.5 kg) with the subject standing motionless on the weighing scale, and with the weight distributed equally on each leg.

2. **Height** - It was measured (to the nearest 0.5 cm) with the subject standing in an erect position against a vertical scale and with the head positioned so that the top of the external auditory meatus was level with the inferior margin of the bony orbit (Frankfurt’s plane).

3. **Body Mass Index** - The body mass index, or BMI (weight in kilograms divided by the square of the height in meters), is recommended by the World Health Organization as the most useful epidemiological measure of obesity.

4. **Waist Circumference** - It was measured at the narrowest level and hip circumference was measured at the maximal level over light clothing, using a non-stretchable measuring tape, without any pressure to the body surface, and both were recorded to the nearest 0.1 cm. As the measurements were taken over light clothing, participants were asked to remove tight or loose garments and belts intended to alter the shape of the body, and the person performing the measurement inspected the tension of the tape on the subject’s body to ensure that it had the proper tension (not too loose or too tight). The narrowest waist is easy to identify in most subjects. However, for some subjects there is no single narrowest waist because of either a large amount of abdominal fat or extreme thinness. In the present study, when the narrowest point of waist was difficult to identify (particularly in obese subjects), we measured waist circumference immediately below the end of the lowest rib, because in most subjects the narrowest waist is at the lowest rib.

5. **Waist Hip Ratio** - WHR was calculated as WC divided by hip circumference. To reduce subjective error all measurements were taken by the same person. The cut-off used for the waist-hip ratio (WHR) for males was 0.9 and for females it was 0.8 to define obesity.

6. **Triceps Skin fold Thickness** – Triceps skin fold thicknesses were measured using a Harpenden caliper. It was measured from the left hand when it is totally relaxed. A vertical pinch, parallel to the long axis of the arm is made at the level of mid-point between the acromial process of Scapula and the olecranon process of Ulna, on the mid-line of the posterior surface of the arm.

Inclusion Criteria:

1. All apparently healthy students of Faculty of Medicine of Datta Meghe Institute of Medical Sciences, Deemed University, Wardha.

2. Age group between 18-25 years of both sexes.

Exclusion Criteria: History of taking Cardio active drugs like antihypertensive, antilipidemic, etc, Students who leave the examination midway due to any reason.
Appropriate statistical tools namely percentage, chi square test have been employed to analyze the data and validate the findings.

Results

Table 1: Characteristics of Study group – Age Distribution (as on the day of the examination)

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>19</td>
<td>7</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>20</td>
<td>7</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>21</td>
<td>23</td>
<td>13</td>
<td>36</td>
</tr>
<tr>
<td>22</td>
<td>18</td>
<td>15</td>
<td>33</td>
</tr>
<tr>
<td>23</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>24</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>25</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Interpretation: Maximum number of participants (23 males and 13 females of age 21 and 18 males and 15 females of the age 22) belonged to the age of 21-22. However, the range of age went from 10 students (7 males and 3 females) of the age 19 to one male student of the age 25.

Table 2: Distribution of participants in relation to Blood Pressure

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive parents</td>
<td>31 (49.20)</td>
<td>19 (51.35)</td>
<td>50 (50.00)</td>
</tr>
<tr>
<td>Normotensive parents</td>
<td>32 (50.80)</td>
<td>18 (48.65)</td>
<td>50 (50.00)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>63 (100)</td>
<td>37 (100)</td>
<td>100 (100)</td>
</tr>
</tbody>
</table>
**Interpretation:** Among the 100 participants studied, 63% were male (Table 2) and the average age was 19.76 years (SD ±2.01) with a median of 20 years, varying from 18 to 24 years.

Table 3: Relation of height of the individual to Parental History of Blood Pressure in males

<table>
<thead>
<tr>
<th>Height Range</th>
<th>Hypertensive Parents</th>
<th>Normotensive Parents</th>
<th>Total in the range</th>
</tr>
</thead>
<tbody>
<tr>
<td>145-149</td>
<td>1 (100%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>150-154</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>155-159</td>
<td>0</td>
<td>1 (100%)</td>
<td>1</td>
</tr>
<tr>
<td>160-164</td>
<td>1 (50%)</td>
<td>1 (50%)</td>
<td>2</td>
</tr>
<tr>
<td>165-169</td>
<td>4 (44.4%)</td>
<td>5 (55.5%)</td>
<td>9</td>
</tr>
<tr>
<td>170-174</td>
<td>8 (47%)</td>
<td>9 (53%)</td>
<td>17</td>
</tr>
<tr>
<td>175-179</td>
<td>9 (69%)</td>
<td>4 (31%)</td>
<td>13</td>
</tr>
<tr>
<td>180-184</td>
<td>5 (38%)</td>
<td>8 (62%)</td>
<td>13</td>
</tr>
<tr>
<td>185-189</td>
<td>3 (43%)</td>
<td>4 (57%)</td>
<td>7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
<td><strong>32</strong></td>
<td><strong>63</strong></td>
</tr>
</tbody>
</table>
**Interpretation:** The findings show a random distribution of the range of Height and their relation to the Blood Pressure state of their Parents in Males.

Table 4: Relation of height of the individual to Parental History of Hypertension in females

<table>
<thead>
<tr>
<th>Height Range</th>
<th>Hypertensive Parents</th>
<th>Normotensive Parents</th>
<th>Total in the range</th>
</tr>
</thead>
<tbody>
<tr>
<td>145-149</td>
<td>1 (33%)</td>
<td>2 (66%)</td>
<td>3</td>
</tr>
<tr>
<td>150-154</td>
<td>1 (25%)</td>
<td>3 (75 %)</td>
<td>4</td>
</tr>
<tr>
<td>155-159</td>
<td>5 (50%)</td>
<td>5 (50%)</td>
<td>10</td>
</tr>
<tr>
<td>160-164</td>
<td>11 (57 %)</td>
<td>8 (43%)</td>
<td>19</td>
</tr>
<tr>
<td>165-169</td>
<td>1 (100%)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>18</td>
<td>37</td>
</tr>
</tbody>
</table>

**Interpretation:** According to this study, as the range of height (in cms) increases, it moves more towards those females who have a positive parental history of Hypertension i.e. the Study group.
Table 5: Distribution of Body Mass Index in relation to family history of hypertensive parents

| Body Index | Male | | Female | | Total |
|------------|------||--------|------|------|
|            | Mass | Body Mass Index | Mass | Body Mass Index | Mass |
| Hypertensive parents | <25 | 20 (64.52) | >25 | 11 (35.48) | <25 | 14 (73.69) | >25 | 5 (26.31) | 50 (50) |
| Normotensive parents | <25 | 28 (87.49) | >25 | 04 (12.51) | <25 | 17 (94.45) | >25 | 01 (5.55) | 50 (50) |
| **Total** | | 48 (48) | | 15 (15) | | 31 (31) | | 06 (6) | 100 |

p < 0.01* (significant)

**Interpretation:** Males with BMI of 25 or more were 35.48% with history of Hypertensive parents, while only 12.5% of males were having BMI of 25 or more with history of normotensive parents.
**Interpretation:** Females with BMI of 25 or more were 26.31% with history of Hypertensive parents, while only 5.55% of females were having BMI of 25 or more with history of normotensive parents (Table 5).

Table 6: Distribution of Waist-hip ratio in relation to family history of hypertensive parents

<table>
<thead>
<tr>
<th></th>
<th>Male Hypertensive parents</th>
<th>Male Normotensive parents</th>
<th>Female Hypertensive parents</th>
<th>Female Normotensive parents</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist-hip ratio &lt; cut-off</td>
<td>13 (41.94)</td>
<td>28 (87.49)</td>
<td>09 (47.37)</td>
<td>15 (83.34)</td>
<td>33 (33.00)</td>
</tr>
<tr>
<td>Waist-hip ratio &gt; cut-off</td>
<td>18 (58.06)</td>
<td>04 (12.51)</td>
<td>10 (52.63)</td>
<td>03 (16.66)</td>
<td>67 (67.00)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>31 (100)</td>
<td>32 (100)</td>
<td>19 (100)</td>
<td>18 (100)</td>
<td>100 (100)</td>
</tr>
</tbody>
</table>

p < 0.01* (significant)
Interpretation: Among the male subjects, while 58.06% of the males with history of hypertensive parents had a waist-hip ratio equal to or more than 0.9. 12.51% males with history of normotensive parents had a waist-hip ratio equal to or more than 0.9.

Interpretation: In females 52.63% with history of hypertensive parents had a waist-hip ratio equal to or more than 0.8. Among the female subjects, 16.66% with history of normotensive parents had a waist-hip ratio equal to or more than 0.8 (Table 6).

Table 7: Distribution of Triceps Skin fold Thickness in relation to the state of Blood Pressure of the Parents

<table>
<thead>
<tr>
<th>Units</th>
<th>Male Hypertensive parents</th>
<th>Male Normotensive parents</th>
<th>Female Hypertensive parents</th>
<th>Female Normotensive parents</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
<td>7</td>
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<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>Males</td>
<td>Females</td>
<td></td>
<td></td>
</tr>
<tr>
<td>----</td>
<td>-------</td>
<td>-------</td>
<td>---------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td></td>
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<tr>
<td>12</td>
<td>4</td>
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<tr>
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<td>6</td>
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</tr>
<tr>
<td>14</td>
<td>5</td>
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<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td></td>
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</tr>
<tr>
<td>18</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31 (100)</strong></td>
<td><strong>32 (100)</strong></td>
<td><strong>19 (100)</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Interpretation:** The Triceps skin fold thickness of Males students having Normotensive parents remained between 7 and 15 units, whereas more range, (6 units to 16 units) was seen in male students of Hypertensive parents.

**Interpretation:** The Triceps Skin fold Thickness of Females students having Normotensive parents was confined between the range of 12 units to 15 units on the Harpenden’s Caliper whereas the Skin fold thickness of Female students having Hypertensive parents ranged between 11 units to 18 units. It also shows that fat
distribution under the Triceps was more in females having Hypertensive parents than Normotensive parents.

Discussion

Out of the Total 15 males who were reported to have the Body Mass Index greater than 25, 11 belonged to the study group i.e. those who have positive parental history of Hypertension. This shows a positive relation of the increasing Body Mass Index and its association in becoming an increasing risk factor to develop Hypertension in future. Out of the 6 females who have their Body Mass Index greater than 25, 5 belonged to the study group. This fact also shows the positive relation of the increasing Body Mass Index and its association for becoming an increasing risk factor to develop Hypertension in future. A similar co-relation was found in the study of Maria C et al \(^{18}\) in the year 2007 where they investigated the risk factors associated with essential arterial hypertension in adolescents. Nutritional status was assessed by means of body mass index. Data were also obtained on waist circumference, height, family history of arterial hypertension, birth weight and pubertal development. Body mass index was associated with hypertension.

Height had a positive association with hypertension only among the girls. The Positive association of height with hypertension among girls as observed in the study given above is also seen in this study where as the Height range increases, it moves more towards those females who belong to the study group. Hence, when seen together in both the Sexes, the number of students who have their Body Mass Index greater than 25 are more in case of those students who showed a positive parental history of Hypertension (Study group) than in comparison to those who did not show positive parental History of Hypertension (Control Group). Similar findings were seen in the study conducted by Glowińska et al\(^{13}\) in the year 2002. According to his study, children with positive family history of cardiovascular diseases have significantly higher body mass index. (25.4 vs 23.8 kg/m\(^2\)).

The cut off for the Waist Hip ratio (WHR) for Males to define obesity is 0.9. In this study, out of the 31 males in the study group, 18 have their WHR above the standard defined cut off mark for obesity and 13 males have their WHR below the standard mark. This shows that these 18 participants can be classified as obese which is a strong risk factor to develop Hypertension. Out of the 32 males in the control group, only 4 have their WHR above the standard cut off for obesity. This also proves that lower value of WHR provides less chances of developing obesity and thus Hypertension in future. Similarly, the cut off for the Waist Hip Ration for females to define obesity is 0.8. The study comprises of 19 females in the study group out of which 10 have their WHR above the standard cut off and thus can be classified as obese. Being obese again predisposes such females to an increasing risk of developing Hypertension. Out of the 18 females in the control group, only 3 have their WHR above the standard cut off defined to be declared as obese.

The observations of this study shows that the differences between the Triceps Skin fold Thickness in males and females of the Study and Control group was always more than 1 unit on the Harpenden’s Caliper used. Thus, it clearly showed that those students who have a positive parental history of Hypertension have more deposition
of fat under the skin. This in future adds to the risk factor for developing Hypertension at older age. The findings echoed with the findings of Bruke et al7 in the year 1991 where they observed that Age- and sex-adjusted Triceps skin fold thickness was 1.0 mm greater in those young adults with a positive parental history of hypertension.

Limitation of the study

Despite the attempt to obtain a complete assessment of parental history, a substantial number of participants were unaware of their parents' disease status (especially paternal history). Because we classified unknown responses as a negative history, this tendency would bias our results toward the null. Therefore, the differences presented probably underestimate the true risk factor difference attributable to parental history. Another potential drawback of these data is the lack of validation of parental disease by medical record review. Other investigators have detected a relatively good concordance (78%) between a reported family history and medical record validation, suggesting that, despite some imprecision, the reported history gives a reasonable estimate of family history for the diseases we have assessed in this paper29. Even if some discordance occurs, there is no reason to suspect that this would result in artifactual risk differences; rather, as with any misclassification error, it would be more likely to increase the variability of the parental history measures and lead to an underestimate of the real risk factor differences between these groups.

Conclusion

The findings of the present study suggest the need of monitoring the BP of children of hypertensive parents. Health care providers, therefore have an important role to play in educating families and children about approaches that are useful in preventing hypertension.

References


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Transcultural Differences in Alcohol Use among Slavic, Arabian And Nigerian Students: A Case Study in Belarus

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Abstract

Background: Alcohol use by university students is a major public health problem in Belarusian campuses. The patterns of alcohol use might vary among students of different cultural backgrounds.

Aims & Objectives: Differences in alcohol use and related problems among undergraduates of various ethnic groups - Slavs, Arabians and Nigerians in Minsk, Belarus were examined.

Methods / Study Design: The study was randomized and anonymous, involving a total of 1549 respondents: 1345 Slavic, 120 Arabian and 84 Nigerian students in Minsk, Belarus. All respondents were administered questionnaire containing the AUDIT, CAGE, MAST and other alcohol related questions.

Results / Findings: Overall, 91.08% Slavs, 63.33% Arabs and 56.82% Nigerians were alcohol users. A total of 16.28% Slavic, 32.50% Arabian and 22.73% Nigerian problem drinkers were identified using the AUDIT. Generally, the use of weak strength alcoholic beverages (beer) was higher in the students’ population of all ethnicities.

Conclusion: The level of alcohol use and related problems in the general Belarusian students’ population is high. Differences in the pattern of alcohol use and related problems exist among students of various ethnicities (Slavs, Arabians and Nigerians) in Minsk, Belarus. Alcohol related problems were higher among the Arabs and Nigerians, compared to the Slavs. Similarities in the average AUDIT, CAGE and MAST scores amongst the Slavs and Nigerians, as well as preference for alcoholic beverages among the students of all ethnicities were noted. Higher scores were recorded only on the AUDIT and MAST for the Arabs.
Introduction

Alcohol use is a risk factor for health and significantly contributes to the burden of disease worldwide (Razvodovsky 2008; Catherine 2004). According to some researchers one of the major risks for health is associated with heavy alcohol use (Welcome et al, 2008; Wechsler et al, 1994; Weitzman et al, 2004).

Recent epidemiological data have consistently shown that the level of alcohol problems is high among the students’ population (Wechsler et al, 1994; Weitzman et al, 2004). High level of alcohol problems in the general students’ population calls for the necessity of carrying out preventive measures aimed at early detection of alcohol problems, with subsequent consultation and therapeutic intervention. In the general students’ population alcohol use results in low academic performance. Expulsions from school, traffic offences and accidents, asocial behaviors, injuries, blackouts etc are all effects of alcohol use by students (Wechsler et al, 1994; Weitzman et al, 2004; Manuel & Walt, 2005; Paschall & Freisthler, 2003).

In Belarus, there is a paucity of data addressing the problem of students’ alcohol use. This has contributed partly to the increase in the prevalence of alcohol use and related problems, as no intervention program is carried out (Welcome et al, 2008; Razvodovsky 2008; Catherine 2004). The pattern of alcohol use might differ among various ethnic groups, even in the same cultural settings (Catherine 2004; Caetano et al, 1998; Dong-Eok & Jorge, 2004; Emmanuel et al, 2005). A screening result that will address the prevalence of alcohol use and related problems in the general students’ population of various ethnic groups will be of great importance. Also, the students’ population is easily accessible, and every data suggest that screening for the prevalence of alcohol use in the student’s population, and subsequent intervention is of great benefit to public health (Elissa & Toben 2004; Federico & Diane 2007).

Presently, in epidemiological research, for determining the level of problems related with alcohol use in the general population, certain psychometric screening instruments are widely used. The most commonly used instruments are the AUDIT (The Alcohol Use Disorders Identification Test), MAST (Michigan Alcohol Screening Test), and CAGE (the Cut, Annoyed, Guilty and Eye questionnaire) (Welcome et al, 2008; Gache et al, 2005; Hays et al, 1995). These instruments are highly sensitive (85-94%) and specificity (79-93%) for early detection of alcohol problems (Welcome et al, 2008; Hays et al, 1995).

The aim of this survey was to screen for the prevalence of alcohol use and related problems among university students of different ethnicities: the Slavs, Arabians and Nigerians in Minsk, Belarus.

Materials and methods
**Study population:** Minsk is the capital city of Belarus with the highest number of students (foreigners and natives). There are four major universities (the Belarusian State University, Belarusian State Medical University, Belarusian National Technical University and Belarusian State Agrarian Technical University) in Minsk, where the native Belarusians, Arabians and Nigerians study. Presently, about 93 Nigerians; 350 Arabians and about 12000 Slavs study in these universities. Majority of students in these universities are Christians (94%). Others are Muslims (5%), atheists and non-religious (1%).

**Sampling size and technique:** A total of 2210 Slavic; 250 Arabian and 90 Nigerian students at random were explained the study aims and objectives, only those who agreed to participate were considered for interview in their various universities. Overall, 1549 students: 1345 Slavs (mean average age = 21 yrs) (352 males and 993 females), 120 Arabians (mean average age = 21.5 yrs) (89 males and 31 females) and 84 Nigerians (mean average age = 21.5 yrs) (73 males and 11 females) agreed to participate. All Arabians and Nigerians are foreigners studying in Minsk. Arabians were Iraqi and Saudi Arabian origin. While a majority of the Slavic students were Belarusians (97%), others were Russians (2%) and Ukrainians (1%). The participants: Slavic students were 96% Christians, 3% Muslims, atheists/non-religious (1%); Arabian students were 98% Muslims and 2% Christians; Nigerian students were 99% Christians and 1% – Muslims.

**Procedure:** The Ethics and Research Committee of the various universities approved the study protocol and informed consents were obtained from the respondents after the aims and objectives of the study had been explained. All students were administered questionnaire containing the AUDIT, CAGE, MAST and other alcohol related questions. All questionnaires were distributed evenly among students of year one to final year of university education in all four major universities.

**Measures:** A score of \( \geq 8 \) on the 10-item AUDIT defines alcohol related problems (Welcome et al, 2008). Non-problematic alcohol use was determined on the AUDIT from scores of 1 through 7. Abstinence was defined as a score of zero on the AUDIT. Students with scores \( \geq 1 \) were considered as alcohol users (Welcome et al, 2008; Gache et al, 2005). A score of 2 through 4 on the CAGE was considered clinically significant. Students with scores of \( \geq 3 \) on the MAST were defined as problem drinkers (i.e. students with alcohol related problems). A standard drink was set at 8g of absolute ethanol (Welcome et al, 2008; Gache et al, 2005; Hays et al, 1995).

**Data analysis:** All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) 16.0 version for Windows; the criteria of Pearson, \( \chi^2 \) and Student’s t tests (Bland 2000). The probability value for significance was set at \( p<0.05 \). All volumes of alcohol are given in values of absolute ethanol. Results are displayed as means and standard error of means (M ± m), as well as in percentages, %.

**Results**

The mean statistical results of all respondents (Slavs, Arabians and Nigerians) on the AUDIT, CAGE and MAST are given in table 1. The average scores were significantly
higher on the AUDIT and MAST for the Arabians, compared to scores for the Slavs and Nigerians (p<0.02). There were no significant differences in the average AUDIT, CAGE and MAST scores of the Slavs and Nigerians (Table 1).

Table 1: Total average AUDIT, CAGE and MAST scores of students of various ethnic groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>AUDIT</th>
<th>CAGE</th>
<th>MAST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slavs (n=1345)</td>
<td>4.38 ± 0.14</td>
<td>0.56 ± 0.03</td>
<td>0.94 ± 0.05</td>
</tr>
<tr>
<td>Arabs (n=120)</td>
<td>6.70 ± 0.88</td>
<td>0.89 ± 0.10</td>
<td>2.76 ± 0.38</td>
</tr>
<tr>
<td>Nigerians (n=84)</td>
<td>4.18 ± 0.87</td>
<td>0.68 ± 0.17</td>
<td>1.20 ± 0.32</td>
</tr>
</tbody>
</table>

Overall, 91.08% (n=1225) Slavs, 63.33% (n=76) Arabians and 60.71% (n=51) Nigerians were alcohol users (Table 2). On the AUDIT, a total of 16.28% (n=219) Slavs, 32.50% (n= 39) Arabians and 22.62% (n=19) Nigerians were problem drinkers (Table 2). The total percentage of Arabian problem drinkers was significantly more than the Slavs by approximately 2.0 times ($\chi^2=19.97$, p<0.005) on the AUDIT; 2.1 times ($\chi^2=21.38$, p<0.005) on the CAGE and 3.4 times ($\chi^2=20.70$, p<0.005) on the MAST. Although, the total number of problem drinkers among the Arabians was slightly more than the Nigerians, there was no statistical significance. Also, in respect to the percentages of problem drinkers no value for significance was recorded between the Slavs and Nigerians.

Table 2: Gender differences in the percentages of alcohol users and problem drinkers among the Slavs, Arabs and Nigerians on the AUDIT, CAGE and MAST

<table>
<thead>
<tr>
<th>Ethnicities</th>
<th>Sex</th>
<th>Alcohol users, %</th>
<th>Problem drinkers, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AUDIT</td>
<td>CAGE</td>
</tr>
<tr>
<td>Slavs</td>
<td>M (n=352)</td>
<td>94.32 (n=332)</td>
<td>34.66 (n=122)</td>
</tr>
<tr>
<td></td>
<td>F (n=993)</td>
<td>89.93 (n=893)</td>
<td>9.77 (n=97)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>91.08 (n=1345)</td>
<td>16.28 (n=219)</td>
</tr>
<tr>
<td>Arabs</td>
<td>M (n=89)</td>
<td>61.80 (n=55)</td>
<td>35.96 (n=32)</td>
</tr>
<tr>
<td></td>
<td>F (n=31)</td>
<td>58.06 (n=18)</td>
<td>22.58 (n=7)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>63.33 (n=76)</td>
<td>32.50 (n=39)</td>
</tr>
<tr>
<td>Nigerians</td>
<td>M (n=73)</td>
<td>61.64 (n=45)</td>
<td>23.29 (n=17)</td>
</tr>
<tr>
<td></td>
<td>F (n=11)</td>
<td>54.55 (n=6)</td>
<td>18.18 (n=2)</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>60.71 (n=51)</td>
<td>22.62 (n=19)</td>
</tr>
</tbody>
</table>

The number of alcohol users and problem drinkers was lower among the females of both ethnicities. But, a significant proportion of both male and female Slavic students had higher alcohol users, compared to other ethnic groups (Table 2). Despite the higher rate of alcohol use by Slavic females, they had lower percentage of problem drinkers, compared to the Arabian and Nigerian females. The percentages of problem alcohol users among the Slavs on the MAST were lower than that of the AUDIT and CAGE (Table 2).
Table 3: Quantity of alcohol use and percentages of some alcohol related problems among the Slavs, Arabs and Nigerians. Only Alcohol users

<table>
<thead>
<tr>
<th>Ethnicities</th>
<th>Dose/person/month (ml)</th>
<th>Loss of control, %</th>
<th>Hangover, %</th>
<th>Blackouts, %</th>
<th>Injuries, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slavs (n=1225)</td>
<td>123.9</td>
<td>22.35</td>
<td>16.26</td>
<td>32.1</td>
<td>27.08</td>
</tr>
<tr>
<td>Arabs (n=73)</td>
<td>116.1</td>
<td>47.68</td>
<td>41.23</td>
<td>49.53</td>
<td>46.77</td>
</tr>
<tr>
<td>Nigerians (n=51)</td>
<td>104.0</td>
<td>29.17</td>
<td>16.67</td>
<td>25.25</td>
<td>20.83</td>
</tr>
</tbody>
</table>

Analysis of the quantity of alcohol use showed no significant differences among students of all ethnic groups, although the amount was higher among the Slavs by 7.8ml and 19.9ml, than the values for the Arabs and Nigerians respectively (Table 3). The monthly frequency of alcohol use was also very low for both Arabs and Nigerians (1-2 times), compared to the Slavs who use alcoholic beverages 2-4 times on the average. Cases of some alcohol related problems like injuries, blackouts, hangover and loss of control was more in the Arabian students’ population than in the Slavic and Nigerian population. But no significant differences were noted between the Slavs and Nigerians (Table 3).

Table 4: Preference for different alcoholic beverages by different ethnic groups; Only Alcohol users

<table>
<thead>
<tr>
<th>Ethnicities</th>
<th>WSAB, %</th>
<th>ASAB, %</th>
<th>SSAB, %</th>
<th>WASSAB, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slavs (n=1225)</td>
<td>70.29 (n=861)</td>
<td>7.51 (n=92)</td>
<td>10.04 (n=123)</td>
<td>12.16 (n=149)</td>
</tr>
<tr>
<td>Arabs (n=73)</td>
<td>46.58 (n=34)</td>
<td>20.55 (n=15)</td>
<td>21.92 (n=16)</td>
<td>10.96 (n=8)</td>
</tr>
<tr>
<td>Nigerians (n=51)</td>
<td>56.86 (n=29)</td>
<td>23.53 (n=12)</td>
<td>11.76 (n=6)</td>
<td>7.84 (n=4)</td>
</tr>
</tbody>
</table>

N/B: WSAB – weak strength alcoholic beverages (beer); ASAB – average strength alcoholic beverages (wine); SSAB – strong strength alcoholic beverages (vodka and other spirits); WASSAB – weak/average/strong strength alcoholic beverages (beer, wine, vodka and other spirits). Composition of alcohol in the various alcoholic beverages: beer – <7%; wine – 7-17%; vodka/other spirits – ~40% (Welcome et al, 2008).

From table 4, generally, the use of weak strength alcoholic beverages was higher among students of all ethnicities; however weak strength alcohol users were significantly higher among the Slavs, compared to the Arabs and Nigerians. The use of average and strong strength alcohol or its combination was lowest in the general student population. The percentage of strong strength alcohol users showed an increase among the Arabs (up to ~22%, compared to only 10% and 12% for the Slavs and Nigerians respectively). Among average strength alcohol users, the percentage was also higher for both the Arabs and Nigerians than in the Slavic population by 2.7 times and 3.1 times respectively.
The major factors that encourage alcohol use in the general students’ populations of all ethnicities were drinking to reduce bad mood, on days of wages, for the sweet qualities of alcohol and to get drunk.

Discussion

The cut-off point for problematic alcohol use in this study is in agreement with the recommended cut-off for the various screening tools in Belarus (Welcome et al, 2008).

Before entrance into the university (before arrival in Belarus) approximately half of all Arabian and Nigerian students reported abstinence. The high proportion of alcohol users and relatively low problem drinkers among the Slavs, compared to the Arabians and Nigerians with lower number of alcohol users, but relatively higher proportion of problem drinkers (Table 2) might be linked to many factors (see below). The higher level of alcohol related problems in the Arabian students’ population, compared to the Slavs and Nigerians might be partly due to their socialization peculiarities and even differences in biological constitution (for example, the high Km enzymes of alcohol metabolism have been confirmed to be of low prevalence in Asian decent, as a result, they are more prone to experiencing greater effect of alcohol use, compared to other ethnic groups) (Wall et al, 1997). It has been suggested that Muslims (as 98% of the Arabs in this study were Muslims) might find it very difficult to cope in a society where alcohol use is part of the daily life of the people (Catherine 2004; Caetano et al, 1998; Dong-Eok & Jorge 2004; Emmanuel et al, 2005). Subsequently, their means of socialization are affected, which might probably result in alcohol use (Caetano et al, 1998; Dong-Eok & Jorge 2004). According to Durkheim’s theory, rapid cultural change causes a condition called anomic - the absence within a society of common social norms and controls. Under those conditions, people lack clear behavioral guidelines, possibly resulting in self-destructive tendencies (e.g., depression and alcohol abuse, alcohol dependence). In the same way, Leighton argued that rapid social change and disruptions (e.g. conflicting cultural values and fragmented communication) cause high stress levels that can result in deviant behaviors and psychological disorders, which might subsequently result in alcohol use and abuse (Welcome et al, 2008; Caetano et al, 1998; Frone 1999). Religion also plays a major role in peoples’ attitude toward alcohol use. A low level of alcohol consumption in Muslim societies is a classical example of the protective influence of religion on alcohol use (Welcome et al, 2008; Catherine 2004; Caetano et al, 1998; Wall et al, 1997). Epidemiological data suggest that Muslims might experience high rate of alcohol problems in case of alcohol use, as a result of their lack of experience regarding alcohol use (Caetano et al, 1998; Bloomfield et al, 2005; Heath 1995). This could likely be one of the reasons why even for approximately equal quantity of alcohol use among students of all ethnic groups, the Arabian students still had higher alcohol related problems compared to their Slavic counterparts.

Generally, among the various ethnic groups – Slavs, Arabians and Nigerians, there were no significant differences in the type of alcoholic beverages used as majority of the students of all ethnicities prefer weak strength alcoholic beverages like beer (Table 4).
It has been noted in earlier studies that the MAST might show minimal sensitivity when used for determining the level of alcohol related problems in some populations. And that the CAGE might be highly sensitive among the Slavic population (Welcome et al, 2008; Catherine 2004; Gache et al, 2005; Hays et al, 1995; Bohn et al, 1995). This was the rationale for using multiple screening tests in this study. It is probable, that the MAST is less sensitive, compared to the AUDIT and CAGE among the Slavic students’ population as seen in the screening results (Table 1 & 2). All three screening tests (AUDIT, CAGE and MAST) showed almost the same results (in regards to the percentage of problem drinkers) among the Arabian and Nigerian students’ population (Table 2). Making general conclusion about the sensitivity of the various screening instruments used is rather difficult as a result of the limitations of this study.

Limitations: Some respondents with alcohol related problems may have under-reported them in the AUDIT, MAST and CAGE. This might have affected the reliability value of the screening results. Another limitation of this study is that the questionnaire was administered ones and so the reliability indices of the various tests were not assessed. The fewer sample of both the Nigerians and the Arabians (especially the female respondents), compared to the Slavs, could have affected the reliability and significance of the results. This was because a fewer number of Arabians and Nigerians (and especially very few females) study in Minsk (Belarus).

Conclusion

The level of alcohol use and related problems among the Slavic, Arabian and Nigerian students’ population in Minsk, Belarus is high. Significant differences in the pattern of alcohol use exist between students of various ethnic groups (Slavs, Arabians and Nigerians) in Minsk, Belarus. The percentage of Slavic alcohol users (91.08%) was higher, than the Arabians (63.33%) and Nigerians 56.82%. The proportion of problem drinkers on the AUDIT was higher among the Arabs (32.50%) and Nigerians (22.73%), compared to the Slavs (16.28%). The use of weak strength alcoholic beverage (beer) is highest among students of all three ethnic groups. Although among the Slavs, weak strength alcohol (beer) users were slightly higher than the Arabians and Nigerians. There was a slight increase in the percentage of strong strength alcohol users among the Arabs, compared to other ethnicities.

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Determinants of Quality of Life for Jamaica Women

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Brief Synopsis: On an average the mean quality of life of Jamaican Woman is 6.8 ±1.7: Range 10: 10– 0. The model shows that 6 factors explain 18.5% of the variance in quality of life of this gender. The 3 most influential variables are social class (4%), employment (2.9%) and income of a person; with religiosity being the fourth most influential of the 6 factors.

Abstract

Objective: The current study seeks to examine the quality of life (or subjective wellbeing) of Jamaican women by building a model that will capture socio-demographic and economic determinants of their quality of life.

Method: The current study uses a sample of 723 women, with a mean age of 34.33yrs ±13.4 yrs. This study is taken from a general study conducted by the Centre of Leadership and Governance, Department of Government, The University of the West Indies between July and August 2006 of some 1,338 Jamaicans. The survey was a stratified random sample of the fourteen parishes of Jamaica, using the descriptive research design. Data were collected and stored using the Statistical Packages for the Social Sciences (SPSS); and multiple regressions were used to build a quality of life model for Jamaican Women.

Findings: The study reveals that the model explains 18.5% (Adjusted R-squared) of the variability of quality of life of women; with 6 variables accounting for this variance. Further examination of the sociodemographic determinants revealed that subjective social class (Beta = 0.198; b=0.725; 95%CI:0.380, 1.070) is the most influential factor followed by employment status (Beta = 0.167; b=0.691; 95%CI:0.304, 0.1.077), religiosity(Beta = 0.152; b=0.594; 95%CI:0.214, 0.974), income (Beta = 0.155; b=0.058; 95%CI:0.015, 0.101), the administration of the governance of the nation (Beta = -0.139; b=-0.548; 95%CI:0.893, -0.203) and lastly by interpersonal trust (Beta = 0.094; b=0.348; 95%CI:0.020, 0.676).

Conclusion: In summary, the factors of quality of life of a Jamaican Woman are social class, employment, income and religiosity, with social class being the most influential of all the variables. Employment does not merely about the income, but it is about the independence, the choices, the sense of freedom, the positive psychological attributes that this freedom gives as well as the self-advancement that it is likely to provide why this variable is of that importance in determining the quality
of life of Women. The current work does not provide all the answers, but it is catalysts upon which we are able to build, modify and refute research as this provide a platform upon which this is probable in the future.

**Keywords:** Quality of life, Women health, Jamaica, developing countries, cross-section study

**Introduction**

The current study seeks to examine the quality of life (i.e. subjective or self-reported wellbeing) of Jamaican women by building a model that will capture socio-demographic and economic determinants of quality of life of this cohort. The rationale that underpins the current work is principally driven by lack of academic literature on the subjective wellbeing or quality of life on the particular gender. Most studies on quality of life have incorporated gender as a predictive factor or a determinant of subjective wellbeing studies (or quality of life) (Bourne, 2009, 2007; Murphy and Murphy 2006; Hambleton et al. 2005; Hutchinson et al. 2004; Stutzer and Frey 2003, 2001; Easterlin 2001a, 2001b, 1995; Lyubomirsky 2001; Cummins 2000; Diener 2000, 1985; Smith and Kington 1997; Grossman 1972). One study examining a particular quality of life of an elderly man shows how medical practitioners over many years sought to address a particular issue that was eroding the wellbeing of a patient who had a certain physiological dysfunctions (Ali and colleagues 2007). Can medical practitioners and social researchers assume that the quality of life of sexes is the same, given that they are of the same species? Such a situation is simple, as the physiological composition of the sexes is different, purchase power party differs, gender culturalization is dissimilar as well as the disparity between gender opportunities. Within this context, researchers, medical practitioners and policy makers need to understand the factors that influence quality of life of each gender as they are sex specify in enhancing the specificity that is needed to planning for the sex differential. A primary rationale for this awareness is owing to the opportunity differential because of one sex in society.

In 1991, the unemployment rate was 22.2 per cent for females compared to 9.4 per cent for males and in 2007, the figure fell to 6.2 per cent for males and 14.5 per cent for females. The more drastic reduction in the unemployment rate for women cannot constitute any form of betterment of females over their male counterparts as in 2007 the unemployment rate for female was twice more than that of males. The statistics reveal that men enjoy a 17 per cent higher employed labour force than females; and this indicates the opportunity of greater economic resources. Another good measure that has been used to evaluate betterment (quality of life) between the sexes is economic resources (i.e. wages or salaries, income or wealth) (Becker et al., 2004; Gaspart, 1998; Summers & Heston 1995). In the Economic and Social Survey of Jamaica (2004, p. 21.9), the publication showed that on an average the earnings of males (mean wage = $2.4 million) was 2 times more than that of females ($ 1.7 million); and that 76 per cent of senior positions were held by males although 54 per cent of executive and managerial positions were held by females. If males are still receiving greater salaries compared females and they experience high degrees of employment, we cannot concur with Miller nor Chevannes or Gayle that they are marginalized despite the fact that they are living fewer years than females (Table 1.1).
From a study, using survey data from 1988 to 1999, conducted in Argentina, Brazil and Costa Rica, the researchers found that there is no general trend of economic marginalization of males in those societies (Omar Arias, 2001), which is evident from some of economic indicators in Jamaica. On the other hand, what about our women?

The importance of women in fertility as well as the fact that they have a greater life expectancy compared to their male counterparts (Table 1.0); it is timely that a research be done on this cohort to unearth ‘what constitute their quality of life?’ Scholars who have done studies on different Caribbean nations like Bourne, 2007; Eldemire 1997, 1996, 1995a, 1995b, 1994, 1987a, 1987b; Hambleton et al. 2005; Brathwaite, their works on the quality of life have been substantially on elderly people (ages 60 years or older or 65 years and older) with no particular interest on a certain sex. Studies on the same region have examined psychological wellbeing of the total population, with women having a lower psychological wellbeing and life satisfaction than men (Hutchinson et al. 2005) and rural women of the reproductive ages 15 to 49 years (Bourne and Rhule, 2009). Hutchinson et al.’s work used a sample of young adults (ages 15 to 50 years), and therefore omits the all other age cohort of Jamaicans. Bourne and Rhule on the other hand did not example the gamut of women as they excluded urban and semi-urban women. Caribbean societies have patriarchal roots and so economic resources are primarily in the hands of males; but of the quality of life of female? How are they living in Jamaica?

Is there is disparity between the quality of life of the sexes? However, a survey done by Rudkin found that women have lower levels of wellbeing (i.e. economic) than men (Rudkin 1993 222). This finding is further sanctioned by Haveman et al (2003) whose study reveal that retired men’s wellbeing was higher than that of their female counterparts, because men usually received had more material resources, and more retired benefits compared to women ages 65 years and older. Thus with men receiving more than women, and having a more durable possession than women, their material wellbeing is higher is later life.

Generally, from the United Nations statistical databases, life expectancy for male is lower than of females. This is particular true for females in the old aged cohorts (United Nations 2004; Moore et al. 1997). Moore et al. (1997) added, “Females’ life expectancies are likely to remain above that for males [Elo 2001] for the foreseeable future, among both the population as a whole and the elderly” (Moore et al. 1997, 12). Among the justification for the differential between life expectancy the sexes is linked with the health consciousness of women and their approach to preventative care. Unlike women, worldwide men have a reluctance to ‘seek health-care’ compared to their female counterpart. It follows in truth that women have bought themselves additional years in their younger years, and it is a practice that they continue throughout their life time which makes the gap in age differential what it is – which is approximately a 4-year difference in Jamaica.

A study conducted by McDonough and Walters (2001) revealed that women had a 23 percent higher distress score than men and were more likely to report chronic diseases compared to males (30%). It was found that men believed their health was better (2% higher) than that self-reported by females. McDonough and Walters used data from a longitudinal study named Canadian National Population Health Survey (NPHS). The study was initiated in 1994, and data were collected every second year for a duration
of six years. The information was taken form 20,000 household members who were 12 years and older.

A research carried out by a group of economists (Headey and Wooden) revealed that “…women are slightly more likely to report higher levels of life satisfaction than men (mean=78.3, compared with 77.1 for men…” (Wooden and Headey 2003, 14). Based on the nature of the study, ‘…subjective wellbeing and ill being’, the reported wellbeing (measure by life satisfaction) of women is higher than that for men but that males have a higher financial wellbeing than females (Headey and Wooden 2003, 16). Thus, the discourse is inconclusive and we will not add to the literature in this regard but will examine quality of life of women as this is the first of its kind in Jamaica and in the wider Caribbean literature.

Theoretical Framework

The overarching theoretical framework that will be adopted in this study is an econometric model that was developed by Grossman (1972), and further modified by Smith and Kington 1997. The initial model (i.e. Eqn. [1]) by Michael Grossman reads:

\[ H_t = f (H_{t-1}, G_o, B_t, MC_t, ED) \] …………… [1]

where \( H_t \) - current health in time period \( t \), stock of health \( (H_{t-1}) \) in previous period, \( B_t \) - smoking and excessive drinking, and good personal health behaviours (including exercise \( - G_o \)), \( MC_t \) - use of medical care, education of each family member \( (ED) \), and all sources of household income \( (including \ current \ income) \). Grossman’s model further expanded upon by Smith and Kington to include socioeconomic variables (Eqn.2).

\[ H_t = H^* (H_{t-1}, P_{mc}, P_o, ED, E_t, R_t, A_t, G_o) \] ….. Eqn. [2]

Eq. (2) expresses current health status \( H_t \) as a function of stock of health \( (H_{t-1}) \), price of medical care \( P_{mc} \), the price of other inputs \( P_o \), education of each family member \( (ED) \), all sources of household income \( (E_t) \), family background or genetic endowments \( (G_o) \), retirement related income \( (R_t) \), asset income \( (A_t) \). Thus, the current study will test this general hypothesis in seeking to establish a quality of life model for Jamaican Women (Eqn. [3]):

\[ QoL_j = f(G_j, PPI_j, Y_j, R_j, lnA_j, C_j, O_j, T_j, SS_j, AR_j, X_j, E_j, ES_j, RA_j, WS_j) \] …………Eqn.[3]

Method

The current study uses a sample of 723 women, with a mean age of 34.33yrs ±13.4 yrs. This study is taken from a general study conducted by the Centre of Leadership and Governance, Department of Government, The University of the West Indies between July and August 2006 of some 1,338 Jamaicans (Powell, et al. 2007). The survey was the first of its kind as it collected data on Jamaican’s Political Culture. The
survey uses a questionnaire of some 166 items. The themes ranged from democracy; civic culture; trust and confidence; perception of wellbeing using Abraham Maslow's 5 Needs Item; preference for private or public sector solving problems in the economy; political participation and civic engagement; and, leadership, party, and electoral preferences. Face-to-face interviews were used to collect the data on an instrument which took about 90 minutes. The instrument consisted of 166 items that were taken from Latino barometer and Euro barometer cross-cultural survey; the American National Election Studies series; the Harvard/Washington Post Leadership survey, the New Zealand Election Surveys and the Cross-cultural Variations in Distributive Justice Perception survey and Carl Stone surveys. The instrument was vetted by senior scholars, researchers as well as by interviewers within the data divisions of the Statistical Institution of Jamaica (STATIN) and Social Development Commission (SDC). After the vetting phase, the questionnaire was pretested in a number of communities across the 14 parishes of Jamaica as well as among UWI faculty and student population. Modifications were made at a training symposium based on the comments of the different interviewers and remarks of trained researchers. All the interviewers employed by the CLG’s team were either data collectors by STATIN or SDC. Although the interviewers are trained data collectors, they were trained by the CLG team for a one-day period.

The survey was a stratified random sample of the fourteen parishes of Jamaica, using the descriptive research design. The steps involved in computing the sample size is explained in the next sentences. The proportion of Jamaicans residing in each parish was calculated as well as gender and age composition. The sample size was proportionate to the population; and this was in keeping with the gender and age distribution of the population. Data were collected and stored using the Statistical Packages for the Social Sciences (SPSS). Descriptive statistics were done to provide background information on the sample; tests were done for Cronbach alpha to examine the validity of the construct – i.e. wellbeing and political participation. Multiple regressions were used to build a model for quality of life of Jamaican Women.

Measures:

\[ Q_{oL_j} = \frac{1}{10} \sum L_{ij} \]

where \( L_i \) denotes each Need Item of Abraham Maslow’s 5-Need Hierarchy

\[ i=1 \]

(Each is a 10-point Likert Scale: Health status; Basic Necessities; Social Needs; Self-Esteem; Self-Actualization). Reliability analysis of the 5-Need Likert Scale Item is 0.748 (or 75%). Quality of Life Index ranges from: 1≤Quality of Life Index≤10; where from 1 to 3.9 are low, 4 to 6.9 are moderate and with high being from 7 to 10.
Area of residence. This means the geographic location of one’s place of abode. It is a dummy variable, 1=St. Andrew, Kingston and St. Catherine, 0=Other\textsuperscript{1}

Subjective Social Class. This is people’s perception of their social and economic position in life, based on social stratification.

- socialcl1 1=Middle class
- socialcl2 1=Upper class

Referent group is lower class.

Interpersonal Trust. The survey instrument asked the question ‘Generally speaking would you say that most people are essentially good and can be trusted, or that most people are not essentially good and cannot be trusted. The variable was then dummied, 1 if most people essential good and can be trusted, 0 if otherwise. Trust is on a continuum, and so low trust is a proxy for distrust.

Occupation is a dummy variable, 1 if in high occupation, 0 if otherwise. Those categories which are classified within this are – teachers, doctors, lawyers, businessmen, managers and/or supervisors whereas in the low category the following were included – farmers, tradesmen, unskilled worker, shopkeeper, haggler, vendor, office workers and so on.

Confidence in sociopolitical institutions. This is the summation of 22 Likert scale questions, with each question on a scale of (4) a lot of confidence, (3) some confidence, (2) a little confidence, to (1) no confidence. The heading that precedes the question reads: I am going to read to you a list of major groups and institutions in our society. For each, tell me how much CONFIDENCE you have in that group or institution. Confidence index = summation of 22 items, with each question being weighted equally; and 0≤confidence index≤88, with a Cronbach α for the 22-item scale being 0.896. The higher the scores, the more people have confidence in sociopolitical institutions within the society. Thus, the confidence index is interpreted as from 0 to 34 represents very little confidence; 35 to 61 is low confidence; 62 to 78 is moderate confidence and 79 to 88 is most confidence.

Age. Age is a continuous variable, which is recorded in years.

\textsuperscript{1} Others constitute St. Thomas, Portland, St. Mary, St. Ann, Trelawny, St. James, Hanover, St. Elizabeth, Westmoreland, Manchester, and Clarendon.
Religiosity. The frequency with which people attend religious services, which does not include attending functions such as (1) graduations, (2) weddings, (3) christenings, (4) funerals. This variable was recorded as:

Religiosity1 1=High religiosity (i.e. church attendances more than once per week)
Religiosity2 1=Moderate religiosity (i.e. church attendance once per week or fortnightly)
Referent group is low religiosity (i.e. none to several times per year)

Income. Income is an ordinary variable with twenty-categories, ranging from (1) under $5,000 to (20) $250,000 and above. Based on the nature of this variable, it will be treated as a continuous variable.

Political Participation Index. Based on Trevor Munroe’s work, ‘political participation’ “…the extent to which citizens use their rights, such as the right to protest, the right of free speech, the right to vote, to influence or to get involved in political activity” (Munroe, 2002:4; Munroe, 1999:33), we use that construct to formulate a PPI = \( \sum b_i \), \( b_i \geq 0 \), and \( b_i \) represents each response to a question on political behaviour, such as voting, involvement in protest, with \( 0 \leq \text{PPI} \leq 19 \). The Cronbach alpha for the 22-item scale, which is used to constitute this Index, is 0.828.

Governance of the country, G, is defined as people’s perception of administration of the society by the elected officials. This is a dummy variable, where 1 denotes in favour of a few powerful interest groups or the affluent, 0 is otherwise.

Employment status, E, where 1=employed and 0 is otherwise

Extent of the Welfare System of governance:

Results: Sociodemographic Characteristics of Sampled Population

The findings of the current research has a sampled population of 723 women ages 16 to 85 years with a mean age of 34.3 years ± 13.4 years. Most of the respondents report that they are Blacks (78%) with some indicates Browns – i.e. Mixed - (14%), Caucasians (6%). Approximately 6 out of 10 women indicate that they are in the lower class. The demographic characteristics of the sample also reveal that approximately 7 out of every 10 women indicate that they are employed (i.e. full-time, part-time, temporarily, seasonally and self-employed). On an average the quality of life of the sample was high (i.e. 6.8 ±1.7: Range 10: 10– 0). Furthermore, the findings (Table 1.1) indicate that political participation for Jamaican Women is
low (i.e. 3.6 ±3.5: Range 17: 17–0). On the contrary, the population has moderate confidence in the various socio-political institutions in Jamaica (56.3±10.8: Range 79:86 – 7); with a sample report a high ‘welfare system of governance’ of the Jamaican state.

Findings: Multivariate Analysis

Using econometric analysis (i.e. multiple regressions) – of the surveyed research data of some 723 Jamaican women – we found that the final model (Eqn. [3]) explains 18.5% (Adjusted R-squared) of some 6 variables. The model is a good fit (F statistic [15, 410] = 7.413, p value = 0.001). (Table 1.2).

\[
QoL_j = f(G_j, \text{PPI}_j, Y_j, R_j, \ln A_j, O_j, T_j, SS_j, AR_j, X_j, E_j, ES_j, RA_j, WS_j, \varepsilon_j) \quad \text{Eqn.}[3]
\]

where:
- \(QoL_j\) is the quality of life of person j;
- \(G_j\) is self-reported administration of the governance of the nation of person j;
- \(\text{PPI}_j\) is the political participation index of person j;
- \(Y_j\) is the income of person j;
- \(R_j\) is the religiosity of person j;
- \(\ln A_j\) is the logged age of person j;
- \(O_j\) is the occupation of person j;
- \(T_j\) is the interpersonal trust of person j;
- \(SS_j\) is the subjective social class of person j;
- \(AR_j\) is the area of residence (i.e. parish of residence) of person j;
- \(X_j\) is the gender of respondent of person j;
- \(E_j\) is the educational level of person j;
- \(ES_j\) is the employment status of person j;
- \(RA_j\) is the ethnicity of person j;
- \(WS_j\) is the extent of welfare state of a nation as reported by person j.

\[
QoL_{ij} = f(Y_j, R_j, T_j, G_j, SS_j, ES_j, RA_j, WS_j, \varepsilon_j) \quad \text{Eqn.}[4]
\]

Examination of the sociodemographic determinants in Eqn. [4] revealed that subjective social class – middle class with referent to lower class - (Beta = 0.198; b=0.725; 95%CI:0.380, 1.070) is the most influential factor followed by employment status (Beta = 0.167; b=0.691; 95%CI:0.304, 0.1.077), income (Beta = 0.155; b=0.058; 95%CI:0.015, 0.101), religiosity - high religiosity - (Beta = 0.152; b=0.594; 95%CI:0.214, 0.974), the administration of the governance of the nation (Beta = 0.139; b=-0.548; 95%CI:-0.893, -0.203) and lastly by interpersonal trust (Beta = 0.094; b=0.348; 95%CI:0.020, 0.676) (Table 1.2).
Further examination of the findings will now be forwarded to provide a more in-depth understanding of determinants in model (i.e. Eqn. [4]). An individual who is in the self-reported middle class with referent to lower class contributes the most to quality of life of Jamaican Women. However, those in the upper class with referent to lower class contribution are marginally more than interpersonal trust that influence is the least. A woman who trusts other people has a greater quality of life compared to another who reported that she does not trust other people. A similar result was observed for employment status as an employed woman has greater quality of life compared to those who are unemployed, and the greater the income of a person the higher is the quality of life of that individual. Religiosity is the fourth most significant factor of quality of life of sampled population. The religiosity with which we speak is high church attendance (i.e. church attendance at least twice per week) with referent to low religiosity (i.e. from no church attendance to once per year). Those who reported that the governance of the nation (i.e. political administration) benefits mostly equally with referent to those who indicated that it favours the rich have a lower quality of life. In addition to what has been reported so far, those who cited being in moderate religiosity had a greater quality of life compared to those with had a low religiosity. Thus, a woman’s quality increases with greater church attendance.

**Limitation of the Model**

Although the current model used data from a cross-sectional study by way of stratified probability sampling technique, it has an adjusted R-square of less than 20%. Some statisticians argue that a cross-sectional study that is less than 30% and over is not a good predictor of the phenomenon. The current research is the first of its kind, and is more so a platform for future studies than a conclusion on the matter of quality of life of women in Jamaica. Another limitation for the non-collection of some critical variables such as living arrangement and marital status which may aid in explain quality of life of females.

**Discussion**

The physiological composition of the sexes explains the rationale of some typologies of diseases affecting a particular sex (WHO 2005). One health psychologist, Phillip Rice, in concurring with WHO, argued that differences in death and illnesses are the result of differential risks acquired from functions, stress, life styles and ‘preventative health practices’ (Rice 1998). Biomedical studies showed that there are gender specific diseases. The examples here are prostate cancer (affect only men) and cervical cancer (plague only women). In Jamaica the health conditions disparity between the sexes include malignant neoplasms (rates are 39% higher for males than females); cerebrovascular diseases (rates are 14% higher for females than males); heart disease (71.2 per 100,000 for females and 66.1 per 100,000 for males); diabetes mellitus (females have a 64% greater mortality rates than males in diabetes) (Ward and Grant, 2005). Concomitantly, the 5 leading cause of mortality for males 5 years and older in descending order were external causes, cerebrovascular disease, diabetes mellitus, ischaemic heart disease and malignant neoplasm of prostate. For males, in
descending order, the 5 leading cause of death of same age cohort as males were diabetes mellitus, cerebrovascular disease, hypertensive disease, ischaemic heart disease and external causes (Statistical Institute of Jamaica, 2008). Rice believed that this health difference between the sexes is due to social support. According to Rice (1998), Rodin and Ickovics (1990) this can be explained by epidemiological shifts. Lifestyle practices may justify the advantages that women enjoy compared in men concerning health status. However, a survey done by Rudkin found that women have lower levels of wellbeing (i.e. economic) than men (Rudkin 1993 222). This finding is further sanctioned by Haveman et al (2003) whose study reveal that retired men’s wellbeing was higher than that of their female counterparts, because men usually received had more material resources, and more retired benefits compared to women ages 65 years and older. Thus with men receiving more than women, and having a more durable possession than women, their material wellbeing is higher is later life.

The issue extends beyond those two types of chronic illnesses as Courtenay (2003) noted from research conducted by the Department of Health and Human Services (2000) and Centers for Disease Control (1997) that from the 15 leading causes of death except Alzheimer’s disease, the death rates are higher for men and boys in all age cohorts compared to women and girls. Embedded within this theorizing are the differences in fatal diseases that are explained by gender constitution (Seltzer and Hendricks 1989, 7), to which Courtenay (2003) explained are due to behavioural practices of the sexes and goes to explain the fact that men are dying 6 years earlier than females (U.S. Preventive Services Task Force, 1996). The current research does not expand on past literature, but provides new information on factors that explain variability in quality of life of females (or women) in Jamaica.

Among the fundamental characteristics of research are that adding something new to the discourse, modifying what exists and so in keeping with these epistemological traditions, we will maintain these traditions in the current work. Religion is gender bias, and this dates back to nation’s slavery past. In contemporary Jamaica, church attendance is substantially a woman issue; and many theologians continue to argue that there are reality benefits to have from this practice. It is well accepted that religiosity is positively associated with wellbeing; and that is goes beyond the theologians’ views (Krause 2006; Moody 2006; Jurkovic and Walker 2006; Ardelt 2003; Graham et al. 1978). According to Kart (1990), religious guidelines aid wellbeing in that through restrictive behavioural habits which are health risk such as smoking, drinking of alcohol, and even diet. The current study has concurred with the literature that religiosity is positively associated with quality of life; and this is the fourth most influential predictor of quality of life of a Jamaican Woman. We go further to say that the quality of life Jamaican Woman is the highest when she has the greatest degree of church attendance followed by moderate religiosity and lastly by the lowest religiosity.

Traditionally income was used to proxy wellbeing (i.e. economic wellbeing), and that Richard Easterlin (2001a, 2001b) showed that income is important to happiness, but that income does not buy unlimited happiness. In a paper titled Poverty and Health, Murray (2006) argued that there is a clear interrelation between poverty and health. She noted that financial inadequacy prevents an individual from accessing – food and good nutrition, potable water, proper sanitation, medicinal care, preventative care, adequate housing, knowledge of health practices - and attendance at particular
educational institutions among other things. The issue of resource insufficiency affects the ability and capacity of the poor from accessing the quality of goods and services comparable to the rich that are better able to add value to wellbeing. This is succinctly forwarded by Murray in her monograph that:

Poverty also leads to increased dangers to health: working environments of poorer people often hold more environmental risks for illness and disability; other environmental factors, such as lack of access to clean water, disproportionately affect poor families (Murray 2006, 923)

Michael Grossman’s work had established the direct link between income and health (Smith and Kington 1997; Murray 2006; Sen 1999); and that income’s contribution to the quality of life of a Jamaican Woman is highly important as the current study reveals that it (income) is the third most influential factor in determining quality of life of the sampled population. This contradicts the work of Edward Diener. Diener (1984), states that the correlation between income and subjective wellbeing was small in most countries. According to Diener (1984, 11), “…, there is a mixed pattern of evidence regarding the effects of income on SWB [subjective wellbeing]”. The current research was subjective wellbeing (i.e. self-reported quality of life using Abraham Maslow’s 5 Need Item scale), and it shows that income is the third most valued predictor of quality of life of a Jamaican woman. Arendt, using ordered logistic models, found that “it cannot be rejected that the income effects are causal” and this proceeded the finding that “[a] robust relations exist between income and some measures of wellbeing of [the] elderly” (Ardent 2005, 327). Although the current work counter the findings of Edward Diener’s work (1984), what contributes the most to quality of life of a Jamaican woman?

The answer is social class followed by employment status (ie employed women). The quality of life of a Jamaican Women is primarily determined by her social class; with middle class women having the greatest quality of life and working class female experiencing the least quality of life. In this study education was not related to quality of life, which contravenes the finding of many studies (Diener 1984; Grossman, 1972; Hambleton et al. 2005; Bourne, 2007). Hambleton et al.’s work, on the other hand, found that the statistical relation was a weak one. Employment’s contribution to the quality of life of woman is highly important because of significant of employment in socio-economic independent, opportunities, choices and freedom and power of independency in this regard.

**Conclusion**

In summary, the factors of quality of life of Jamaican women are social class, employment, income and religiosity, with social class being the most influential of all the variables. Employment does not merely about the income, but it is about the independence, the choices, the sense of freedom, the positive psychological attributes that this freedom gives as well as the self-advancement that it is likely to provide why this variable is of that importance in determining the quality of life of Women. The current work does not provide all the answers, but it is a catalyst upon which we are able to build, modified and refute as these are pillows upon which research is based.
References


### Table 1.0: Expectation of Life at Birth by Sex, 1880-1991, Jamaicans

<table>
<thead>
<tr>
<th>Period</th>
<th>Average Expected Years of Life at Birth</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>e₀</td>
<td>e₀</td>
</tr>
<tr>
<td>1880-1882</td>
<td></td>
<td>37.02</td>
<td>39.80</td>
</tr>
<tr>
<td>1890-1892</td>
<td></td>
<td>36.74</td>
<td>38.30</td>
</tr>
<tr>
<td>1910-1912</td>
<td></td>
<td>39.04</td>
<td>41.41</td>
</tr>
<tr>
<td>1920-1922</td>
<td></td>
<td>35.89</td>
<td>38.20</td>
</tr>
<tr>
<td>1945-1947</td>
<td></td>
<td>51.25</td>
<td>54.58</td>
</tr>
<tr>
<td>1950-1952</td>
<td></td>
<td>55.73</td>
<td>58.89</td>
</tr>
<tr>
<td>1959-1961</td>
<td></td>
<td>62.65</td>
<td>66.63</td>
</tr>
<tr>
<td>1969-1970</td>
<td></td>
<td>66.70</td>
<td>70.20</td>
</tr>
<tr>
<td>1979-1981</td>
<td></td>
<td>69.03</td>
<td>72.37</td>
</tr>
<tr>
<td>1989-1991</td>
<td></td>
<td>69.97</td>
<td>72.64</td>
</tr>
<tr>
<td>1999-2001</td>
<td></td>
<td>70.94</td>
<td>75.58</td>
</tr>
<tr>
<td>2002-2004</td>
<td></td>
<td>71.26</td>
<td>77.07</td>
</tr>
</tbody>
</table>

Sources: Demographic Statistics (1972-2006); Statistical Yearbook of Jamaica, 1999 and
*Economic and Social Survey, Jamaica 2005 (Quoted in Bourne, 2007, p. 150)  
Note e₀ is life expectancy at birth

### Table 1.1: Demographic Characteristics of Sampled Population, N=723

<table>
<thead>
<tr>
<th>Subjective Social Class</th>
<th>Number</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working (lower) class</td>
<td>409</td>
<td>58.7</td>
</tr>
<tr>
<td>Middle class</td>
<td>259</td>
<td>37.2</td>
</tr>
<tr>
<td>Upper class</td>
<td>29</td>
<td>4.2</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>46</td>
<td>6.4</td>
</tr>
<tr>
<td>Blacks</td>
<td>562</td>
<td>77.9</td>
</tr>
<tr>
<td>Browns</td>
<td>104</td>
<td>14.4</td>
</tr>
<tr>
<td>Other</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Educational Level</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal Education</td>
<td>8</td>
<td>1.2</td>
</tr>
<tr>
<td>Primary/Preparatory and All Age school</td>
<td>116</td>
<td>16.8</td>
</tr>
<tr>
<td>Secondary</td>
<td>246</td>
<td>35.5</td>
</tr>
<tr>
<td>Post-secondary</td>
<td>127</td>
<td>18.4</td>
</tr>
<tr>
<td>Tertiary</td>
<td>195</td>
<td>28.1</td>
</tr>
<tr>
<td>Employment Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployed</td>
<td>222</td>
<td>31</td>
</tr>
<tr>
<td>Employed</td>
<td>494</td>
<td>69</td>
</tr>
<tr>
<td>Age</td>
<td>34.33yrs ±13.4 yrs.: Range 69: 85 – 16 yrs.</td>
<td></td>
</tr>
<tr>
<td>Quality of Life</td>
<td>6.8 ±1.7: Range 10: 10 – 0.</td>
<td></td>
</tr>
<tr>
<td>Political Participation Index</td>
<td>3.6 ±3.5: Range 17: 17 – 0.</td>
<td></td>
</tr>
<tr>
<td>Extent of Welfare System of governance</td>
<td>6.8 ± 1.5: Range 8.7:10 – 1.2.</td>
<td></td>
</tr>
<tr>
<td>Confidence in sociopolitical institution index</td>
<td>56.3±10.8: Range 79:86 – 7.</td>
<td></td>
</tr>
</tbody>
</table>
Table 1.2: Quality of Life of Jamaican Women by Some Explanatory Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized Coefficient</th>
<th>Std. Error</th>
<th>Beta</th>
<th>t</th>
<th>P</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>4.317</td>
<td>1.060</td>
<td></td>
<td>4.072</td>
<td>0.000</td>
<td>2.233 - 6.401</td>
</tr>
<tr>
<td>Secondary or tertiary</td>
<td>0.252</td>
<td>0.225</td>
<td>0.064</td>
<td>1.122</td>
<td>0.263</td>
<td>-0.189 - 0.693</td>
</tr>
<tr>
<td>High religiosity</td>
<td>0.594</td>
<td>0.193</td>
<td>0.152</td>
<td>3.073</td>
<td>0.002</td>
<td>0.214 - 0.974</td>
</tr>
<tr>
<td>Moderate religiosity</td>
<td>0.466</td>
<td>0.194</td>
<td>0.116</td>
<td>2.406</td>
<td>0.017</td>
<td>0.085 - 0.847</td>
</tr>
<tr>
<td>Kingston/St Catherine</td>
<td>-0.031</td>
<td>0.204</td>
<td>-0.007</td>
<td>-0.152</td>
<td>0.879</td>
<td>-0.432 - 0.370</td>
</tr>
<tr>
<td>Extent of Welfare System of Governance Lower Occupation</td>
<td>0.034</td>
<td>0.053</td>
<td>0.028</td>
<td>0.641</td>
<td>0.522</td>
<td>-0.071 - 0.139</td>
</tr>
<tr>
<td>Middle class</td>
<td>0.050</td>
<td>0.209</td>
<td>0.013</td>
<td>0.236</td>
<td>0.813</td>
<td>-0.362 - 0.461</td>
</tr>
<tr>
<td>Upper class</td>
<td>0.725</td>
<td>0.175</td>
<td>0.198</td>
<td>4.134</td>
<td>0.000</td>
<td>0.380 - 1.070</td>
</tr>
<tr>
<td>†Lower class</td>
<td>0.820</td>
<td>0.387</td>
<td>0.096</td>
<td>2.121</td>
<td>0.035</td>
<td>0.060 - 1.581</td>
</tr>
<tr>
<td>Interpersonal trust</td>
<td>0.348</td>
<td>0.167</td>
<td>0.094</td>
<td>2.086</td>
<td>0.038</td>
<td>0.020 - 0.676</td>
</tr>
<tr>
<td>Governance of country</td>
<td>-0.548</td>
<td>0.176</td>
<td>-0.139</td>
<td>-3.124</td>
<td>0.002</td>
<td>-0.893 - 0.203</td>
</tr>
<tr>
<td>(Benefits most equally)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Income</td>
<td>0.058</td>
<td>0.022</td>
<td>0.155</td>
<td>2.670</td>
<td>0.008</td>
<td>0.015 - 0.101</td>
</tr>
<tr>
<td>Employed</td>
<td>0.691</td>
<td>0.197</td>
<td>0.167</td>
<td>3.514</td>
<td>0.000</td>
<td>0.304 - 1.077</td>
</tr>
<tr>
<td>Race: Black or brown</td>
<td>0.235</td>
<td>0.293</td>
<td>0.036</td>
<td>0.801</td>
<td>0.424</td>
<td>-0.341 - 0.810</td>
</tr>
<tr>
<td>Index of Political Participation</td>
<td>-0.042</td>
<td>0.022</td>
<td>-0.088</td>
<td>-1.867</td>
<td>0.063</td>
<td>-0.086 - 0.002</td>
</tr>
<tr>
<td>Logged Age</td>
<td>0.222</td>
<td>0.254</td>
<td>0.044</td>
<td>0.874</td>
<td>0.383</td>
<td>-0.277 - 0.721</td>
</tr>
</tbody>
</table>

R = 0.462
R-squared = 0.213
Adjusted R-squared = 0.185
N=425
F-test [15, 410] = 7.413, P = 0.001< 0.05
Standard error of the estimate 1.598; Reference group †
Total Phenolic Contents of Selected Fruits and Vegetables Commonly Found Locally in Malaysia

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Abstract

Background: Polyphenol compound is an antioxidant types that can be commonly found in phytonutrient-bearing food such as fruits, vegetables, legumes, and grains. Some of the common examples of phenolic compounds found in food are phenolics, flavonoids, and anthocyanins. Phenolic compounds appears to contain multifunctional antioxidants properties and one of the studies conducted on extractable polyphenols present in grapes and wines plays a positive role in human nutrition.

Aims & Objectives: The aim of this study is to evaluate the amount of phenolic contents on selected local fruits and vegetables. The selected local fruits are banana (Musa sapientum), dragon fruit (Hylocereus undatus), seedless guava (Psidium guajava), papaya (Carica papaya) and star fruit (Averrhoa carambola). Whereas selected local vegetables are such as beetroot (Beta vulgaris), carrot (Daucua carota), green spinach (Amaranthus spp.), water spinach (Ipomoea aquatica) as well as tomato (Lycopersicum esculentum). The phenolic contents of these selected samples were determined.

Methods/Study Design: Local fruits and vegetables were purchased from a local wet market in Chow Kit Central Market, Kuala Lumpur, Malaysia. Six different samples of each of the fruits and vegetables were randomly selected. Total phenolic content was determined by using Folin–Ciocalteu reagent.

Results/findings: This study has found that the total phenolic contents were different in various types of selected local fruits and vegetables (P<0.05). Seedless guava (130.67±6.52mg GAE/L) and green spinach (170.28±0.00mg GAE/L) have the highest phenolic content among the selected local fruits and vegetables. Banana (36.83±2.31mg GAE/L) and tomato (19.89±0.00mg GAE/L) exhibits the lowest total phenolic content among selected local fruits and vegetables.
Conclusion: Green spinach contains the highest phenolic content among the selected local fruits and vegetables in this study.

Keywords: Polyphenolic, Total phenolic content (TPC), Folin-Ciocalteu reagent, gallic acid equivalent (GAE).

Introduction

Several epidemiological studies have shown that a high intake of food rich in natural antioxidants such as fruits and vegetables can increase the antioxidant capacity of the plasma and reduces the risk of some cancers, heart diseases, and stroke (Grajek et al. 2005). Studies also explain that cancer patients have low level of antioxidants in their bloods (Larrauri et al. 1996). Therefore, antioxidants are compounds that are capable in reducing the harmful oxidation of other molecules by inhibiting the initiation or propagation of oxidizing chain reactions (Al-Mamary 2002).

The studies suggested that the antioxidant compounds are characterized in variety of components such as vitamin C, vitamin E, carotenoids, and polyphenolic antioxidants (Wang et al. 1996) are playing an important role in preventing the free radicals from damaging the human body cells. Phenolic antioxidant is an antioxidant that found in phytonutrient-containing food including fruits and vegetables (Sellapan et al. 2002). Phenolic compounds appears to contain multifunctional antioxidants and one of the studies conducted on extractable polyphenols were present in grapes and wines plays a positive role in human nutrition (Larrauri et al. 1996). The examples of phenolic compounds that can be found in food are phenolic, flavonoids, and anthocyanins.

Most polyphenol compounds are commonly found in fruits and vegetables. They are usually freshly-eaten among the members of various communities in Malaysia. The fruit and vegetable industry in Malaysia is small and fragmental. All aspects of horticulture are readily available in Malaysia including fruit growing, vegetable production in the open and protected structures (fertigation) as well as ornamental cultivation. Tropical fruits are widely grown either in mixed or single fruit orchards. Temperate vegetables and flowers are grown in the highlands whereas tropical vegetables and flowers are grown in the lowlands (Alias 2005).

Most of these fruits and vegetables contain minerals, vitamins as well as antioxidant properties which may have beneficial effects. Generally, many studies have demonstrated that the antioxidants activities present in fruits and vegetables may decrease the risk of chronic diseases (Amin & Cheah 2003; Grajek et al.2005). Example of phytochemicals in fruits and vegetables are phenolics, flavonoids and carotenoids. They may play an important role in reducing chronic disease risk (Al-Mamary 2002; Liu 2003).

The aim of this present study is to determine the total phenolic contents of selected fruits and vegetables grown locally in Malaysia.
Materials and Methods

Samples

All fruits and vegetables were purchased from a local wet market at Chow Kit Central Market, Kuala Lumpur, Malaysia. The samples of fruits are papaya (Carica papaya), banana (Musa sapientum), star fruit (Averrhoa carambola), dragon fruit (Hylocereus undatus), and seedless guava (Psidium guajava) while the samples of vegetables are tomato (Solanum lycopersicum), green spinach (Amaranthus spp.), carrot (Daucus carota), water spinach (Ipomoea aquatica), and beetroot (Beta vulgaris).

Chemicals and equipments

In this study, chemicals are prepared including distilled water, Folin-Ciocalteu reagent (Fluka, 2N), gallic acid, absolute ethanol, and sodium bicarbonate (Na₂CO₃) were purchased from Sigma Chemical Co. (St.Louis, MO, USA). Equipments are required for this study such as sharp knife, blender (MX-291N National), orbital shaker (Heidolph Unimax 1010, Schwabach, Germany), air-tight container, aluminium foil, freezer, conical flask, beaker, filter paper (Whatman No. 1), filter funnel, vortex mixer (Stuart Scientific SA8), UV-1601 UV-Visible spectrophotometer, cuvette, 50ml volumetric flask, 10ml measuring cylinder, spatula, and timer.

Samples preparation

The fruits and vegetables were washed under tap water and excessive water were dripped off. The fresh and healthy of fruits and vegetables were then weighed. 50g of the edible portions from each of the samples were cut into small pieces and homogenised by using a blender (MX-291N National) for approximately two minutes to a paste form.

Guava and star fruit were blended without peeling the skin whereas the other three fruits were homogenised after the skin was removed. The homogenised sample was transferred into an air-tight container and kept at -20°C for further studies. All procedures were carried out carefully without much exposure to light (Amin & Cheah 2003).

Samples extraction

The 10% of sample extraction was prepared by mixing 10g of samples with 100ml of distilled water in a conical flask. The mixture was shaken at 200rpm for 2 hours at room temperature (28°C) by using an orbital shaker (Heidolph Unimax 1010, Schwabach, Germany). The extracts were filtered through a filter paper (Whatman No. 1) using filter funnel to obtain a clear solution. This clear solution is used for further tests. All samples were extracted in triplicates.
Determination of Total Phenolic Content

The method used to investigate antioxidant capacity in fruits and vegetables is Folin–Ciocalteu method. Total phenolic content was determined using Folin–Ciocalteu reagent (St.Louis, MO, USA) with using gallic acid as a standard reference (Velioglu et al. 1998). An aliquot (200µl) of clear extract was mixed with 1.5ml Folin-Ciocalteu reagent (diluted 10 times with distilled water) in the test tube and allowed to be shaken using vortex mixer (Stuart Scientific SA8) at room temperature. After 5 minutes, 1.5ml of 6% sodium bicarbonate solution (Na₂CO₃) was added to the mixture in the same test tube for 90 minutes. After 90 minutes, the absorbance was read at 725nm by using spectrophotometer (UV-1601 UV-Visible). Gallic acid (St.Louis, MO, USA) was used as the standard reference for estimating the total phenolic content of the vegetable extracts. A standard calibration curve of 0.010–0.050mg/ml gallic acid in distilled water was plotted. The total phenolic content of the fruit and vegetable extracts were expressed as gallic acid equivalents (GAE) in mg per Litre (L).

Statistical Analysis

All analyses were run in triplicates. Data were analysed using one-way analysis of variance (ANOVA), and the differences were considered to be significant at P<0.05. All statistical analyses were performed with SPSS.

Results and Discussion

The water extraction was used rather than ethanol extraction in the present study as the water mimics the human environment. The studies show that the ethanol extraction has the potential to bind the active antioxidant compounds compared to the water extraction (Soong & Barlow 2004) but it could not be used for further in vivo studies. This is to imply that human do not consume fruits and vegetables with presence of alcohol.

The comparison on total phenolic contents among selected local fruits and vegetables are shown in Table 1. Among the selected vegetables, green spinach has the highest phenolic content followed by water spinach (167.63±2.76mg GAE/L), beetroot (123.08±2.81mg GAE/L), carrot (25.71±2.71mg GAE/L), and tomato (19.89±0.00mg GAE/L). Green spinach and water spinach has no significant differences (P>0.05) while carrot and tomato also shows no significant differences (P>0.05) in mean.

The previous studies have shown that phenolic contents in spinach are higher compared to other vegetables (Al-Mamary 2002; Amin et al. 2006). Al-Mamary (2002) reported that coriander, parsley, and chilli contain higher phenolic contents compared to other vegetables including spinach.

The reason spinaches have higher in phenolic content among selected fruits and vegetables are due to the flavonoids present in the spinach leaves (Pandjaitan et al. 2005; Amin et al. 2006). Green spinach and water spinach are similar spinach family.
and inherited with flavonoid compounds in genotypes when it comes to breeding lines.

Beetroot belongs to the spinach family that has bred into different species and possess a slightly higher phenolic content in this present study. Betalain is an antioxidant commonly found in beetroot family has similar structure to anthocyanin (Pandjaitan et al. 2005). Furthermore, the previous study conducted has discovered that flavonol compounds are rich in the leafy vegetables (Herrmann 1976). Therefore, the leafy vegetables including spinaches and beetroots contain a larger amount of phenolic contents when compared to non-leafy vegetables such as tomatoes and carrots in this study.

Among the selected fruits, the seedless guava has the highest phenolic content (130.67±6.52mg GAE/L) followed by star fruit (53.63±10.12mg GAE/L), dragon fruit (47.00±0.35mg GAE/L), papaya (45.62±1.20mg GAE/L), and banana (36.83±2.31mg GAE/L). Star fruit, dragon fruit, papaya and banana has no significant differences and are considered to contain a low phenolic content in this study. The seed and seedless guava has shown a higher phenolic content as well as antioxidant properties compared to other selected fruits in previous studies (Koo & Mohamed 2001; Lim et al. 2006).

This is due to the presence of ellagic acid found in skin guava that contains high phenolic contents (Koo & Mohamed 2001). One of the previous studies proves that the seed as well as seedless guava contain high phenolic contents as well as antioxidant properties when compared with other selected fruits (Lim et al. 2006). Moreover, the studies have shown that the phenolic contents such as myricetin, apigenin, ellagic acid, and anthocyanins are also highly abundant in guava (Thaiponga et al. 2006).

The phenolic contents in star fruit, dragon fruit, papaya, and banana were lesser when compared to seedless guava. The low level of phenolic contents is probably due to the action of sunlight (Mélo et al. 2006). The previous study has explained that the phytochemical contents such as flavonol compounds found on the outer leaves where it is more exposed to sunlight compared to inner leaves. The concentration of phytochemicals markedly drops from the outer to the inner leaves (Herrmann 1976). Therefore, the samples of the selected local fruits (starfruit, dragon fruit, papaya, and banana) in this study were taken from inner tissues where it contains low phenolic contents compared to the outer skin layers. Furthermore, the outer layer skin of fruits is less likely to be consumed by human.

The comparison on total phenolic contents between selected local fruits and vegetables are shown in Table 1 as well as Figure 1. Figure 1 shows that the amounts of total phenolic contents were different in various types of fruits and vegetables. It also show that there was significant difference of total phenolic contents between selected local fruits and vegetables (P<0.05).

The concentration of total phenolic contents in the samples of the selected local fruits and vegetables examined has a range between from 19.89 to 170.28mg GAE/L. By comparing total phenolic contents between fruits and vegetables whereby green spinach, water spinach and seedless guava has shown no significant differences (P>0.05) in total phenolic content but has a show significant difference (P<0.05) among other selected local fruits and vegetables in this study. However, carrots
(25.71±2.71mg GAE/L) and tomatoes (19.89±0.00mg GAE/L) has the lowest total phenolic content compared to other selected local fruits and vegetables.

Al-Mamary (2002) reported that various amount in total phenolic contents might be due to the differences in structures of phenolic compounds in different fruits and vegetables. Each fruit and vegetable studied has its own variety of polyphenol compounds that might influence their total phenolic contents.

In addition, Bravo (1998) reported that the variation polyphenol contents in plant foods are greatly influenced by genetics, sunlight, reliable rainfall, topography, soils, location, season, soil fertilization, and maturity of plants.

Table 1: The Comparison of Total Phenolic Content among Selected Local Fruits and Vegetables

<table>
<thead>
<tr>
<th>Type of samples</th>
<th>Samples</th>
<th>Concentration ± SD (mg GAE/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruits</td>
<td>Seedless guava&lt;sup&gt;b&lt;/sup&gt;</td>
<td>130.67 ± 6.52</td>
</tr>
<tr>
<td></td>
<td>Starfruit&lt;sup&gt;c&lt;/sup&gt;</td>
<td>53.63 ± 10.12</td>
</tr>
<tr>
<td></td>
<td>Dragon fruit&lt;sup&gt;c&lt;/sup&gt;</td>
<td>47.00 ± 0.35</td>
</tr>
<tr>
<td></td>
<td>Papaya&lt;sup&gt;c&lt;/sup&gt;</td>
<td>45.62 ± 1.20</td>
</tr>
<tr>
<td></td>
<td>Banana&lt;sup&gt;c&lt;/sup&gt;</td>
<td>36.83 ± 2.31</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Green spinach&lt;sup&gt;d&lt;/sup&gt;</td>
<td>170.28 ± 0.00</td>
</tr>
<tr>
<td></td>
<td>Water spinach&lt;sup&gt;a&lt;/sup&gt;</td>
<td>167.63 ± 2.76</td>
</tr>
<tr>
<td></td>
<td>Beetroot&lt;sup&gt;b&lt;/sup&gt;</td>
<td>123.08 ± 2.81</td>
</tr>
<tr>
<td></td>
<td>Carrot&lt;sup&gt;d&lt;/sup&gt;</td>
<td>25.71 ± 2.71</td>
</tr>
<tr>
<td></td>
<td>Tomato&lt;sup&gt;d&lt;/sup&gt;</td>
<td>19.89 ± 0.00</td>
</tr>
</tbody>
</table>

Different letters indicate there are significant different in amount of total phenolic content among fruits and vegetables at p<0.05 whereas same letters show that there are no significant different in amount of total phenolic content at p>0.05 (a – green spinach & water spinach; b – seedless guava & beetroot; c – starfruit, dragon fruit, papaya & banana; d – carrot and tomato).
Conclusion

In conclusion, our study found that green spinach has high phenolic content among the selected local fruits and vegetables in this study. The selected local fruits and vegetables have different in amount of phenolic contents.

Acknowledgements

The authors would like to acknowledge the research grant and technical assistance from Universiti Kebangsaan Malaysia.

References


The role of Information Technology in preventing Medical Errors

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Abstract

Patient safety is “the environment, infrastructure and technology emphasizing the reporting, analysis and prevention of medical error and adverse events that might cause a patient ‘harm’. American Medical Association reported as mentioned in a recent paper2 almost 200,000 people die in U.S. hospitals each year as the result of lapses in patient safety. This article primarily deals with the application of Information Technology in preventing medical errors and preserving patient safety. We are certain that there are other nations where medical errors happen at a much more significant rate. How technology can help? Two major ways we can immediately mention. 1) computerized physician order entry (CPOE, a system in which a doctor enters a medication order directly into a software application designed to detect errors) and (2) bar coding medications to ensure that the right hospital patient gets the right dose of the right prescription at the right time3. In this paper we shall talk about several applications of Information Technology that have been developed to act against the epidemic. The topic is crucial, informative and necessary for the medical community as well as medical scholars.

Keywords: Medical error, Patient safety, Information Technology, Healthcare

Introduction

The primary customer of the business of healthcare is the ‘patient’. Healthcare is a professional setting which is established to restore, persevere and ensure physical and psychological health of patients. This definition can be applied to a Hospital, Long-term care facility, Public health institution or a Physician’s clinic, among other forms of establishments. Specific objectives of healthcare include, but not limited to:


3 Saul Spigel. Information technology and medical error reduction. OLR Research Report, 2005
• Diagnose the cause of discomfort or poor health condition.

• Organize and apply procedures, treatment, medication and technology to *restore* ‘good health’.

• Preserve patient safety.

• Prevent medical or treatment errors which may cause physical or psychological harm to the patient.

• Suggest preventive medications or treatment protocols to *maintain* ‘good health’.

While the scope of healthcare is vast and in many cases unknown, this paper primarily concerns the role of Information Technology in preserving patient safety. There are various types of safety violations. Following is a list from the literature:

• Medication error.

• Erroneous diagnosis.

• Wrong site surgery.

• Errors in Surgical procedures.

• Wrong equipment handling.

• Wrong Lab reports or test results.

• Patient fall.

• Neglects during patient monitoring process by nurses and other medical staff.

**Typical cause and prevention methods for medical errors and patient safety violations: Observations in the U.S healthcare systems**

A good explanation is provided by AHRQ (Ahrq.gov) “Most errors result from problems created by today's complex health care system. But errors also happen when doctors and their patients have problems communicating. For example, a recent study supported by the Agency for Healthcare Research and Quality (AHRQ) found that doctors often do not do enough to help their patients make informed decisions. Uninvolved and uninformed patients are less likely to accept the doctor's choice of treatment and less likely to do what they need to do to make the treatment work.”

By exploring further into AHRQ investigations, the agency reports:  


One of the landmark studies on medical errors indicated 70 percent of adverse events found in a review of 1,133 medical records were preventable; 6 percent were potentially preventable; and 24 percent were not preventable. A study released last year, based on a chart review of 15,000 medical records in Colorado and Utah, found that 54 percent of surgical errors were preventable.

Other potential system improvements include:

- Use of information technology, such as hand-held bedside computers, to eliminate reliance on handwriting for ordering medications and other treatment needs.
- Avoidance of similar-sounding and look-alike names and packages of medication.
- Standardization of treatment policies and protocols to avoid confusion and reliance on memory, which is known to be fallible and responsible for many errors.

Relevant incidences and statistics are well summarized in a Patient Safety Summit. Following are additional measures to preserve patient safety:

- Computerized physician order entry (CPOE), smart IV pumps and other drug dispensing systems, bar coding and systems to detect the frequency of adverse events.
- Up-to-date documentations and strategies for effectively implementing CPOE, including strategies for securing physician buy-in and effective staff training.
- Integrating CPOE technology into your organization’s existing clinical decision support / clinical computing system.
- Knowledge sharing and standards development initiatives and their impact on medical error reduction.
- The patient safety and productivity benefits of context management and single sign-on in presenting the patient record across multiple legacy systems.

Information Technology in preserving patient safety

Information Technology (IT) in U.S. healthcare started around 1960’s with mainframe computers mainly performing patient demographic record keeping and handling billing. The IT applications in healthcare came a long way establishing

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6 THE SUMMIT ON PATIENT SAFETY & INFORMATION TECHNOLOGY. September, 2002. San Diego, CA, USA
powerful COPE systems, Clinical Decision Support Systems, Laboratory, Drug management and Pharmacy systems and expanding ground with wireless communications using desktop and hand held devices. Along those lines, we also see sophisticated computing algorithms to predict potential medical errors, safety violations and benchmarking databases as tools of “Continuous Quality Measurement (CQM)” as well as “Evidence Based Medicine (EBM)”. In the following section we have discussed common Information Technology applications that are being used towards preserving patient safety.

**Computerized Physician Order entry (CPOE)**

CPOE appears to have a significant effect of preventing medical errors. As stated earlier, we estimate in U.S alone almost 130,000-140,000 patients die or experience severe complications due to prescription errors. It has been well established that CPOE systems, with or without a decision support tool appears to provide well documented electronic records and audit trails in reducing the chances of prescribing errors. This is true for physicians, nurses, pharmacy and other professionals who are authorized to administer drugs to patients. An alarming statistics was pointed out “Ward clerks or nurses make 80% of the errors in transcribing doctor’s handwriting. Entering medication order directly into the computerized physician order entry system without going through the transcribing process can reduce errors by 40%-60.”

Significant number of prescriptions is still administered through hand written orders. An article in the New England Journal of Medicine stated “*Information technology can reduce the rate of errors in three ways: by preventing errors and adverse events, by facilitating a more rapid response after an adverse event has occurred, and by tracking and providing feedback about adverse events.*”

Other benefits of CPOE systems are:

1. Output and display of legible orders, ability to order drugs, lab tests and radiology reports in electronic format.
2. Automatic order submission to pharmacies through electronic means or communication networks.
3. Standardized and accurate documentation, with logs.
4. A direct support component for Electronic Health Record Systems.

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8 Giangnguyen “Preventing Medical Errors: Use of Information Technology To Reduce Adverse Drug Events. Read more: [http://www.brighthub.com/health/technology/articles/7297.aspx#ixzz0cbeHPh0N](http://www.brighthub.com/health/technology/articles/7297.aspx#ixzz0cbeHPh0N)
All of the above invariably decrease the probability of medication errors and potential to commit patient safety violation.

**A number of recommendations from IEEE-USA**\(^{10}\)

*IEEE-USA believes that increased use of information technology can play an important role in improving patient safety and the quality of health care. The Federal government, working collaboratively with health care providers and other interested parties should take proactive steps to enhance the utilization of information technology in health care delivery.*

- Implementing the National Health Information Network (NHIN) and online Electronic Health Records (EHRs), with the potential to reduce the number of medical errors by providing quick access to patient history and medical guidelines.

- Encouraging ePrescription systems, which offer promising new alternatives to reducing errors, such as illegible handwriting. Electronic prescriptions also offer immediate access to possible drug interactions, with closer monitoring of patient use of medications and/or duplicate prescriptions.

- Improving patient identification through interoperable, secure and private lifetime EHRs. In-patient errors due to misidentification can be further reduced by using electronic data capture, such as bar coding, RFID and biometric technology.

- Using advanced IT technologies, such as clinical decision support systems and data mining, to assist in diagnosis and reduce errors and unintended consequences.

**Some references to recent vendor based systems**

- Various types of “Medical Error Reporting Systems” have been proven effective in reducing errors by effectively educating caregivers and clinicians, benchmark with national databases and regulatory agency audits.

- Advanced Radiology workflow and integrate information systems working together with imaging systems to remove inefficiency at all points.\(^ {11}\)

\(^{10}\) The Institute of Electrical and Electronics Engineers. PATIENT SAFETY: THE ROLE OF INFORMATION TECHNOLOGY IN REDUCING MEDICAL ERRORS. Bard of Directors Position Statement. 2008.

• One access point to optimize cardiovascular care workflow called Xcelera. “Philips Xcelera provides access to multimodality cardiac imaging as well as powerful exam review, analysis, quantification, and reporting tools from a single patient-centric workstation. Xcelera delivers vital patient information across the care continuum via enhanced connectivity with other hospital information systems and the patient’s electronic medical record.”

The integrated system is geared to electronically document patient records with multiple access points and audit trails so that medical errors can be prevented.

• In addition to sophisticated healthcare systems, IBM took a different approach to issues relating medical error prevention. IBM analytics and business intelligence engine are directed towards automation and predictive aspects of cause, effect and symptoms where prevention of medical errors is an integral part. A recent news release covers the story “Focusing on healthcare analytics, business intelligence, electronic medical and health records, identity management and unified communications, the Centre will offer experiential demonstrations; architecture consultancy; proof of concept and prototype demonstrations; integration of partner solutions; and, complex solutions design. It will also provide prototyping across areas such as RFID, telemedicine, regional and national health portals, telematics and mobile applications.”

• Microsoft seems to have stayed close to the theory “Close Loop Cycle” of prescribing information management in its Amalga Hospital Information System. In a white paper it claims “With a shared record that provides identical views of patient and medication information to everyone involved in a patient’s care, the Amalga HIS medication management system helps capture, protect, and communicate medication information and features built-in safeguards for a high level of accuracy.”

• There are numerous vendors implementing patient-safety technologies like bar coding and RFID which appear to be effective “bedside” measures.

**A few hurdles to overcome**

Information Technology has a very prominent role in Patient Privacy, Patient Safety as well as maintaining images, documentations of patients in case such records are

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required during later treatment of the patient.\textsuperscript{17} However, there remains to be some issues, at least in the U.S medical community.

1. Significant healthcare cost upraise requires rapid automation. As an example; almost 80% of workflow documentation, both medical and clinical are undertaken in pure hand written form. Thus, the challenge of automation is much widespread than what most think. \textit{A recent study by the Rand Institute estimates that if 75-90% of all healthcare providers adopted Health IT potential savings could average $80-$100 billion per year. An effective Health IT system would cut costs by reducing the duration of hospital stays, the amount of time that nurses spend performing administrative tasks, and drug and radiology usage.}\textsuperscript{18}

2. Inadequate safety reporting standards from providers. Wacher writes \textit{“The difference lies in our continued reliance on provider self-reports to count most safety outcomes (versus quality performance, which can often be ascertained by reviewing existing clinical or administrative records).”}\textsuperscript{19}

3. Despite of all efforts in the past 10 years, hospitals in U.S., supposedly well equipped with preventive technology, continue to make severe medical errors. Very recently, according to a report that was made public, California state officials recently fined 13 hospitals for medical errors that either killed or injured patients.\textsuperscript{20}

4. While physicians in general support the notion of EMR and patient record automation, patient privacy and confidentiality is a key concern. Studies show \textit{“About 71 percent of the more than 1,000 survey respondents expressed concern about the potential for privacy breaches. A 63 percent of the respondents were less willing to include "highly confidential" patient information in an EMR than in a paper chart.”}\textsuperscript{21} Thus, EMR and EHR use in the U.S is still not uniformly accepted and the practice of paper records will continue to contribute to medication and medical errors.

Looking at the global medical community, the use of Information Technology decreases the probability of medical errors and regarded to be a predominant measure. With more acceptances, implementation, better training of physicians and caregivers along with ‘\textbf{easy to use} systems’ we are hopeful that the error rates will continue to decrease. The key is implementation of close loop integrated systems with good audit trails and easy user interface.

\textsuperscript{17} Dey, Sukhen, “Role of Informatics in Patient Safety”. \textit{Quality Colloquium at Harvard University}. June, 2008.
\textsuperscript{18} Adopted from Kelly Montgomery “Health Information Technology”. About.com editorial.
Knowledge of First Year Medical Students on HIV/AIDS

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Abstract

A cross-sectional descriptive study was carried out in Bangladesh Medical College to assess the depth of knowledge of 1st year medical students about HIV/AIDS. A structured questionnaire was used for data collection and socio-demographic profile and information related to HIV. The sample size is of 100. Most of the respondents were in the age group of 19-20 years estimating 85% and their gender distribution was closely even distributed. The survey ended up with 45% male and 52% female respondents. The religious distribution was also reflecting the Islamic dominancy in Bangladesh. Most of the respondents were from higher middle class to upper class based on the monthly income status. More than half of the respondents (55%) thought that the prevalence of AIDS were increased, 29% thought normal, 15% thought it was decreased. Respondents were not well aware HIV/AIDS cases were detected in Bangladesh. They were also not aware fully about how many people were affected by the disease. According to 63% of the respondents both developed and developing countries are mostly affected by the disease whereas 13% thought affection is in developed countries and rest 24% answered that affection is in the developing countries. They think Africa has the highest number of HIV patient followed by America. 65% knew about the age group of affected people and according to them the young people were affecting more and sex workers (88%) were in the realm of great danger of affecting HIV/AIDS. Sexual transmission was responded as a predominant route for HIV/AIDS transmission beside parental transmission and perinatal transmission. Respondent were clear that they could not be affected by shaking hands, hugging or sharing glass and they also thought there is a link between HIV and other Sexually transmitted disease (STD’s). 83% of the respondents knew that there were no vaccine against AIDS as they thought it as a non-curable, treatment less and lifelong virus. According to the respondents, Influenza (43%) is supposed to be resembled at the early stage of HIV. 27% for hepatitis, 22% for diarrhea. About 60% respondents thought HIV positive means “presence of HIV antibody in blood” and about 37% thought HIV positive means “presence of HIV antigen in blood”. About 32% of the respondents thought there is 90% chance to develop AIDS from HIV. About 20% thought about 80% probabilities, 27% about 70% probabilities and 18% thought about 50% probabilities. For the protection against HIV/AIDS, among the 100 respondents 21.1 % thought ‘use of condom’ as a major protection method against AIDS. 15.5% by ‘Safe blood transfusion’, 5.6% by ‘Safe sexual relation’, 8.5% by ‘Awareness of AIDS’, 2.8% by ‘Avoiding multiple sex partner’, 6.3% by ‘Prevent sharing needle’, 1.4% by ‘Following religious values’. Finally, the awareness regarding the HIV/AIDS still had some lacking and need to be aware as early as
possible as these first year MBBS students will be the future pioneer for the rest of the generations.

**Introduction**

Bangladesh has a narrow window of opportunity to act decisively to prevent the spread of HIV/AIDS among vulnerable groups. HIV prevalence and the number of AIDS cases remain low in Bangladesh, but they are on the increase in some risk groups. There have been little change in high-risk behaviors and vigorous and prompt action is needed now to prevent the virus from taking hold.

The HIV epidemic in Bangladesh is evolving rapidly. While overall prevalence rates are still low, high risk groups sex workers and injecting drug users record much higher rates. In a pocket of injecting drug users in one area in central Bangladesh, HIV prevalence rates jumped from 1.4% to 4% to 8.9% over a period of 3 years. This level of infection among IUDS poses a significant risk as the infection can spread rapidly within the group then through their sexual partners and their clients into the general population. Another of IUDS in the country who sell their blood professionally Bangladesh relies on professional blood-sellers to meet most of the transfusion needs of its people.

Although overall HIV infection rates are low, Bangladesh is highly vulnerable to an HIV/AIDS epidemic due to the prevalence, behavior patterns and risk factors that facilitate the rapid spread of the virus. Risk factors include: Large commercial sex industry, condom use, sexually transmitted infections, needle sharing among injecting drug users, lack of knowledge etc.

Treatments of AIDS and HIV can slow the course of the disease. There is currently no vaccine or cure. Antiretroviral treatment reduces both the mortality and morbidity of HIV infection.

Prevention of HIV infection is a key aim in controlling the AIDS epidemic, with health organizations promoting safe sex and needle-exchange program in attempts to slow the spread of the virus. Although data derived from the different sources are being used by our planners, findings based on actual study about the knowledge of HIV/AIDS in Bangladesh are a few. Authentic information on transmission and prevention of HIV/AIDS in Bangladesh is scarce and deficient, although the study on transmission and prevention in developing countries is an important issue in public health programs. This study has been undertaken to fulfill this gap.

**Justification of the study**

HIV/AIDS is a burning issue in the modern world. It’s being fatal untreatable and spread over the globe makes it imperative for the medical system to make the situation universally.

AIDS is fatal once contracted. There is yet no established treatment. Thus prevention and early detection of HIV is essential. The sole way to do this it to create awareness
especially amongst the young adults who are most exposed to the infection. Thus our research targeted the 1st year student teenagers entering the world of science with only a layman’s idea of AIDS.

The commonest mode of transmission of HIV infection is through sexual contact along with blood transfusion, drug abuse, sharing of needles and razors etc. Thus, it is evident that the target group, are adolescents and young adults. It has been proved that the modern day teenagers are changing the patterns of sexual behavior and thus, increasing the risk of contracting HIV and ultimately AIDS. The only way to escape the disease is awareness and prevention. A thorough knowledge of the signs and symptoms of HIV, the test used for its diagnosis, methods of prevention such as practicing of safe sex, avoiding promiscuity, screening of blood etc must order to reduce the mortality and morbidity due to AIDS.

Methodology

This cross-sectional type of descriptive study was conducted in Bangladesh Medical College, Dhanmondi R/A, Dhaka during June to November, 2008. This particular private college was chosen because this is the institute where who are studying and it was very convenient for us to collect data side by side during our regular classes; so as, the study result revealed quickly and cost-effectively. One hundred (100) students of first year present in the class during the study period were included in the study. A structured pre-tested questionnaire was supplied to the respondents to obtain information. After Collection of data, each questionnaire was checked meticulously for any error, omission or ambiguity. The data were analyzed by using computer software SPSS (Statistical Package for Social Sciences). Results were presented in tables and figures.

Results and Discussion

I conducted my survey on the First year MBBS students of Bangladesh Medical College, Dhanmondi R/A, Dhaka on the topic of AIDS awareness among them. As they are in the realm of the learning medical studies they are supposed to be aware of the world’s most talked topics ‘AIDS’.

In our survey we had selected 100 first year MBBS student by non-probability convenient sampling method to answer the questionnaire that was uniquely designed for them. Around 85% of the respondents were between the age limit of 19 to 20 years of old. Approximately, 12% respondents were about 18 years old and rest of them was about 21 years old. We had closely even gender distribution in the sample and the Muslim dominancy was also found by their religious distribution as Bangladesh is an Islamic country by its origin.

Respondents were very reluctant to answer about some questions like monthly income of the family. Only 30% respondents respond positively about this question where as 70% refused to give this information as they thought financial information as confidential. About 5% respondents had family income from 20,000 - 40,000 taka and
20% had income ranges from 50,000-100,000 taka. Rest of the respondents had above 100,000 taka monthly family income.

We found more than half of the respondents (55%) thought that the prevalence of AIDS was increased. They did not know the first recognition of AIDS in Bangladesh. Very few of the respondents answered close to the original answer and most of them choose randomly for this question.

More than 50% didn’t know the number of affected people by AIDS and their randomness in the consecutive question proved the status of their unknowns. Around 57% respondents thought that African countries had the highest number of affected patients and 25% thought in America and rests thought in Asian region like India.

According to them the young generation is most likely to affect by HIV/AIDS and sex workers have the top risk (88%) for this. Among the respondents, 8% thought about the ‘lab technologist’ and rests thought about the ‘nurses’. As high as 90% of the surveyed respondents considered ‘sexual transmission’ as predominant mode for HIV/AIDS transmission; 6% responded ‘parenteral transmission’ and 2% thought about ‘perinatal transmission’.

Most of the respondents (71.0%) thought there is a link between HIV and STDs. More than one-fifths (22%) said there is no connection and rests didn’t answer. Precisely 88% of the respondents didn’t think that one couldn’t get AIDS by shaking hands, hugging or sharing glass. Respondents thought use of condom, safe blood transfusion, safe sexual relation, awareness of AIDS, avoiding multiple sex partner, prevent sharing needle, following religious values can protect one from having HIV/AIDS. But use of condom was supported at top against HIV protection.

Most of the respondents knew that there were no vaccine for HIV/AIDS and it’s a life long virus and it’s a fatal disease as it might ended up ones life with death, destroying immune system, non treatment and not curability.

Almost half (43%) of the respondents thought ‘influenza’ as a disease at early age of HIV whereas 27% thought ‘hepatitis’ and 22% thought ‘diarrhea’. Most of the respondents thought that there are tests for detection of HIV/AIDS and according to them the HIV positive means “presence of HIV antibody in blood”. About 37% thought HIV positive means “presence of HIV antigen in blood”.

Not all the respondents knew exactly about the severity of the HIV/AIDS but 25% thought it’s very severe and fatal (by 9%). About 32% of the respondents thought there is 90% chance to develop AIDS from HIV. Almost 20% thought about 80% probabilities, 27% about 70% probabilities and 18% thought about 50% probabilities.

Above all, 92% of the respondents thought HIV/AIDS is a non curable disease. By this survey it can be said that the respondent had a very fuzzy idea about the HIV/AIDS. Their prior knowledge about the topic was poor to moderate. They should be aware more and more.
Conclusion

Reviewing findings of the data of this study it is concluded that some of the students knew about the disease HIV/AIDS. They also knew about the causes of the disease and methods of prevention. Though the percentage of students knew about the prevalence and transmission of HIV/AIDS is low, the study showed that the students had poor to moderate knowledge about HIV/AIDS. Even though the minority of them are being awarded and motivating others to get awarded of HIV/AIDS. The overall level of awareness of students regarding knowledge of HIV/AIDS is not satisfactory.

Recommendations

- The First year students should provide enough knowledge about HIV/AIDS at the very beginning of their entry.
- Government should take proper steps to enlighten the peoples of all phase nationally.
- Students at the primary, secondary and higher secondary level should be introduced by the different phase of this fatal disease.
- Social awareness should be increased.
- Religious obligation should be imposed more strictly.
- Mass media should work for the awareness of uneducated people.
- NGO’s should take different awareness programs at the grass root level of our country.
- Self awareness and self willingness can be a good way to learning about HIV/AIDS.

Reference


6. WHO (2005), Weekly Epidemiological Record

7. AIDS Research and Therapy; Anton A. Niekenk and Loretta M. Kopelman


11. Petu-Duesber, Inventing the AIDS virus, Regeny USA, 1996:760-792


Table 1: Idea about prevalence of AIDS in Bangladesh

<table>
<thead>
<tr>
<th>Prevalence</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>29</td>
<td>29.0</td>
</tr>
<tr>
<td>Increased</td>
<td>55</td>
<td>55.0</td>
</tr>
<tr>
<td>Decreased</td>
<td>15</td>
<td>15.0</td>
</tr>
<tr>
<td>Not answered</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 2: Countries having the highest number of HIV/AIDS patient

<table>
<thead>
<tr>
<th>Name of Country</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>17</td>
<td>17.0</td>
</tr>
<tr>
<td>Africa</td>
<td>57</td>
<td>57.0</td>
</tr>
<tr>
<td>America</td>
<td>25</td>
<td>25.0</td>
</tr>
<tr>
<td>Wrongly answered</td>
<td>1</td>
<td>1.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Why fatal disease

Figure 1: Why AIDS is fatal
How severe the problem is

Figure 2: Severity of the problem

Figure 3: Protection methods against AIDS frequency

Figure 4: The frequency of response to the fact whether HIV/AIDS is curable or not
Value of pleural fluid Adenosine deaminase in Tuberculosis

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Abstract

Background: A definitive diagnosis of TB pleural effusion requires the presence of granulomas in pleural tissue or a stained AFB or positive culture from the pleural tissue or pleural fluid. However the bacillary population in TB effusion is small and the most likely pathogenic mechanism is essentially immunologic. Correcting this diagnostic deficiency, our main interest is pleural fluid chemical analysis of measuring the Adenosine Deaminase (ADA)activity to search for tuberculosis in pleural space.

Aim and Objective: The Aim is to study the value of pleural fluid adenosine deaminase (ADA) in the diagnosis of tuberculous pleural effusion. Our objective is to find out the cut-off value of ADA for diagnosing tuberculous pleural effusion and to calculate the sensitivity, specificity, positive and negative predictive values of ADA at that level.

Methods: This study was a hospital based analytical cross sectional study performed at Chest Medical Ward, Yangon General Hospital, Myanmar. Study period from 2004 January to 2005 January. Total of 187 patients were included. In each patient, pleural biopsy, pleural fluid cytology, pleural fluid ZN staining and AFB culture were sent for diagnosis. The main test of this study, Pleural fluid Adenosine Deaminase activities were determined by Giusti and Galanti method.

Results: There were (120) men and (67) Women with a mean age of (51.0 ±17.56) years (range 12-85 years). TB pleurisy accounted for 108 (58 %) of the effusions, 73 with neoplastic effusions (39 %) .Diagnostic utility of ADA for tuberculous pleural effusion was evaluated using receiver operating characteristic (ROC) curve analysis. The best cut off points of ADA to diagnose tuberculous pleural effusion was 42.5 U/L where sensitivity and specificity were 0.87 (87 %) and 0.89 (89 %) respectively. The area under the curve (AUC) that represents the diagnostic accuracy was 0.96(lower boundary 0.936, upper boundary 0.983). Positive Predictive value (PPV) was 96 % and Negative Predictive Value (NPV) was 83 %.
**Conclusion:** In this study, pleural fluid ADA assay is highly sensitive and specific test suitable for rapid diagnosis of tuberculous pleural effusion. The cut off values of high sensitivity and specificity are consistent with the value reported in other studies.

**Keywords:** Tuberculosis, Adenosine Deaminase (ADA), Pleural effusion, UCSI University, Giusti and Galanti, Myanmar

**Introduction**

Tuberculosis is a worldwide killer whose occurrence is on the rise especially in developing countries. Pleural effusion is one of the common complications of tuberculosis. The diagnosis of Tuberculous Pleural Effusion (TPE) can be difficult to make because of the low positivity of the various diagnostic tests. The bacillary population in TB effusion is small, and it’s most likely pathogenic mechanism is essentially immunologic and fluid collects as a result of delayed hypersensitivity reaction to tuberculoprotein. This immunologic reaction causes the stimulation and differentiation of lymphocytes, which released lymphokines, which in turn activate macrophages for an enhanced bactericidal effect (Kataria YP, Khurshid I, 2001).

ADA is a polymorphic enzyme involved in purine metabolism, catalyses the deamination of ADA to inosine and ammonium. The enzyme is widely distributed in animal and human tissues. It is present in the cytoplasmic fraction and a certain amount is located in the nucleus. Although found in most tissue, ADA activity is greatest in lymphoid tissue its activity being 10-20 times more active in T lymphocytes than in B lymphocytes and plays a part in the differentiation of lymphoid cells and the maturation of monocytes to macrophages (Barton RW and Goldshneider I 1979). Lymphocyte ADA levels can be considered a parameter of immune response. In pleural fluid it reflects the cellular immune responses in the pleural compartment, especially the activation of T lymphocytes.

Two isoenzymes of ADA coded by different gene loci exist, namely ADA1 and ADA2, each with unique biochemical properties. The ADA1 isoenzyme is found as a monomer (ADA1m) and as a dimer (ADA1c), where two ADA1m molecules are combined with a combining protein. The ADA1 isoenzymes are found in all cells, with the highest activity in lymphocytes and monocytes, where as ADA2 isozyme gene products appear to be found only in monocytes.

Our clinical experiences in Myanmar patients showed that the positivity of pleural fluid Ziehl Neelson stain or culture is quite low. Pleural biopsies using Abram’s biopsy needle often reveal chronic nonspecific pleuritis and need repetitions. Sometimes more invasive procedures such as bronchoscopy, lymph node biopsy or percutaneous direct needle biopsy were performed to get the diagnosis. Correcting this diagnostic deficiency, our main interest is pleural fluid chemical analysis of measuring the Adenosine Deaminase (ADA) activity to search for tuberculosis in pleural space.
ADA activity has been proposed as a diagnostic test for tuberculous pleurisy since 1978 (Piras & Gakis et al, 1978). A study of ADA estimations was performed on the pleural fluid from 368 effusions (Maritz FJ et al, 1982). In their study the mean (+/- SD) ADA concentration in TPE was 92.11 +/- 37.05 U/l. A paper from Mexico including 218 patients revealed that the activity of adenosine deaminase in TPE had significantly higher ADA activity than patients with non tuberculous pleural effusions (p less than 0.0001). (Banale JL et al, 1991).

Value of ADA in the diagnosis of TB pleural effusion in young patients in a region of high prevalence of TB was also studied (Valdes L et al, 1995). In their study all TB cases had pleural fluid ADA level of > 47IU/L (mean (SD) 111.1(36.6) U/L).

Another study of ADA in TPE was published in Portuguese (Chalhoub M et al, 1996). They have conducted a cross-sectional study of 221 patients with pleural effusion. Pleural fluids were analyzed by routine tests plus determination of ADA activity using Giusti’s method. According to a Receiver Operating Curve (ROC) analysis of the data, sensitivity of ADA activity at 40 U/L was 93.5%, resulting in a positive predictive value of 97.2% and a negative predictive value of 85.3%, in this confirmed tuberculosis by histopathology or culture.

Valdes L et al (1998) studied 254 patients with tuberculous pleural effusions. They found that all but 1 effusion (99.6%) had adenosine deaminase (ADA) concentration higher than 47U/L. Their comment was high ADA concentration was a highly sensitive diagnostic test.

The diagnostic value in TB pleurisy was also determined (Chen ML et al, 2004) by using ROC curve. In their study 147 exudative were non tuberculous (non TB) and 63 were tuberculous (TB). There was statistically significantly difference (p < 0.0001) between the mean of pleural fluid ADA levels among the TB and non-TB populations. The value for diagnosing TB effusions was > 55.8 IU/L, with a sensitivity of 87.3% (95% CI: 76.5 – 94.3 %) and specificity of 91.8% (95% CI: 86.2-95.7%). The positive predictive value (PPV) was 82.1% and the negative predictive value (NPV) was 94.4%. A pleural fluid ADA value < 16.81 IU/L suggests that a tuberculous effusion is highly unlikely (100% sensitive with 100% NPV and 0% negative likelihood ratio for a pleural fluid ADA level >/= 16.81 IU/L). In addition, the area under the ROC curve was 0.933 (S.E. = 0.0230, 95% CI: 0.890-0.963). They concluded that pleural fluid total ADA assay is a sensitive and specific test suitable for rapid diagnosis of TB pleurisy.

Although several studies have shown the diagnosis use of ADA in TB pleural effusion, some studies have shown that ADA levels are limited value. Van Keimpema AR et al, (1987) had measured ADA in pleural effusions of 95 patients, using a method optimised for rapid determination on a Hitachi 705 analyzer. They concluded that in a country with a low tuberculosis incidence, a high ADA activity in pleural effusion in neither sensitive nor specific enough to rely on the diagnosis of tuberculous pleurisy.

Maartens G and Bateman ED et al (1991) determined the use of adenosine deaminase activity in pleural fluid as a diagnostic test for tuberculosis. They concluded that adenosine deaminase does not provide as valuable a diagnostic test of pleural tuberculosis as has been suggested.
In our experiences, clinicians frequently encounter the diagnostic problems of pleural effusion even with exhaustive investigations. Closed Pleural biopsies are frequently reported as chronic nonspecific pleuritis. Pleural fluid cytology and microbiological examinations are sometimes not informative. Measurement of ADA, which is relatively simple, has a potential for use in area with limited resources and expertise. There is no document or published data on measurement of pleural fluid ADA in Myanmar and it may help to solve the diagnostic dilemma in many patients with undiagnosed pleural effusions. Our aim is to study the value of pleural fluid adenosine deaminase (ADA) in the diagnosis of TPE by finding out the best cut-off value of ADA and to calculate the sensitivity, specificity, positive and negative predictive values at that level.

Patients and methods

This study was a hospital based analytical cross sectional study performed at the Department of Respiratory Medicine, Rangoon General Hospital (RGH), Myanmar from January 2004 through January 2005. All patients with clinical features of pleural effusion confirmed by Chest X ray were included without age and sex limitation. Written informed consent was obtained from patient. Before requesting consent, the individual was explained in an understandable language about the aims of the study, the methods of conduct, expected duration of subject participation, benefits, foreseeable rights or discomfort, the extent of confidentiality, extent of investigators responsibility, provision of medical services, the right to refuse to participate and withdraw from the study without affecting further medical care. A total of 187 patients with various causes of pleural effusion were studied.

Exclusion criteria

1. Transudative effusions (using Light criteria)

2. Raised blood urea and creatinine

Patients with renal insufficiency may present high values of ADA

3. Acute hepatitis and liver failure.

Patient having signs and symptoms of hepatitis or acute/chronic liver failure will be excluded for possible false positive results by hyper-amoniemia.

4. Undiagnosed pleural effusion

5. Multiple pathology

Patients with more than single cause of pleural effusion will be excluded.

6. HIV serology positive
ADA level significantly correlates with the number of CD4+ lymphocytes and HIV serology positive patients will be excluded.

**Procedures**

Determination of pleural fluid protein and LDH concentration were done. The ratio of pleural fluid: serum protein and LDH were calculated to exclude transudates according to Light criteria. Pleural biopsy, pleural fluid cytology, pleural fluid ZN staining and AFB culture were performed on all patients. Pleural fluid ADA activities were measured by using Giusti and Galanti method.

**Procedure of the Giusti and Galanti method**

The pleural fluid specimen was collected and the test was performed on the same day. HBO 25 in-vitro diagnostic test kit from Cypress diagnosis laboratory, Belgium was used (Figure 1). ADA is assayed by measuring the amount of ammonia formed during the 60 minutes of incubation at 37°C. Ammonia reacts in presence of sodium nitrolypentacyanoferrate as a catalyst, with sodium hypochlorite and phenol, in alkaline solution, producing a deep blue indophenol.

The steps of the procedure are:

a. Following solutions were transferred to four test tubes as mentioned below.

<table>
<thead>
<tr>
<th>Solution</th>
<th>Sample</th>
<th>Blank of Sample</th>
<th>Standard</th>
<th>Blank of reagents</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A 1</td>
<td>A 2</td>
<td>A 3</td>
<td>A 4</td>
</tr>
<tr>
<td>Phosphate buffer</td>
<td>-</td>
<td>-</td>
<td>50µl</td>
<td>550µl</td>
</tr>
<tr>
<td>Adenosine</td>
<td>0.5 ml</td>
<td>0.5 ml</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Standard solution</td>
<td>-</td>
<td>-</td>
<td>0.5 ml</td>
<td>-</td>
</tr>
<tr>
<td>Sample</td>
<td>50 µl</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

b. All test tubes were shook well and incubated for 60 minutes at 37°C.

<table>
<thead>
<tr>
<th>Phenol catalyst</th>
<th>1.5 ml</th>
<th>1.5 ml</th>
<th>1.5 ml</th>
<th>1.5 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample</td>
<td>-</td>
<td>50 µl</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Alkaline hypochlorite</td>
<td>1.5 ml</td>
<td>1.5 ml</td>
<td>1.5 ml</td>
<td>1.5 ml</td>
</tr>
</tbody>
</table>

  c. After 60 minute incubation period, all test tubes were shook well again and incubated at room temperature for 30 minutes.
d. Then, read photometrically with the aid of a tube reader at a wavelength of 630nm.

Interpretation of results as

$$\frac{A1 - A2}{A3 - A4} \times 50$$

ADA activity in U/L

One U/L of ADA activity corresponds to 3 nmoles of ammonia released into the reaction mixture per hour at 37 degree C.

![Figure 1: Vials in HBO 25 in-vitro diagnostic test](image)

**Diagnostic classification**

The diagnoses were made according to the predetermined operational definition.

TB pleurisy was diagnosed if one or more of the followings criteria were present.

(a) Positive AFB in pleural fluid by ZN stain or AFB culture,

(b) Presence of granuloma in the biopsy tissue.

(c) Histiocyte and Langhans multinucleated giant cells, admixed with and surrounded by lymphoid cells in biopsy tissue.

(d) Caseation necrosis in biopsy tissue.

Malignancy was diagnosed if histological features of malignancy is detected in pleural tissue and/or positive malignant cells in pleural fluid.
If one associated with acute febrile illness, pulmonary pneumonic infiltrates, purulent sputum and identification of organism in pleural fluid culture in the absence of any evidences of tuberculosis or malignancy, he or she was diagnosed as parapneumonic effusion.

Other aetiologies of exudative effusion were defined if definitive diagnosis were obtained such as pancreatitis, Dressler's Syndrome, collagen vascular disease such or rheumatoid arthritis, SLE, pulmonary infarction etc. In all cases there must be absence of malignancy and pulmonary infiltrates.

Patients having effusion of unknown origin, after exhausted investigations, were classified as undiagnosed and were excluded.

Data Analysis

A ROC curve was drawn to find out the best cutoff value of ADA activity to diagnose TPE. Area under the curve (AUC) was also measured. The values of ADA levels for the diagnosis of tuberculous pleurisy were evaluated in terms of its sensitivity, specificity, and positive predictive value (PPV) and negative predictive value (NPV);

\[
PPV = \frac{\text{Prevalence} \times \text{sensitivity}}{[(\text{prevalence} \times \text{sensitivity}) + (1-\text{prevalence})(1-\text{specificity})]}
\]

\[
NPV = \frac{(1-\text{prevalence}) \times \text{specificity}}{[(1-\text{prevalence}) \times \text{specificity} + \text{prevalence} \times (1-\text{sensitivity})]}
\]

For the purpose of this study "prevalence" refers to the numbers of cases of a given kind of pleural effusion divided by the total number of pleural effusions studied.

The use of ADA as a diagnostic tool for tuberculosis was evaluated at various cutoff levels by calculating sensitivity, specificity and positive (PPV) and negative (NPV) predictive values which were compared by means of ROC curve.

Results
Figure 2: Frequency of different etiologies of pleural effusion

Table 1: Positivity of microbiological procedures for TPE

<table>
<thead>
<tr>
<th>Procedure</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ZN Stain of pleural fluid</td>
<td>1</td>
<td>0.93</td>
</tr>
<tr>
<td>Culture of pleural fluid in LJ medium</td>
<td>6</td>
<td>5.65</td>
</tr>
<tr>
<td>Culture of biopsy tissue in LJ medium</td>
<td>2</td>
<td>1.86</td>
</tr>
</tbody>
</table>

Table 2: Positivity of pleural biopsy in patients with TPE

<table>
<thead>
<tr>
<th>Diagnostic positivity of pleural biopsy to obtain definite tissue diagnosis</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st biopsy</td>
<td>91 (84.3 %)</td>
</tr>
<tr>
<td>2nd biopsy</td>
<td>15 (13.8 %)</td>
</tr>
<tr>
<td>3rd biopsy</td>
<td>2 (1.9 %)</td>
</tr>
<tr>
<td>Total</td>
<td>108</td>
</tr>
</tbody>
</table>

Table 3: Percentage positivity of pleural biopsy in patients with malignant pleural effusion
Diagnostic positivity of pleural biopsy to obtain definite tissue diagnosis

<table>
<thead>
<tr>
<th>Diagnostic positivity</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st biopsy</td>
<td>48 (65.7 %)</td>
</tr>
<tr>
<td>2nd biopsy</td>
<td>14 (19.1 %)</td>
</tr>
<tr>
<td>3rd biopsy</td>
<td>3 (4.1 %)</td>
</tr>
<tr>
<td>Negative Biopsy but positive pleural fluid cytology of malignant cells</td>
<td>8 (11.1 %)</td>
</tr>
<tr>
<td>Total</td>
<td>73</td>
</tr>
</tbody>
</table>

Within the study period, 187 patients with various causes of pleural effusion were studied. There were (120) men and (67) Women with a mean age of (51.0 ±17.56) years (range 12-85 years). According to the predetermined diagnostic criteria, TB pleurisy was accounted for 108 (58 %) of the exudative effusions. The rest were 73 with neoplastic effusions (39 %) and 6 patients with various other causes of exudates (3 %) as shown in Figure 2. In the group of other exudates (6 patients) included 3 parapneumonic patients, 2 empyema patients and 1lymphoma patient (Figure 2).

The positivity of microbiological and histological procedure is shown in table (1) and table (2) respectively. Among them, only one patient (0.9%) had positive AFB smear in pleural fluid. After one to two months later, culture of pleural effusion and pleural biopsy report was returned, with positive result of 5.6% and 1.9% respectively.

Out of seventy three malignant effusions, sixty five patients (88.9%) were diagnosed by identification of malignant pleural tissue. Eight patients (11.1%) were diagnosed by identification of malignant cells in the pleural fluid cytology because subsequent biopsies revealed chronic non specific pleuritis (Table 3).

**Receiver operating characteristic (ROC) curve**

Diagnostic utility of ADA for tuberculous pleural effusion was evaluated using receiver operating characteristic (ROC) curve analysis. The best cut off points of ADA to diagnose tuberculous pleural effusion was 42.5 U/L where sensitivity and specificity were 0.87 (87 %) and 0.89 (89 %) respectively. In this ROC curve analysis, data were calculated based on 181 patients (108 tuberculous pleural effusions and 73 malignant pleural effusions) excluding 6 other causes of pleural effusions. If calculating a very small sample size in constructing ROC curve, statistic of larger sample sizes may be biased. The area under the curve (AUC) that represents the diagnostic accuracy was 0.96. (lower boundary 0.936 , upper boundary 0.983) Positive Predictive value (PPV) was 96 % and NPV was 83%.

**ROC Curve**

Figure 3: Receiver operating characteristic (ROC) curve

**Area Under the Curve**

Test Result Variable(s): ADA

<table>
<thead>
<tr>
<th>Area</th>
<th>Std. Error(a)</th>
<th>Asymptotic Sig.(b)</th>
<th>Asymptotic Confidence Interval</th>
<th>95%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>.960</td>
<td>.012</td>
<td>.000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>.960</td>
<td>.012</td>
<td>.000</td>
<td>.936</td>
</tr>
</tbody>
</table>

The test result variable(s): ADA has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a  Under the nonparametric assumption

b  Null hypothesis: true area = 0.5
Coordinates of the Curve

Test Result Variable(s): ADA

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Discussion

In this study, 58 % of pleural effusions were caused by tuberculosis and 39 % were caused by malignancy. Exudative pleural effusion due to other causes was uncommon in Myanmar. There is a preponderance of male sex and highest incidence is in the productive age group reflecting a general state of pulmonary tuberculosis (Valdes L et al 1995). In this study commonest age group in malignancy was between 61 and 70 years which is significantly higher than patients with tuberculous effusion.

The positivity rate of first session of pleural biopsy was 84.3 % of TB pleural effusion and 65.7 % of malignant pleural effusion in this study. In this study second and third biopsy were needed in 29 patients and 10 patients respectively to confirm the diagnosis. Repeat performance of pleural biopsy is obviously an inconvenience to the patients. Some patients may not produce useful information even after third procedural session and were excluded. In our study, direct examination of pleural
fluid, pleural fluid culture and pleural biopsy has proven to be insufficient for the aetiological diagnosis of pleural effusion.

Closed pleural biopsy is a fairly blind procedure rendering it into a diagnostic procedure with less than desired positivity rate. Pleuroscopy resolve this problem but the procedures require more material resources and expertise, and are also relatively more invasive. It would probably be impractical to recommend this procedure in place where incidence and prevalence of tuberculosis is high. A simple, inexpensive and rapid test to support the diagnosis of TPE would be of great value in these areas. Further more, pleural biopsy would be an inappropriate diagnostic procedure in very young patients in whom, although age per se might exclude malignancy fairly well in majority of cases, there is still a need for clarification of aetiology of effusion in many cases.

The nature of tuberculous pleural effusion was that of an exudate which is easily demonstrable by measuring protein and LDH in serum and pleural fluid, applying the Light criteria (Light RW et al, 1972).

Smear examination of pleural fluid using Ziehl-Neelson stain had a very low positivity rate i.e 0.9 % of cases in this study and so was the positive culture of AFB from the fluid i.e 5.6 % of patients. Mycobacteria can be cultured from pleural tissue but the time required and the positivity rate was still unsatisfactory to be of value in routine clinical management. Pleural biopsy culture was positive in 1.9 % in the present study. This may reflect the paucibacillary status of pleural fluid which results at least partly from immunologic mechanism.

The positivity rate of microbiological tests in this study was consistent with another study from 105 patients in which pleural fluid AFB staining, pleural fluid AFB culture and pleural biopsy AFB culture were positive in 0 %, 5 % and 2 % respectively (Mihmanli A et al, 2004). But the positivity rate was higher in the study by Valdes L et al (1998) which showed a positive smear of pleural fluid was 5.5 % and positive culture was 36.6 % of patients. Pleural biopsy tissue culture also was high at 56.4 %.

Mean (SD) ADA activity of tuberculous pleural effusion in the present study was 73.90 (33.96) U/L and median value of 64.0 U/L. Various cut-off level of ADA activity were tested from the ROC curve for the diagnosis of tuberculosis. In deducting sensitivity and specificity from ROC curve, sample size is important. Including very small sample in a larger study could cause bias in constructing ROC curve. Thus two most commons causes of effusion (i.e TB and malignancy) were used for determining the sensitivity and specificity from ROC. Mean ADA activity of TB group was significantly higher than malignant group (73.91 Vs 33.96).

In our study the best cutoff level of ADA activity was tested at 42.5 IU/L when sensitivity was 87% and specificity was 89%. Positive Predictive value (PPV) was 96 % and NPV was 83%. Several studies have suggested that an elevated pleural fluid ADA level predict tuberculous pleural effusion with sensitivity of 90 to100 % and specificity of 89 to 100% when the Giusti method is used (Roth BJ, 1999).

The activity of ADA was also determined in 79 pleural effusions in Spain (Perez de Oteyza et al, 1989). In their experience, ADA determination had a sensitivity of 92%
and specificity of 94%; with a predictive value of 89% and a negative predictive value of 96%.

The activity of ADA in the pleural fluid of 218 consecutive patients was studied by Banales JL et al (1991) and reported that patients with pleural tuberculosis presented significantly higher ADA activity than patients with non tuberculous pleural effusion (p < 0.0001). This result indicated that in a population with a relatively high prevalence of tuberculosis, the analysis of ADA levels in pleural effusion constitutes a useful marker for diagnosis which, in addition, can be made quickly and cheaply.

In a study measuring ADA activity in TB pleural effusion in young patients in a region of high prevalence of tuberculosis, the diagnostic threshold for tuberculosis was 47 U/ L with the sensitivity and specificity of 100 % and 87.5 % respectively for patients 35 years and younger ages. (Valdes L et al, 1995)

Burgess LJ et al (1995) studied the ADA analysis of 462 pleural fluid samples. Various levels of ADA were tested as a cut-off level for the diagnosis of tuberculosis, 50 U/L was found to yield the best result, where sensitivity, specificity, PPV and NPV were 90 %, 89 %, 81 %, 94 % receptivity. Valdes L et al (1998) studied the 254 patients with tuberculous pleural effusion. All but 1 effusion (99.6 %) had an ADA concentration higher than 47 U/L. They concluded that ADA activity remains a useful test in the evaluation of pleural effusions as it is higher than any other diagnostic group and at a level of 50 U/L the sensitivity and specificity for the identification of TB was 90% and 89% respectively.

Conclusion

The Gold standard for diagnosis of tuberculosis is demonstration of mycobacteria in ZN stain or AFB culture. Although it is highly specific, sensitivity of microbiological examinations on pleural fluid does not reach the degree required for a single diagnostic investigation for tuberculosis. Pleural biopsy will be useful as an ultimate procedure in cases with diagnostic problem as it is a procedure which can give a definitive tissue diagnosis.

In this study, pleural fluid ADA assay is highly sensitive and specific test suitable for rapid diagnosis of TPE. The sensitivity and specificity of the ADA depend on the prevalence of tuberculosis in the population. With the decline in the prevalence of TPE, the PPV of pleural fluid ADA also declines, but the NPV value remains high. So this test is still useful even in area with low prevalence to exclude tuberculosis. At the ADA level of 42.5 1U/L, sensitivity of ADA in diagnosing TPE is higher (87%) compared to first time pleural biopsy (84.3%). In areas where facilities and expertise for proper conduct of histological and microbiological examinations are lacking, ADA measurement of pleural fluid would be an alternative, cheap and affordable for the patients.

However the test should be performed only by trained medical technologist to get accurate results. It is also important that all reagent bottles must be kept in 0°C to 4°C which requires continuous electricity and laboratory refrigerator. The electricity in certain parts of Myanmar is cut off frequently. A spectrophotometer which can read
the test tube at a wavelength of 630 nm is essential equipment for the test which is not available in some township and district hospitals.

As we already mentioned, the gold standard for diagnosis of tuberculosis is demonstration of mycobacteria in ZN stain or AFB culture or pleural biopsy. As such, it will be very useful that the use of combining ADA measurement in pleural fluid and these gold standard procedures for the diagnosis of tuberculous pleural effusion.

References


Introduction

In recent times, hip resurfacing has emerged as a viable alternative to the traditional hip replacement arthroplasty in cases of hip osteoarthritis secondary to childhood orthopaedic disorders. This is especially so given the younger profile of paediatric orthopaedic patients, who will benefit from the various advantages hip resurfacing have over traditional hip arthroplasty. For example, hip revisions with less complications and better post-operative results with higher Harris Hip scores. Hip resurfacing has been done in centers in the United States with encouraging results, however resurfacing has not taken off as rapidly in Singapore, with no published cases till date. This case report aims to highlight the positive experience of the National University Hospital (NUH) in performing hip resurfacing in a patient with Perthes disease complicated by secondary osteoarthritis. We propose resurfacing as a viable alternative to the traditional hip arthroplasty in the Asian setting as well.

The patient was informed that data concerning the case would be submitted for publication, and he consented.

Case study

A 26-year-old Chinese male with a past history of Perthes’ Disease presented to our Orthopaedic clinic with a 2 month history of left hip pain. This was associated with a left hip deformity and significant functional impairment—he was unable to sit cross-legged and had difficulty ambulating up and down the stairs. He first presented to the Orthopaedic Department 14 years ago in 1995 with persistent left hip pain, which was
eventually diagnosed as avascular necrosis of the left hip (Perthes disease). He was subsequently treated conservatively with lower limb skin traction, and was on crutches for 2.5 years before seeking traditional Chinese treatment in Beijing, China. Subsequently, he developed back pain associated with a left lower limb shortening, and investigations revealed a collapse of the left femoral head of about 3 cm. He underwent a left lower limb lengthening procedure in 2004, which involved the insertion of a fit bone. Subsequent removal of fitbone antenna revealed an intact antenna. The patient underwent a course of physiotherapy for hamstring stretching, as a result of relative hamstring shortening. Three months post-operatively, the patient returned with the complaint of progressive left hip pain persisting even at rest, associated with weakness and muscle wasting, precipitating frequent falls at home. Investigations revealed a loosened distal locking screw, which was subsequently re-inserted.

On physical examination, our patient was alert and comfortable. His vital signs were stable and he was afebrile. Multiple well-healed surgical scars and slight muscle wasting was noted on the left hip. Range of motion of the left hip was limited, with internal rotation at 15 degrees, and external rotation at 30 degrees. A limb length discrepancy of 1 cm (left lower limb 95cm, right lower limb 94cm). There was no fixed flexion deformity. Neurological examination was unremarkable.

Investigations revealed an elevated white cell count at 9.81 x 10^9/L (normal 3.30-9.96), slightly elevated neutrophil count at 7.48 x 10^9/L (normal 1.41 - 6.83). Culture was negative for MRSA and infection. X-Ray pelvis revealed flattening and deformity of the left femoral head with underlying osteoarthritic changes involving the left hip joint (Figure 1.1). Sclerosis and cortical thickening along the left femoral shaft was also noted. This was concurred by the CT scan, which showed a similar flattening and deformity of the left femoral head. Irregularity of the surface of the left femoral head was noted with subchondral cystic changes. The left acetabulum was noted to be deformed. No obvious left hip joint effusion was noted. This was in keeping with the diagnosis of hip osteoarthritis secondary to Perthes disease.
Fig. 1.1 Note deformity and flattening of the left femoral head. Subchondral sclerosis suggests an underlying left hip osteoarthritis. The left hip joint space is noted to be slightly widened.

Taking into account his relatively young age, a decision was made for him to undergo a hip resurfacing as opposed to the traditional hip arthroplasty (Figure 1.2). Post-operative recovery was uneventful and no complications were noted. DVT scan post-op was normal. At this time of writing (10 months post-operatively), the patient remains well and pain free. He is currently avidly involved in sports especially baseball, and does not experience difficulty or pain walking or climbing stairs. Harris Hip score 8 months post-operatively was excellent at > 95. Radiographic investigations done 8 months post-operatively were also normal with no evidence of prosthetic loosening, or peri-prosthetic lucency (Figure 1.3)
Figure 1.2 X-Ray pelvis done 1 day post-operatively. Note the well alignment of prosthetic implant. No peri-prosthetic fractures seen.

Figure 1.3 X-Ray left hip taken 7 months post-operatively. No evidence of prosthetic loosening, or peri-prosthetic lucency. Patient remains well, ambulant and pain-free.

Discussion

Childhood hip disorders, in particular Legg-Calve-Perthes and acetabular dysplasia are well-established risk factors for the development of early osteoarthritis of the hip, with patients at an increased risk of a total hip arthroplasty later on in life. A higher Stulberg classification was associated with an increasing incidence of secondary
osteoarthritis. The prevalence of secondary osteoarthritis in Stulberg Class II stands at 37% and 70% in Stulberg Class IV\textsuperscript{7}. The prognosis of Perthes disease is also known to be related to age of diagnosis. Diagnosis after the age of 9 is associated with a poorer prognosis, with most patients ending up in Classes III, IV or V\textsuperscript{7}. Given that our patient was diagnosed at 12 years of age with a Stulberg Class IV/V, this is associated with a poor prognosis and increased risk of development of secondary osteoarthritis, which he presented with 14 years later at the young age of 26. We advocated the usage of hip resurfacing over the traditional hip arthroplasty in our patient after taking into consideration his young age and activity needs. The 5-year results of the Birmingham Hip Resurfacing Arthroplasty in Oxford reported that young patients with osteoarthritis treated with resurfacing exhibited the most excellent post-operative results.\textsuperscript{8}

A huge factor in our decision to opt for a hip resurfacing in our patient was due to our patient’s young age. At 26 years old, our patient would be looking at a further 3-4 hip revisions in his lifetime. Due to the retention of less bone stock in total hip arthroplasty, this would make each subsequent hip revision more difficult and technically challenging, and more complications might ensue\textsuperscript{9}. There was also no concomitant hip infection which would otherwise have been an important contraindication to surgery\textsuperscript{9}.

Our patient was of normal weight with a BMI of 23kg/m\textsuperscript{2}. This is another favourable factor in our choice of resurfacing as obesity (BMI of 30kg/m\textsuperscript{2} or higher) is associated with a higher incidence of femoral neck fractures\textsuperscript{10}. It should also be of note that the Surface Arthroplasty Risk Index (SARI) of our patient was low at 2 points (for a cyst greater than 1cm in femoral head). A 12-fold increased risk in early implant failure is reported to be associated with a high SARI score\textsuperscript{11} of more than 3.

We also considered possible disadvantages for the patient. One is the complications associated with resurfacing such as femoral neck fracture, acetabular component loosening and metal hypersensitivity. However, such complications have been shown to be rare\textsuperscript{12}, with clinical outcomes of resurfacing comparable to that of total hip arthroplasties. The technical difficulties associated with hip resurfacing have to be taken into consideration as well. Such technical difficulties include a head-cup size mismatch amongst others, which might have impeded post-operative recovery and function.

\textit{Post-operatively, the patient was followed up and we noted excellent Harris hip scores of >95 8 months post-operatively. The patient is currently being followed up to monitor the development of any future complications.}

\textbf{Conclusion}

Hip resurfacing is a viable alternative to total hip arthroplasty with statistically similar or even better post-operative outcomes. However, to fully benefit from the advantages of hip resurfacing, discriminate choice of patients need to be exercised to prevent associated complications. With the good results that we’ve achieved with our patient, we advocate the use of resurfacing in patients with osteoarthritis secondary to
childhood hip disorders. This is especially more so for younger patients, where preservation of bone stock might be required for future hip revisions.

References


Role of titanium prosthesis in ossiculoplasty

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Abstract

Background: Ossicular chain damage from chronic middle ear diseases is a significant problem in India. The ideal ossicular chain reconstruction procedure is yet to be defined. In our study, we have dealt with the use of titanium prosthesis for ossiculoplasty.

Aim: To prospectively assess the results of titanium partial and total ossicular replacement prostheses in chronic ear disease.

Methods: It is a prospective study on 87 patients, carried in 2 different tertiary hospitals in India in 2 spells from September 2005 to December 2008 and February 2009 to June 2009. 36 titanium partial and 51 total ossicular replacement prostheses were performed in either primary or revision surgery by a single surgeon (Dr. Guha) and with a single microscope. All patients were followed for at least 3 month, with mean follow up being 5.6 months. Preoperative and 3 months post-operative averages of pure tone audiograms, done over a frequency range as per American Academy of Otolaryngology Head and Neck Surgery criteria (0.5–3 kHz), were compared. Baseline demographic and surgical characteristics including middle ear risk index (MERI) and postoperative complications were also noted.

Results: Successful rehabilitation of conductive hearing loss (less than or equal to 20 dB air-bone gap) was obtained in 29 out of 36 patients with titanium partial ossicular replacement prostheses (80.5%) as compared to 32 out of 51 patients with total ossicular replacement prostheses (62.7%), while hearing had improved in 100% cases. Pure tone thresholds improved by an average 18 dB in the partial reconstruction group and 25 dB in the total reconstruction group. Overall Extrusion Rate was 8% (7 cases). No other complication was noted. Hearing results were better for primary versus revision cases, for intact canal wall procedures versus canal wall-down procedures and also for lower preoperative MERI.

Conclusion: Titanium is an ideal material for ossicular chain reconstruction due to its biocompatible nature, ease of insertion, low rate of complications and superior hearing outcomes, but it is also very costly and needs an expert to handle. Hence it
should be prescribed judiciously and operated with proper precautions by an experienced hand.

**Study limitations:** Less number of cases is covered as fewer titanium prosthesis ossiculoplasties are done in India due to the higher price of titanium. Also the follow up period is quite less (mean 5.6 months), as most patients cease to come for regular check ups once their hearing gets improved.

**Keywords:** titanium, prosthesis, ossiculoplasty, PORP, TORP, ABG

**Introduction**

The sense of hearing has been one of the most useful assets to human life. Humans owe their civilization to the fact that we can communicate with our fellow beings through hearing. Middle ear is the key apparatus in the mechanism of hearing. It provides the impedance matching which transmits sound energy from the tympanic membrane to the inner ear. It also provides protection from loud sound and minimizes internal effects of vocalization. Chronic middle ear diseases such as chronic suppurative otitis media, causing damage to the ossicular chain is very common in India (WHO, 2004) and causes severe jeopardy in the mechanism of hearing. 77% of the affected persons in India suffer significant hearing loss (WHO, 2004).

The purpose of middle ear surgery is to provide improved hearing to the patient. Ossiculoplasty is a surgical procedure for restoring the ossicular chain as near to normal as possible or to achieve continuity and transmission in an entirely different way after abandonment of the natural system. The earliest recorded attempts to re-establish connection between the tympanic membrane and the oval window in cases of missing or damaged ossicles dates to Matte’s myringostapediopexy in 1901 (Matte, 1901). Autologous ossicles often cannot be used due to underlying disease and homologous ossicles may transmit infections, thus alloplastic materials are considered as an option. In the last three decades, various ossiculoplasty methods have evolved and good results were achieved. Nevertheless, ossiculoplasty continues to be a process in evolution (Janssen de Varebeke, Govaerts, Somers & Offeciers, 1996).

Ossicular repositioning was first performed by Hall and Rytzner in 1957 (Hall & Rytzner, 1957). In 1960s, biocompatible solid polymeric materials were being introduced for ossicular reconstruction which included ultra high molecular weight polyethylene, Teflon, and metallic implants. Shea was the first to use a length of polyethylene 90 tubing to reconstruct sound conducting mechanism in the middle ear in a tympanoplasty (Shea JJ, 1958). Later Austin used Teflon tubing (Austin, 1963) and Palva used metallic implants (Palva T, Palva A, & Karja, 1971). The results were very poor with migration, extrusion; foreign body reactions and penetration into inner ear, hence were abandoned. In the late 1970s nonreactive, high density polythene sponge known as “plastipores” and “polycels” were used, they had the additional advantage of being easy to sculpt but they too had higher extrusion rate (Mangham & Lindeman, 1990). In 1985, Schuknecth and Shi (Schuknecht & Shi, 1985) reported that incus and malleus grafts show less evidence of erosion. To reduce the high rate of
extrusion, Coyle Shea had proposed cartilage interposition (Shea MC & Glasscock, 1967). Bioinert materials like Aluminum oxide ceramic ($\text{Al}_2\text{O}_3$) and bioactive glass and bioceramics were popular in the 1970s but had higher erosion (Mangham & Lindeman, 1990). Since late 1980s gold prosthesis was gaining popularity, but then it was found to be heavy (Gjurić & Rukavina, 2007). In 1992, acoustic comparison of the various existing ossiculoplasty materials revealed that hydroxyapatite prosthesis has the best acoustic results (Nishihara & Goode, 1993).

Use of titanium for ossicular reconstruction began in Germany in 1993, which were produced by the German company Kurz GmbH (Stupp CH, Stupp HF, & Grun, 1996). The partial implant was used in the presence of an intact and mobile stapes and the total prosthesis was used when the stapes superstructure was absent. Since then it is been extensively used by oto-surgeons in the developed countries. In this study we have prospectively assessed the use of titanium as partial and total ossicular replacement prostheses and have tried to discover its relevance as a successful prosthesis material in India.

Patients and Methods

It is a prospective study on 87 adult patients requiring ossiculoplasties and admitted to 2 different tertiary hospitals in India. The study was conducted in 2 spells from September 2005 to December 2008 in one of the hospitals and from February 2009 to June 2009 in the other hospital. A written consent was taken from every patient and the study was approved by the ethical committee of the institution.

36 titanium partial (PORP) and 51 total ossicular replacement prostheses (TORP) were performed, which were either a primary or a revision surgery. Sliced cartilage was used as a standard to cover all prostheses and reconstruction of the tympanic membrane was carried out with temporalis fascia. All the surgeries were performed by a single surgeon (Dr. Guha) and with a single microscope to avoid manual (individual) and instrumental bias. All patients were followed for at least 3 months, with mean follow up being 5.6 months.

A proforma was made for every patient, which documented the baseline demographic characteristics, initial complaints, Middle Ear Risk Index (MERI), the preoperative and the postoperative air-bone gap (ABG) and the postoperative complications. The improvement in air-bone gap in the two different groups of were analyzed and compared with their preoperative determinants. Preoperative and 3 months postoperative averages of pure tone audiograms, done over a frequency range 0.5–3 kHz (0.5/1/2/3 kHz), as per American Academy of Otolaryngology Head and Neck Surgery criteria, were also compared. Audiometries were done using Elkon 3N3 Multi audiometer.

Statistical Analysis
All data were analyzed using SAS software, version 9.1. Chi-square test and Fisher’s exact test was used to compare the proportions. A both sided p value of < 0.05 was considered statistically significant.

**Results**

Among the 87 patients studied, 33 were male and 54 were female- ranging in age from 18 years to 54 years. 66 cases (75.86 %) were primary surgeries and 21 (24.14 %) were revision surgeries. 11 (12.64 %) surgeries were done by canal wall down procedure, while the rest had intact canal wall. The demographic and preoperative details of the patients are given in Table 1. The MERI was calculated (Table 2) for each patient based on several pre and intra operative findings. 22 patients (25.28 %) had MERI ≥ 7 (indicating severely diseased ear) [Figure 1] while 31 (35.63 %) patients had preoperative air-bone gap > 30 (indicating poor prognosis). 45 ossiculoplasties were accompanied with mastoid surgery, in the rest 8 were only ossicular reconstructions and 34 required additional graft placement (Figure2).

Post surgery, subjective sensation of hearing ability improved in 100% cases and not much difference was found between the hearing outcome in TORP group and PORP group, although the degree of improvement was much higher in TORP group (Table 3). The mean improvement of ABG in TORP is 19.1 dB compared to 14.4 dB in PORP (p = 0.026). Pure tone thresholds improved by an average of 25 dB, 3 months post surgery, in TORP compared to an improvement of 18 dB in PORP (p < 0.0001).

Results with PORP for ABG closure are marginally better than TORP, as would be expected in the presence of an intact stapes superstructure; however the difference in the results were not found to be statistically significant (p = 0.073). Less than or equal to 20 dB postoperative ABG is defined as a successful rehabilitation of the conductive hearing loss, as per American Academy of Otolaryngology–Head and Neck Surgery guidelines ( Monsell et al, 1995), which was obtained in 29 out of 36 patients with titanium PORP (80.5%) as compared to 32 out of 51 patients with TORP (62.7%) [Table 4].

Overall Extrusion Rate was 8% (7 cases), all of them on revision surgeries revealed improper placement of cartilage sandwich as a reason behind the extrusion. No other complication was noted. Hearing results were not found to be significantly better for primary versus revision cases (p = 0.798), but were better in intact canal wall procedures versus canal wall-down procedures (p = 0.042). MERI was found to have a crucial role in the improvement of hearing results, i.e. postoperative ABG (p = 0.001) [Table 5].

**Discussion**

Titanium prostheses have been successfully used for ossicular reconstruction with favorable results (Wang, Song, & Wang, 1999; Begall & Zimmermann, 2000; Ho, Battista, & Wiet, 2003; Martin & Harner, 2004; Krueger et al, 2002; Siddiq & Raut, 2007). The success of bone-anchored hearing aid devices testifies the affinity of
titanium to bone – termed osseointegration. Its thin shaft and perforated head allow visualization of the stapes head or footplate during placement. Moreover, it is inert and no foreign body or macrophage reaction has been noted in titanium prostheses obtained from revision surgery (Schwager, 2000). Titanium has better acoustic properties and showed improved results at particularly 2–3 kHz maintained over 24 months (Zenner, Stegmaier, Lehner, Baumann, & Zimmermann, 2001). The low prosthesis weight and good coupling allows good sound transfer which is lost with heavier prostheses.

In our study, successful restoration of hearing, i.e. postoperative ABG < 20dB, was found slightly more in the PORP group than the TORP one, although the degree of improvement of both postoperative ABG and pure tone thresholds were more for the TORP group. Earlier there has been controversy regarding the efficacies of the procedures certain studies have found that patients undergoing TORP procedures did better (Zenner, Stegmaier, Lehner, Baumann, & Zimmermann, 2001), whereas some others found that PORP patients did better (Dalchow, Grun, & Stupp, 2004; Gardner, Jackson, & Kaylie, 2004; Martin & Harner, 2004). Graphical comparison of the preoperative and postoperative ABG for PORP and TORP are given in Figure 3 and Figure 4.

In line with other studies (Martin & Harner, 2004; Schmerber, Troussier, Dumas, Lavieille, & Nguyen, 2006), hearing outcomes in canal wall down procedures were found less successful compared with that of intact canal wall procedures. The effect of MERI on hearing outcomes have been studied for the first time in this study and has been found to play a vital role, this supports the popular belief that middle ear status has a major role in the hearing outcome post ossiculoplasty. Also this study revealed that hearing outcome doesn’t considerably differ in a revision surgery, as long as the surgical expertise isn’t compromised.

In our study, the partial titanium prosthesis gave marginally better hearing results than the total prosthesis, although the degree of improvement was higher in the total one. Our results indicate that titanium is an ideal material for ossicular chain reconstruction prostheses because of its biocompatible nature, ease of insertion, low rate of complications and superior hearing outcomes. But it is also very expensive in an economy like ours, more so when the rates of CSOM are exceedingly high in the poorer communities (Okafor, 1984). Also the extrusion cases illustrate that it needs an expert to handle. Hence it should be prescribed judiciously and operated with proper precautions by an experienced surgeon.

References


**TABLES**

**TABLE 1:** Demographic and preoperative details of the patients

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<td>≥ 30 dB</td>
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<td>35.6%</td>
</tr>
</tbody>
</table>

**TABLE-2:** Calculation of MERI for each patient

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Risk Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Otorrhea</strong> (Bellucci classification)[Bellucci, 1973]</td>
<td></td>
</tr>
<tr>
<td>Dry</td>
<td>0</td>
</tr>
<tr>
<td>Occasionally wet</td>
<td>1</td>
</tr>
<tr>
<td>Persistently wet</td>
<td>2</td>
</tr>
<tr>
<td>Wet, cleft palate</td>
<td>3</td>
</tr>
<tr>
<td><strong>Perforation</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td><strong>Cholesteatoma</strong></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
</tbody>
</table>
### Ossicular status (Austin/ Kartush classification) [Austin, 1985]

<table>
<thead>
<tr>
<th>Status</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: M+I+S+</td>
<td>0</td>
</tr>
<tr>
<td>A: M+S+</td>
<td>1</td>
</tr>
<tr>
<td>B: M+S-</td>
<td>2</td>
</tr>
<tr>
<td>C: M-S+</td>
<td>3</td>
</tr>
<tr>
<td>D: M-S-</td>
<td>4</td>
</tr>
<tr>
<td>E: Ossicle head fixation</td>
<td>2</td>
</tr>
<tr>
<td>F: Stapes fixation</td>
<td>3</td>
</tr>
</tbody>
</table>

### Middle ear: Granulation or Effusion

<table>
<thead>
<tr>
<th>Status</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
</tbody>
</table>

### Previous surgery

<table>
<thead>
<tr>
<th>Surgery</th>
<th>Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Staged</td>
<td>1</td>
</tr>
<tr>
<td>Revision</td>
<td>2</td>
</tr>
</tbody>
</table>

### TABLE 3: Postoperative improvement of ABG and PTA

<table>
<thead>
<tr>
<th>TEST</th>
<th>TORP</th>
<th>PORP</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean Improvement in ABG</td>
<td>19.1 dB</td>
<td>14.4 dB</td>
<td>0.026</td>
</tr>
<tr>
<td>Mean Improvement in PTA</td>
<td>25 dB</td>
<td>18 dB</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### TABLE 4: Postoperative ABG closure for PORP and TORP

<table>
<thead>
<tr>
<th>Postoperative ABG</th>
<th>PORP</th>
<th>TORP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Percent</td>
<td>Number</td>
</tr>
<tr>
<td>≤ 20 dB</td>
<td>29</td>
<td>80.5%</td>
</tr>
<tr>
<td>&gt;20 dB</td>
<td>07</td>
<td>19.5%</td>
</tr>
</tbody>
</table>

### TABLE 5: Hearing results as per MERI (Middle ear risk index)

<table>
<thead>
<tr>
<th>MERI</th>
<th>Postoperative ABG &lt; 20</th>
<th>Postoperative ABG &gt; 20</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>4-6</td>
<td>34</td>
<td>14</td>
</tr>
<tr>
<td>7-12</td>
<td>10</td>
<td>12</td>
</tr>
</tbody>
</table>
Figures:

**Figure 1:** Distribution of the patients according to their MERI

![Bar Chart](image1)

**Figure 2:** Pie chart showing different surgical procedures done in the patients

![Pie Chart](image2)
Figure 3: Pre and postoperative comparison of air-bone gaps in PORP cases

Figure 4: Pre and postoperative comparison of air-bone gaps in TORP cases
Effects of homeopathy remedy *Syzygium jambolanum* on glucose level, lipid profile and histology of pancreas of Streptozotocin induced diabetes rat

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Abstract

**Background:** Polyphenol compound is an antioxidant types that can be commonly found in phytonutrient-bearing

**Background**

The hyperglycemic condition can cause various complication in diabetes mellitus patients and various new treatments with promising therapeutic results and minimized side effects were being researched. This study was to see the effect of homeopathy remedy *Syzygium jambolanum* on glucose level, lipid profile and pancreas histology of streptozotocin (STZ) induced rats.

**Methods**

32 male rats of Sprague-dawley with body weight 250-300g divided randomly into four groups. Two groups of rat were injected with single dose of STZ with the dose of 45mg/kg intravenously. On the third day, STZ injected rat was confirmed diabetic with measurement of blood glucose level. Homeopathy remedy *S. jambolanum* was administrated through force feeding for 28days. Then, the rats were sacrificed and the blood sample and the pancreas was collected. Biochemical analysis of glucose, lipid profile and the histology of pancreas was carried out. the data obtained is analysed using One-way Anova with significance value of p<0.05.

**Results**

Mean plasma glucose level of treated diabetes group rats, showed a significantly (p<0.05) reduced (61.71%) compared to non treated diabetes group rats. The treated diabetes group rats showed significantly (p<0.05) reduced mean level of plasma total cholesterol (61.71%), triglyceride (70.84%) and LDL-cholesterol (79.14) compared to
the non treated diabetes group rats. Mean plasma HDL-cholesterol level was significantly (p<0.05) increased (364.86%) in treated diabetes group rats compared to the non treated diabetes group rats. H&E and Maldono staining was used to stain the pancreas. The histology examination showed the presence of denser beta cell distribution and larger islet of Langerhans of treated diabetes group rats compared to the non treated diabetes group rats.

Conclusion

From the result of this study (glucose, lipid profile and histology result), it's concluded that the homeopathy remedy \textit{S. jambolanum} can be used as a treatment to diabetes patients.

Background

Diabetes is a group of metabolic disorders that result in hyperglycemia due to decreased insulin production (Type 1) or insufficient insulin utilization (Type 2) (Marshal & Bangert 2004). Dyslipidemia is a secondary complication of diabetes (Shamim et al. 2009). LDL and HDL plays important role in transportation of cholesterol and triglyceride. Cholesterol and triglyceride carried by LDL from liver into the blood circulation (West et al. 1983). The HDL carries the cholesterol and triglyceride to liver to be metabolised and excreted (Briones et al. 1984). The commonly practised treatments of diabetes include oral antidiabetic drugs, insulin injection and management through diet and physical exercise (Vats et al. 2002). Unfortunately, none of the oral hypoglycaemic agents have been successful in maintaining euglycaemia, and in addition have a number of side effects (Holman and Turner, 1991). In spite of the presence of number of oral synthetic oral antidiabetic drugs in the market, researchers are now diverted their attention to different herbs and medicinal plants in order to find out new active principal with less side effects and better antidiabetic activity (Beigh et al. 2002). Therefore, it has become necessary to look for an economical as well as therapeutically effective treatment without side effects (Grover et al. 2002).

\textit{Syzygium jambolanum} from the family of Myrtaceae, is also commonly known as ‘jambol fruit’, ‘jamun’ or ‘rose apple’ in English. It's a large, evergreen tree found primarily in India, Pakistan Southern Asia and Brazil (Grover et al. 2002). \textit{S. jambolanum} is a well known Indian folk medicine for the treatment of diabetes mellitus and prickly heat (Samba-Murthy & Subrahmanyam 1989). The antidiabetic potential of the fruit and seed extracts of \textit{S. jambolanum} have been shown by several studies (Sridhar et al. 2005, Sharma et al. 2003). \textit{S. jambolanum} used in this research is a commercially available homeopathy remedy in the dosage of mother tincture and used for diabetes patients by homeopathy practitioners. Mother tincture of \textit{S. jambolanum} is prepared from the ethanol extract of powdered \textit{S. jambolanum} seeds (William Boericke 2002). However the effectiveness of \textit{S. jambolanum} as a homeopathy remedy has not been studied yet. Therefore, in this study, effect of homeopathy remedy \textit{S. jambolanum} on glucose level, lipid profile and pancreas histology of STZ induced rats was tested. STZ, an antibiotic produced by
Methods

32 male Sprague-Dawley rats, body weight range of 210-250g from Unit Haiwan UKM was used in this study (UKMAEC approval number: FSKB/BIOMED/2008/HAWA/12-AUGUST/230-SEPT-2008-FEB-2009). The rats were divided into four groups randomly. After a week of adaptation period, two groups were induced diabetes by injecting STZ via intravenous and the other two groups were the nondiabetic rats. The dose used was 45mg/kg. The volume of STZ injected was 1ml/kg (Fonteles et al. 1996). The four groups were the non diabetes mellitus rats without treatment (NDMNoTX), non diabetes mellitus rats with treatment (NDMTx), diabetes mellitus rats without treatment (DMNoTx) and the diabetes mellitus rats with treatment (DMTx). STZ was freshly prepared.

After three days, the blood glucose level was measured using the Advantage II glucometer (Roche Diagnostics, New Zealand) via tail prick. Blood glucose level higher than 13.8mmol/L was considered diabetes condition. Then the treatment of homeopathy remedy S. jambolanum was carried out for 28days daily via force feeding the NDMTx and DMTx group rats. The S. Jambolanum mother tincture was mixed with water and the volume force fed was 1ml/kg. The mixing of remedy was done according to the local homeopathy practitioner. The NDMNoTx and DMNoTx group rats were force feed with distilled water.

After 28 days, the rats were weighted. Cardiac puncture was done to collect blood sample for the biochemical tests and the tail of pancreas was collected for histology purpose. Blood sample was collected in litium heparin tube for the lipid analysis and the sodium oxalate tube was used for glucose analysis. Blood sample was centrifuged at 3500rpm, 4ºC for 15 minutes. The plasma was kept at -45ºC. The pancreas sample was washed with normal saline and divided into two equal pieces. One part was fixed with 10% formal saline for 24hours and the the other part was fixed in Bouin solution for 12 hours.

The plasma glucose level was determined using glucose oxidase kit from Thermo electron corporation (USA). The plasma total cholesterol (TC) level was measured using the Loeffler et al. (1963) method. The plasma triglyceride (TG) level was measured using Triglyceride kit from Randox laboratories (UK). The plasma high density lipoprotein (HDL) level was measured using modified Lape-Virella and Feris (Wooton 1974). The plasma low density lipoprotein (LDL) level was calculated using Friedawald formula (Genst & Cohn 1998). The pancreas samples were fixed and processed. The sliced tissues fixed on slaid were stained. The Bouin solution fixed samples were stained using Maldono (Luna 1968) staining and the 10% formal saline fixed samples were stained using Hematoxylin & Eosin (Clayden 1971) staining. Results were recorded and expressed as mean ± SD. The data were analyzed by ANOVA test. Differences were considered as statistically significant when p<0.05.
Results

Figure 1: Plasma glucose concentration according to groups

a – significant compared to NDMNoTx.
b – significant compared to NDMTx.
c – significant compared to DMNoTx.

Figure 1 shows plasma glucose level according to groups after 4 weeks of study. Mean plasma glucose of NDMTx group (109.62 ± 11.48) shows no significant difference compared with NDMNoTx group (90.61 ± 13.64). Mean plasma glucose of DMNoTx group (313.89 ± 45.07) was higher significantly compared to NDMTx group and NDMNoTx group. DMTx group (132.41 ± 17.59) shows mean plasma glucose significantly lower compared with DMNoTx group, no significant difference compared with NDMTx group and significantly higher compared to NDMNoTx group.

Plasma total cholesterol analysis

Figure 2: Plasma total cholesterol concentration according to groups

a – significant compared to NDMNoTx.
b – significant compared to NDMTx.
c – significant compared to DMNoTx.
Figure 2 shows mean plasma total cholesterol according to groups after 4 weeks of study. Mean plasma total cholesterol of NDMTx group (67.49 ± 7.09) was significantly higher compared to NDMNoTx group (39.58 ± 5.79). DMNoTx group (117.85 ± 21.87) shows mean total cholesterol significantly higher compared with NDMTx group and NDMNoTx group. Mean plasma total cholesterol of DMTx group (45.10 ± 8.39) was significantly lower compared with DMNoTx group and NDMTx group and no significant difference compared to NDMNoTx group.

Plasma Triglyceride analysis

![Plasma triglyceride concentration according to groups](image)

Figure 3: Plasma triglyceride concentration according to groups

- a – significant compared to NDMNoTx.
- b – significant compared to NDMTx.
- c – significant compared to DMNoTx.

Figure 3 shows mean plasma triglyceride according to groups after 4 weeks of study. Mean plasma triglyceride of NDMTx group (59.98 ± 5.12) was significantly higher compared to NDMNoTx group (39.48 ± 7.36). DMNoTx group (101.73 ± 19.71) shows mean plasma triglyceride significantly higher compared to NDMTx group and NDMNoTx group. Mean plasma triglyceride of DMTx group (29.66 ± 9.64) was significantly lower compared with DMNoTx group and NDMTx group and no significant difference compared to NDMNoTx group.

Plasma HDL analysis
Figure 4 shows mean plasma HDL according to groups after 4 weeks of study. Mean plasma HDL of NDMTx group (10.18 ± 1.88) shows no significant difference compared to NDMNoTx group (11.46 ± 2.40). DMNoTx group (4.24 ± 2.22) shows a significantly lower mean plasma HDL compared with NDMTx group and NDMNoTx group. Mean plasma HDL of DMTx group (19.71 ± 5.78) was significantly higher compared with DMNoTx group, NDMTx group and NDMNoTx group.

**Plasma LDL analysis**

Figure 5 shows mean plasma LDL according to groups after 4 weeks of study. Mean plasma LDL of NDMTx group (45.31 ± 6.53) was significantly higher compared to NDMNoTx group (20.22 ± 3.75). DMNoTx group (93.26 ± 21.57) shows mean plasma LDL significantly higher compared with NDMTx group and NDMNoTx group.
group. Mean plasma LDL of DMTx group (19.45 ± 4.42) was significantly lower than DMNOtx group and NDMTx group and no significant difference compared to NDMNOtx group.

Analysis of pancreas histology

a) H&E staining

![Figure 6: Histology of pancreas of DMNOtx group. H&E staining. Magnification 400x. Light microscope.](image)

![Figure 7: Histology of pancreas of DMTx group. H&E staining. Magnification 400x. Light microscope.](image)

H&E staining revealed the presence of necrosis and the islets of Langerhans can be differentiated from the exocrine region. However the β cells cannot be differentiated with α cells. DMTx group shows islets larger in size and less necrosis compared to DMNOtx group.

b) Maldono staining

![Figure 8: Histology of pancreas of DMNOtx group. Maldono staining. Magnification 400x. Light microscope.](image)

![Figure 9: Histology of pancreas of DMTx group. Maldono staining. Magnification 400x. Light microscope.](image)
Maldono staining revealed the presence of necrosis and islets of Langerhans can be differentiated from the exocrine region. The β cells can be differentiated with α cells. DMTx group shows islets larger in size, less necrosis and more β cells compared to DMNoTx group.

Discussion

Destruction of β cells causes lower production of insulin and this disturbs carbohydrate metabolism (Chatterjee & Shinde 2000). Glucose in blood circulation could not be taken up by body cells and the body stays in fasting state. Impuls would be send to produce more glucose via the glucagon action. This causes the hyperglycemia and dyslipidemia state as found in DMNoTx group rats (Pansy et al 1989). Homeopathy remedy *S. jambolanum* shows antidiabetic activity and indicated by the significant (p<0.05) decrease in glucose level, total cholesterol, triglyceride, LDL and an increase in HDL in DMTx group rats compared to DMNoTx group rats. This result supports the usage of *S. jambolanum* seed traditionally as antidiabetic agent (Anonymous 1985). The possible mechanism of action of homeopathy remedy *S. jambolanum* was by increasing the insulin level either by increasing the release of insulin hormone from β cell or by increasing the insulin from its bound form (Kumar et al 2008). Homeopathy remedy *S. jambolanum* could also increased insulin level via increasing the cathepsin B activity. Cathepsin B plays role in formation of insulin from proinsulin (Bansal et al. 1981). An increase in insulin level increases the uptake of glucose by cells and stops the glucagon activity and improves the hyperglycemia and dyslipidemia condition.

Earlier study of Ravi et al. (2004) indicates *S. jambolanum* posses antioxidant activity. This study also suggests the homeopathy remedy *S. jambolanum* posses the antioxidant activity which destroys the free radicals and complication of hyperglycemia and dyslipidemia could be avoided. STZ destroys the β cells in Islets of Langerhans via the free radical production. The antioxidant property protects the β cells from destruction and this to increase the insulin level in body (Ravi et al. 2004). The histology observation indicates the denser β cell distribution in Islets of Langerhans in DMTx group rats compared to DMNoTx group rats. This supports the suggestion of protective effect of homeopathy remedy *S. jambolanum* on β cells.

Glycemic control is the major factor that influences the level of VLDL and triglyceride (Markku 1995). It is suggested that homeopathy remedy *S. jambolanum* have effect on glycemic control and lowers the triglyceride level in DMTx group rats.

Study have shown diabetes condition and lack of insulin action leads to high levels of triglyceride and total cholesterol compared to normal individual as insulin stimulates synthesis of adipose tissue by lipoprotein lipase (Matshushita 1982). This study also suggests the homeopathy remedy *S. jambolanum* causes increased production of HDL as in DMTx group rats which transports the cholesterol and triglyceride to liver to be metabolised and excreted and thus causing the decreased level of cholesterol and triglyceride as in DMTx group rats (Sharma et al. 2003). A decreased production of LDL also leads to lack of transportaion for cholesterol and triglyceride to be carried to blood circulation and leads to lower level of cholesterol and triglyceride in DMTx group rats. The presence of diatery fibers in *S. jambolanum* seed decreases the
absorption of cholesterol in intestine (Lansky 1993). A decreased absorption of cholesterol decreases the blood cholesterol level in blood and could be another mechanism of action of homeopathy remedy S. jambolanum in DMTx group rats (Kar et al. 1999).

NDMTx group rats showed a nonsignificantly increased glucose level, significantly (p<0.05) increased total cholesterol, triglyceride and LDL and nonsignificantly decreased HDL level. These results might be caused by the destructive effect of the remedy on the islets of Langerhans in NDMTx group rats. However more study should be done. These result indicates homeopathy remedy S. jambolanum is not suitable to be used as supplement and should only be used in diabetes patients.

**Conclusion**

The present study demonstrates the homeopathy remedy *S. jambolanum* can be used as a treatment for diabetes patient. this study shows the homeopathy remedy *S. jambolanum* has hypoglycemia and hypolipidemia activity. the homeopathy remedy *S.jambolanum* decreases plasma glucose, total cholesterol, triglyceride and LDL and increases the plasma HDL level of DMTx group. From the histology observation, homeopathy remedy *S. jambolanum* protects β cell from free radical destruction and repairs the hyperglycemia and dyslipidemia condition in DMTx group. The homeopathy remedy *S. jambolanum* is not recommended to be used in nonpathological condition.

**References**


Changing demographics of rheumatic heart disease in western world: A case report of mitral stenosis and brief review of literature

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Abstract

Rheumatic heart disease related mitral stenosis in United States is a rarely seen entity. Classically, valve problems develop 5 - 10 years after the rheumatic fever. In North America and Europe, this classic history of MS has now been replaced by an even milder delayed course with the decline in incidence of rheumatic fever. We report an interesting case of untreated rheumatic mitral stenosis (MS) with atrial fibrillation and fatal multi-organ thromboembolism demonstrating the altered natural course of this entity in developed world. This case provides an excellent educational opportunity for both new and old generation of physicians. It illustrates a typical scenario of altered natural history of rarely seen severe MS in the developed world and emphasises the importance of timely intervention including adequate anticoagulation to prevent thromboembolism, as these can and have proven to be fatal.

Keywords: Rheumatic heart disease, Mitral stenosis, Thromboembolism

Background

Rheumatic heart disease related mitral stenosis in United States is a rarely seen entity. Mitral stenosis (MS), resulting from thickening and immobility of the mitral valve leaflets, causes an obstruction in blood flow from the left atrium to left ventricle. As a result, there is an increase in pressure within the left atrium, pulmonary vasculature, and right side of the heart, while the left ventricle is unaffected in isolated MS. However, MS often coexists with mitral regurgitation and occasionally with aortic valve dysfunction, which may cause left ventricular dysfunction [1]. Mitral valve disease is associated with atrial fibrillation (AF), which may lead to serious and fatal thromboembolic complications. We report an interesting case of untreated rheumatic MS with AF and fatal multi-organ thromboembolism. This case provides an excellent educational opportunity for both new and old generation of physicians. It illustrates a typical scenario of altered natural history of rarely seen severe MS in the developed world and emphasises the importance of timely intervention including adequate anticoagulation to prevent thromboembolism, as these can and have proven to be fatal.
Case Report

A 56 year old female presented with nausea, vomiting, headache, abdominal pain, and sudden onset of bilateral leg pain. Her past medical history was significant for two previous strokes with residual left hemiparesis, a heart condition (unknown diagnosis at the time of admission), and atrial fibrillation on warfarin therapy. Patient denied any similar presentation in the past. On examination, patient was found to be in atrial fibrillation with absent distal pulses in lower extremities bilaterally, diffuse abdominal tenderness and diminished bowel sounds. Rest of the physical examination was unremarkable. Laboratory investigations revealed normal blood count and metabolic panel with subtherapeutic INR of 1.3 at the time of admission. Chest Xray showed cardiomegaly with prominent aorto-pulmonary window suggestive of pulmonary hypertension typical of mitral stenosis [Figure 1]. The trans-thoracic echocardiogram revealed severe MS, thickened mitral valve cusps without any vegetations, and an enlarged left atrium without any clots [Figure 2]. CT scan of brain confirmed a large subacute infarct in right parietal region [Figure 3]. Computerised tomography (CT) of the abdomen revealed multiple infarcts in the spleen and kidneys, mesenteric ischemia and acute bilateral iliac artery occlusions [Figure 4]. Abdominal aortic angiogram was performed together with an emergent intra-arterial thrombolysis of the occlusive thrombi in iliac arteries. Post-procedure, she received systemic heparin and alteplase infusion for 24 hours. A trans-esophageal echocardiogram was scheduled, but the patient expired before its completion due to cardiac arrest with pulseless electrical activity that did not respond to advanced life support.

Discussion:

Rheumatic fever is the predominant cause of MS. Isolated MS occurs in 40% of all patients presenting with rheumatic heart disease [2,3], although only 50 to 70 percent of patients report a history of rheumatic fever [2,3]. Isolated MS is twice as more common in women than in men [2-4]. Other causes of MS, though rare, include left atrial myxoma, ball valve thrombus, mucopolysaccharidosis, and severe annular calcification.

In patients with MS due to rheumatic fever, the pathological processes include leaflet thickening and calcification, commissural fusion, chordal fusion, alone and / or in combination [5,6]. These ultimately result in a funnel-shaped mitral apparatus with reduced size of mitral valve orifice. Interchordal fusion obliterates the secondary orifices, and commissural fusion narrows the principal orifice [5,6].

Classically, valve problems develop 5 - 10 years after the rheumatic fever. Rheumatic fever is becoming rare in the United States, so MS is also very rarely seen. In North America and Europe, this classic history of MS has now been replaced by a milder delayed course with the decline in incidence of rheumatic fever [7]. The mean age of presentation is now in the fifth to sixth decade [7] and more than one third of patients undergoing valvotomy are older than 65 years [8]. Our patient was 58 years old and this exemplifies the changing demographics of this condition. In developed countries, there is a long latent period of 20 to 40 years from the occurrence of rheumatic fever.
to the onset of symptoms. Once symptoms develop, there is another period of almost a decade before symptoms become disabling [2].

The symptoms induced by MS are primarily related to the severity of the valvular stenosis as reflected by the left atrial pressure, pulmonary pressures, pulmonary vascular resistance, and cardiac output. However, many patients with severe MS deny symptoms because slow progression of disease is "matched" by a gradual reduction in activity. As a result, a careful history is often required to document a slow decline in exercise tolerance. Any situation that increases the cardiac output, thus raising transmitral flow, or causes tachycardia, which reduces diastolic filling time, can markedly increase the transmitral pressure gradient and precipitate symptoms such as dyspnea or hemoptysis, even in patients with mild MS. In some patients, the diagnosis of MS is first made when the patient is exposed to such stresses. Others present only with a secondary complication, such as AF or an embolic event.

Atrial fibrillation (AF) is common in patients with MS due to the elevation of left atrial pressure and consequent left atrial enlargement. The prevalence of AF is higher with more severe disease, increasing age, and the presence of other valvular abnormalities. Munoz et al in their study of 854 patients with MS, reported incidence of AF as 47 percent overall; the rate was higher in those with other valvular abnormalities [9]. The 2006 ACC/AHA valvular disease guidelines and 2008 Eighth ACCP consensus conference recommended long-term oral anticoagulation (target INR 2.5, range 2.0 to 3.0) in patients with MS who have a prior embolic event, left atrial thrombus, or paroxysmal, persistent, or permanent AF, since all forms of AF carry a similar risk for thromboembolism [10-12]. The 2006 American College of Cardiology/American Heart Association (ACC/AHA) and the 2007 European Society of Cardiology (ESC) guidelines on the management of valvular heart disease concluded that the primary indications for intervention were moderate to severe MS and the presence of symptoms [10,13]. The main indication for intervention in asymptomatic patients was moderate to severe MS and pulmonary hypertension (pulmonary artery systolic pressure >50 mmHg at rest or >60 mmHg with exercise).

Overall, the 10-year survival of untreated patients presenting with MS is 50% to 60%, depending on symptoms at presentation [3,4]. In the asymptomatic or minimally symptomatic patient, survival is greater than 80% at 10 years, with 60% of patients having no progression of symptoms [3,4]. However, once significant limiting symptoms occur, there is a dismal 0% to 15% 10-year survival rate [2-4,14]. Once there is severe pulmonary hypertension, mean survival drops to less than 3 years [15]. The mortality of untreated patients with MS is due to progressive pulmonary and systemic congestion in 60% to 70%, systemic embolism in 20% to 30%, pulmonary embolism in 10% and infection in 1% to 5% [4,5].

**Conclusion**

This case provides an excellent educational opportunity for both new and old generation of physicians. It illustrates a typical scenario of altered natural history of rarely seen severe MS in the developed world and emphasises the importance of timely intervention including adequate anticoagulation to prevent thromboembolism, as these can and have proven to be fatal.
References


Figure 1: Chest Xray demonstrating cardiomegaly with prominent aorto-pulmonary window suggestive of pulmonary hypertension typical of mitral stenosis
Figure 2: Transthoracic echocardiogram showing severe mitral stenosis
Figure 3: Computerised tomography of brain showing right middle cerebral artery territory ischemic infarct
Figure 4: Computerised tomography of abdomen showing bilateral multiple kidney infarcts and persistent delayed nephrogram compatible with decreased transit of contrast through renal parenchyma indicative of diffuse renal parenchymal injury.
Nutritional Assessment of Dialysis Patients at a Malaysian National Kidney Foundation Center

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Abstract

Background: Nutritional compliance is known to play a pivotal role in enhancing the quality of life for end-stage renal failure patients. However, nutritional compliance has been reported to be significantly low among haemodialysis (HD) patients. By improving the nutritional status of dialysis patients, the rate of morbidity and mortality associated with nutritional impairment in dialysis patients can be reduced.

Objective: To assess the level of nutritional (dietary and fluid) compliance among patients in a dialysis centre of National Kidney Foundation (NKF) and to identify the common reasons behind the lack of compliance.

Methods: An interview was conducted on 52 randomly recruited patients to obtain their knowledge of dietary and fluid restrictions related to dialysis, personal and medical characteristics and self-reported compliance. Nutritional compliance of the patients was derived from comparing the resting energy expenditure (REE) with the total calories consumed by a patient in a typical day.

Results: Self-reported nutritional compliance among HD patients was 94% when compared to actual compliance of 48%. Common reasons behind lack of compliance amongst HD patients were lack of family support, financial constraints, co-existing morbidities, misinformed calorie intake and unwillingness to change lifestyle. Seventy five percent of patients from National Kidney Foundation (NKF) were uncertain of their dietary requirement and sought advice to enhance their nutritional status.

Conclusion: Health care providers should be aware of the common factors behind noncompliance in HD patients. Patients at-risk of noncompliance should be identified early to institute appropriate interventional practices. Patient education with family involvement and concentrated effort towards lifestyle intervention should be part of health care provision to HD patients.

Keywords: Hemodialysis, End-Stage Renal Failure, Nutritional Compliance
Introduction

Nutritional status plays an essential role in enhancing the quality of life for ESRD patients (Locatelli F, et al., 2002). Patients undergoing dialysis are advised to practice salt free diet, low potassium containing foods and limited fluid intake as it delays the deterioration of glomerular filtration rate thus restricting the progression to ESRD (Luis DD, et al., 2008). Nonadherence to fluid restriction can lead to fluid overload and complications such as hypertension and pulmonary congestion. Likewise, nonadherence to dietary recommendation can result in elevated serum phosphate levels which play an important role in the development of secondary hyperparathyroidism, renal osteodystrophy as well as coronary artery disease (Block GA et al., 2004).

Balanced intake of protein is also vital to HD patients. Though protein adds up to uremia, ESRD patients are required to consume a high protein diet (1-1.2 g/kg/day) so as to meet the extra demands for body repair functions and immunity (Jones M et al., 2003). However, several surveys have reported protein-calorie malnutrition in up to 40% of this patient population (Mehrotra R, 2001). Reports indicate that frequently observed gastrointestinal complaints in this patient population are likely to contribute to decreased protein intake and malnutrition (Strid H, 2003). Treating underlying issues that prevent adequate intake can improve nutrition status, and improved nutrition along with compliance to the prescribed regimen has the potential to reduce morbidity for those with ESRD.

Dietary compliance has been reported to be significantly poor in dialysis patients (Denhaerynck K, et al., 2007). According to the Annual General Report of the Malaysian NKF, about 75% of patients are uncertain of their dietary requirement and seek advice to enhance their nutritional status (Annual General Meeting Report by National Kidney Foundation, 2007). Counseling sessions on the right diet have been given in the dialysis center by the nurses. However, it is not known if the patients adhere to the advice given or whether the advice was adequate. The objectives of this study are to assess whether the dialysis patients fulfill the recommended dietary requirement and if not, to investigate the common factors behind it.

Materials and Methods

In this cross-sectional study, data were collected from the study participants. The study population consisted of patients undergoing hemodialysis at the NKF Dialysis Center situated in Klang Valley. The inclusion criteria were patients aged above 21 years, of sound mind and had provided informed consent. Structured interviews with questionnaires were used to collect information about patients’ knowledge of dietary and fluid restrictions related to dialysis, personal characteristics and self-reported compliance regarding prescribed diet and fluid regimen. Nutritional compliance of the patients was derived from comparing the resting energy expenditure (REE) with the total calories consumed as reported by the patient in a typical day.
Measure of patients’ knowledge

A questionnaire was developed together with an experienced dietician to assess patients’ knowledge of diet and fluid regimens. The questions were based on the content of an information booklet that was developed by the Malaysian NKF which is routinely given to HD patients. The questionnaire included items on general knowledge about the ESRD, dietary prescriptions for HD, recognition of restricted/nonrestricted food, fluid allowance and the consequences of noncompliance. The responses were in yes/no format, and the number of correct responses was totaled to obtain the patients’ knowledge score.

Measure of self reported compliance

Study participants were asked to rate the level of dietary compliance with based on caloric value during the past week on a 7-point rating scale, where responses ranged from ‘0’ (poor) to ‘7’ (excellent). Patients were classified as compliant if the rating was above ‘4’.

Measure of actual dietary compliance

Dietary compliance for each patient was determined by comparing the Resting Energy Expenditure (REE)\(^{22}\) with the total calories consumed by a patient in a typical day. REE was calculated as explained by the Harris-Benedict principle.

\[
\begin{align*}
\text{REE}_{\text{male}} &= (66.5 + 13.8 \times \text{weight}) + (5.0 \times \text{height}) - (6.8 \times \text{age}) \\
\text{REE}_{\text{female}} &= (665.1 + 9.6 \times \text{weight}) + (1.8 \times \text{height}) - (4.7 \times \text{age})
\end{align*}
\]

The total calories consumed by each patient on a typical day were calculated by adding up the respected caloric value of each food mentioned by the patient. As REE tends to overstate calorie needs by 5% (Frankenfield DC, 1998), patients with a caloric intake within 5% of the lower range of REE were accepted as compliant.

Patient demographic data that were collected included age, gender, religion, level of education, occupation, marital status, number of family members, family income, co-morbidities and duration of HD. The study protocol was approved by the Monash University Standing Committee on Ethics in Research.

Results

Demographic Distribution

\(^{22}\)Amount of calories required for a 24-hour period by the body during a non-active period.
Sixty patients undergoing dialysis in NKF were recruited to participate in the study. However, only 52 patients were eligible and consented to participate. Of the study population, 35 patients were males and 17 were females. Thirty six subjects were retirees, 7 were employed and 9 were housewives. Forty eight percent of the subjects had coexistent diabetes mellitus and hypertension and 33% had hypertension alone. Eighteen (35%) patients admitted to be active smokers and alcoholics.

Patients’ knowledge

The maximum score for the knowledge scale was 100. Eight subjects (15%) had a score of >90; 71% scored between 70 and 90 and 14% of HD patients obtained a score of <70. No correlation was observed between the score of dietary knowledge and the measure of actual compliance.

Self reported and actual nutritional compliance

Self reported compliance is defined as the patients’ perception of the appropriate calorie intake whereas actual compliance reflects the true calorie intake acquired from the calculation of the calorie value of food consumed per day. Although 94% of the study participants self–reported to be compliant, actual compliance to the dietary advice was found only in 48% of the patients based on the REE by gender, age group and co-morbidity.

Based on the data collected from HD patients, common reasons behind lack of compliance were: (a) insufficient family support, (b) financial constraints, (c) co-existing morbidities, (d) misinterpretation of dietary intake and (e) unwillingness to change lifestyle (Table 1). Of these, unwillingness of the dialysis patients to change their habits and lifestyle was found to be main reason for the lack of compliance (87%). Ninety percent of the patients in the study population indicated that a dedicated dietician may help in the maintenance of nutritional compliance by reinforcing appropriate dietary habits on the subsequent visits.
Figure 1: Actual and self reported dietary compliance among haemodialysis patients

Table 1: Common Reasons to Patients’ Non-compliance in Dietary Intake

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of family support</td>
<td>60%</td>
<td>31</td>
</tr>
<tr>
<td>Financial constraints</td>
<td>42%</td>
<td>22</td>
</tr>
<tr>
<td>Co-existing morbidities</td>
<td>19%</td>
<td>10</td>
</tr>
<tr>
<td>Misinformed of dietary intake</td>
<td>73%</td>
<td>38</td>
</tr>
<tr>
<td>Unwillingness to change lifestyle</td>
<td>87%</td>
<td>45</td>
</tr>
</tbody>
</table>

Discussion

The main finding of this study is the lack of nutritional compliance in 52% of patients undergoing haemodialysis although, 96% of participants self-reported to be compliant with the prescribed dietary regimen. This is significantly less compared to previous studies of reported compliance ranging from 50-85% (Cummings et al., 1982). Such difference in the prevalence rate might be attributed to the different criteria used for measuring compliance and different confounding factor such as culture and type of food consumption. The patients in our study were observed to be consuming lesser calories as compared to the recommended caloric intake as stated by the REE. Several studies have also stated that dialysis patients’ nutrient intake is lower than recommended (Hakim RM, 1993), possibly due to the depressed appetite, effects of
uremia (Bergstrom J, 1994) along with loss of albumin and amino acids during dialysis (Ikizler TA, 1994, 1995).

Patient’s self reported compliance rate was significantly higher than the measured actual compliance in our study population. As reported earlier, it may be due to patients’ fear of embarrassment or lack of knowledge of their recommended food source (Hudson et al., 1994). Inadequate dietary awareness may also lead to false sense of satisfaction that they are consuming enough food to fulfill their energy requirement. Patient’s denial of their condition may also contribute to higher self reported compliance rate (Yanagida EH et al., 1981). This suggests that more communication and explanations on the interpretation of compliance behavior as well as dietary advice are required to assist the patients in achieving the desired level of compliance.

Our results also indicate that patients’ awareness do not correlate with compliance. This is supported by other studies that indicate no relationship exists between knowledge and compliance (Chan & Molassiotis, 1999). This suggests that knowledge alone may not be sufficient in enhancing the level of compliance among dialysis patients.

Unwillingness to change lifestyle, lack of family support and dietary knowledge are the common factors behind lack of dietary compliance in our patients. Previous studies have reported contradictory results on the role of family support on compliance level (Christensen et al., 1992; Cameron, 1996). However, it should be admitted that these factors are common pitfalls of inadequate control of any chronic illness and an uphill challenge for health care community. These issues could be overcome by increasing awareness among the health care providers and the family members of the importance of working together in the management of HD patients. Positive patient staff relationship is known to increase self reported compliance efforts and behaviours of patients and also enhanced self-efficacy capacities (Zrinyi M et al., 2003). The health care professional should evaluate the perception of the patient towards the illness and assess carefully the role of the family in the patient’s treatment program, before attempting to steer the patients towards better compliance. Recent studies have reported that patient counselling centered on dialysis compliance, diet and medications are effective strategies to improve the quality of life and awareness in ESRD (Thomas D, 2009). It is also vital that these strategies are reinforced and monitored at regular intervals by the health care team working towards the patients’ empowerment of self management.

This study has a few limitations. The sample size was relatively small (n = 52). In addition, the usage of predictive equation for REE as well as the calculation of the typical dietary intake for each patient provides only estimates but not true figures.

**Conclusion**

Dietary management is an essential component for patients with EDSR. Identifying the underlying issues early and implementing appropriate interventional strategies can improve nutrition status, and has the potential to reduce morbidity for those on chronic haemodialysis.
References


Nutritional Anemia in Medical Students

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Abstract

Background: Nutritional anemia is very much prevalent and largely undiagnosed among students in Professional Institutes. Various socio-demographic characteristics like age, sex, social class, dietary habits, and infections are the etiological factors for nutritional anaemia.

Objectives: To study nutritional anemia and its’ correlates among the Medical Students of Rural Medical College, Loni.

Methods: The study was done on 100 MBBS students. Hemoglobin estimation was performed by Sahli’s Haemoglobinometer and observations were interpreted as per the WHO criteria. The data was collected on a predesigned and pretested questionnaire. The data was analyzed by SPSS Statistical software and chi-square test of significance was applied to assess the significance level by calculation of p-value of the observations.

Results: In the present study on 100 Medical students, 32.0% students were anaemic, out of which 44.0% were girls and 20.0% boys. 25.0% students had mild anemia. Majority (81.8%) of anaemic students were undernourished as per their Body Mass Index.

Conclusion: Hemoglobin estimation of students at the time of entrance to Medical Colleges should be done. Iron and folic acid tablets and deworming drugs in therapeutic doses should be provided to anemic students. The students should be motivated and educated to take balanced diet, rich in green leafy vegetables and fruits as nutritional anemia is totally preventable.

Keywords: Nutritional Anemia, Hemoglobin level, Body Mass Index

Introduction
Nutritional anemia affects all age and sex groups in India. Iron deficiency anemia is the most common micronutrient deficiency in the world affecting more than 700 million persons. Anemia is particularly severe among pregnant women, lactating mothers, adolescent girls and pre-school age children. Nutritional anemia is a disease syndrome caused by malnutrition in its widest sense\(^2\). It has been defined by WHO as "a condition in which the hemoglobin content of blood is lower than normal as a result of a deficiency of one or more essential nutrients, regardless of the cause of such deficiency"\(^2\). By far the most frequent cause of nutritional anemia is iron deficiency, and less frequently folate or vitamin B\(_{12}\)\(^3\). Iron deficiency anemia is a major nutrition problem in India and many other developing countries\(^4\). In addition, many subjects have iron deficiency without anaemia\(^5\). The incidence of anemia is highest among women and young children, varying between 60 to 70 percent\(^6\). In a study by Kapoor and Aneja\(^7\) (from public and government schools in Delhi, anaemia among adolescent girls was as high as 50.8%. Compared to the vast amount of work done in pregnant mothers and young children, there are relatively few published studies on the prevalence of anaemia in medical students and probably none in boys, and none from the town of Loni.

**Materials and Methods**

**Type of Study**: Cross Sectional

**Study Participants**: 100 Medical Students

- **Inclusion criteria:**
  1.) Students enrolled in MBBS from first year to final year.
  2.) Students without any systemic disorders like diabetes, hypertension, bleeding diathesis.

- **Exclusion criteria:**
  1.) Students from other allied health branches like Dental, Physiotherapy, Nursing.
  2.) Those adolescents with chronic illness or receiving long-term drugs and needing hospitalization in the last two weeks before the study were excluded.
  3.) Those who did not volunteer to give blood for examination.

**Sampling technique**: Purposive sampling

**Study Setting**: Rural Medical College & Pravara Rural Hospital (PRH)

**Statistical analysis**: SPSS Statistical software.

**Statistical methods**: Chi-square test of significance.
Methodology

The present study was conducted on 100 Medical students to study the magnitude of nutritional anemia in them. A social demographic profile including parents’ education, family structure and diet consumed (vegetarian, non-vegetarian) was noted. A detailed general physical examination was done to look for pallor, icterus, edema, hyperpigmentation, lymphadenopathy, bleeding spots and signs of vitamin deficiency and was noted on a predesigned proforma.

Physical examination was done to rule out any systemic abnormality. The anthropometric measurements (weight and height) were made by single observer eliminating inter observer variability and errors. Finally 100 medical students were included in the study & their hemoglobin estimation was performed by Sahli’s hemoglobin meter and results interpreted as per the WHO criteria. Anemia is established if the hemoglobin is below the cut-off points as recommended by WHO8.9.

Cut-off points for the diagnosis of anemia.

<table>
<thead>
<tr>
<th>Category</th>
<th>Venous Blood (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult males</td>
<td>13.0</td>
</tr>
<tr>
<td>Adult Females (non-pregnant)</td>
<td>12.0</td>
</tr>
</tbody>
</table>

The students detected as anaemic were further investigated by laboratory tests like Packed Cell Volume (PCV), Mean Corpuscular Volume (MCV), Mean Corpuscular hemoglobin (MCH), Mean Corpuscular hemoglobin Concentration (MCHC) to rule out non-nutritional causes of anemia. Statistical analysis was done by chi-square test of significance by SPSS Statistical software.

Results

In the present cross sectional study on 100 Medical students, 32.0% students were anaemic, with 44.0% girls and 20.0% boys. The association between normal hemoglobin level and anaemic status was statistically highly significant p-value < 0.01 (p=0.0078) on applying chi-square test of significance (table 1). Majority of students had mild grade of anemia (25.0%), which was more common in girls (36.0%) than boys (14.0%). None had severe anemia (table 2). Majority (81.8%) of anaemic students were undernourished as per their Body Mass Index. The relation of anemia with under nutrition was highly significant since p-value < 0.001 (p-value= 0.00064) (table 3). Almost all the non vegetarian student, except one was found to be anemic. The relation between the dietary pattern of the students & anemic status was highly significant with p-value<0.01 (p=0.005432) (table 5).Most of students were vegetarians (94.0%) though only 51.0% were taking green leafy vegetables and fruits.
regularly. Only 7.0% students were taking nutritional supplements, iron tablets, multivitamins etc. (table 5). The possible role of infections and socio-economic status was not significant. Associated micronutrient deficiencies included xerophthalmia in 18 and knuckle hyperpigmentation in two adolescents and all of them were anaemic. None of adolescents had icterus, lymphadenopathy, edema or bleeding spots.

Table I: Sex wise distribution of anemia among students

<table>
<thead>
<tr>
<th>Status of Anemia</th>
<th>Boys No. (%)</th>
<th>Girls No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Hemoglobin</td>
<td>40 (80.0%)</td>
<td>28 (56.0%)</td>
</tr>
<tr>
<td>Anemic</td>
<td>10 (20.0%)</td>
<td>22 (44.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100.0%)</td>
<td>50 (100.0%)</td>
</tr>
</tbody>
</table>

Chi-Square test; p< 0.01 (p=0.0078); highly significant association

Table II: Sex wise grading of severity of Anemia (WHO Criteria)

<table>
<thead>
<tr>
<th>Grading</th>
<th>Boys No. (%)</th>
<th>Girls No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>40 (80.0%)</td>
<td>28 (56.0%)</td>
<td>68 (68.0%)</td>
</tr>
<tr>
<td>Mild</td>
<td>7 (14.0%)</td>
<td>18 (36.0%)</td>
<td>25 (25.0%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>3 (6.0%)</td>
<td>4 (8.0%)</td>
<td>7 (7.0%)</td>
</tr>
<tr>
<td>Severe</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>50 (100.0%)</td>
<td>50 (100.0%)</td>
<td>100 (100.0%)</td>
</tr>
</tbody>
</table>

Table III: Association of nutritional status with anemic status of students

<table>
<thead>
<tr>
<th>Body Mass Index (BMI) (kg/m²)</th>
<th>Total no. of Students No. (%)</th>
<th>Anemic Students No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under nutrition (&lt; 18.5 kg/m²)</td>
<td>11 (11.0%)</td>
<td>9 (81.8%)</td>
</tr>
<tr>
<td>Normal (18.5 – 24.9 kg/m²)</td>
<td>51 (51.0%)</td>
<td>21 (41.2%)</td>
</tr>
<tr>
<td>Overweight (25.0- 29.9 kg/m²)</td>
<td>23 (23.0%)</td>
<td>2 (8.7%)</td>
</tr>
<tr>
<td>Obese (&gt;= 30 kg/m²)</td>
<td>15 (15.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>100 (100.0%)</td>
<td>32 (32.0%)</td>
</tr>
</tbody>
</table>

Chi-Square test; p< 0.001 (p-value= 0.00064); highly significant association
Table IV: Association of dietary pattern with anemic status of students

<table>
<thead>
<tr>
<th>Dietary Pattern</th>
<th>Anemic No.</th>
<th>Non-Anemic No.</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetarians</td>
<td>27</td>
<td>67</td>
<td>94</td>
</tr>
<tr>
<td>Non-Vegetarians</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>68</td>
<td>100</td>
</tr>
</tbody>
</table>

Chi-Square test; p< 0.01 (p-value= 0.005432); highly significant association

Table V: Diet pattern of students. (Multiple response table)

<table>
<thead>
<tr>
<th>Dietary pattern</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vegetarians</td>
<td>94</td>
<td>94.0</td>
</tr>
<tr>
<td>Non-vegetarians</td>
<td>06</td>
<td>6.0</td>
</tr>
<tr>
<td>Only mess food</td>
<td>63</td>
<td>63.0</td>
</tr>
<tr>
<td>Junk foods/snacks</td>
<td>46</td>
<td>46.0</td>
</tr>
<tr>
<td>Fruits/Green leafy vegetables regularly</td>
<td>51</td>
<td>51.0</td>
</tr>
<tr>
<td>Nutritional supplements / Iron tablets / Vitamins</td>
<td>07</td>
<td>7.0</td>
</tr>
</tbody>
</table>

Discussion

Nutritional anemia is a worldwide problem with the highest prevalence in developing countries. An estimation of hemoglobin should be done to assess the degree of anemia. If the anemia is "Severe", 10 g/dl high doses of iron or blood transfusion may be necessary. If hemoglobin is between 10-12 g/dl, the other interventions are like iron and folic acid supplementation and other strategies such as changing dietary habits, control of parasites and nutrition education. It is found especially among women of child-bearing age, young children and during pregnancy and lactation. It is estimated to affect nearly two-thirds of pregnant and one-half of non pregnant women in developing countries. Recent data from the District Nutrition Project (Indian Council of Medical Research) in 16 districts of 11 states, on prevalence of anaemia in non pregnant adolescent girls (11-18 years) showed rates as high as 90.1% with severe anaemia (Hb <7 g/dL) in 7.1%. In a recent study conducted in semi urban Nepal, the prevalence of anaemia in adolescent girls aged 11-18 years was found to be about 68.8%. In some of the less developed countries like Peru, Indonesia and Bangladesh, the prevalence of anaemia in girls has been found to be around 25-30%. Aggarwal; et al. in a government school based study from middle socioeconomic group of North East Delhi reported a prevalence of anaemia as 45%. Similarly, studies on prevalence of anaemia from different states of rural India, reported a prevalence of anaemia from 46% to 98%. Iron deficiency can arise either due to inadequate intake or poor bioavailability of dietary iron or due to excessive losses of iron from the body. Although most habitual diets contain adequate
amounts of iron only a small amount (less than 5 per cent) is absorbed\textsuperscript{18}. This poor bioavailability is considered to be a major reason for the widespread iron deficiency\textsuperscript{19}. Women lose a considerable amount of iron especially during menstruation. Some of the other factors leading to anemia are malaria and hookworm infestations.

**Study Limitation**

For Hemoglobin estimation, only Sahli’s Haemoglobinometer was used. No other methods were used to determine hemoglobin level of the blood. Also iron store estimation by detecting serum ferritin by ELISA was not done

**Conclusion**

In the present cross sectional study on 100 Medical students, 32.0\% students were anaemic. Nutritional anemia especially iron deficiency anemia is more prevalent among females especially adolescent girls due to causes like menstrual blood loss, poor diet and under nutrition as compared to males. Periodical and routine health check-up and Haemoglobin estimation of the students at the time of entrance to Medical Colleges should be done. Iron and folic acid tablets and deworming drugs in therapeutic doses should be provided to the anaemic students. Students should be motivated and educated to take balanced diet, rich in green leafy vegetables and fruits. Nutritional anemia is easily preventable as well as treatable and the available control measures are affordable.

**References**

6. ICMR. Recommended dietary intake for Indians, New Delhi; 1990.


The risk factors of device-related infection in nurse practice

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Abstract

Background: Healthcare associated infections (HAIs) concern 5-15% of hospitalized patients and lead to complications in 25 to 33% of those patients admitted to intensive care units (ICUs). The spread of device-related infection cases in ICUs is influenced by the number of invasive procedures as well as the severity of the patients' condition and the environment of the ICU. More than 50% of device-related infections are due to the combined effect of the patient's own flora and invasive devices. In the NNIS (National Nosocomial Infections Surveillance System), the risk of acquiring nosocomial pneumonia, bloodstream infection, or urinary tract infection is significantly associated with device exposures.

Aim of the study: To determine the risk factors of device-related infection in nurse practice performed invasive procedures: patients’ care with tracheostomy or intubation tube, peripheral venous catheter and urinary catheter insertion and care at the time.
Material and methods: The research was carried out in the ICUs and in the surgical units of Latvia's regional multi-profile hospitals (n=2), using the quantitative research method: questionnaire (n=288), and qualitative research methods: clinically structured empiric plan (n=85) and microbiological tests (n=92): a) with a Count-Tact applicator and a special culture medium, b) with a swab, and c) with catheter sedimentation method.

Results: A common problem in ICUs and in surgical units is the lack of unified nursing protocols on performing invasive procedures. During the research it was discovered that many respondents (average 18%) hadn't been introduced to the hospital-developed guidelines. Less than half of the observed nurses adhered to the principles of hand hygiene and appropriate visual appearance during invasive procedures. This tendency was especially pronounced in the case of insertion and handling of peripheral venous catheters. During 72 hours or less, intravascular catheters were changed in 83.3% of the observed cases and urinary catheters only in 27% of the cases. Microbiological tests showed a high level of bio-contamination during invasive procedures: the amount of microorganisms on the nurses' hands exceeded acceptable levels sixteen-fold, and medium to high levels of bio-contamination were discovered on patient's changed bed linen as well as in nurses' hair and their work wear.

Conclusions: The main risk factors of device-related infection in nurse practice are: the lack of unified nursing protocols, aseptic and antiseptic mistakes, excessive workload and insufficient knowledge of the care-givers, as well as a high level of bio-contamination in the units.

Keywords: Invasive devices, device-related infection, urinary catheter, peripheral venous catheter, tracheostoma care

Introduction

The risk of device-related infection, more than anything else, has forced medicine to accept the necessity for infection control. More than 50% of invasive device-related infections are due to the combined effect of the patient's own flora and invasive devices (Madeo et al, 2009). The immune systems of critically ill patients are in a severity state which increases the probability of beneficial conditions for a colonization by pathogenic microorganisms due to invasive procedures (Graves et al, 2008). Furthermore, the action of inserting an invasive device (urinary catheter, peripheral venous catheter, tracheostoma or intubation tube) disrupts the natural defence mechanisms by itself. Scanning electron microscopy of an infected devices shows the surface covered by an amorphous biofilm containing numerous host proteins and microcolonies of the infecting organism, all embedded in a thick matrix of exoglycocalyx (Stoodley et al, 2002). Within this matrix, bacterial cells evade the host immune response and survive antimicrobial chemotherapy, resulting in persistent infections that are difficult to treat (Donlan 2008; Weigel et al, 2007). The most common device-related infection pathogens are Staphylococcus aureus, Staphylococcus epidermidis, Klebsiella, Enterobacter, Serratia, Candida.
*albicans*, *Pseudomonas aeruginosa*, *Citrobacter freundii*, *Corynebacterium*, *Escherichia coli* (Wilson 2006; MMWR 2002; Stamm 1998).

**Aim, material and methods**

The purpose of the study to determine the risk factors of device-related infection in nurse practice performed invasive procedures: patients’ care with tracheostomy or intubation tube, peripheral venous catheter and urinary catheter insertion and care at the time.

The research was performed in the intensive care units (ICUs) and in the surgical units of Latvia's regional multi-profile hospitals. The quantitative research method: questionnaire (n=288), and qualitative research methods: clinically structured empiric plan (n=85) and microbiological investigations (n=92) were used. To determine the nurses knowledge as well as practical skills performing patients care with invasive devices, a structured questionnaire was developed. To determine aseptic invasive procedures technique and patients’ care with peripheral venous catheter (n=30), urinary catheter (n=15), tracheostomy (n=20) or intubation tube (n=20) as well as the nurses' work environment in the ICUs and in the surgical units (sufficient material and technical means, the presence or lack of nursing protocols, the number of nursing staff in the units and the visual appearance of the nurses), a clinically structured empiric plan was developed. By means of microbiological investigation the contamination level of the ICUs and surgical units was determined during invasive procedures: a) Count-Tact applicator and a culture medium specially selected for this method was used for determination the bio-contamination level of the work environment, work surfaces, nurses' work wear and patients' bed linen, b) the swab method was used for determination the microbiological contamination of the equipment and the nurses hands, c) the catheter sedimentation method was used for determination the microbial contamination on the invasive devices. The samples taken with the aim of identifying bacterial species present were put on selective culture mediums. Interpretation of the Count-Tact method results was performed according to the risk level present and the colony forming unit (CFU) count on a 25 cm² surface.

The obtained data was analysed with the help of the following software: SPSS 16.0 for MS Windows, Confidence Interval Analysis (CIA), \( \chi^2 \) test and MS Office Excel.

**Results**

In total were analysed 288 questionnaires. The results showed that a nurse from the surgical units takes care of 18 to 40 patients per day and 2 to 3 patients per day in the case of ICUs. The obtained results by questionnaire showed that most of the nurses were informed about the hospital-developed guidelines for insertion and patients’ care with peripheral venous catheters in 77 cases (77%; 77/100), for insertion and patients’ care with urinary catheters in 77 cases (87.5%; 77/88). There were not available hospital-developed guidelines for patients’ care with tracheostomy or intubation tube in the ICUs. The obtained results by clinically structured empiric plan showed that adherence of these guidelines in nurses’ daily work was limited. Peripheral vein
catheterization in 16 cases (53.3%; 16/30) and urinary catheterization in 5 cases (33.3%; 5/15) were recorded in the ordination list, the patient's care protocol or the manipulation journal. However patients’ care with tracheostomy or intubation tube were not recorded (40/40; 100%) in unified nursing protocols of ICUs. Less than half of the observed nurses adhered to the principles of hand hygiene performed invasive procedures: during the peripheral vein catheterization only 3 nurses (10%; 3/30) treated their hands before putting on gloves and 10 nurses (33.3%; 10/30) treated their hands after removing the gloves, but none of them used an adequate technique for treating their hands. By comparison, when dealing with insertion of urinary catheters, 3 nurses (13.3%; 3/15) treated their hands before putting on gloves and 6 nurses (40%; 6/15) treated their hands after removing the gloves, and 3 of them (13.3%; 3/15) used adequate hands treatment techniques. In case of patients’ care with tracheostomy or intubation tube, 20 nurses (50%; 20/40) treated their hands before putting on gloves and 20 nurses (50%; 20/40) treated their hands after removing the gloves, and 14 of them (35%; 14/40) used adequate hands treatment techniques (Figura 1). In 23 cases (77%; 23/30) of the observed peripheral vein catheterization and in 4 cases (27%; 4/15) of urinary catheterization, as well as in 14 cases (70%; 14/20) performed patients’ care with tracheostomy or intubation tube, there was jewellery on the nurses' hands (Figura 2). Performed tracheobronchial suction the protective means such as disposable masks were used in 8 cases (40%; 8/20) of tracheostoma care and in 5 cases (25%; 5/20) in patients’ care with intubation tube, sterile gloves were used in 4 cases (20%; 4/20) of tracheostoma care and in 6 cases (30%; 6/20) in patients’ care with intubation tube, goggles used in 4 cases (20%; 4/20) of tracheostoma care as well as in 4 cases (20%; 4/20) in patients’ care with intubation tube, and protective apron used in 7 cases (35%; 7/20) of tracheostoma care and in 2 cases (10%; 2/20) in patients’ care with intubation tube. The results of tracheobronchial suction showed that disposable catheters were changed in 34 cases (85%; 34/40), but oral hygiene before tracheobronchial suction was provided in 28 cases (70%; 28/40). According to the questionnaire, 79% (79/100) of the respondents agreed that peripheral venous catheters have to be changed once in at most 72 hours but only 40.9% (36/88) of the nurses agreed that the urinary catheters has to be changed in similar intervals. The observation study results showed that change of the peripheral venous catheters no rarer than once in 72 hours was observed in 25 cases (83.3%; 25/30), the timely changing of urinary catheters - in 4 cases (27%; 4/15) (Figura 1).

Microbiological investigation with the Count-Tact method of samples taken from the hands of ICU nurses carried out invasive procedures determined that the number of microorganism colonies exceeds the acceptable levels (the permissible level on 25cm$^2 \leq 5$ CFUs) as much as nine-fold to sixteen-fold (44 colony forming units (CFUs) and 83 CFUs; n=2). Similarly, the bio-contamination of the hands of surgical nurses also exceeded acceptable levels (permissible level on 25 cm$^2 \leq 50$ CFUs) as the 25cm$^2$ surface produced more than 100 colony forming units (128 CFUs and 241 CFUs; n=2) (Table 1). There was different contamination between clinic A and B, which was confirmed by an analysis of statistics ($\chi^2=36,349; p<0,01$). Microbiological investigation of the patients' changed bed linen and nurses' work wear using the Count-Tact method revealed a medium to high level of bio-contamination in patients’ care with tracheostomy or intubation tube and performed urinary catheterization (Table 1). The number of bacteria colonies on nurses’ work wear exceeded the norm in 44 of the investigated cases (78.5%; 44/56), Mucor fungi were found in 44 cases (78.5%; 44/56) and the bacteria colonies count in the nurses' hair exceeded
permissible levels in 48 cases (85.7%; 48/56). There was different contamination between clinic A and B, which was confirmed by an analysis of statistics ($\chi^2=340,357; p<0.01$). The microbiological results of the urinary catheters' connection with the collectors 72 h and 7 days after the insertion of the catheters showed that in 6 cases (50%; 6/12) pathogenic microorganisms like the *E. coli*, β haemolytic *Streptococcus spp.*, and fungi, like the *C. albicans* were identified. The research performed with the swab method and by catheter sediment analysis 72 h and 96 h after the insertion of a peripheral venous catheters revealed the presence of such pathogens as *Pseudomonas aeruginosa, Staphylococcus aureus* in the sterile zone of the peripheral vein catheter in one out of four cases (25%). Likewise the analysis of the urinary catheters’ sediments showed presence of at least one and in some cases several of the following pathogens as *S.aureus, P.aeruginosa, Ecoli, β haemolytic Streptococcus spp.* and fungi like *C.albicans* and *C.tropicalis* in 6 cases (100%; 6/6) both after 72 hours and 7 days of the insertion of the catheter.

![Figure 1: Aseptic patients’ care with invasive devices (n=85).](image)
appropriate work wear

Discussion

Every nurse can play a significant role in minimizing the risk of device-related infections. The identification of risk factors and prevention of device-related infections are the key procedures in quality of patients care (Wilson 2006). The study of the risk factors in patients’ care with invasive devices help to identify areas of clinical practice that could be improved and to optimize the hospital work, the use of more efficient and financially advantageous methods for prevention of device-related infections. This is the first report on risk factors of device-related infection in Latvian
nurse practice. Obtained results reflect problem areas in patients’ care with invasive devices and necessity for guidelines creation and implementation in nurses’ practice, especially, guidelines based to visual appearance of nurses and development of unified nursing protocols for patients’ care with invasive devices.

As shown by several studies, a significant role in limiting the risk of device-related infections are care guidelines and nursing protocols for the development and implementation in practice (Gotelli et al, 2008; Loeb et al, 2008; Morris & Hong Toy, 2008; Quattrin et al, 2004; Saint et al, 2009; Spencer & Clifford, 2009). Our results showed that a common problem in ICUs and in surgical units is the lack of unified nursing protocols on performing invasive procedures. Patients’ care with invasive devices were recorded in the ordination list, the patient's care protocol or the manipulation journal.

Our study, like observational study by Hugonnet (2007), confirmed another important risk factor in the nurses' practice that is the excessive workload in nurses’ daily work, which significantly exceeded the limits of patients’ care (1-2 patients per nurse in ICU and 15 patients per nurse in surgical units). While the leading measure for quality of patients care is a hand hygiene that essential reduce device-related infections, more and more, the authors support the principle of adequate hand hygiene (Allegranza et al, 2009; Farmer 2009; Kusachi 2006; Weinstein 1998).

In our studies, less than half of the observed nurses adhered to the principles of hand hygiene as well as microbiological investigations showed a high level of bio-contamination in patients’ care with invasive devices. The amount of microorganisms on the nurses' hands exceeded the acceptable levels sixteen-fold, and medium to high levels of bio-contamination were discovered on patient's changed bed sheets as well as in nurses’ hair and their work wear. Our data demonstrate some evidence that the pathogenic flora (β haemolytic Streptococcus, E. coli) remains unchanged both 72 h and 7 days after the insertion of the urinary catheter. It leads to the conclusion that the urinary catheter is contaminated during the first 72 hours after insertion and should be changed at least once every 72 hours instead of once a week as indicated by the manufacturer of the catheters. Conclusions of epidemiologic research are inconsistent when evaluating the effect of changing intravascular or urinary artificial implants less frequently than once every 72 hours (Moureau 2009; Morris et al, 2008; Ramritu et al, 2008). Some authors point out that 24 hours is a sufficient period of time for a biofilm to form on the catheter surface, consisting of microorganisms such as Staphylococcus epidermidis, Staphylococcus aureus, Pseudomonas aeruginosa, etc. making the catheter a source of bacteremia (Donlan 2001; Ferrieres et al, 2007). The most of devices-related infections are not severe and self-limiting, therefore microbiological investigations in such cases are not performed routinely in regional multi-profile hospitals of Latvia. This study showed that microbiological investigation is essential in patients’ care with invasive devices and ensure the checking of hospital environment for better prevention of devices-related infections.

Conclusions

The main risk factors of device-related infection in nurse practice are: 1) lack of unified nursing protocols on performing invasive procedures in the intensive care
units and in surgical units, 2) disregard of basic principles of hand hygiene while carrying out invasive procedures, 3) antiseptic and aseptic mistakes during patients' care with invasive devices, 4) excessive workload of nurses working in ICUs and in surgical units, 5) high levels of microbiological contamination during invasive procedures, including medium to high levels of bio-contamination of changed patients' bed sheets, nurses' work wear and hair.

Acknowledgements: This study has been supported by the project of European Social Fond (ESF).

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Cure for Hemophilia: Gene, Stem Cell or Transplant?

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Abstract

Background: Hemophilia has been a major focus of research due to its low minimum therapeutic range required (>5% of normal) and importance (1 per 8000 birth and high cost of replacement therapy). Vector-based gene therapy, stem cell or endothelial cell therapy and gross surgical transplantation are 3 modalities that have gained interest with breakthroughs in recent years. They are holy grails as they result in a permanent phenotypic correction of hemophilia. In the future, these may eventually supersede expensive and troublesome exogenous replacement therapy, which is the only current accepted mainstay treatment.

Aim & Objectives: Many reviews in hemophilia literature focus mainly on one modality. We attempt a highly referenced extensive review of the latest literature in these 3 ‘holy grail’ modalities of potential permanent exogenous cures to give an idea of the current status across the fields.

Methods/Study Design: Review of literature via MEDLINE and scientific/medical journals.

Results/Findings: Vector-based gene therapy includes viral and transposons. They have been successful in animal models. Human phase I trials have not been promising due to current hurdles include low achieved therapeutic levels, loss of transgene expression, potential mutagenesis, high vector doses required and small therapeutic index for vectors.

Cell therapy and transplantation includes hematopoietic stem cells, hepatocytes, endothelial cells and have been achieved in animal models. Concerns include the toxicity of immunosuppressive or tissue remodelling therapy needed, development of FVIII inhibitors, difficulty of integration into liver architecture and long-term safety. A plethora of interesting advances have been developing that will spearhead breakthroughs, including non-viral vectors, transposons, iPSC and various enrichment factors (MGMT, FLP) and immunomodulators and clinical phase I trials may be imminent.

Surgical liver transplantation, though uncommon in hemophilia, is the only consistently permanent phenotypic correction of hemophilia demonstrated reliably in
humans and animals. Current barriers include transplantation associated mortality and morbidity, lack of transplant donors and ethics regarding concurrent HIV and Hepatitis C infected recipients.

**Study Limitations:** Unpublished data may not be available to reviewers.

**Conclusion:** Liver transplantation is an appropriate and viable therapy for hemophiliacs with end stage liver disease, curing both liver disease and hemophilia. With future surgical research that reduces transplant morbidity and mortality, it may become more acceptable in mainstream. Genetic and Cell therapy are more ideal as they are less invasive. However, though they are showing promising progress in animal studies, many hurdles remain before success in human clinical trials can be obtained.

**Keywords:** Liver Transplantation, Gene Therapy, Cell Therapy, Hemophilia

**Introduction**

Hemophilies are a heterogeneous group of sex-linked bleeding disorders due to mutated genes on the X chromosome which result in pathological deficiency of coagulation factors. They are usually inherited but can be occasionally spontaneous up to 30% of the time (Mannucci & Tuddenham, 2001). The most common are Hemophilia A (Factor VIII-FVIII) and B (Factor IX-FIX) with incidence of 1 in 5000 and 1 in 30 000 male live births respectively (Tuddenham, et al., 2008). In most patients, the plasma level of FVIII/FIX predicts the clinical severity of the disease. Hemophilias is stratified to mild, moderate, and severe forms (corresponding to plasma coagulation factor levels of 6 to 30 percent, 2 to 5 percent, and 1 percent or less of normal, respectively) (Mannucci, 2003b). Although patients with mild hemophilia usually bleed excessively only after trauma or surgery, those with severe hemophilia have an annual average of 20 to 30 episodes of spontaneous or excessive bleeding after minor trauma, particularly into joints (hemarthrosis) and muscles. Treatment consists of replacing the missing coagulation factor from exogenous clotting factor concentrates, either plasma-derived or recombinant. For the past decades, data of various major efforts to phenotypically cure haemophilia have been emerging.

The Aim of this study is to highly reference an extensive review of the latest literature in these 3 ‘holy grail’ modalities of potential permanent exogenous cures to ascertain the current status across the fields and their respective challenges. The two authors co-review and discussed literature via PUBMED, MEDLINE and scientific/medical journals searched with the keywords “Hemophilia, Haemophilia and/or Gene, Cell, Therapy and Transplant”.

**History**

Therapy has evolved much over the years. In earliest descriptions found in the Egyptian papyri and Talmud, no treatment was available and affected males of
families uniformly died from fatal bleeding after minor surgery, such as circumcision (Rosner, 1969). The rather strange name 'hemophilia' meaning 'love of blood' was first coined in Hopff's treatise of 1828 (Ingram, 1976). The public interest associates hemophilia as the royal gene from the famous lineage of royal haemophiliacs, especially in the royal Russian Romanov family (Mannucci & Tuddenham, 2001). In the mid-nineteenth century it was recognised that transfusion therapy could treat bleeding in hemophilia patients (Ingram, 1976). In 1929 the first plasma substitution therapy for hemophilia was introduced by precipitation of a globulin from plasma with low pH water (Hecht, 1966). The breakthrough which is our modern mainstay management of exogenous concentrated forms of plasma-derived coagulation factors occurred in the 1970s after extensive research (Mannucci, 2003a).

Challenges

This modality is fraught with challenges. During the 1980s, up to 90% of hemophiliacs were infected with blood-borne viruses, including hepatitis C and HIV, from plasma derivatives manufactured from pooled plasma obtained from thousands of donors and invariably contaminated before good viral-cidal measures and screening were in place (Mannucci, 2003a). Improvements in viral inactivation methods and improved donor selection have significantly reduced the threat of contamination with HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV). The screening of plasma samples using polymerase chain reaction testing was made obligatory in Europe in 1999 (Mannucci, 2003b). However, the risk still exists for parovirus, hepatitis A virus (HAV) and emerging pathogens such as prions (Evatt, Farrugia, Shapiro, & Wilde, 2002). Access to treatment in developed countries has improved the quality of life for patients by dramatically increasing their level of education and employability.

Recombinant clotting factors offer less risk but are more expensive and associated with development of antibody inhibitors. The interest in developing recombinant FVIII/FIX concentrates was driven by the concept of safer therapies for hemophilia. The human FVIII gene was cloned in 1984 (Gitschier, et al., 1984; Toole, et al., 1984) and subsequently inserted in a plasmid vector and transfected to mammalian cells that express and secrete the FVIII protein. Mammalian cells are the only cells that have the capacity to perform the required post-translational glycosylation of the FVIII protein. In the late 1980s, pharmaceutical companies developed two preparations of full-length recombinant FVIII (rFVIII): Recombinate® (Baxter Healthcare) and Kogenate® (Bayer Healthcare). The main advantages of recombinant factor concentrates are safety in terms of potential of viral transmission, and that the manufacturing process of recombinant products does not rely on plasma supply (Dargaud & Negrier, 2007). In hemophilia patients who have previously been treated with plasma-derived FVIII concentrates, rFVIII rarely triggers inhibitor development (Schwartz, et al., 1990). Conversely, the incidence of inhibitor development in previously untreated patients is estimated to be 15 – 30% (Lusher, et al., 2004). The development of neutralizing inhibitor antibodies against FVIII is up to 30% of hemophilia A patients, rendering them unresponsive to further FVIII protein Infusions.

Acute treatment for high-titer inhibitor patients includes the use of fVIII-bypassing agents, e.g., prothrombin complex concentrates, activated prothrombin complex
concentrates, or recombinant activated factor VII, all of which can provide short-term hemostasis, but are not amenable to long-term use owing to financial cost, lack of efficacy in chronic arthropathy, and difficulty of using these agents in a prophylactic manner (Dargaud, Lambert, & Trossaert, 2008). Long-term treatment for inhibitor patients involves frequent high-dose hFVIII infusion, termed immune tolerance induction, which effectively eradicates inhibitory antibodies in 60–80% of inhibitor patients. But it is extremely expensive. Historically, infusion of plasma-derived porcine fVIII can work also. This treatment was effective because of the general lack of inhibitory reactivity of anti-hFVIII antibodies to porcine fVIII. Future improvements on bioengineered FVIII/FIX Concentrates are targeting at increased efficacy with longer half-life and decreased immunogenicity (Dargaud & Negrier, 2007).

**Future-Gene as Cure**

Hemophilia is a condition most attractive for gene therapy because of a combination of reasons. Extensive researches have made many hemophiliac animal models available for preclinical testing. Response to treatment of the disease is also well-defined by easy quantifiable coagulation assays, eliminating a problem that hampers efforts for other disease entities. The clinical manifestations of this monogenic condition are also entirely attributable to the lack of a single gene product, which circulates in minute amounts in plasma. Only a low therapeutic threshold of success is needed. Hemophilia B also has a relatively small size of FIX cDNA for ease of insertion into different gene transfer vectors and allows the addition of numerous transcriptional regulatory elements to both improve and restrict transgene expression in select cell types. Long-term expression of 2–3% of normal levels achieves a substantial reduction in the clinical manifestations of the disease (Herzog, et al., 2002; Sarkar, Gao, Chirmule, Tazelaar, & Kazazian, 2000). Expression of greater than 30% of the normal level of the coagulation factor would result in a phenotypically normal patient even in haemostatic challenges(Plug, et al., 2006), ("Natural history of primary infection with LAV in multitransfused patients. By the AIDS-Hemophilia French Study Group," 1986). Moreover, many different types of cell are capable of making coagulation factors, and the site of synthesis is not critical to function. Tissue-specific expression of transgenic FVIII is not required, only that the protein is secreted into the bloodstream.

There have been numerous enduringly successful gene therapies in hemophiliac murine and canine models (Chuah, et al., 2003; Nichols, et al., 2009), of which persistent therapeutic levels of clotting factors was demonstrated for years. However, the same cannot be said for humans. To date, the 6 Phase I human clinical trials on hemophilia gene therapy only have limited clinical efficacy (Table 1).

**Challenges**

Although the preliminary data are encouraging, several challenges remain. With regards to therapy efficacy, the plasma levels of factor VIII or IX reached so far with the use of gene therapy (1 to 2% of normal, but often less) are insufficient to free
patients from the need for exogenous coagulation factors (Mannucci, 2002). Levels of at least 5% of normal are required to prevent episodes of spontaneous bleeding and to guarantee that supplementary factors are needed only in cases of trauma or surgery (Mannucci, Mendolicchio, & Gringeri, 2001). The risk of developing inhibitors is still of concern, particularly in previously untreated patients. HIV-infected patients who are receiving highly active antiretroviral therapy may have a poor response to retrovirus-based approaches; those with chronic hepatitis may have a poor response to the insertion of viral vectors into the liver (Manno, et al., 2003).

The root problem is related to host immune responses, emphasising that immunological barriers continue to represent the main obstacle to achieving successful gene transfer in patients (Lillicrap, VandenDriessche, & High, 2006). For example, in a clinical trial of gene therapy for hemophilia B (Manno, et al., 2003), one patient receiving the highest dose achieved 10% of normal plasma FIX activity for 8 weeks but had a subsequent decrease of FIX levels associated with a substantial elevation of transaminase levels. This was due to destruction of transduced hepatic cells by cytotoxic T lymphocytes attacking liver cells expressing viral capsid proteins. Other concerns are the possibility of germline transmission (Kazazian, 1999), systemic inflammatory responses related to the use of high doses of adenoviral vectors (Ehrhardt & Kay, 2002) and insertional mutagenesis resulting in cancer. Out of ten children, two developed T cell leukaemia after gene therapy for severe combined immunodeficiency (SCID) using a retroviral vector (Hacein-Bey-Abina, et al., 2003).

Alternatives

There are also nonviral vectors for gene delivery, which are promising alternatives because they avoid the immunological problems associated with viral vectors, have reduced production costs, and have no size limitations of the delivered DNA (Liu, Mah, & Fletcher, 2006). The previous lack of long-term expression from nonviral vectors has recently been overcome by the use of specialized vectors such as strong endogenous promoters. Examples are the integrating DNA transposable elements such as Sleeping Beauty (SB) transposon and the phage fC31 integrase in several animal models (Liu, et al., 2006), including hemophilia (Ehrhardt, Xu, Huang, Engler, & Kay, 2005; Kren, et al., 2009; Ohlfest, et al., 2005; Olivares, et al., 2002; Yant, et al., 2002).

One model used intravenous administration of the FVIII-expressing Sleeping beauty transposon with a promoter complexed with polyethyleneimine (PEI) DNA to correct Hemophilia A mice phenotypically (Liu, et al., 2006). Another used dispersed atomisation of hyaluronan and asialoorosomucoid-coated nanocapsules containing FVIII-expressing Sleeping Beauty transposons over liver sinusoidal endothelial cells and hepatocytes before injecting intravenously (Kren, et al., 2009). The results are promising with hemophilia A mice exhibiting activated partial thromboplastin times comparable to wild-type mice even at 50 weeks.

In summary, challenges to gene success include insufficient transgene expression levels of Factor VIII, inhibitor antibody formation, vector immunogenicity and potential mutagenesis. Gene therapy has been dominated by the use of viral vectors and the immunogenic and oncogenic concerns that accompany these strategies. The
development of nonviral DNA delivery methods may provide an efficient and safe alternative for the treatment of hemophilia A. New types of nonviral strategies, such as transposons and the success of several nonviral animal studies, suggest that nonviral gene therapy has curative potential and justifies its clinical development, which may be in the near future (Gabrovsky & Calos, 2008).

**Future-Stem cell as Cure**

Stem cells and gene therapy are invariably related therapies distinguished by the main difference that in Stem cell therapy ex vivo gene transfer occurs first with pre-transplanted cells if any, before in vivo transplantation. The risks and challenges such as in vivo immunogenicity and mutagenesis remain similar.

Hematopoietic stem cells (HSCs) are an attractive target cell population for hemophilia A gene therapy because they are readily accessible for ex vivo genetic modification and allow for the possibility of sustained expression of a FVIII transgene in circulating peripheral blood cells for the lifetime of the patient following bone marrow transplantation. HSCs has been tested clinically as a treatment option for a variety of human autoimmune disorders, including multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, and Crohn disease (Doering, Gangadharan, Dukart, & Spencer, 2007). Endothelial cells found in liver, peripheral blood, lung are the main producers of clotting factors and are another main target of therapy (Follenzi, et al., 2008; Kumaran, et al., 2005).

Recently, several studies established the possibility of phenotypic cure of hemophilia mice with various transplanted stem cells (Table 2).

Of special mention are innovative ways of improving engraftment. One way is using Fibronectin-like Polymer (FLP) which engages extracellular matrix receptors to facilitate stem cell engraftment to liver tissue matrix without causing cell damage (Follenzi, et al., 2008). More research on identification of compounds that promote proliferation of transplanted cells should provide impetus for further success.

Another interesting model of transplantation is the use of a subcutaneous implant of endothelial cells in a basement membrane scaffold (Matsui, et al., 2007). This allows for sequestration of potentially mutagenic cells at an anatomic site and avoids disseminated delivery. This is supported by Matsui et al in their model where there was no evidence of any significant in vivo expansion of the implants or in other endothelial tissues. Implant removal and replacement can be easily done. However, at 30 weeks no FVIII was detected in any of the mice and the scaffold degraded by 35 weeks.

A novel approach that helps to overcome FVIII antibodies is to sequester FVIII within quiescent platelets using a platelet-based promoter transfer–based strategy. These platelets will deliver FVIII after platelet activation at sites of vessel injury, avoiding inhibitory antibody inactivation even in its presence and achieving hemostasis (Shi, et al., 2008). Even a small proportion of platelets (1%) that contained FVIII improved hemostasis in hemophilic A mice with pre-existing FVIII immunity.
Enrichment of the gene-modified cells after engraftment of bone marrow cells is also possible. This is via clonal expansion through methylguanine methyltransferase (MGMT) drug resistance gene selection (Chang, Stephan, Lisowski, & Sadelain, 2008). These MGMT-selected erythroid stem cells were capable of expanding without loss of repopulating ability as demonstrated by sustained high levels of transgene expression for a total of 18 months with relatively low initial cell numbers. Hemoglobin synthesis and red blood cell development were not disrupted too.

Non-bone marrow cells are used also. Fibroblast cells were induced back to a pluripotency stage (induced Pluripotent Stem (iPS) cells) and differentiated to endothelial progenitor cells which expressed the FVIII protein (Xu, et al., 2009). They engrafted within the hepatic parenchyma via injection and functionally integrated to provide the therapeutic benefit necessary for phenotypic correction of hemophilia. Interestingly, higher levels of FVIII mRNA were also detected in spleen, heart, and kidney tissues of injected animals despite local therapy to the liver only.

**Challenges**

The ideal therapy is that of transplant immune hyporesponsiveness and stable long term tolerance to an expressed transgene product. Some challenges include achievement of sustained production of therapeutic levels of FVIII, toxicity of conditioning regimens (Cyclophosphamide, irradiation, monocrotaline, acetaminophen) needed to achieve good engraftment of transduced cells. For example, good engraftment of transplanted hepatocytes into liver architecture require disruption of the sinusoidal endothelial barrier (Follenzi, et al., 2008). Others include suboptimal transgene expression as a result of poor vector design, low gene transfer in HSCs and gene silencing after vector integration, as well as the risk of insertional mutagenesis associated with the use of long terminal repeat–driven retroviral vectors (H. Lu, et al., 2008).

**Future-Gross Transplant as Cure**

According to Lerut et al, liver transplantation is the best treatment modality for patients with end-stage liver diseases (Ng & Lo, 2009) and also the standard treatment for many inherited metabolic disorders (Lerut, et al., 1995). It has been landmarked as one of the most important advances in the medical field. The history of liver transplantation dates back to 1963 when Starzl first attempted cadaveric liver transplantation (CLT) in a male. Immunorejection and hepatic artery thrombosis plagued the first few operations and resulted in a survival less than the first post-transplantation year (Starzl, et al., 1969).

Though much has advanced since, curing hemophilia through liver transplantation is a well established but not commonly done therapy (Gordon, Mistry, Sabin, & Lee, 1998). This is because of the morbidity associated with transplantation and the established efficacy of the current FVIII replacement regime. To date, only 40 plus
such cases have been reported in literature internationally but is increasing (Bontempo, et al., 1987; Delorme, et al., 1990; Federici, Mannucci, Stabile, Rossi, & Piseddu, 1995; Fischbach & Scharrer, 1993; Ghosh, Marotta, & McAlister, 2005; Gibas, et al., 1988; Lerut, et al., 1995; Lewis, Bontempo, Spero, Ragni, & Starzl, 1985; McCarthy, et al., 1996; Meron, Delius, Campbell, & Turcotte, 1988; Ragni, Dodson, Hunt, Bontempo, & Fung, 1999; Scharrer, Encke, & Hottenrott, 1988; Schliefer, et al., 2000). The first was performed by Lewis in 1985 (Lewis, et al., 1985). The main indications for liver transplant in hemophiliacs are end stage liver disease due to Hepatitis B and/or C where the risk/benefit ratio is justified (Gordon, et al., 1998). These are chronic infections that are always terminally fatal without liver transplant. HIV, Hep B and C are blood-borne diseases and commonly transmitted from pooled plasma before reliable virus-cidal therapy was introduced.

Liver transplantation cures hemophilia; although the patient remains genetically hemophiliac, the new liver synthesizes clotting factors at normal levels within 24 hours of the operation(Gordon, et al., 1998). With appropriate factor replacement prior to the operation, the immediate risks of bleeding during surgery, and arterial thrombosis after transplantation are similar in both hemophiliac and non-hemophiliac patients (Fischbach & Scharrer, 1993). However, there are many benefits to the use of liver transplantation. The expense of transplant surgery and the subsequent anti-rejection therapy may be considerably less than the yearly cost of factor replacement therapy(Gibas, et al., 1988). Authors also note that the survival of HIV-negative hemophiliac liver recipients is similar to that of nonhemophiliacs (Gordon, et al., 1998).

**Challenges**

The drug-induced immune suppression is necessary to prevent organ rejection puts transplant recipients at risk for many of the same opportunistic infections associated with AIDS. Thus, the caveat is that surgical transplantation is only suitable for end-stage liver disease, when the benefits outweigh the risks of transplantation mortality and morbidity (McCarthy, et al., 1996). If transplantation morbidity can be reduced acceptably in the future, liver transplant might be a common and acceptable cure of hemophilia.

Another unfortunate challenge is that even after transplant, if the viral load is not managed, Hepatitis B or C can reinfest the new transplanted organ. In a case, Hep C cirrhosis recurred five years after the transplant (Lerut, et al., 1995).

There is also the operative challenge of maintaining a fine line between coagulopathy and hepatic artery thrombosis. At one extreme, end-stage liver disease together with hemophilia exposes patients to greater risks of bleeding complications during the perioperative period with consequent difficulties in managing coagulopathy (De Pietri, et al., 2008; Gordon, et al., 1998). At the other extreme, thrombosis of the surgically “traumatised” and anastamosed hepatic artery can occur if overuse of coagulation factors occurs(Dargaud, Meunier, & Negrier, 2004). The limited experiences reported by different investigators and the various strategies for clotting factor replacement make it difficult to define a single approach with respect to the
optimal dose and method of administering FIX to achieve perioperative hemostasis and this warrants further research (De Pietri, et al., 2008).

Also, there is the ethical issue of whether liver donors, both live and cadaveric, which are valuable healthcare resources always in shortage, should be used for carriers of Hep C and HIV, which is hard to answer. However with advances in current anti-viral therapy, the prognosis of both Hep C and HIV has improved tremendously. Of course, in Living Donor Liver Transplant (LDLT), the donor’s wishes take paramount importance over such healthcare utility considerations.

It must be emphasised that the main therapeutic purpose of transplant surgery is resection and ‘cure’ of end stage liver disease which have a poor prognosis. Curing hemophilia is an added bonus that should not be the primary purpose of surgery until risks of morbidity associated with transplant can be addressed adequately. Currently, the benefits of saving on the costs and trouble of FVIII replacement do not outweigh the morbidity and mortality risks of transplantation. Current guidelines still advocate the proven exogenous factor replacements (Goodnough, Lublin, Zhang, Despotis, & Eby, 2004; Hoots & Nugent, 2006; White, et al., 2001).

**Conclusion:**

Since hemophiliacs already have a safe and effective mode of clotting factor replacement, any new therapeutic modality must be equally efficacious and provide assurances of the long-term safety. Till date, only the method of liver transplantation is practical and enduringly successful on humans thus far.

The tissue and genetic level of therapy are less invasive and can be deemed as ‘holy grails’ of curing hemophilia. However, they are currently still under trials on animals and humans. So far, they have been proven to be enduringly successful on mice and dogs. Human phase I trials have not been promising due to problems of inadequate takeup and persistent production of therapeutic level of FVIII. A plethora of interesting advances have been developing that will spearhead breakthroughs, including non-viral vectors, transposons, iPES and various enrichment factors (MGMT, FLP) and immunomodulators.

We live in exciting times where we may eventually see a permanent endogenous cure of hemophilia within our lifetimes. We may eventually achieve these holy grails in the future but in the meantime, one should not forget about the surgical avenue of gross liver transplantation.

**References**


sustained in vivo factor VIII expression from lentivirally engineered endothelial progenitors. *Stem Cells, 25*(10), 2660-2669.


Table 1: Human Clinical Gene Therapy Trials

<table>
<thead>
<tr>
<th>Clinical Trial</th>
<th>Hemophilia Type</th>
<th>Vector</th>
<th>Target Cell</th>
<th>Number of Subjects</th>
<th>Success Results</th>
<th>Duration of Factor VIII/IX Expression</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>(D. R. Lu, et al., 1993)</td>
<td>B</td>
<td>Retroviral</td>
<td>Skin Fibroblast</td>
<td>2</td>
<td>1 patient: FIX&gt; 1 IU/dL</td>
<td>6 months</td>
<td>No significant side effect</td>
</tr>
<tr>
<td>(Kay, et al., 2000)</td>
<td>B</td>
<td>AAV</td>
<td>Skeletal Muscle</td>
<td>3</td>
<td>1 patient: FIX&gt;1 IU/dL 3 patients: reduction in Factor Use</td>
<td>4 months</td>
<td>No significant side effect</td>
</tr>
<tr>
<td>(Roth, Tawa, O'Brien, Treco, &amp; Selden, 2001)</td>
<td>A</td>
<td>Fibroblast transfected with FVIII plasmid</td>
<td>Omentum</td>
<td>6</td>
<td>3 patients: FVIII&gt;1 IU/dL</td>
<td>10 months</td>
<td>Invasive laparoscopy No significant side effect</td>
</tr>
<tr>
<td>(Powell, et al., 2003)</td>
<td>A</td>
<td>Retroviral</td>
<td>Blood Mononuclear cells</td>
<td>13</td>
<td>9 patients: FVIII&gt;1 IU/dL 5 patients: reduced bleeding frequency</td>
<td>1 month</td>
<td>Transient positive PCR signal of vector in semen</td>
</tr>
<tr>
<td>(Manno, et al., 2003)</td>
<td>B</td>
<td>AAV</td>
<td>Liver</td>
<td>7 (3 doses each)</td>
<td>2 patients at highest dose: FVIII&gt;&gt;1 IU/dL</td>
<td>2 months</td>
<td>Elevation of liver transaminases Vector DNA in semen</td>
</tr>
<tr>
<td>(Jiang, et al., 2006)</td>
<td>B</td>
<td>AAV</td>
<td>Skeletal muscle</td>
<td>2</td>
<td>1 patient: FIX&gt;1 IU/dL</td>
<td>6 months</td>
<td>No significant side effect</td>
</tr>
</tbody>
</table>

AAV: Adeno-associated virus; FIX: Factor IX; FVIII: Factor VIII; IU: International Units; PCR: Polymerase chain reaction.
Table 2: Stem Cell Cure of Hemophilia in Animal Experiments

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Hemophilia Type</th>
<th>Cell Line</th>
<th>Target Organ</th>
<th>Engraftment procedure</th>
<th>Success Results</th>
<th>Duration of Factor VIII/IX Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Yadav, et al., 2009)</td>
<td>Murine A</td>
<td>Bone Marrow Cells (BMC)</td>
<td>Liver (via Intravenous tail vein)</td>
<td>Acetaminophen to induce liver injury and regeneration incorporating BMCs</td>
<td>25/31 survived tail clip average FVIII level: 20.4%</td>
<td>18 months</td>
</tr>
<tr>
<td>(Kumaran, et al., 2005)</td>
<td>Murine A</td>
<td>Liver Sinusoidal Endothelial Cells (LSEC)</td>
<td>Peritoneal cavity (via Intraperitoneal)</td>
<td>None</td>
<td>6/7 survived tail clip average FVIII level: up to 12%</td>
<td>1 month ongoing</td>
</tr>
<tr>
<td>(Moayeri, Hawley, &amp; Hawley, 2005)</td>
<td>Murine A</td>
<td>Bone Marrow Cells (BMC)</td>
<td>Peritoneal cavity (via Intraperitoneal)</td>
<td>Irradiation or Busulfan</td>
<td>5/6 survived tail clip FVIII level: up to 48%</td>
<td>&gt; 6 months</td>
</tr>
<tr>
<td>(Yadav, et al., 2009)</td>
<td>Murine A</td>
<td>Bone Marrow Cells (BMC)</td>
<td>Liver (via Intravenous tail vein)</td>
<td>Acetaminophen</td>
<td>25/31 survived tail clip average FVIII level: 20.4%</td>
<td>18 months</td>
</tr>
<tr>
<td>(Doering, et al., 2007)</td>
<td>Murine A with anti hFVIII antibodies</td>
<td>Bone Marrow Cells (BMC) encoding porcine FVIII</td>
<td>Blood (intravenous)</td>
<td>Irradiation</td>
<td>11/11 survived tail clip FVIII level: &gt;1U/ml</td>
<td>9 months</td>
</tr>
<tr>
<td>(Matsui, et al., 2007)</td>
<td>Murine A</td>
<td>Blood outgrowth endothelial cells</td>
<td>Subcutaneous depot on neck in a Matrigel scaffold,</td>
<td>Cyclophosphamide</td>
<td>6/6 survived tail clip FVIII level: 22.5mU/ml</td>
<td>7 months</td>
</tr>
<tr>
<td>(Follenzi, et al., 2008)</td>
<td>Murine A</td>
<td>Liver Sinusoidal Endothelial Cells (LSEC)</td>
<td>Liver (via intravenous portal vein)</td>
<td>Fibronectin-like polymer (FLP), Monocrotaline and Low dose cyclophosphamide</td>
<td>13/15 survived tail clip FVIII level: 19.4%</td>
<td>3 month</td>
</tr>
<tr>
<td>(Shi, et al., 2008)</td>
<td>Murine A with anti hFVIII antibodies</td>
<td>Bone Marrow Cells (BMC) encoding platelet only expressed FVIII</td>
<td>Blood (intravenous)</td>
<td>Irradiation</td>
<td>14/16 survived tail clip FVIII level: 0.48 mU/10^8 platelets</td>
<td>12 months</td>
</tr>
<tr>
<td>(Chang, et al., 2008; Jiang, et al., 2006)</td>
<td>Murine B</td>
<td>Haemopoietic Stem cell- derived erythroid cells</td>
<td>Blood (intravenous)</td>
<td>Methylguanine methytransferase (MGMT) and busulfan</td>
<td>All survived tail clip FIX level: (&gt;500 ng/ml).</td>
<td>18 months</td>
</tr>
<tr>
<td>(Xu, et al., 2009)</td>
<td>Murine A</td>
<td>Fibroblast-derived induced Pluripotent Stem (iPS) cell differentiated endothelial cells and progenitors</td>
<td>Liver (direct injection)</td>
<td>Irradiation</td>
<td>6/6 survived tail clip FVIII level: up to 12%</td>
<td>3 months</td>
</tr>
</tbody>
</table>
Efficacy of Prophylactic Measures for Malaria

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Abstract

**Background:** Malaria is a major health problem with over 8 percent of the Indian population exposed to malaria risk in varying degrees. Around 10 percent of malaria cases are reported from the urban areas. Unplanned rapid expansion of urban areas, industrialization without proper drainage facilities, poorly constructed overhead tanks in old buildings, stagnant water at construction sites and abandoned mills have led to mosquitoigenic conditions. The development of supporting infrastructures like rail and roads without keeping in mind the natural flow of surface water have led to the formation of extensive vector breeding grounds.

**Aim & Objectives:** This study aims to determine personal and household measures undertaken for malaria prophylaxis in an endemic area in Mumbai and estimate their efficacy. It will also be analyzed whether the study sample has received accurate health education on malaria related protective measures. The general occurrence of malaria in the study sample will then be ascertained, as well as the cases in the last year and in the last month. It will be determined if any associations can be made between the practiced protective measures and recurrence of malaria. In this way, efficacy of the measures in preventing the incidence of malaria will be estimated.

**Methods:** Using a questionnaire, 200 households from Mumbai’s “E” Ward were covered during the monsoons. Data was analyzed using tables and stacked and clustered column graphs. Variables representing practiced protective measures were cross-tabulated in proportions and frequencies. Logistic regression was used on some variables to determine functional relationships and chi-square test for associations.

**Results:** 73.5% respondents had not received malaria education. 87% respondents mistakenly blamed dirty water for malaria. Only 16.5% knew that construction sites could constitute breeding grounds. There were large gaps between awareness and use of protective measures especially for mosquito nets. 77% households were aware of nets but only 8% employed them. Chi-square test showed a statistically significant association between ongoing construction work and malaria occurrence. Logistic regression also showed construction sites increased the chances of malaria recurrence. 44% respondents practiced ineffective measures like cleaning surroundings and using coils. Chi-square test confirmed that repellent creams and insecticides were effective. Comparison of two groups was done: people who have never had malaria (Group1) and people who have had malaria last year (Group2). Nearly 77% of Group 2 had not used any protective measures while over 65% of Group1 used two-four protective
measures. 70% patients visited private practitioners and 26.5% went untested, and thus undetected, by active government surveillance.

**Study Limitations:** The correct use of preventive measures by respondents could not be verified by observation. The diagnosis of malaria by doctors of laboratories could not be confirmed by an independent test. As with the nature of qualitative research, the results are limited in their ability to be generalized to the wider population.

**Conclusion:** Education focusing on distinction between malaria prevention and anti-mosquito measures, along with the correct usage of protective measures would help prevent malaria. Research into more effective protective measures, containing substances less harmful to human health, such as plant-based repellents is needed.

**Keywords:** Malaria, Prophylaxis, Prevention, Efficacy

**Introduction**

According to the World Health Organization, the number of malaria cases in India account for 60% of cases in the South-East Asia region. Malaria is a major health problem with over 8% of the Indian population exposed to malaria risk in varying degrees. Around 10% of malaria cases are reported from the urban areas. Yet, the actual incidence of malaria may be much higher, as much as 30-fold. Malaria remains endemic in all of India except at elevations above 1800 meters and in some coastal areas.

The private medical care sector is popular and flourishing in India. Private institutions often do not keep or report information related to malaria incidence to Government agencies. Sometimes breakdown of active surveillance machinery causes low reporting of malaria cases. Therefore, the officially reported incidence is considered grossly underestimated. A study in Ahmedabad found that estimated malaria incidence was found to be nearly 9 times more than the numbers reported.

The situation has been made more complicated by rapid development and construction activities in urban areas. A survey conducted in Delhi slums shows that majority of urban slums lack proper sanitation and have poor drainage facilities resulting in water stagnations. The other reasons for the urban malaria problem include non-promulgation of civic laws for elimination of mosquito breeding places, poor case-finding mechanisms and insufficient staff for carrying out anti-larval operations. In Mumbai itself, there were 1,687 cases of malaria in June 2008, while 1,739 people have tested positive for malaria in July 2008 in the civic hospitals alone. Unplanned rapid expansion of urban areas, industrialization without proper drainage facilities, poorly constructed overhead tanks in old buildings, stagnant water at construction sites and abandoned mills have led to mosquitoigenic conditions. The development of supporting infrastructures like rail and roads without keeping in mind the natural flow of surface water have led to the formation of extensive vector breeding grounds. The lower immunity of urban residents to malaria makes these areas more epidemic prone. The main urban malaria vector, *Anopheles Stephensi*
breeds in stored water and domestic containers. Focus is needed more on preventive aspects than treatment of the disease.

This study aims to determine the personal and household measures undertaken for malaria prophylaxis in an endemic area in Mumbai and estimate their efficacy. It will be analyzed whether the study sample has received accurate health education on malaria related protective measures. The general occurrence of malaria in the study sample will be ascertained, as well as the cases in the last year and in the last month. It will be determined if any associations can be made between the practised protective measures and recurrence of malaria. Efficacy of the measures in preventing the incidence of malaria will be estimated.

Use of prophylactic measures are dependent on socioeconomic status which is an important factor associated with malaria. Therefore, households from a middle income group have been enrolled.

This study will demonstrate that the correct and stringent use of personal and household prophylactic measures can in fact prevent malaria and its recurrence to a large degree. The study will also help emphasize that a stronger educational component should be introduced in the National Vector Borne Disease Control Programme (NVBDCP) and the Urban Malaria Scheme (UMS). Health education is necessary to impress upon a population the benefits of personal and household protective measures against malaria. This will prevent and control the incidence of malaria infection in the future.

Material and Methods

Study Area

Mumbai is governed by the civic body Brihan Mumbai Mahanagarpalika. It is divided into 6 zones which include 23 wards for administrative purposes. This cross-sectional exploratory study was conducted in “E” Ward; chosen because it reported maximum number of malaria cases in Mumbai in 2007. From the list of vulnerable areas for malaria in “E” Ward, the Tadwadi Health Post was randomly selected. The Health Officials informed that this malaria endemic Health Post Office covers 18,463 houses and a population of 83,656 people.

Study Population

The households were stratified into residential buildings and chawls.

The sample size was based on the hypothesis that at least 50% of households would be aware of one or the other protective measures against malaria. This is because of the awareness campaign against monsoon related diseases which is under way since the launch of Disaster Management Plan after the deluge of 26th July 2005. The sample size was calculated according to the formula, \( n = \frac{1.96^2 P(1-P)}{e} \) where \( n \) is the sample, “P” is the expected proportion of households aware and “e” is the error of the estimate (+10%).
The sample “n” was multiplied by two because of the design effect associated with cluster sampling. This led to a sample size of 192.

A list of residential colonies was obtained from the Health Post Office and 25 colonies were selected randomly. Selection of the first household was made randomly using the last digit on the currency note. Thereafter eight houses were covered consecutively keeping pace with the time at hand. Thus 200 households in the middle income group were covered.

The interviewed household members were in the age group of 18 years and above and have been living in the specified area for at least one year. Persons were included in the study only if they wished to participate/were co-operative and there was no communication barrier. Locked households on first visit were excluded.

**Ethical Considerations**

The study was initiated after approval from the Ethics Committee of K.J. Somaiya Medical College & Hospital, Mumbai and carried out as per the Ethical Guidelines for Biomedical Research on Human Participants, Indian Council Of Medical Research 2006. A written Free and Informed Consent was taken from all participants.

**Study Methods and Duration**

The structured questionnaire was pilot-tested before being administered and appropriate revisions were made. It was prepared in English and if necessary, verbally translated into Hindi. Door to door interviews were conducted during the months of July and August 2008 because malaria becomes an even more major cause of morbidity and mortality in the midst of the monsoon season.

**Statistical Analysis**

The data was entered in Microsoft Excel 2003 and was analyzed using SPSS 16 (Statistical Packages For Social Sciences Software).

Data has been tabulated and represented graphically in the form of tables and graphs. Some variables have been cross-tabulated in proportions and frequencies. As there are multiple factors, especially behavioral factors, which may be associated with the causation and recurrence of malaria, logistic regression has been used to show the functional relationship between certain variables in our findings more effectively. For the nominal qualitative data, chi-square test has been used to check associations.

**Results**
63% of the respondents were females and 37% were males. None of the households denied participation in the survey. Table 1 gives the age and sex breakdown of the recipients. The mean age of the respondents was 39.

Table 1- Age and Sex Breakdown Of Recipients

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Female</th>
<th>Male</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-25</td>
<td>22.22%</td>
<td>21.62%</td>
<td>22%</td>
</tr>
<tr>
<td>26-55</td>
<td>72.22%</td>
<td>31.08%</td>
<td>57%</td>
</tr>
<tr>
<td>&gt;55</td>
<td>5.56%</td>
<td>47.30%</td>
<td>21%</td>
</tr>
<tr>
<td>Totals</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

94 households were located in chawls, a name for a common housing system in India. The buildings are often 4-5 stories with about 10-20 tenements on each floor. A usual tenement consists of one all purpose room and a kitchen. Families on a floor have to share a common block of 4-5 latrines. 106 households were located in residential buildings.

89.5% of respondents admitted that mosquitoes caused them trouble.

Figure 1 displays the times of the year at which respondents are troubled by mosquitoes.

Figure 2 shows that mosquitoes seem to bite people most at night.
82% of the respondents claimed that they protected themselves from mosquitoes.

**Health Education Related To Malaria**

73.5% respondents claimed that they never received health education related to malaria. Respondents were quizzed on their awareness of potential breeding grounds for malaria-transmitting mosquitoes. They were also asked whether they had stagnant water collection in/around their homes. Their responses are tabulated in Figure 3.

Most respondents specified that open tanks were classified as breeding grounds only if they let the water get really dirty, which they claimed they did not.

When the presence of ongoing construction work was tested for association with the occurrence of malaria in any member of the household in the last one year, using chi square test, the association was found to be statistically ($\chi^2 = 3.187$, D.F. = 1, P value = 0.0742 P<0.1) significant.
Multiple responses were allowed from each respondent \( n=200 \)

![Graph showing potential breeding grounds of malaria-transmitting mosquitoes]

**Figure 3**

**General Malaria Prophylaxis**

The results tabulated in Figure 4 explain which measures respondents took to protect themselves against malaria. “Keeping surroundings clean” was a malaria preventative measure suggested by a conspicuous 77% of the respondents.
Multiple responses were allowed from each respondent \((n=200)\)

**Figure 4**

Over 84% users of coils and/or creams reported only night-time use and only 12% used these measures at dusk and night. Regarding *indoor insecticides*, it was seen
that **mats, vaporizers** and **sprays** were the insecticides of choice. 20.5%, 13.5% and 13% households used mats, vaporizers and sprays respectively. Many used more than one type of insecticide. Of the 25% households that had spraying done in the last twelve months as a prophylactic measure against malaria, **94% thought that the number of bites post-spraying had decreased.** 66% of the respondents said that a household member did the spraying. 28% and 6% engaged a private company to do the spraying and had their home sprayed by a government worker/program respectively.

56% of the participants did not even express any interest in owning a net.

**Episodes of Malaria in the Household**

A total of 971 people have been covered in our survey of 200 households.

**71.2% sought malaria treatment from private establishments.** 5.9% have obtained malaria medication directly from a pharmacy without medical consultation or testing.

A majority of 61.8% do not remember what treatment was given. Less than half were able to recall the name “chloroquine”, the main drug for malaria treatment.

![Figure 5](image)

Figure 5

From Figure 5, it is clear that a large number of malaria cases last year, in this study sample at least, missed the net of government surveillance and were officially undetected.

To study whether or not the recurrence of malaria of any member of the household was affected by the breeding grounds for mosquitoes and use of the preventive measures, **logistic regression** was performed. The variables in Table 2 are found to be statistically significant as p-value (Sig in the Table 3) P< 0.10 for these variables.
Table 2: Variables in the Equation

<table>
<thead>
<tr>
<th>Step 1(a)</th>
<th>B</th>
<th>S.E.</th>
<th>Wald</th>
<th>df</th>
<th>Sig.</th>
<th>Exp(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing Construction Work</td>
<td>0.961</td>
<td>0.477</td>
<td>4.05</td>
<td>1</td>
<td>0.044</td>
<td>2.614</td>
</tr>
<tr>
<td>Potted Plants</td>
<td>1.803</td>
<td>0.597</td>
<td>9.114</td>
<td>1</td>
<td>0.003</td>
<td>6.067</td>
</tr>
<tr>
<td>Using Insecticides and sprays</td>
<td>-0.877</td>
<td>0.414</td>
<td>4.494</td>
<td>1</td>
<td>0.034</td>
<td>0.416</td>
</tr>
<tr>
<td>Using Creams/ Lotions</td>
<td>-0.778</td>
<td>0.423</td>
<td>3.384</td>
<td>1</td>
<td>0.066</td>
<td>0.459</td>
</tr>
<tr>
<td>Constant</td>
<td>-0.786</td>
<td>0.446</td>
<td>3.104</td>
<td>1</td>
<td>0.078</td>
<td>0.456</td>
</tr>
</tbody>
</table>

The following variables are found to be statistically significant as p-value (Sig in Table 2) P< 0.10 for these variables:

1. Presence of ongoing construction work around the house
2. Presence of plants outside the house
3. Use of insecticides/ sprays as a protective measure for prevention of malaria
4. Use of creams as a protective measure for prevention of malaria

Efficacy of Protective Measures

To confirm the results obtained by logistic regression for the protective measures, chi-square test was performed using those variables which denoted the most popularly used protective measures of our respondents:

- Creams/Lotions
- Coils
- Insecticides/Sprays
- Keeping surroundings clean
- Use of traditional plants

Mosquito nets and other methods which were used by less than 10% of the study sample were not tested for association.

It may be noted that of the minority 8% households that used a mosquito net, all the respondents found the net effective and none who had been using the net had ever had malaria. (These were mostly children)

When the use of repellent creams/lotions as a preventive measure was tested for association with the recurrence of malaria in any member of the household, using chi square test, the association was found to be statistically ($\chi^2 = 3.910$, D.F. = 1, P value = 0.048 P<0.1) significant.
When the use of coils as a preventive measure was tested for association with the recurrence of malaria in any member of the household, using chi square test, the association was found to be statistically ($\chi^2 = 0.767$, D.F. = 1, P value = 0.381 $P>0.1$) insignificant.

When the use of insecticides/sprays as a preventive measure was tested for association with the recurrence of malaria in any member of the household, using chi square test, the association was found to be statistically ($\chi^2 = 7.550$, D.F. = 1, P value = 0.006 $P<0.1$) significant.

When the practice of keeping surroundings clean as a preventive measure was tested for association with the recurrence of malaria in any member of the household, using chi square test, the association was found to be statistically ($\chi^2 = 3.841$, D.F. = 1, P value = 0.05 $P<0.1$) significant.

When the use of plant based repellents as a preventive measure was tested for association with the recurrence of malaria in any member of the household, using chi square test, the association was found to be statistically ($\chi^2 = 0.884$, D.F. = 1, P value = 0.347 $P>0.1$) insignificant.

In Figure 6 and Figure 7, a comparison has been done between

- People who have never had malaria: These have been more inclined to use protective measures with many people using multiple protective measures.

- People who have had malaria last year: Majority were not using any protective measures or were employing one or more protective measures very sparsely.

![Figure 6](image_url)

Figure 6
**Discussion**

63% respondents were found to be female and about 72% of these were in the age group of 26-55 years reflecting the fact that interviews were carried out during daytime when most women were at home and men were out working. This is supported by the fact that in the older (retired) age groups there were more male than female respondents. The sex bias is not considered problematic since women of child-bearing age are not only the care-takers of the household but also considered the gatekeepers to household adoption of protective measures against malaria.

Though mosquito density is highest in the monsoons, almost 66% respondents have complained of mosquito trouble throughout the year. This may be due to the perennial nature of mosquito breeding sites in urban areas such as construction sites and open
drains/gutters. Also, studies\textsuperscript{14} show that \textit{Anopheles stephensi} is an important vector of malaria in urban areas, especially in India and is found throughout the year.

43\% and 18.4\% respondents complained of mosquitoes biting at nights and at dusk extending into the night respectively. The malaria transmitting mosquitoes – \textit{Anopheles} species- are known to bite at night including \textit{Anopheles stephensi} which bites mostly at nights before midnight\textsuperscript{14}. A significant 30.2\% respondents alleged daytime biting which is a cause of concern too as the dengue-transmitting Aedes mosquito is a daytime biting mosquito.

As this is an urban study, monetary restrictions or lack of availability of protective measures were not marked obstacles and at least one method of malaria prevention was in use by most respondents. 73.5\% respondents cited that they had never received any form of health education related to malaria. The apathetic state of health education on malaria has probably led to inadequate personal and household malaria preventive practices. Using Lao PDR\textsuperscript{15} as a model, school children could act as health information messengers from schools to communities for malaria control. Health education was found to play a major role in malaria control and was the main reason for increase in knowledge of the disease in Equador and Nicaragua\textsuperscript{16}.

The respondents’ awareness levels of various potential breeding grounds of malaria-transmitting mosquitoes shed light on several important facts.

- 87\% knew that open toilets were breeding grounds while only 16.5\% knew of construction sites.
- The recent and current spate of intense construction activity in Mumbai with the erection of numerous high rises is evident when 74\% respondents say that there is ongoing construction activity in the neighborhood. Yet, too few are aware that it implies a neighboring mosquito breeding ground. A one year long longitudinal study\textsuperscript{17} found that the habitat-wise proportion of \textit{Anopheles stephensi} was highest in masonry tanks followed by overhead tanks, curing water at construction sites etc.
- Open gutters were also incriminated by respondents though only 17\% had open toilets near their home.
- Most of the respondents, who chose “open tanks” as a potential mosquito breeding ground in a multiple choice question, specified that it classified as a potential mosquito breeding ground only when the water lasted more than a week and got dirty. Evidently, a higher percentage of respondents consider \textit{dirty} stagnant water (open toilets, open gutters/drains) to be potential malaria mosquito breeding grounds as compared to simply stagnant or clean stagnant water.

The above is further emphasized when it is learnt that 77\% respondents suggested that “Keeping surroundings clean” was a malaria preventive measure. In another recent study\textsuperscript{18} majority of the respondents had mentioned that malaria vectors breed in dirty stagnant water. The most likely reason for this is the incorrect dissemination of malaria education messages. The message “Clean up the surroundings of the house” (which means cutting grass, clearing up water containers and puddles) is aimed at reducing mosquito breeding and hence malaria. However, although some mosquito
species breed in close association with humans, Anopheles mosquitoes do not breed in dirty water (preferring small bodies of unpolluted water usually some distance from human habitation). Anopheles stephensi may breed in jars or cisterns. As an intervention, clearing up around houses has no impact on malaria disease whatsoever. In malaria related health education messages, we may need to address this inaccuracy directly and focus on preventing malaria by preventing mosquito bites alone and not by trying to reduce mosquito breeding sites.

As expected, when logistic regression method was used in our study, the impact of the presence of open toilets and open gutters/drains on the recurrence of malaria in any member of the household was seen to be insignificant. This helps prove that the malaria transmitting Anopheles are partial to clean stagnant water.

In our study, a significant association was found between ongoing building construction work and the occurrence of malaria in any member of the household in the last one year by chi square test. Since in Table 2, the value B=0.961, we can say that as the number of households having ongoing construction work around the home increases, the chance of having recurrence of malaria in the household increases. Legislative measures and building by-laws must be in place and rigidly followed during the construction phase and proper maintenance should be ensured to prevent mosquito breeding.

Open tanks do not appear to have any impact on the recurrence of malaria in any member of the household as per logistic regression method. These would be potential Anopheles breeding grounds, but the question was misunderstood. Respondents confused “drums” and “tanks”. These drums did not contain stagnant water as the water was constantly disturbed by daily removals. It logically follows that these would not be responsible for malaria.

In our study, recurrence of malaria was seen to depend on the presence of potted plants. This was noticed in an urban Delhi study too. Since in Table 2, the value B=1.803, we can say that as the number of households having potted plants in/around the home increases, the chance of having recurrence of malaria in the household increases. Plants make excellent resting sites for Anopheles mosquitoes during the day. In many urban homes in Mumbai, potted plants were seen to be arranged in long trays on shelves outside the window. Excess water from pots, as well as clean water spilled during watering, stagnate here and develop into a breeding ground.

While tracking the episodes of malaria in each household, it emerged that over 70% people visited private practitioners for treatment. 26.5% of those who had malaria last year were not tested and of these 72% and 28% went to private establishments and pharmacies respectively. There is no denying that there has been an impressive growth of India’s private health sector during the past decade. Yet, a similar study in Mumbai found that many practitioners did not rely on a peripheral blood-smear test to make a diagnosis and gave one day treatments in response to patient demands and to retain their popularity and patronage. A large number of malaria cases, as proved in our study, were undetected by active government surveillance.

In the study a large gap was obvious between awareness and usage of various malaria preventive measures. The most prominent gap was seen for mosquito nets with 77% being aware but only 8% households using them. 56% of our respondents were not
even interested in owning a net. In this study, logistic regression showed no relation between mosquito nets and malaria prevention as the sample using nets was miniscule.

However there can be no doubt that insecticide treated mosquito nets remain one of the most fool-proof measures of malaria prevention.

In recent years, Insecticide Treated Nets (ITN)/ Long Lasting Insecticidal Nets (LLIN) have proved effective against vector borne diseases especially malaria. In a previous study amongst fever patients in India, respondents mentioned mosquito net as a prime preventive measure against mosquito bite. Numerous studies in Gambia and Suriname have demonstrated that mosquito nets provide privacy and a barrier to mosquito’s nuisance.

Creams and lotions when applied to all exposed portions of the body especially the necks, wrists and ankles, may confer protection even up to 4-6 hours. Since, in Table 4, the value $B=-0.778$, we can say that as the number of people who use creams as the protective measure increases the chances of having recurrence of malaria decreases. The chi-square test too confirmed the association between use of creams and prevention of malaria recurrence.

The recurrence of malaria in any household member appeared to be independent of the use of coils by logistic regression and chi-square test. This is due to a variety of reasons. Studies have shown that coils are not very effective against malaria. A WHO Report states that coils are of “doubtful effectiveness”. Yet, they do confer a certain degree of protection. Unfortunately, majority of the respondents use coils at nights only. Coils have to be switched on at dusk and rooms should not be well-ventilated. Breeze may dampen the effect of the coil. In Mumbai homes, especially in summer, this is not feasible. There are health concerns over the use of coils too.

Considering indoor insecticides and sprays, logistic regression method (Table 2) showed that as the value $B=-0.877$, we can say that as the number of people who use insecticides(mats and vaporizers) and sprays as the protective measure increases, the chances of having recurrence of malaria decreases. Chi square test confirmed this association. Yet, these should not be used indiscriminately for fear of spawning insecticide resistance or affecting health adversely. For the purpose of calculation, these two measures were clubbed together. It must be realized that many respondents used more than one type of mats, vaporizers or sprays. Like coils, mats and vaporizers too, are subject to ventilation.

25% of our respondents have used sprays of which 66% used household sprays available in the market and carried out the spraying themselves. This casts doubts on the effectiveness of the spraying technique as not all the home spraying may have been done adequately all over their home or enough number of times. Peak vector biting occurs at night when people are asleep and during the day mosquitoes rest in the unsprayed rooms, so there is urgent need to inform people about the significance of spraying all of their rooms including the kitchen and worship-room to boost the malaria control program.
Not all available household sprays utilized are effective. It is also not clear if household members sprayed only at floor level or whether hanging fabrics such as curtains have been sprayed regularly.

In fact, the main malaria vector in Mumbai, *Anopheles stephensi*, is discovered to rest at a height of at least 30cm above ground level and selects hanging objects for resting.14

Unlike the logistic regression method, the chi-square test showed an association between keeping surroundings clean and recurrence of malaria in any member of the household. As discussed before, keeping the surroundings clean has no impact on malaria transmitting mosquitoes while it does prevent other mosquitoes breeding. Yet, Figure 6 also shows that people who have never had malaria have concentrated on keeping their surroundings clean unlike those who had malaria in the previous year. This disparity can be explained when we consider that those are the more health-conscious and/or educated people, who adopt multiple malaria preventive measures and have a more positive attitude towards health and its promotion, especially at prevention level. They would be likely to keep their surroundings clean to prevent other diseases besides malaria hence the result of the chi-square test.

Logistic regression method (Table 2) and chi-square method showed that plant-based repellents did not influence the recurrence of malaria. However, our study shows that of the plant-based repellents in use, nearly 74% consisted of just placing the *Tulsi* plant at home to ward off mosquitoes. This would have limited, if any, effect on the incidence of malaria. *Neem* and other plant-based products, as discussed later are showing promise in terms of malaria prevention.

From Figure 6 and Figure 7, we can come to only one indisputable conclusion. Even if the individual capacity of various practiced protective measures to actually prevent malaria is debatable and the exact methods of use are ambiguous, there is no doubt that when they are combined randomly, they are proving efficient. The cumulative effect serves to offer some degree of protection.

In Mumbai, people’s capacity to buy repellents is increasing steadily. Most commercially available repellents i.e. coils, creams/lotions, mats, sprays, vaporizers contain pyrethroids as the principal ingredient. Studies30 show a myriad of health hazards and risks posed by hydrocarbon and other fillers in these repellents such as changes in the tracheal and alveolar epithelium, reproductive dysfunction, development impairment and cancer. Pyrethroids and DEET (N, N-Diethyl-meta-toluamide) themselves, have had adverse effects on human health.

Though burning mosquito coils indoors generates smoke that can control mosquitoes to some extent, the smoke contains pollutants of health concern. A study31 identified carcinogens in the coil smoke and suggested that exposure to the smoke of one mosquito coil would release the same amount of PM2.5 mass as burning 75-137 cigarettes.

As per the WHO and NVBDCP, Indoor Residual Spraying (IRS) is a highly effective measure against mosquitoes and hence malaria. If carried out by trained personnel on the walls and ceilings of dwellings, it is a cost-effective and efficient vector control method. Yet indiscriminate use of household sprays by the public has led to
development of resistance. Of the six principal vector species, two, namely An.culicifacies and An.stephensi have begun to show wide spread resistance. Chemical sprays are in any case very dangerous to the environment and human health.

Neem oil, extracted from the seeds of Azadirachta indica was used in a study. Neem cream was found to be a safe and suitable alternative to insecticide impregnated coils.

An effective result was obtained by vaporizing neem oil from mats: 5% neem oil was more effective at reducing both biting and numbers of resting mosquitoes than 4% allethrin on mats. Neem oil (0.01-1 %) mixed in kerosene and used as an insecticide reduced biting of human volunteers and catches of mosquitoes resting on walls in the rooms. Several other studies propagate the use of neem, derivatives of lemon eucalyptus plant and essential oils for preventing mosquito bites.

It is suggested that further research be done in the area of plant-based repellents as they show tremendous potential fighting the onslaught of malaria. More detailed studies should be undertaken in urban areas of India to determine volume of use and subsequent health effects of various protective measures, such as coils, creams, mats, vaporizers and sprays of Indian brands.

Conclusions

Large gaps are present between awareness and correct practice of protective measures. A few grey areas have been identified. The line between anti-malaria measures and eradication of mosquito menace needs to be distinctly defined since vague awareness does not translate as complete knowledge. Educating urban residents on all aspects of malaria (such as Anopheles breeding grounds) is the need of the hour. Prophylactic measures are being undertaken but as they are based on the shaky foundation of out-dated concepts and sketchy hearsay, they are proving deficient. The high rate of occurrence and recurrence of malaria in the urban population is being masked due to lack of testing and fractional reporting by private practitioners, as is seen in this study. Discovery and research into more effective, longer-acting personal and household protective measures which incorporate substances less damaging to human health, such as plant-based repellents, is the order of the day. To this end, innovative approaches and alliances must be forged to increase financing and improve research efforts.

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Therapeutic and Clinical Applications of L-Carnitine and its Congeners as a Potent Nutrigenomic Membrane Molecular Antioxidants in Health and Disease

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Abstract

L-Carnitine (LC) otherwise known as Vitamin B₆ (β-hydroxy-γ-trimethyl amino butyric acid), a conditionally essential quaternary amine, plays a vital role in lipid metabolism and production of ATP through β-oxidation and subsequent oxidative phosphorylation. Although L-carnitine was originally discovered in 1905, its crucial role in metabolism was not elucidated until 1955, and primary L-carnitine deficiency was observed in a variety of nutritional deficiencies, diabetes, male infertility and aging was not described until 1970s. Therapeutic applications and pharmacological effects of L-Carnitine and its congeners were studied through a systematic review of the literature by searching MEDLINE, Current Contents, Entrez PubMed from 1960 to Dec 2009 and delineated the molecular mechanism of Levo-carnitors as a nutrigenomic regenerative antioxidants. On administration L-Carnitine will be converted in to its acyl derivatives and can easily penetrate in to the membranes and blood brain barriers. There is a decrease in the concentration of carnitine in blood and tissues in a variety of nutritional deficiencies, metabolic syndromes, pathological conditions and xenobiotics-induced toxicities including antibiotics and antineoplastic agents and heavy metals. Carnitine enhances glycolytic and TCA cycle enzymes, insulin-like growth factor (IGF-1) and exerts insulin mimetic effect and prevents the formation of advanced glycation end products (AGEPs). On supplementation carnitine and its derivatives interacts in the membrane molecular level and enhances expression of uncoupler of oxidative phosphorylation, leptins and adipokinins and certain lipolytic enzymes, thyroid hormone receptor activity, alleviates alcohol induced toxicities and spares choline and methionine hence exerts hypolipidemic antiatherosclerotic effects. Carnitine increases lipoprotein lipase activity, prostacyclin (PGI₂), HDL-C and heat-shock protein biosynthesis and decreases LDL-C, plasma fibrinogen and serum homocysteine levels and hence reduces the risk factors of thrombogenic burden and Cardiovascular Diseases (CVS). Carnitine exerts hypolipidaemic effect by augmenting β-oxidation of long chain fatty acids, inhibiting the activity of HMG-CoA reductase the rate limiting enzyme in cholesterol biosynthesis as well increasing bile salts and bile acid synthesis by sparing vitamin C which is also one among the precursor of carnitine biosynthesis in vivo. Carnitine alters membrane fluidity and increases membrane stability, inhibits xanthine oxidase.
(XO) and neutrophil superoxide radical formation, prevents the accumulation of protein carbonyl content (PCC), sequestrates calcium, chelates iron and hence prevents lipid peroxidation (LPo) and exerts anti-anaemic effect, increases poly(ADP)ribose polymerase and hence prevents DNA single strand breaks and ameliorates point mutations and exerts anti-mutagenic and anticancer effects. L-Carnitine increases mitochondrial electron transport chain (ETC) complex enzymes, prevents mitochondrial myopathies, increases urea cycle enzymes. A 3-hour pre-treatment with L-Carnitine increases the expression of brain m-RNA in aged rats and augments neuronal DNA biosynthesis and neurotrophic factors and hence exerts anti-ageing effects. L-Carnitine enhances immunity, spares / increases protein synthesis, increases melatonin biosynthesis in addition maintains normal metabolism in a variety of pathological conditions and experimental studies. L-Carnitine prevents oxidative stress, apoptosis and enhances nitric oxide radical (NO) and prostaclin (PGI₂) synthesis and enhances sperm count and motility activity and beneficial in erectile dysfunction. L-Carnitine and its derivatives are potent hypoglycemic, lipotropic, immuno-modulatory, xenobiotics-detoxifying, proteogenic, membrane stabilizing, iron-chelating, antiperoxidative, antimutagenic, anti-aging antioxidants. Hence Levo-carnitines are potent nutrigenomic regenerative molecular medicines, and its supplementation will be beneficial in health and disease as well as aquaculture and agriculture especially during infection.

Keywords: L-Carnitine, hyperlipidaemia, erectile dysfunction, immunomodulation, nutrigenomics, anti-aging antioxidants.

Introduction

L-carnitine is a conditionally essential quaternary amine plays a vital role in the metabolism (Rebouchi and Engel, 1981). Ascorbic acid, lysine, methionine, vitamin B₆ and iron are the precursor molecules and cofactors required for the biosynthesis of carnitine (Rebouche, 1991). Carnitine deficiency is associated with innumerable pathological conditions and nutritional deficiencies (Walter, 2003; Thoma and Henderson, 1984; Stevens et al., 1996; Loots du et al., 2004). Iron deficiency limits carnitine biosynthesis and at the same time impedes haematopoiesis. Acetyl-L-carnitine, can easily cross the blood-brain barrier to improve energy transport and repair mechanisms in nerve tissue. Supplementation of carnitine improves overall energy metabolism and ameliorates toxicities induced by a variety of genotoxic agents and xenobiotics (Loots du et al., 2004; Challoner et al., 1971). Carnitine exerts neuroprotective effect by forming acyl derivatives with a variety of xenobiotics and enhances the clearance and mitigates the toxic onslaught of the xenobiotics (Mazzio et al., 2003; Virmani et al., 2002). Administration of several antibiotics causes carnitine depletion and hence carnitine supplementation is recommended (Arrigoni-Martelli & Caso, 2001; Deeks, 1998; Melegh et al., 1990, 1993 & 1997; Kopple et al., 2002). Carnitine enhances thermonerin and bile acids biosynthesis and hence prevents obesity (Sundin et al., 1987; Cha, 2008). Fe²⁺ and Fe³⁺ ions are involved in the triggering of peroxidation reactions, with radicals, and their consequent catalytic effects, being released in a primary reaction. These hydroxyl radicals (OH) continue the peroxidation reaction, which eventually results in the destruction of membrane.
Propionylcarnitine appears to sequester the Fe$^{2+}$ ions (Reznick et al., 1992) thus preventing them from taking part in the primary reaction. Supplying L-carnitine can prevent the formation of radicals and propionyl carnitine itself need not be given since L-carnitine is converted into propionyl carnitine inside the cell. Reichmann et al (1994) found that erythrocytes contain about four times as much L-carnitine (240 μmol/l) as the ambient blood plasma (60 μmol/l). In erythrocytes, L-carnitine occurs mainly in its esterified form (approximately 10 times the concentration found in plasma), and helping to stabilise the cell membrane and acting as a buffer for Na-K-ATPase. Carnitine enhances membrane stability (Berard & Idorche, 1992), ameliorates metal ions and ammonia induced toxicities (Belli, 1988; Matsuoka, H; Igisu, 1993; Tremblay & Bradley, 1992) in addition chelates iron (Reznick et al., 1992), sequestrates Ca$^{2+}$ (Messineo et al., 1982), and increases liver P450 detoxification support by enhancing drug-metabolizing enzymes and prevents lipid peroxidation induced by environmental pollutants (Messineo et al., 1982; Alvarez, 2005; Dayanandan et al., 2001). It has been shown that acyl carnitine can facilitate the ATP-free incorporation of both long and short-chain activated fatty acids into phospholipids of the erythrocyte membrane (Arduini et al., 1993), thus contributing to a loosening of molecular packaging of polar phospholipids in the bilayer region. Through administration of L-carnitine and the resulting improvement of membrane properties it is probably possible to increase the life of the erythrocyte membrane and reduce haemolysis (Ahmad et al., 1992). As a result, for a constant rate of haematopoiesis there is an increase in haematocrit value, thus facilitating more economical use of the expensive haematopoietic hormone, erythropoietin. A deficiency of L-carnitine in blood plasma resulted in weakening of the erythrocyte membrane and an increased rate of haemolysis and ultimately anaemia (Tein et al., 1992). The key to improving oxygen supply and increasing erythrocyte stability lies modulating lipid composition of the erythrocyte membrane and in increasing the activity of Na-K-ATPase. Donatelli et al (1987) observed that administration of L-carnitine resulted in an increase in Na-K-ATPase activity, in erythrocyte count, and also in haematocrit and haemoglobin values. In a placebo-controlled study with 24 patients, each of whom received 1,000 mg L-carnitine every time they had dialysis treatment, it was possible to save 38% of administered haematopoietic hormone, erythropoietin (Labonia et al., 1995). Carnitine detoxifies potent hepatotoxic/carcinogenic xenobiotics and exerts antimutagenic/anticarcinogenic effects (Yatim & Sachan, 2001; Sachan & Yatim, 1992; Boerrigter et al., 1993). Carnitine prevents anthracycline-induced toxicities in sarcoplasmic reticulum by sequestering calcium (Ronca-Testoni et al., 1992). No toxicity related to L-carnitine therapy was observed and dose reductions were not necessary (De Simone et al., 1982; Franceschi et al., 1990). Pola et al (1991) observed as a result of L-carnitine a reduction in the time taken for haemofiltration and an increased erythrocyte flow rate. Fritz et al (1991) were able to show that, in contrast to choline or β-methylcholine, L-carnitine prevented fibrinogen-mediated aggregation of erythrocytes, and thus discouraged thrombosis (Martinez, et al., 1993). Corsico et al (1993) noted that free L-carnitine and short-chain L-carnitine esters protect against the occurrence of vascular lesions. Other studies have shown that L-carnitine enhances the blood supply to peripheral vessels (Corsico et al 1993), and protects endothelial cells against permeability changes caused by lipopolysaccharides, tumor necrosis factor-α (TNF-α) or other inflammatory factors (Uhlenbruck, 1996). The vascular dilatational effect, and the resulting improvement in circulation, might also be responsible for side effects such as increased alertness, hyperactivity and sleeplessness, which have
frequently been reported (Tesch et al., 1994). Carnitine possesses a versatile immunoprotective effect in a variety of experimental studies (Deufel et al., 1984). Carnitine increases the monoclonal antibody production of mouse-hybridoma cells in culture (Athanassakis et al., 2001). Carnitine increases humoral immune response, antigen-specific IgG and overall immunity, and improves metabolic parameters of AIDS patients (Patrick, 2000). Dietary L-carnitine supplementation (100 mg carnitine/kg added to feed) increases antigen-specific IgG production in broiler chickens (Mast et al., 2000). L-carnitine therapy also led to a drop in the frequency of apoptotic CD4 and CD8 lymphocytes and increases T cell counts (Athanassakis et al., 2003). L-carnitine modifies the humoral immune response in mice after in vitro or in vivo treatment, preliminary observations suggest that L-carnitine-preloading also protected peripheral blood lymphocytes from old donors when such cells were exposed to an oxidative stress (Boerrigter et al., 1993).

L-carnitine treatment which was accompanied with a significant enhancement of chemotactic and phagocytic activity being restored to control levels, these findings demonstrated that L-carnitine is capable of restoring the age-related changes of neutrophil functions (Moraru et al., 1990). L-carnitine increases the proliferative responses of both murine and human lymphocyte following mitogenic stimulation and increase polymorphonuclear chemotaxis (Moraru et al., 1990). Increase of specific antibody response to bovine serum albumin in pigeons due to L-carnitine supplementation has been reported (Janssens et al., 2000). A new class of carnitine derivative antimicrobial amphiphile, "soft", quaternary ammonium L-carnitine esters, of the type (CH$_3$)$_3$N$^+$-CH$_2$-CHOCO(R$_1$)-CH$_2$-COO(R$_2$) Cl$^-$, shows good activity against a wide range of bacteria, yeasts, and fungi, and exerts antiviral effect (Kang et al., 1992). L-carnitine reduces lymphocyte apoptosis and oxidant stress in HIV-1-infected subjects treated with zidovudine and didanosine (Deeks, 1998).

Leukocytes (granulocytes, monocytes and lymphocytes) are relatively rich in L-carnitine (Deufel et al., 1990). This provides an initial indication of the importance of L-carnitine in respect to immunological processes. Böhles et al (1994) observed a massive increase in L-carnitine content in granulocytes and lymphocytes in cases of bacterial infection and Crohn's disease. Activated leukocytes consume up to 50% of their intracellular L-carnitine reserves within just one hour, and are thus dependent on a rich supply if they are to maintain a high level of activity (Guzman et al, 1996), through the administration of L-carnitine it is also possible to produce a dose-dependent increase in leukocyte ATP production.

AIDS patients were found to have depressed levels of plasma L-carnitine and low T-lymphocyte counts. Leukocyte L-carnitine levels were also depressed and administration of 2-6 g/d L-carnitine supplement improved these patients immune status (De Simone et al (1994). Jirillo et al (1991) and (1993) found that as an immunostimulant L-carnitine was capable of helping in the treatment of infections such as tuberculosis and leprosy. Various authors have reported on the mitigating and protective effects of L-carnitine in the treatment of septic shock (Fritz and Arrigoni-Martelli, 1993; Uhlenbruck, 1996; Famularo and De Simone, 1995). Eighteen patients, who had been unresponsive to other forms of therapy, were given L-carnitine. In 14 of the patients (80%) the trophic lesions and ulceration of the skin disappeared completely. In another study, improved healing of ulceration wounds on the extremities was observed (Pola et al., 1991).
Carnitine and its derivatives interacts in the molecular level and anneals the DNA-single strand breaks (DNA-SSBs) induced by xenobiotics (Boerrigter et al., 1993) and age-related mitochondrial DNA deletions (Hagen et al., 2002) by increasing poly (ADP)-ribose polymerase (Monti et al., 1992), prevents apoptosis and alters gene expression (Moretti et al., 1998; Angelucci et al., 1988; Horiuchi et al., 1992). L-carnitine and its derivatives increases cytochrome oxidase subunits (Gadaleta, et al., 1990), enhances age-related reduction of mitochondrial DNA transcription (Gadaleta et al., 2005), increases heat shock protein HSP in the brain (Abdul et al., 2006). Several studies on pigs, fish, foal, quail and broiler chickens demonstrate a positive nitrogen balance and growth improvement by feeding extra dietary L-carnitine (Greenwood et al., 2001; Owen et al., 2001). Carnitine enhances the biosynthesis of DNA, RNA and ultimately proteins (Juliet et al., 2005; Torreele et al., 1993) and exerts hypolipidemic effect (Dayanandan et al., 1994) and alters acetyl CoA/CoA pool and enhances acetyl CoA decarboxylase (Hotta et al., 1994). Carnitine exerts sparing effect on protein, lysine, vitamin C, methionine, thiol, reduced glutathione, creatine phosphate and erythropoietin (Takada et al., 1987; Hoffman et al., 1992; Hibbert et al., 1986; Sushamakumari et al., 1989; Khairallah & Wolf, 1985; Takada et al., 1987; Horl, 2002; Levine et al., 2003). Brevetti et al (1988) observed in patients with circulatory disorders of the legs, peripheral occlusive arterial disease, Claudicatio intermittens, (shop-window leg) a doubling of the pain-free distance that could be covered in 33 male test persons following administration of 2x2 g of L-carnitine / day. In Untrained test persons, supplementation of LC 3g/day led to a significant reduction in muscle pains, in muscle weakness following exertion, and in damage to the musculature compared with those who had been given a placebo (Giamberdino et al., 1996). The test persons performed identical levels of physical exertion to the point of muscle damage, following which the damage was ascertained. L-Carnitine produced better results than the placebo. A series of pathological disorders, including cardiac arrhythmias and fibrillation as a result of ischaemia and oxidative stress are closely linked with the integrity of membranes (Fritz and Arrigoni-Martelli, 1993). Researchers have observed that the addition of L-carnitine and propionylcarnitine facilitates the repair of damaged phospholipids (Arduini, 1993 & 1995). In rowers, cyclists and marathon runners, L-carnitine was found to increase physical performance and reduce recovery times (Angelini 1986; Cooper, 1986; Corbucci 1984; Dragan 1984; Eclache 1984; Frösch, 1994; Lehmann-Bouri, 1994). In the case of poliomyelitis patients, the increase in physical strength and bodily performance achieved through the administration of L-Carnitine is so great that it is now recommended globally by the Polio Association (1993) (Frosch, 1994), while in Germany the health insurance companies reimburse the costs of treatment. The described clinical data have been confirmed in muscle biopsies, which have demonstrated a L-carnitine-mediated increase in muscle energy production and oxygen uptake (Angelini, 1986; Cederblad, 1976; Maggiani et al., 2000).

Considering the large number of studies demonstrating a reduction in plasma triglycerides by

L-carnitine, one is bound to ask whether they were actually used in energy production, or instead perhaps incorporated into fatty tissue or excreted. Evidence that L-carnitine increases fatty acid oxidation has been reported by various research groups (Scholte et al., 1979). Administration of L-carnitine was found to increase lipolysis, and thus improve the utilisation of body fat reserves. Following
administration of L-carnitine, an increased rate of long-chain fatty acid oxidation was observed, indicating improved energy production; in addition, a positive nitrogen balance was achieved more speedily (Heller et al., 1986). Owen et al (1996) were able to demonstrate that L-carnitine supplementation increased palmitate oxidation, the amount of branched amino acids, and protein synthesis in the liver of live pigs. At the same time, a significant reduction in total body fatty in the L-carnitine group, compared with the control group, was observed. Increased levels of branched amino acids as a consequence of L-carnitine administration has also been reported by Berchiche et al (1994). L-carnitine increased the proportion of branched amino acids from 22% to 41%. In *in vivo* experiments with human skin tissue, Tein et al (1990) found increases in fatty acid oxidation, protein synthesis and protein content (BCAA’s) following topical application of L-carnitine (Scholte et al 1979). Heller et al (1986) observed that administration of carnitine promoted the burning of long chain fatty acids (LCFAs), thus improving energy production, and also promoting the re-establishment of a positive nitrogen balance. L-Carnitine was found to increase BCAA’s from 22 to 41%, which, following physical stress, means that more of these amino acids are available for protein synthesis and muscle building, thus producing a better training effect (Berchiche, 1994). Lohninger et al (2000) elucidated the genetics of how the administration of L-carnitine results in an increased production of IGF-I. Ahmad et al (1990), found that long-term L-carnitine supplementation increased physical performance and had a trophic effect on the skeletal muscles of haemodialysis patients, while the levels of urea, serum creatinine and phosphate in the patients' blood were decreased. Spagnoli (1990) found that one year of L-carnitine supplementation had an anabolic effect on the skeletal muscles of haemodialysis patients, producing an increase in muscle size and in body weight. Within 12 months L-carnitine led to growth of type-I muscle fibres, but after L-carnitine supplementation was discontinued muscle fibre diameter decreased. Serum albumin also increased during supplementation by increased hepatic protein biosynthesis, as did the haematocrit value. Brevetti et al (1988) found that long-term L-carnitine supplementation increased physical performance and had a trophic effect on skeletal muscle in patients with peripheral vascular occlusion disease. L-Carnitine has long been given to patients being fed parenterally, in which it reduces significantly the catabolism of muscle tissues (Böhles, 1985).

IGF-I is a potent growth factor which promotes the production of fat-free muscle tissue in the body. In a study with pregnant sows, which were given L-carnitine, the piglets developed more red muscle fibre and contained less fat while still in their mother's womb. Following birth, 1-2 more piglets per litter survived and were stronger; they grew more quickly and retained their favourable fat to muscle ratio (Eder et al., 2000). Musser et al (1999) found that giving L-carnitine to sows increased the levels of glucose, insulin and IGF-1 in their blood plasma. These new findings may offer an explanation for a new mode of action of L-carnitine. De Simone (1999) found that in AIDS patients the mean level of IGF-I increased from 0.06 ng/100 mL to 3.17 ng/100 ml over a period of 8 weeks as a result of administering 3 g L-carnitine per day. Hudson et al (1996) were able to show that IGF-I significantly increases the activity of the carnitine acyl transferases CPT-I and CPT-II. L-carnitine stimulates pyruvate dehydrogenase complex (Arenas., et al., 1994) and acetyl-L-carnitine decreases glycation of lens proteins *in vitro* studies (Swamy-Mruthinti & Carter, 1999). Cavallini et al (2004) reported that carnitine is more active than testosterone for improving symptoms of male aging such as sexual...
dysfunction, depressed mood, and fatigue (Laurie Barclay & Charles Vega, 2004). Acetyl-L-carnitine reduces penile curvature significantly in the therapy of acute and early chronic Peyronie’s disease (Biagiotti & Cavallini, 2001). Carnitine enhances sperm motility against xenobiotic induced toxicities in experimental studies (Mangano et al., 2000). It is reported that seminal carnitine concentration may be an appropriate marker of sperm and epididymal function and L-carnitine/L-acetyl carnitine treatment may be an effective therapy to improve mainly functional seminal parameters (De Rosa et al., 2005). L-carnitine and its derivatives exerts potent immuno-modulatory, xenobiotics-detoxifying, proteogenic, hypolipidemic, membrane stabilizing, iron-chelating, antiperoxidative and anti-ageing antioxidant effects. Hence Levo-carnitine and its acyl derivatives are potent nutrigenomic regenerative molecular medicines, and its supplementation will be beneficial in health and disease as well as aquaculture and agriculture especially during infection.

References


Determinants of school dropouts in children

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Abstract

Background

Education is attainment of knowledge, a source of employment, enrichment of culture. It is one of the most important factors for the social and economical development of the nation. India is a country of villages; the government of India is trying its level best to ensure proper growth and development of the villages by providing education. The problem of drop out has been continually troubling the primary education system not only in India but in other developing countries also. Dropout does not mean mere rejection of school by children; it leads to wastage of funds invested in school buildings, teachers’ salaries, and equipment, textbook and so on. It also means the existence of some deficiencies in the organization of primary education system².

Objectives

1. To know the prevalence of school dropouts in the tribal community of Chandrapur.

2. To study the socio-demographic profile of school dropouts.

3. To determine the reasons for the same.

4. To know the health status of school dropouts.

5. To suggest recommendation.

Methods
**Design of Study:** Cross-sectional prospective study.

**Study Area:** Tribal community of Chandrapur village under field practice area of RMC, Loni.

**Study subject:** Children of age 6-14 years who were not attending school for 6 months or more.

**Study sample:** All children belonging to the age group 6-14 years who had never enrolled or were not attending school from past 6 months or more.

**Statistical Analysis:** Chi square test and logistic regression model used to analyze the data.

**Consent:** Informed and written consent to be taken from community leader for the cooperation from the community, as well as informed and verbal consent to be obtained from parents/guardian/elder sibling who will be present at home at the time of survey. Help of Aanganwadi worker, female health volunteer and Medical social worker will be taken.

**Results**

The results found showed that out of 286 children, 153 were dropout, 67% were females, 33% males and 76% in the age group of 10-14 years and 24% in the age group of 6-9 years irrespective of their standard. Hindu girls showed 88.1% dropouts and Muslim boys showed 36.4% dropouts. About 25.4% females never enrolled in school. 48% dropped out in primary and 33% dropped out in primary. 68% of the dropouts had dropped out on account of domestic work and 56% as they had to look after their siblings.

Whereas 73% of dropouts parents were unaware of importance of education. A high proportion of dropouts said they found difficulty in understanding language in school, about 63%, while strict teachers and failure in school was 40% and 37% respectively. 77% were not interested in studying and 82% were not aware of importance of education.

**Study Limitation**

Suggestions could not be given to all the members of the family as everyone was not present at the time when survey was done. Thus, not all the members of the family could be educated regarding the importance of going to school.

**Conclusion**

The prevalence of school dropouts was high in the urban slums. This prevalence was significantly higher in females than males and in general more in the age group of 10-15.
The dropouts are due to involvement in domestic work, harassment by classmates and teachers, earning money and failing in the exams.

**Keywords:** Education, School dropouts, Village

**Introduction**

Education is attainment of knowledge, a source of employment, enrichment of culture. It is one of the most important factors for the social and economical development of the nation. It is stated in the doctrine of human rights 1948 that everyone has right to education; even than many are deprived of it. The government has planned several projects to counter education to the children as its goal. It is in perspective the constitution states under article 45 of directive principles that "state shall endeavor to provide free and compulsory education for all the children up to the age of 14 yrs. The goal for universal elementary education should have been achieved within a period of 10 yrs." But since then it has remained a long cherished dream. Education is the major factors affecting the health, employment, socio-economic status, literacy and progress of the nation.

India is a country of villages; the government of India is trying its level best to ensure proper growth and development of the villages by providing education. But, even then results obtained are less than satisfactory. The problem of drop out has been continually troubling the primary education system not only in India but in other developing countries also. Dropout does not mean mere rejection of school by children; it leads to wastage of funds invested in school buildings, teachers’ salaries, and equipment, textbook and so on. It also means the existence of some deficiencies in the organization of primary education system. There are schools dropouts, the estimated school dropout are around 50-60%, while almost 300 million people in India can't read their own name, there are various causes that leads to school dropouts like poverty, malnutrition, ill health, lack of awareness in both children and parents etc. almost 50-60% children do not go beyond their primary school. Alone in Maharashtra 60% school dropouts are seen. This condition is even worst in tribal communities. This alarming rate of school dropouts and illiteracy is a major setback to country’s social and economical development.

The sixth five year plan, pointed out the critical role of education in the process of economic development and how it was the principle means of creating human capital of trend, competent manpower for implementing the process of development. Its approach was to ensure essential minimum education to all children up to the age of 14 years within the next 10 years, particularly giving attention to the school drop outs and to those groups which were in danger of being left behind because of their special circumstances. During the sixth plan period, a primary school was opened in every village in the state having a population of about 2000 and above.

Since education is very important for the development of both the individual and the country, it becomes inevitably crucial to study the determinants causing this
grave problem of school dropouts. It's high time to take up the cudgels against this menace. This study aims at achieving the same in the children between 6-14 years in tribal community of Chandrapur village in rural Maharashtra.

Materials and Methods

**Design of Study:** Cross-sectional prospective study.

**Study Area:** Tribal community of Chandrapur village under field practice area of RMC, Loni.

**Study subject:** Children of age 6-14 years who were not attending school for 6 months or more.

**Duration of study:** The duration of study will be of 2 months.

**Study sample:** All children were belonging to the age group 6-14 years who had never enrolled or were not attending school from past 6 months or more. This 100% population will be considered for calculating prevalence.

- **Inclusion criteria:** Following criteria were used to involve subjects in the present study.
  1. The children who had left school between 6-14 years of age.
  2. The absence from school for 6 months and more.

- **Exclusion criteria:** Following criteria were used to exclude the subjects from the present study.
  1. Children who were residing in the study area for less than 6 months.

**Data Collection:** House to house survey to be conducted to cover all children of school age group 6-14 years, who were not attending school for 6 months or more than 6 months to determine the prevalence and causal factors of school dropouts.

Data to be collected on pre tested structured proforma from each study subject and to confirm reliability, information will be cross checked from senior family member present at the time of data collection. Information will be collected regarding personal data, father's and mother's literacy and occupation status, family background and the various reasons like school dropout pertaining to family, pertaining to school and to self of school dropouts which was followed by the physical examination of each subject.
Statistical Analysis: - Chi square test and logistic regression model used to analyze the data.

Consent: - Informed and written consent to be taken from community leader for the cooperation from the community, as well as informed and verbal consent to be obtained from parents /guardian / elder sibling who will be present at home at the time of survey. Help of Aanganwadi worker, female health volunteer and Medical social worker will be taken.

Results

The present study was conducted in the tribal area of Chandrapur village in which total number of children belonged to age group 6-14 years was 286 children from which 153 children were not attending school. The overall prevalence of school dropouts comes to 53.49%.out of 153 school dropout children, 100 children contacted by house to house survey considering inclusion and exclusion criteria for gathering information.

Table No. I: Distribution of school dropouts according to their personal perspective

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Particulars</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Age group</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>a)6-9years</td>
<td>7(21.2)</td>
<td>17(25.4)</td>
<td>24(24)</td>
<td>0.647</td>
</tr>
<tr>
<td></td>
<td>b)10-14 years</td>
<td>26(78.8)</td>
<td>50(74.6)</td>
<td>76(76)</td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td>Religion</td>
<td></td>
<td></td>
<td></td>
<td>0.004*</td>
</tr>
<tr>
<td></td>
<td>a)Hindu</td>
<td>21(63.6)</td>
<td>59(88.1)</td>
<td>80(80)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b)Muslim</td>
<td>12(36.4)</td>
<td>8(11.9)</td>
<td>20(20)</td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>Educational status</td>
<td></td>
<td></td>
<td></td>
<td>0.066*</td>
</tr>
<tr>
<td></td>
<td>a)never enrolled in school</td>
<td>2(6.1)</td>
<td>17(25.4)</td>
<td>19(19)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b)dropped out in primary</td>
<td>18(54.5)</td>
<td>30(44.8)</td>
<td>48(48)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c)dropped out in secondary</td>
<td>13(39.04)</td>
<td>20(29.9)</td>
<td>33(33)</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05

Table no. 1 shows that, there were maximum numbers of female dropouts (67%) as compared to male children (33%). But according to age group there was no significant
difference (p>0.05) in male and female population. However, there is marked rise in school dropouts in the age group 10-14 years.

It was also observed that, there were more Hindu dropouts, almost 4 times the Muslim school dropouts. There is a marked significance difference in attending school among Hindu girls (88.8%) while school dropouts was seen more in Muslim boys (36.4%). The study reveals a high number of girls who had never enrolled in school and were about 4 times the number of boys, who drops the school in the primary section as well as secondary.

Table 1(a): Distribution of school dropouts according to their family perspective

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Particulars</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.</td>
<td>Fathers education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a)</td>
<td>Illiterate</td>
<td>23(69.7)</td>
<td>46(68.7)</td>
<td>69(69)</td>
<td>0.916</td>
</tr>
<tr>
<td>b)</td>
<td>Literate</td>
<td>10(30.3)</td>
<td>21(31.3)</td>
<td>31(31)</td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Fathers occupation</td>
<td></td>
<td></td>
<td></td>
<td>0.099*</td>
</tr>
<tr>
<td>a)</td>
<td>Unemployed</td>
<td>11(34.4)</td>
<td>27(44.3)</td>
<td>38(40.9)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td>Unskilled labor</td>
<td>17(53.1)</td>
<td>25(41)</td>
<td>42(45.2)</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td>Skilled labor</td>
<td>2(6.2)</td>
<td>9(14.8)</td>
<td>11(11.8)</td>
<td></td>
</tr>
<tr>
<td>d)</td>
<td>Business</td>
<td>2(6.2)</td>
<td>0(0)</td>
<td>2(2.2)</td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Mothers education</td>
<td></td>
<td></td>
<td></td>
<td>0.280</td>
</tr>
<tr>
<td>a)</td>
<td>Illiterate</td>
<td>27(81.8)</td>
<td>60(89.6)</td>
<td>87(87)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td>Literate</td>
<td>6(18.2)</td>
<td>7(10.4)</td>
<td>13(13)</td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Mothers occupation</td>
<td></td>
<td></td>
<td></td>
<td>0.013*</td>
</tr>
<tr>
<td>a)</td>
<td>Working</td>
<td>20(60.6)</td>
<td>23(34.3)</td>
<td>43(43)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td>Not working</td>
<td>13(39.4)</td>
<td>44(65.7)</td>
<td>57(57)</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>Socio-Economic Status</td>
<td></td>
<td></td>
<td></td>
<td>0.066*</td>
</tr>
<tr>
<td>a)</td>
<td>Class 2</td>
<td>2(6.1)</td>
<td>7(10.4)</td>
<td>9(9)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td>Class 3</td>
<td>13(39.4)</td>
<td>11(16.4)</td>
<td>24(24)</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td>Class 4</td>
<td>12(36.4)</td>
<td>38(56.7)</td>
<td>50(50)</td>
<td></td>
</tr>
<tr>
<td>d)</td>
<td>Class 5</td>
<td>6(18.2)</td>
<td>11(16.4)</td>
<td>17(17)</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>Type of Family</td>
<td></td>
<td></td>
<td></td>
<td>0.607</td>
</tr>
<tr>
<td>a)</td>
<td>Nuclear</td>
<td>14(42.4)</td>
<td>34(50.7)</td>
<td>48(48)</td>
<td></td>
</tr>
<tr>
<td>b)</td>
<td>Joint</td>
<td>12(36.4)</td>
<td>18(26.9)</td>
<td>30(30)</td>
<td></td>
</tr>
<tr>
<td>c)</td>
<td>Broken</td>
<td>7(21.2)</td>
<td>15(22.4)</td>
<td>22(22)</td>
<td></td>
</tr>
</tbody>
</table>
The high proportion of school dropout children observes with illiterate fathers (69%), but there is no significant difference between male and female dropouts according to fathers’ education. The study reveals that in general a high number of school dropout belong to the group of fathers being unemployed and engaged in unskilled labor. However, there is borderline significance (p=0.05) in the number of school dropouts being more in girls in unemployed and skilled labored father. While high proportion of boys dropped out of school whose fathers were engaged in unskilled labor and business.

Both male (81.8%) and female (89.6%) dropouts were observed in high proportion with illiterate mothers (87%). However there is no statistical significance observed. High proportion of school dropout males were noted whose mothers were working, where as highest proportion of females remained away from school even though their mothers were not working.

Almost half of the school dropouts were belonging to nuclear type of family but there is no significant sex wise difference noted according to the type of family.

Table 2: Distribution of school dropouts according to causes related to family

<table>
<thead>
<tr>
<th>Sr.No</th>
<th>Reasons pertaining to family</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Involved in domestic work</td>
<td>16(48.5)</td>
<td>52(77.6)</td>
<td>68(68)</td>
<td>0.003*</td>
</tr>
<tr>
<td>2.</td>
<td>Have to change residence frequently</td>
<td>2(6.1)</td>
<td>3(4.5)</td>
<td>5(5)</td>
<td>0.733</td>
</tr>
<tr>
<td>3.</td>
<td>Look after siblings</td>
<td>12(36.4)</td>
<td>44(65.7)</td>
<td>56(56)</td>
<td>0.005*</td>
</tr>
<tr>
<td>4.</td>
<td>Parents unaware of importance of education</td>
<td>26(78.8)</td>
<td>47(70.1)</td>
<td>73(73)</td>
<td>0.360</td>
</tr>
<tr>
<td>5.</td>
<td>Parents separated/died</td>
<td>5(15.2)</td>
<td>14(20.95)</td>
<td>19(19)</td>
<td>0.491</td>
</tr>
<tr>
<td>6.</td>
<td>No books/clothes</td>
<td>7(21.2)</td>
<td>7(10.4)</td>
<td>14(14)</td>
<td>0.145</td>
</tr>
<tr>
<td>7.</td>
<td>Unaffordable fees</td>
<td>9(27.3)</td>
<td>13(19.4)</td>
<td>22(22)</td>
<td>0.372</td>
</tr>
<tr>
<td>8.</td>
<td>Earning money</td>
<td>11(33.3)</td>
<td>9(13.4)</td>
<td>20(20)</td>
<td>0.019*</td>
</tr>
<tr>
<td>9.</td>
<td>Fathers alcoholism</td>
<td>20(60.6)</td>
<td>38(56.7)</td>
<td>58(58)</td>
<td>0.711</td>
</tr>
<tr>
<td>10.</td>
<td>Domestic violence</td>
<td>19(57.6)</td>
<td>35(52.2)</td>
<td>54(54)</td>
<td>0.615</td>
</tr>
</tbody>
</table>

The high proportion of children dropped out of school mainly because parents were unaware (74%) of education followed by involvement in domestic work (68%), fathers alcoholism (58%) and domestic violence (54%). Significantly high proportion of girls were not able to attend school only because they were involved in domestic work (77.6%) and to look after siblings, whereas, significantly higher proportion of
boys said they were not attending school because they were busy in earning money.

There is no significant difference in male and female population with regards to change of residence, parents being unaware of the importance of education, parents having separated or died, unavailability of books and clothes, unaffordable fees, fathers alcoholism and domestic violence.

Table 3: Distribution of school dropouts according to reasons pertaining to school

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Reasons pertaining to school</th>
<th>Male N=33(%)</th>
<th>Female N=67(%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Failed in exam</td>
<td>16(48.5)</td>
<td>21(31.3)</td>
<td>37(37)</td>
<td>0.095*</td>
</tr>
<tr>
<td>2.</td>
<td>Finding language difficult</td>
<td>26(78.8)</td>
<td>37(55.2)</td>
<td>63(63)</td>
<td>0.022*</td>
</tr>
<tr>
<td>3.</td>
<td>Strict teachers</td>
<td>18(54.5)</td>
<td>22(32.8)</td>
<td>40(40)</td>
<td>0.037*</td>
</tr>
<tr>
<td>4.</td>
<td>Fear of punishment</td>
<td>13(39.4)</td>
<td>15(22.4)</td>
<td>28(28)</td>
<td>0.075*</td>
</tr>
<tr>
<td>5.</td>
<td>Harassment by teachers</td>
<td>7(21.2)</td>
<td>3(4.5)</td>
<td>10(10)</td>
<td>0.009*</td>
</tr>
<tr>
<td>6.</td>
<td>Unfriendly classmates</td>
<td>16(48.5)</td>
<td>18(26.9)</td>
<td>34(34)</td>
<td>0.032*</td>
</tr>
<tr>
<td>7.</td>
<td>Distance too much</td>
<td>2(6.1)</td>
<td>8(11.9)</td>
<td>10(10)</td>
<td>0.357</td>
</tr>
<tr>
<td>8.</td>
<td>Time is not convenient</td>
<td>2(6.1)</td>
<td>11(16.4)</td>
<td>13(13)</td>
<td>0.148</td>
</tr>
</tbody>
</table>

The study shows difficult language as the most prevalent (65%) cause of school dropouts followed by strict teachers (40%), failure in examinations (37%), unfriendly classmates (34%) and fear of punishment (28%). Among these reasons, all are showing statistically significance except failure in examination which is of borderline significance. (p=0.005)

Though the harassment by teachers was less prevalent, it was significantly higher in proportion by the boys. (p<0.05)
Table 4: Distribution of school dropouts according to reasons pertaining to self

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Reasons pertaining to self</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>No confidence</td>
<td>16(48.5)</td>
<td>23(34.3)</td>
<td>39(39)</td>
<td>0.172</td>
</tr>
<tr>
<td>2.</td>
<td>No interest in studying</td>
<td>26(78.8)</td>
<td>51(76.1)</td>
<td>77(77)</td>
<td>0.766</td>
</tr>
<tr>
<td>3.</td>
<td>Unaware of the importance of education</td>
<td>28(84.8)</td>
<td>54(80.6)</td>
<td>82(82)</td>
<td>0.603</td>
</tr>
<tr>
<td>4.</td>
<td>Neglected by parents</td>
<td>12(36.4)</td>
<td>29(43.3)</td>
<td>41(41)</td>
<td>0.508</td>
</tr>
<tr>
<td>5.</td>
<td>Mental retardation</td>
<td>0(0)</td>
<td>2(3)</td>
<td>2(2)</td>
<td>0.316</td>
</tr>
<tr>
<td>6.</td>
<td>Mischievous Behavior</td>
<td>23(69.7)</td>
<td>30()</td>
<td>53(53)</td>
<td>0.019*</td>
</tr>
</tbody>
</table>

The study shows that major no. of school dropouts are in the category of unaware of importance of studying and not interested in studying. There is no significant difference in male and female with regards to no confidence, no interest in studying, unaware of importance of education, neglect by parents and mental retardation. However, significant difference found in males and females with regards to mischievous behavior and is more in males about 69.7% than females 44.8%.

Table 5: Stepwise backward logistic variation of all the cause of school dropouts

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Stepwise backward logistic variation of all the causes</th>
<th>OR</th>
<th>p</th>
<th>B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Failed</td>
<td>0.234</td>
<td>0.010*</td>
<td>-1.452</td>
</tr>
<tr>
<td>2.</td>
<td>Unfriendly classmates</td>
<td>0.355</td>
<td>0.044*</td>
<td>-1.036</td>
</tr>
<tr>
<td>3.</td>
<td>Time problem</td>
<td>4.983</td>
<td>0.093*</td>
<td>-1.606</td>
</tr>
<tr>
<td>4.</td>
<td>Domestic work</td>
<td>6.112</td>
<td>0.001*</td>
<td>1.810</td>
</tr>
<tr>
<td>5.</td>
<td>Earning money</td>
<td>0.288</td>
<td>0.039*</td>
<td>-1.271</td>
</tr>
</tbody>
</table>

The study shows that domestic work is the commonest cause of school dropout amongst all causes, being 6 times more in females as compared to males.
The study shows that high proportions (39%) of school dropouts were addicted to mishri and females were highly addicted to mishri. Among smokers all the subjects were males.

Table 6: Distribution of school dropouts on the basis of their behavioral problems

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Behavior</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Theft</td>
<td>2(6.1)</td>
<td>0(0)</td>
<td>2(2)</td>
<td>0.042*</td>
</tr>
<tr>
<td>2.</td>
<td>Threatening others</td>
<td>2(6.1)</td>
<td>4(4)</td>
<td>4(4)</td>
<td>0.461</td>
</tr>
<tr>
<td>3.</td>
<td>Destruction of property</td>
<td>1(3)</td>
<td>2(3)</td>
<td>3(3)</td>
<td>0.990</td>
</tr>
<tr>
<td>4.</td>
<td>Verbal violence</td>
<td>15(45.5)</td>
<td>23(34.3)</td>
<td>38(38)</td>
<td>0.281</td>
</tr>
<tr>
<td>5.</td>
<td>Physical violence</td>
<td>13(39.4)</td>
<td>14(20.9)</td>
<td>27(27)</td>
<td>0.050*</td>
</tr>
</tbody>
</table>

The study reveals a high no. of school dropouts involved in verbal violence to about 38%. However, there is no significant difference between males and females in this group. There is no significant difference in males and females in threatening others, destruction of property. However more males than females are involved in theft and physical violence.
Table 7: Morbidity profile of school dropouts

<table>
<thead>
<tr>
<th>Sr.No.</th>
<th>Health profile</th>
<th>Male N=33(%)</th>
<th>Female N= (67%)</th>
<th>Total N=100(%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Handicap</td>
<td>11(33.3)</td>
<td>6(9)</td>
<td>17(17)</td>
<td>0.002*</td>
</tr>
<tr>
<td>2.</td>
<td>Anemia</td>
<td>24(72.7)</td>
<td>57(85.1)</td>
<td>81(81)</td>
<td>0.139</td>
</tr>
<tr>
<td>3.</td>
<td>Scaly dry skin</td>
<td>10(30.3)</td>
<td>11(16.4)</td>
<td>21(21)</td>
<td>0.109</td>
</tr>
<tr>
<td>4.</td>
<td>Boils</td>
<td>10(30.3)</td>
<td>15(22.4)</td>
<td>25(25)</td>
<td>0.390</td>
</tr>
<tr>
<td>5.</td>
<td>Dermatitis</td>
<td>14(42.4)</td>
<td>20(29.9)</td>
<td>34(34)</td>
<td>0.212</td>
</tr>
<tr>
<td>6.</td>
<td>Fungal</td>
<td>2(6.1)</td>
<td>6(9)</td>
<td>8(8)</td>
<td>0.616</td>
</tr>
<tr>
<td>7.</td>
<td>Bitots spots</td>
<td>1(3)</td>
<td>0(0)</td>
<td>1(1)</td>
<td>0.152</td>
</tr>
<tr>
<td>8.</td>
<td>ASOM</td>
<td>23(69.7)</td>
<td>42(62.7)</td>
<td>65(65)</td>
<td>0.489</td>
</tr>
<tr>
<td>9.</td>
<td>Caries teeth</td>
<td>4(12.1)</td>
<td>2(3)</td>
<td>6(6)</td>
<td>0.070</td>
</tr>
<tr>
<td>10.</td>
<td>Mottling</td>
<td>11(33.3)</td>
<td>31(46.3)</td>
<td>42(42)</td>
<td>0.218</td>
</tr>
<tr>
<td>11.</td>
<td>Stomatitis</td>
<td>2(6.1)</td>
<td>3(4.5)</td>
<td>5(5)</td>
<td>0.733</td>
</tr>
<tr>
<td>12.</td>
<td>ARI</td>
<td>14(42.4)</td>
<td>32(47.8)</td>
<td>46(46)</td>
<td>0.615</td>
</tr>
<tr>
<td>13.</td>
<td>Diarrhoeal</td>
<td>9(27.3)</td>
<td>10(14.9)</td>
<td>19(19)</td>
<td>0.139</td>
</tr>
<tr>
<td>14.</td>
<td>Epilepsy</td>
<td>0(0)</td>
<td>2(3)</td>
<td>2(2)</td>
<td>0.575</td>
</tr>
<tr>
<td>15.</td>
<td>Undernourished</td>
<td>15(45.5)</td>
<td>18(26.9)</td>
<td>33(33)</td>
<td>0.151</td>
</tr>
</tbody>
</table>

The study revealed a high proportion of school dropouts suffering from anaemia (81%) followed by Acute Suppurative Otitis Media (65%, Acute respiratory infection(46%), mottling of teeth(42%) and undernourishment(33%). Though the prevalence of handicap and caries teeth was less, there was higher significance in males in handicap (p<0.05) and borderline significance in caries teeth (p>0.005)

Discussion

The present study highlights the prevalence of school dropouts and the factors influencing it. This study reports school dropouts to be 53%. Khokhar et al in Delhi, found 50-60% of school dropouts. While the study conducted by Subodh V, Sunday times found the overall dropout to be 61.92%. While Subodh V of Sunday Times reports that 50% of dropouts are by primary, this study reports 67% (Table 1) school dropouts in primary itself. While literacy in Indian females is 55%, this study has found 67% of school dropouts in females. From the study it is observed that there is no significant difference according to age group in male and female population. It is observed that there are more Hindu dropouts, almost 4 times the Muslim school dropouts. By the study, it was observed that higher proportion of Hindu girls, 88.8% dropped out (Table 1) while school dropout is seen more in Muslim boys 36.4% (Table 1). In the researches that were found, no study was done on school dropouts on the basis of religion. The high no. of Hindu girls found in the study of school dropouts is probably because the Hindu traditions and norms do not allow a female child to go out of the house but are supposed to learn the culture of household work, care of family members and looking after siblings. Contradictorily, Muslim boys are seen to dropout more than...
Muslim girls. It was observed in the course of the study that the Muslim community prefers to educate the boys in their religion as compared to going to school. Many boys were seen to attend Madarassa.

The current study showed the higher proportion of school dropouts in children whose fathers were illiterate.

The present study revealed that in general a high number of school dropouts fathers were unemployed and engaged in unskilled labor (Table 1a). This indicates poverty as the reason for incomplete schooling.

There is high number of school dropouts in both male and females in cases with illiterate mothers, about 87% and 7 times the dropouts in literate mother cases (Table 1a). High proportion of school dropouts were observed in non-working mothers. This maybe due to high illiteracy of mothers and their unawareness of importance of education. The high no. of school dropouts in illiterate mothers indicates that a female's literacy is of high value in the education of the family. However there is no significant difference between male and female according to mother's education.

While high number of school dropouts are seen in males who have working mothers, high number of school dropouts are seen in females amongst non working mothers. (Table 1a) There is no significant difference noted in school dropouts according to the type the family whether broken, nuclear or joint. (Table 1a) A high proportion of prevalence of school dropouts was observed in nuclear family with siblings. This maybe due to both the parents working and the child being left at home to do the household work.

The study revealed a high number of girls who had never enrolled in school and are about 4 times the number of boys, there are most boys dropping out of school in the primary section as well as secondary (Table 1a). This study has revealed that the main bulk of school dropouts are in the primary section and was found to be 48% and is comparable with the study by Pratinidhi et all who found 60% of their dropouts in primary. 4 77.6% females and 48.5% males involved in domestic work as a reason of school dropout (Table 2). The study by Nidhi Kotwal et al in a study in J & K has found domestic activity as a cause of school dropout in 72% females.”. Pratinidhi et al stated 26% of the male population and 57% of female population engaged with domestic activities. 4 The difference between this and the present study maybe due to the present study being carried out in the slum area where parents are unaware of importance of education (71% for females and 78% for males). Here also the finding of Nidhi Kotwal et al was observed almost similar (78% in females) of females parents unaware of importance of education.11 The current study reports 13.4% females and 33.3% of males being economically active (Table 2). The World Youth Data Sheet stated that 35% of females and 50% of males in the age of 5-18 to be economically active.5 This difference may be due to present study. This may be probably because females must learn domestic work and males must earn money according to the norms of the society. Death in the family as a reason for school dropout is seen in 6% cases in Nidhi Kotwal studies et al. This study shows 20.95% of cases dropped out as a cause of parents having died or separated. (Table 2). This study highlights the fact that total of male and female who dropped out to look after siblings are 56%, while 35% of male and 65.7% female population dropped out as they had to look after siblings. (Table 2). Higher proportion of females 60/140 (42.85) were pulled out of schools by their parent's as
compared to males 21/139 (15.10%) by a study conducted in Delhi by Khokhar et al. This was mainly done so that girls could look after their siblings 32/60 (53.33%). It is seen as it is considered the job of a woman to look after the family members and it has to be learnt by the females from their childhood.

The dropouts in the group who change their residence frequently have been reported as only 5%. It is not significant as probably during the survey, large proportions of the community had already left in search of labour and were not accessible. In their presence the significance of the data would have probably changed.

The reasons of school dropouts on basis of unaffordable fees, no clothes or books are not significant as most of the children were attending school that provided free education, free school books and uniform and mid day meals.

The study by Pratinidhi et al have found 13% males and 5% females having dropped out on account of harassment by the teacher. This study reports 21.2% of males and 4.5% of females dropping school on account of harassment by the teachers and is comparable with the study of Pratinidhi et al (Table 3). Nidhi Kotwal et al found 20% of female dropouts not interested in studying. This study found 76.1% of female population and 78% of male population not interested in studying (Table 4). While Pratinidhi et al found that total of 48% children were not interested in studying, this study found 77% of children not interested in studying. While a study in Delhi by Khokhar et al reports dropouts due to failing in exams as 4.2%, this study reports dropouts due to failing in exams as 37% (Table 3). This may probably be because of lack of interest in studying or lack on behalf of teachers and education system. During the study it was observed that several dropouts complained of lack of attention from the teachers.

Pratinidhi et al have reported 9% males and 12% females having dropped out in account of school being too much and this study is comparable to it as it reports 11.9% males and 10% females having left school on account of distance of school being too much.(Table 3). The study conducted by Pratinidhi et al states that 27% of male and 25% of female population dropped out on account of difficulty in understanding the language and subject matter. This study reports 78.8% of males and 55.2% of females who dropped out as they found the language difficult (Table 3).

Mischievous behavior was found to be a significant cause of school dropout with p value 0.019 (Table 4). The references found had no data regarding mischievous behavior being a cause of school dropout.

While mental retardation, lack of confidence in self and unawareness of importance of education were reasons found to be insignificant.

While the global tobacco survey finds 5-6% adolescents using any form of tobacco, it is comparable with this study which finds 46% of dropouts using any form of tobacco. This study also reports 4% dropouts involved in smoking and is comparable with The Global Youth Survey which reports smoking cigarettes in 1-23% children.

A large no. of children were found to have behavioral problems like theft, threatening others, destruction of others property, verbal and physical violence. 38% were involved in verbal and 27% in physical violence. The references found had no data regarding these behavioral problems. Anaemia has been found to be 95% in
Indian girls. This study reports 85% of anemia in girls, overall anaemia in girls and boys to be 81% and anaemia in boys to be 72% in the school dropouts (Table 7). Acute respiratory tract infection was found to be 46% and disease as 19% (Table 7). Handicap was found to be in 17% cases. Other health problems were related to skin infections like dermatitis, fungal infections, boils. While others like mottling of teeth, caries, dry scaly skin was found to be insignificant. The study reveals that 33% of the children were undernourished. 26.9% females were found to be undernourished and 45.5% males were undernourished. The references found had no data on school dropouts regarding occupation of parents, type of family, change of residence, addictions and health profile.

Conclusion

The prevalence of school dropouts was high in the tribal area of Chandrapur village. This prevalence was significantly higher in females than males and in general more in the age group of 10-14. The dropouts are due to involvement in domestic work, harassment by classmates and teachers, earning money and failing in the exams. The consequence of this is anti-social activities, drug addiction, behavioral problems and lack of awareness of their own health needs. The morbidity health profile shows high no. of children suffering from anaemia, acute respiratory tract infection and diarrhoeal diseases along with skin infection and undernourishment. This picture can change but will show very gradual improvement with a change in the overall family background.

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Self medication with H1-Antihistamines and pain relieving agents among the educated young adult people of Bangladesh

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Abstract

Background: Responsible self medication with OTC drugs has been appreciated as a means of healthcare cost reduction worldwide. Previous studies indicated that the self medication rate with OTC and prescription drugs among Bangladeshi educated young adult population was 16%. In Bangladesh drugs have not been classified into prescription-only and OTC likewise FDA regulations. People can obtain any drug from retailers even in the remote parts of the country.

Aim & Objectives: The objective of this study was to investigate the patterns of self-reported pain relieving and H1 antihistamine medication use, including both prescription and non-prescription drugs, and to assess the possible predictors of self-medication, for young educated population of Bangladesh.

Methods/Study Design: The study was conducted among the students of colleges and universities in Dhaka and Bogra city. 11 categories of highest selling and most commonly used pain relieving agents and H1 antihistamines were printed in the questionnaire. The drug brands were selected after careful consultation with product managers and in house sales data of reputed pharmaceutical companies. The students were asked whether they had used any of the drugs within 6 months prior to survey date. When said yes, they were asked if they had any prescription for using those drugs. By snowball sampling method, 758 students were found who used at least one of the 11 drugs listed; all of them were interviewed within June 2009. The symptoms, diseases and length of therapies of the respective drugs were also noted.

Results/Findings: The self medication rates for the 11 drug products Aspirin (83.1%), Paracetamol (67.8%), Tramadol (100%), Pizotifen (71.4%), Ketorolac (66.7%), Diclofenac (72.3%), Chlorphenamine (79.1%), Loratadine (76.3%), Cetirizine (79.6%), Desloratadine (85.7%), and Promethazine (85.9%) were noted and analyzed.
**Study Limitations:** The study was focused on only educated people and a particular age group within 14 – 32. While the literacy rate of Bangladesh is only 48%, the findings of this study do not implicate the whole population.

**Conclusion:** The prevalence of such a high self medication rate of prescription drugs like tramadol and ketorolac may bring about hazards to public health in Bangladesh.

**Keywords:** Self-medication, H1-Antihistamines, Pain relieving medicine, Antihistamine, Bangladesh

**Introduction**

Although responsible self medication with OTC drugs has been appreciated as a means of healthcare cost reduction worldwide, one report estimated that there were four million over the counter (OTC) drug misusers in the south Asian region with Bangladesh (1) accounting for nearly 500,000. Previous studies indicated that the self medication rate with OTC and prescription drugs among Bangladeshi educated young adult population was 16% (2). OTC medications can be associated with significant morbidity and even mortality in both acute overdoses and when administered in correct doses for chronic periods of time (3). Physicians often do not inquire about OTC medication use, and parents (or other caregivers) often do not perceive OTCs as medications (3).

In Bangladesh drugs have not been classified into prescription-only and OTC likewise FDA regulations (4). People can obtain any drug from retailers even in the remote parts of the country. Therefore the misuse of prescription drugs needs to be probed thoroughly. But no study on use of prescription pain relieving and H1-antihistamine drugs has yet been carried out.

Seventy seven percent (77%) of higher educated people in Bangladesh sought advice from retail medicine sellers for minor ailments, including common cold, allergy, mild fever or diarrhea. Paracetamol (80%) was the single mostly used OTC medicine (5). The status of H1-antihistamine use has also been sought to be unraveled here. A recent survey in several districts of Bangladesh showed that 105 people died from perforation of a peptic ulcer and several thousand suffered from peptic ulceration after injudicious consumption of non-steroidal anti-inflammatory drugs (6, 7).

According to a previous study, 81% of Bangladeshi educated people maintain home medicines like painkillers, antibiotics, vitamins etc (2). The most common reported calls that involve OTC medications to poison control centers in USA are for the ingestion of acetaminophen and cough and cold preparations (8). The duration of use of these medicines is upon the judgment of patients when self medicated. The half-life of loratadine, for example, is typically 10 hours but may be more than doubled in overdose (9). Hence, propensity towards self-medication may have serious consequences for public health in developing countries. The challenge and opportunity for the Bangladesh government, healthcare professionals and providers of self-medication products are to have a responsible framework in place for self-
medication. Hence, this study was carried out to evaluate the potential consequence of this situation.

The objective of this study was to investigate the patterns of self-reported pain relieving and H1 antihistamine medication use, including both prescription and non-prescription drugs, and to assess the possible predictors of self-medication, for young educated population of Bangladesh.

Methods

The study was conducted among the students of colleges and universities in Dhaka and Bogra city. 11 highest selling and most commonly used pain relieving agents and H1 antihistamines were printed in the questionnaire. The drug brands were selected after careful consultation with product managers and in house sales data of reputed pharmaceutical companies. This study included OTC analgesics like Aspirin, Paracetamol and OTC H1-antihistamines like Chlorpheniramine, Loratadine, Cetirizine for survey. This study also included Prescription pain relieving drugs like Tramadol, Pizotifen, Ketorolac, Diclofenac, and Prescription H1-antihistamines like Desloratadine, Promethazine in this survey.

The sample students were asked whether they had used any of the drugs within 6 months prior to survey date. When said yes, they were asked if they had any prescription for using those drugs. By snowball sampling method, 758 students were found who had used at least one of the 11 drugs listed; all of them were interviewed within June 2009. Multiple cases of different drugs from one person was considered separately. The symptoms, diseases and length of therapies of the respective drugs were also noted.

Data management

Supervisors in the field regularly reviewed questionnaires. Field researchers double-checked the responses at the field immediately after conducting interviews. Supervisors directly observed 5% cases during the interview conducted by field workers. Information from the written questionnaires was entered into an electronic database.

Data analysis

The data thus gathered was analyzed using SPSS software version 13.0. The trends in population characteristics across explanatory variables (e.g. Self medication rate etc.) were assessed using Pearson’s chi square test for categorical variables and simple linear regression for continuous variables. The analysis was exploratory.

Ethics
The Department of Pharmacy, State University of Bangladesh, which has been granted the accreditation of the Pharmacy Council, Bangladesh and University Grants Commission, Bangladesh, reviewed the study before approval and approved accordingly. The names of the brands from different pharmaceutical companies have not been elucidated. The analysis was done on the basis of generics.

**Results**

More than 50% of the survey population was male (55.8%, n=423). More than 50% of the population was of age 22-32 (51.7%, n=392). The rest of the population was from age group 14 – 21. (Table 1)

All of the drugs have been self medicated within 6 months prior to survey date (Table 2). The self medication rate is highest among 11 drugs in case of tramadol, 100% of its users haven’t visited doctors and used it upon self judgment. The second and third most highly self medicated pain relieving drugs are aspirin and Diclofenac (72.3%, n=112) and Pizotifen (71.4%, n=5). Paracetamol and Ketorolac have high self medication rates (67.8% and 66.7% respectively).

On average, self medication rate for the H1 antihistamines are higher than the pain relieving medications. Promethazine and Desloratadine showed the highest incidence of self medication (85.9% and 85.7% respectively) among antihistamines. The second highest self medication rate was observed with Cetirizine (79.6%) Chlorpheniramine (79.1%). Loratadine has also been self medicated in more than 75% of cases.

Aspirin was most frequently used to treat Headache during both prescription use (68.8%) or self medication (89%). More than 90% cases of prescription or self medication incidences of Paracetamol use was in Fever. Diclofenac was used to treat pain in more than 80% cases with or without prescription. Ketorolac was mostly (75%) used to treat Eye Diseases with prescription. People self medicated Ketorolac for both Eye Diseases (50%) and Pain (50%). Pizotifen was used to treat Migraine with or without prescription. In one incidence, Pizotifen was self medicated for treating Fever. Tramadol was self medicated to treat Fever. (Table 3 and 4)

Chlorpheniramine and promethazine have high incidences of use (in both Prescription Use or Self medication) in cold and cough respectively (Table 2). 4 misuse cases were found with Chlorpheniramine. It was self medicated to treat Pain (n=2) and Fever (n=2). Loratadine, Desloratadine and Cetirizine were used (Both Prescription and Self Medication) for allergy most frequently. (Table 3 and 4)

The drugs have been self medicated for various durations (Table 5). We investigated whether the duration of therapy varied between Prescription Use or Self Medication Use of drugs.

The duration of use of Loratadine was significantly higher (p<0.05) when used with prescription than self medication. Long term, i.e., more than 7-day usage of drugs was more common when used with prescription; this was noted in 6 out of 7 valid cases. Only Promethazine showed more tendencies to be self medicated for long term duration than prescription. (Table 5)
**Conclusion**

It’s apparent some OTC as well as prescription drugs are being misused in wrong indications. Misuse incidences were found in case of Chlorpheniramine and Pizotifen. Diclofenac has been self medicated in 72.3% cases. 2.8% people who took diclofenac to treat pain without doctors prescription continued the therapy for more than 7 days. It’s not certain whether they used antacids simultaneously to minimize Diclofenac’s harmful effect on stomach acid secretion. Further studies need to be carried out to evaluate the self medication of Diclofenac and Aspirin in depth.

The purchasing of prescription drugs should be thoroughly monitored by a qualified pharmacist. As there is no community pharmacy run by registered pharmacists in Bangladesh, the absence of pharmacists is being filled by self medication and random misuse of medicines. We recommend immediate establishment of community pharmacies run by qualified pharmacists who would spend more time for patients and FDA recommended prescription only status of selected drugs like Pizotifen, Ketorolac, Diclofenac etc. in Bangladesh.

Educational advertisements and campaigns are needed to make people aware of the danger of self medication with Pizotifen, Ketorolac, Diclofenac, Desloratadine, Promethazine etc. prescription drugs. The accurate use of OTC drugs like Aspirin, Paracetamol, Chlorpheniramine, Loratadine, and Cetirizine need to be explained to the general public.

**Limitations of the Study**

The limitation of this study was that the incidences of pain were not classified into musculoskeletal or visceral pain. All therapeutic forms of pains were classified under the theme ‘Pain’.

The study was focused on only educated people and a particular age group within 14 – 32. While the literacy rate of Bangladesh is only 48%, the findings of this study do not implicate the whole population.

**References**

7. Health and Health Sciences, Banglapedia, Asiatic Society of Bangladesh.

TABLES AND FIGURES

Table 1: Age and Gender Distribution among the survey population (Descriptive table)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Based on all sampled individuals (n=758)</th>
<th>% n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td>% n</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>55.8 (423)</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>44.2 (335)</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14 -21</td>
<td></td>
<td>48.3 (366)</td>
</tr>
<tr>
<td>22 - 32</td>
<td></td>
<td>51.7 (392)</td>
</tr>
</tbody>
</table>

Table 2: Rate of self medication among the survey population

<table>
<thead>
<tr>
<th>Therapeutic category</th>
<th>FDA-defined Legal Status</th>
<th>Name of drug</th>
<th>No. of Population Sampled</th>
<th>% self medicated (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain relieving agent</td>
<td>OTC</td>
<td>Aspirin</td>
<td>284</td>
<td>83.1 (236)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Paracetamol</td>
<td>587</td>
<td>67.8 (398)</td>
</tr>
<tr>
<td></td>
<td>Prescription-only</td>
<td>Tramadol</td>
<td>8</td>
<td>100 (8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pizotifen</td>
<td>7</td>
<td>71.4 (5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ketorolac</td>
<td>12</td>
<td>66.67 (8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diclofenac</td>
<td>155</td>
<td>72.3 (112)</td>
</tr>
<tr>
<td>H1-antihistamines</td>
<td>OTC</td>
<td>Chlorphenamine</td>
<td>177</td>
<td>79.1 (140)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Loratadine</td>
<td>38</td>
<td>76.3 (29)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cetirizine</td>
<td>142</td>
<td>79.6 (113)</td>
</tr>
<tr>
<td></td>
<td>Prescription-only</td>
<td>Desloradine</td>
<td>7</td>
<td>85.7 (6)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Promethazine</td>
<td>92</td>
<td>85.9 (79)</td>
</tr>
<tr>
<td>Drug</td>
<td>Symptoms/Diseases</td>
<td>Total Incidence of use with prescription</td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>------------------</td>
<td>-----------------------------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aspirin (n=48)</td>
<td>Fever</td>
<td>&lt;10 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>68.8 (33)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>26.5 (14)</td>
<td></td>
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</tr>
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<td>Paracetamol (n=189)</td>
<td>Fever</td>
<td>94.7 (179)</td>
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<tr>
<td></td>
<td>Headache</td>
<td>&lt;10 (6)</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Pain</td>
<td>&lt;10 (5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diclofenac (n=43)</td>
<td>Fever</td>
<td>&lt;10 (2)</td>
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<tr>
<td></td>
<td>Headache</td>
<td>14 (6)</td>
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</tr>
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<td></td>
<td>Pain</td>
<td>81.4 (35)</td>
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</tr>
<tr>
<td>Ketorolac (n=4)</td>
<td>Pain</td>
<td>25 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Eye disease</td>
<td>75 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tramadol x</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td>Pizotifen (n=2)</td>
<td>Headache</td>
<td>50 (1)</td>
<td></td>
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<td></td>
<td>Migraine</td>
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<td></td>
<td></td>
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<td>Chlorphenamine (n=37)</td>
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<td></td>
<td>Allergy</td>
<td>&lt;10 (3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sedation</td>
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</tr>
<tr>
<td>Loratadine (n=9)</td>
<td>Cough</td>
<td>44.4 (4)</td>
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<tr>
<td></td>
<td>Allergy</td>
<td>55.6 (5)</td>
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<td></td>
</tr>
<tr>
<td>Desloratadine (n=1)</td>
<td>Allergy</td>
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<td></td>
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<td>Cetirizine (n=29)</td>
<td>Cough</td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Cold</td>
<td>&lt;10 (1)</td>
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<td>Allergy</td>
<td>82.8 (24)</td>
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<td>Asthma</td>
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<tr>
<td></td>
<td>Fever</td>
<td>&lt;10 (1)</td>
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<td>Sedation</td>
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<td>Promethazine (n=13)</td>
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<td>Allergy</td>
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<td>Sedation</td>
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**Table 4: Self medication of medicines in different diseases/symptoms**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Symptoms/Diseases</th>
<th>Total Incidence of Self medication</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>%n</td>
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<tr>
<td>Aspirin</td>
<td>Fever</td>
<td>&lt;10 (6)</td>
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<tr>
<td></td>
<td></td>
<td>89 (210)</td>
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<td>&lt;10 (20)</td>
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<td>Paracetamol (n=398)</td>
<td>Fever</td>
<td>91.4 (364)</td>
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<td>&lt;10 (24)</td>
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<td></td>
<td></td>
<td>&lt;10 (10)</td>
</tr>
<tr>
<td>Diclofenac (n=112)</td>
<td>Fever</td>
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<tr>
<td></td>
<td></td>
<td>&lt;10 (2)</td>
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<tr>
<td></td>
<td></td>
<td>97.3 (109)</td>
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<td>Ketorolac (n=8)</td>
<td>Pain</td>
<td>50 (4)</td>
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<td></td>
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<td>50 (4)</td>
</tr>
<tr>
<td>Tramadol</td>
<td>Fever</td>
<td>100 (8)</td>
</tr>
<tr>
<td>Pizotifen (n=5)</td>
<td>Fever</td>
<td>20 (1)</td>
</tr>
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<td></td>
<td></td>
<td>20 (1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>60 (3)</td>
</tr>
<tr>
<td>Chlorphenamine (n=140)</td>
<td>Cough</td>
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<td></td>
<td></td>
<td>51.1 (71)</td>
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<tr>
<td></td>
<td></td>
<td>6.5 (9)</td>
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<tr>
<td></td>
<td></td>
<td>8.6 (12)</td>
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<td></td>
<td></td>
<td>6.5 (9)</td>
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<td>15.1 (21)</td>
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<td></td>
<td></td>
<td>&lt;10 (2)</td>
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<tr>
<td>Loratadine (n=29)</td>
<td>Cough</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>37.9 (11)</td>
</tr>
<tr>
<td></td>
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<td>51.7 (15)</td>
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<tr>
<td></td>
<td></td>
<td>&lt;10 (1)</td>
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<tr>
<td>Desloratadine (n=6)</td>
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<td>100 (6)</td>
</tr>
<tr>
<td>Cetirizine (n=113)</td>
<td>Cough</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>&lt;10 (10)</td>
</tr>
<tr>
<td></td>
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<tr>
<td></td>
<td></td>
<td>&lt;10 (1)</td>
</tr>
<tr>
<td>Promethazine (n=79)</td>
<td>Cough</td>
<td>87.3 (69)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12.7 (10)</td>
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</tbody>
</table>
Table 5: Long term use of drugs in the respective most highly self medicated symptom/disease

<table>
<thead>
<tr>
<th>Drug</th>
<th>Symptom/Disease</th>
<th>Long Term Use (&gt;7 days)</th>
<th></th>
<th></th>
<th>Chi square (Prescription vs Self Medication)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Self medicated most frequently</td>
<td></td>
<td>With</td>
<td>Self</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Prescription</td>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>Headache</td>
<td></td>
<td>6.1 (2)</td>
<td>2.4 (5)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>Fever</td>
<td></td>
<td>4.5 (8)</td>
<td>2.2 (8)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Pain</td>
<td></td>
<td>11.4 (4)</td>
<td>2.8 (3)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Pain</td>
<td></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Eye disease</td>
<td></td>
<td>100 (1)</td>
<td>25 (1)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Tramadol</td>
<td></td>
<td></td>
<td>0 (0)</td>
<td>12.5 (1)</td>
<td>N/A</td>
</tr>
<tr>
<td>Pizotifen</td>
<td>Migraine</td>
<td></td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>N/A</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>Cold</td>
<td></td>
<td>0 (0)</td>
<td>8.5 (6)</td>
<td>N/A</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>Allergy</td>
<td></td>
<td>8.3 (2)</td>
<td>5.8 (5)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Loratadine</td>
<td>Allergy</td>
<td></td>
<td>80 (4)</td>
<td>6.7 (1)</td>
<td>P&lt;0.05</td>
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<tr>
<td>Desloratadine</td>
<td>Allergy</td>
<td></td>
<td>100 (1)</td>
<td>0 (0)</td>
<td>Not Significant</td>
</tr>
<tr>
<td>Promethazine</td>
<td>Cough</td>
<td></td>
<td>10 (1)</td>
<td>11.6 (8)</td>
<td>Not Significant</td>
</tr>
</tbody>
</table>
Date Rape Drug awareness among College Girls

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Department of Community Medicine, Pt. J.N.M. Medical College  
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Abstract
The date rape drugs are being increasingly used in Sexual assault especially among adolescent girls due to their sedative and amnesic effect. Creating awareness among the vulnerable groups is the only effective measure to check this crime. In this backdrop, a cross-sectional study was conducted among 280 girls. A questionnaire was used to assess awareness about drug facilitated sexual assault, to know most common source of information about such drugs and to get feedback on acceptable preventive measures against such sexual assault. This study finds that about 70% of girls were unaware about existence and use of such drugs. In the rest 30% who were aware, 56% didn’t know name of such drugs while remaining 44% who knew specific names reported mainly Sedatives and Hypnotics followed by Alcohol. The awareness was found to be significantly linked with professional course of the subjects while it was not significantly linked with each of the socio-economic status, residential background & level of education. The predominant sources of information were movies (22%) and TV (21%) indicating that electronic media plays important role in creating awareness. The most common circumstance of use of such drugs is Party (7.2%) followed by Bar (2.4%). Institutional sex education is most preferred choice of preventive measure (31.78%) followed by banning of drug (20%).

Key Words: date rape drug, sexual assault, awareness, media, party.

Introduction
Since ages, Rape has always been a social problem. Females have been a victim of this crime in one form or other but in recent past with modernization of society and liberalization of girls in social behavior, it is taking new form.

Studies reveal that Acquaintance rape is the most common type of rape (Mary P. Koss, 1988¹). Most of the time female is raped by someone she knows, trusts, or loves. The perpetrator might be a partner, coworker, friend or neighbor (Office of crime victims advocacy²).
Drug Assisted Rape is a type of acquaintance rape where drugs are used without the consent of the victim (Hensley, 2002). The victim is usually a teenager girl and those in 20’s by an acquaintance (Rickert VI, 1998). With the advent of better, cheap and easy available drugs, the sedative drugs are being increasingly used in Sexual assault. These are also known as Date Rape Drugs because usually they are associated with dating. However apart from dating, cases of date drug rape are also occurring in parties and other frequent hangouts (Sampson). According to the National Institutes of Health, the date rape drug is odorless, colorless and tasteless. It can be put in someone’s drink unknowingly and will incapacitate the victim for hours. Perpetrators make their use due to their amnesic effect. The victim is sedated during Sexual assault and is unable to recall the events thereafter under the influence of drug.

A study (ElSohly MA, 1999) conducted on urine samples collected from victims of alleged sexual assault analyzed samples for alcohol and drugs which may be associated with sexual assault in United States. It showed that, with respect to alleged sexual assault cases, the prevalence of ethanol was very high, followed by cannabinoids, cocaine, benzodiazepines, amphetamines, and GHB (Gamma hydroxybutyrate). While earlier only a couple of substances were supposed to be implicated with sexual assault, this study showed that almost 20 different substances were associated with this crime. This study also raises the concern of illicit and licit drug use in sexual assault cases and suggests the need to test for a range of drugs in these cases. It also highlights the need to test for GHB, which is not generally tested for in a normal toxicology screen.

The studies conducted worldwide reflected low awareness level (6, 7). Creating awareness among the vulnerable groups is the only effective weapon to check this crime. In this backdrop, the above study has been undertaken to find out the level of awareness of this problem among girls students of medical college Raipur. This study intends to know about prevalence of awareness of date rape drugs and what girls generally think of the various preventive measures in this regard.

Aims and Objectives

1. To assess awareness about use of date rape drugs in drug facilitated sexual assault.

2. To assess linkage between the awareness about date rape drugs with various Socio-Demographic factors.

3. To identify most common source of information about such drugs.

4. To get feedback on acceptable preventive measures against such sexual assault.

Method

A cross-sectional study was conducted by interviewing 280 Medical, Dental and Paramedical (Nursing and Physiotherapy) girl students of PT, J. N. M. Medical College, Raipur, Chhattisgarh, India. A pre-tested questionnaire consisting of subject’s details viz Age, Residential background, Socio Economic Status, Marital status, Professional
course they are pursuing and their awareness about use of such drugs, source of awareness and opinion towards different preventive measures was used. The socio-economic status was determined as per Modified Prasad’s Classification which is:

<table>
<thead>
<tr>
<th>Class</th>
<th>Family income per capita per month in Rupees</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>&gt;2399</td>
</tr>
<tr>
<td>II</td>
<td>2399-1200</td>
</tr>
<tr>
<td>III</td>
<td>1199-750</td>
</tr>
<tr>
<td>IV</td>
<td>749-360</td>
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<tr>
<td>V</td>
<td>&lt;360</td>
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</tbody>
</table>

Appropriate statistical tools namely percentage, chi square test have been employed to analyze the data and validate the findings. SPSS was not used. No other statistical package was used. The analysis was done manually and on excel sheet. Sampling was based on non-random purposive method. The ethical approval was taken (No.MCR/Ethical Comm./09/2478 and No.MCR/Ethical Comm./09/2479-82).

**Study Limitations**
1. The Study was limited to Medical, Dental and Paramedical girl students due to ethical issues.
2. Due to paucity of studies on this subject, the prevalence of problem was unknown. Therefore minimum required sample size based on parameters could not be ascertained. Hence a relatively large size of 280 subjects was purposely undertaken.

**Observations:**

<table>
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<th>Background characteristic</th>
<th>Number</th>
<th>Percentage</th>
</tr>
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</tr>
<tr>
<td>Tribal</td>
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<tr>
<td>Rural</td>
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<td>21.42</td>
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<td>Urban</td>
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<tr>
<td>Skip</td>
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<td>Total</td>
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<tr>
<td><strong>Socio-Economic Status</strong></td>
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</tr>
<tr>
<td>I</td>
<td>76</td>
<td>27.14</td>
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<tr>
<td>II</td>
<td>43</td>
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<td>3.57</td>
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<td>32</td>
<td>11.42</td>
</tr>
<tr>
<td>Medium</td>
<td>155</td>
<td>55.35</td>
</tr>
<tr>
<td>Average</td>
<td>57</td>
<td>20.35</td>
</tr>
</tbody>
</table>
## Interpretation:
Two thirds (66.07%) of girls belonged to urban background. Nearly half (50.35%) of the girls were reluctant to tell their family income. In those who mentioned their family income, highest percentage (27.14%) belonged to SES (Socio-Economic Status) I as per Modified Prasad Classification. There were no girls belonging to SES grade V. More than half (55.35%) girls belonged to medium school background. Majority of girls (45%) were students of Nursing College followed by Dental College (25%) and Medical College (20.35%). Majority (41.78%) didn’t tell their year of studying. Among those who did, almost freshman and sophomores together constituted the majority (37.85%).

![Figure 1: Awareness level of girls](image)

**Interpretation:** Awareness level was very low and this is shockingly low in medical and paramedical students who should all aware of such drugs. Only 29.65% girls were aware of date rape drugs.
Table 2: Awareness in association with professional course

<table>
<thead>
<tr>
<th>Professional Course</th>
<th>Awareness</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Medical</td>
<td>24</td>
<td>33</td>
</tr>
<tr>
<td>Dental</td>
<td>4</td>
<td>66</td>
</tr>
<tr>
<td>Physiotherapy</td>
<td>5</td>
<td>22</td>
</tr>
<tr>
<td>Nursing</td>
<td>50</td>
<td>76</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>197</td>
</tr>
</tbody>
</table>

\(x^2: 7.86\), degree of freedom: 3, the p-value comes out to be 0.049 which is < 0.05 hence p-value is significant.

**Interpretation:** The professional course was found to be significantly linked with the level of awareness.

Table 3: Awareness in association with residential background

<table>
<thead>
<tr>
<th>Residential Background</th>
<th>Awareness</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Urban</td>
<td>62</td>
<td>123</td>
</tr>
<tr>
<td>Rural</td>
<td>19</td>
<td>41</td>
</tr>
<tr>
<td>Tribal</td>
<td>0</td>
<td>17</td>
</tr>
<tr>
<td>Skip</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>197</td>
</tr>
</tbody>
</table>

\(x^2: 0.047\), degree of freedom: 1, the p-value comes out to be 0.8284 which is > 0.05 hence p-value is insignificant.

**Interpretation:** The residential background was not found to be significantly linked with the level of awareness.

Table 4: Awareness in association with school background:

<table>
<thead>
<tr>
<th>School Background</th>
<th>Awareness</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Paush</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>Medium</td>
<td>50</td>
<td>105</td>
</tr>
<tr>
<td>Average</td>
<td>22</td>
<td>35</td>
</tr>
<tr>
<td>Skip</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>197</td>
</tr>
</tbody>
</table>

\(x^2: 0.032\), degree of freedom: 4, the p-value comes out to be 0.9999 which is > 0.05 and hence p-value is insignificant.
**Interpretation:** The school background was not found to be significantly linked with the level of awareness.

**Table 5: Awareness in association with socio-economic status:**

<table>
<thead>
<tr>
<th>Socio-Economic Status</th>
<th>Awareness</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>I</td>
<td>23</td>
<td>53</td>
</tr>
<tr>
<td>II</td>
<td>17</td>
<td>26</td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>IV</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Skip</td>
<td>7</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>197</td>
</tr>
</tbody>
</table>

$x^2$: 8.67, degree of freedom: 4, the p-value is comes out to be 0.0699 which is > 0.05 hence p-value is insignificant.

**Interpretation:** The Socio-Economic Status was not found to be significantly linked with the level of awareness.

**Table 6: Awareness in association with year of education**

<table>
<thead>
<tr>
<th>Education Level</th>
<th>Awareness</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Freshman</td>
<td>19</td>
<td>32</td>
</tr>
<tr>
<td>Sophomore</td>
<td>14</td>
<td>41</td>
</tr>
<tr>
<td>Junior</td>
<td>17</td>
<td>21</td>
</tr>
<tr>
<td>Senior</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Skip</td>
<td>25</td>
<td>92</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>197</td>
</tr>
</tbody>
</table>

$x^2$: 2.84, degree of freedom: 4, the p-value comes out to be 0.5849 which is > 0.05 hence p-value is insignificant.

**Interpretation:** The Education Level was not found to be significantly linked with the level of awareness.
Table 7: Name of Drugs

<table>
<thead>
<tr>
<th>Name of Drugs</th>
<th>Number</th>
<th>Percentage of aware girls (83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabinoids</td>
<td>1</td>
<td>1.20</td>
</tr>
<tr>
<td>Alcohol</td>
<td>6</td>
<td>7.22</td>
</tr>
<tr>
<td>Barbiturates</td>
<td>4</td>
<td>4.81</td>
</tr>
<tr>
<td>Opioids</td>
<td>4</td>
<td>4.81</td>
</tr>
<tr>
<td>Sedatives and hypnotics</td>
<td>9</td>
<td>10.84</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>1</td>
<td>1.20</td>
</tr>
<tr>
<td>Multiple</td>
<td>12</td>
<td>14.45</td>
</tr>
<tr>
<td>Skip</td>
<td>46</td>
<td>55.42</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>100</td>
</tr>
</tbody>
</table>

**Interpretation**: Even in 83 girls, 55.42% didn’t know the name of drug while 44.58% knew the name or chemical nature of the drug while. Out of these who knew, the majority of drug reported were multiple drugs (14.45%) followed by Sedatives and Hypnotics (10.84%). The specific names chiefly reported were mainly Alcohol (7.22%) followed by Barbiturates (4.81%) and Opioids (4.81%). None reported name of any Hallucinogen.

Table 8: Source of information regarding Date Rape drugs

<table>
<thead>
<tr>
<th>Source of information</th>
<th>Number</th>
<th>Percentage of aware girls (83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T.V</td>
<td>18</td>
<td>21.68</td>
</tr>
<tr>
<td>Movies</td>
<td>19</td>
<td>22.89</td>
</tr>
<tr>
<td>Newspaper</td>
<td>10</td>
<td>12.04</td>
</tr>
<tr>
<td>Friends</td>
<td>3</td>
<td>3.61</td>
</tr>
<tr>
<td>Novel</td>
<td>1</td>
<td>1.20</td>
</tr>
<tr>
<td>Multiple</td>
<td>27</td>
<td>32.53</td>
</tr>
<tr>
<td>Skip</td>
<td>5</td>
<td>6.02</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>100</td>
</tr>
</tbody>
</table>

**Interpretation**: Out of 83 girls who were aware, 78 (94%) mentioned the source of awareness. The electronic media (T.V & Movies) was chief source of information which together constituted 44.57%. Among printed media, newspaper constituted only 12.04%. None reported Family members or Radio as their source of information. Also none mentioned any real life instance of drug assisted sexual assault.
Table 9: Circumstance of use of Date Rape drugs

<table>
<thead>
<tr>
<th>Instance of real use</th>
<th>Number</th>
<th>Percentage of aware girls (83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Party</td>
<td>6</td>
<td>7.22</td>
</tr>
<tr>
<td>Bar</td>
<td>2</td>
<td>2.40</td>
</tr>
<tr>
<td>Camping</td>
<td>1</td>
<td>1.20</td>
</tr>
<tr>
<td>Multiple</td>
<td>3</td>
<td>3.61</td>
</tr>
<tr>
<td>Not known</td>
<td>73</td>
<td>87.95</td>
</tr>
<tr>
<td>Total</td>
<td>83</td>
<td>100</td>
</tr>
</tbody>
</table>

Interpretation: Party (7.22%) and bar (2.40%) were the most common circumstance of drug use as per the girls. None reported Home or restaurant as circumstances where drug assisted assault is thought to take place.

Table 10: Preferred preventive measure as per respondents

<table>
<thead>
<tr>
<th>Preventive measure</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Banning drug</td>
<td>56</td>
<td>20.00</td>
</tr>
<tr>
<td>Sensitize boys</td>
<td>3</td>
<td>1.07</td>
</tr>
<tr>
<td>Electronic Media exposure</td>
<td>40</td>
<td>14.28</td>
</tr>
<tr>
<td>Institutional Sex Education</td>
<td>89</td>
<td>31.78</td>
</tr>
<tr>
<td>Multiple</td>
<td>61</td>
<td>21.78</td>
</tr>
<tr>
<td>Skip</td>
<td>31</td>
<td>11.07</td>
</tr>
<tr>
<td>Total</td>
<td>280</td>
<td>100</td>
</tr>
</tbody>
</table>

Interpretation: Almost equal support was given to all Preventive measures to increase spread of awareness but the leading accepted preventive measure was institutional sex education (31.78%) as per the girls.

Results

The respondents under study were the girls belonging to 18-24 years of age group. Of these, about **70.35%** were unaware about existence and use of such drugs. In the rest 29.65% who were aware, 44.58% knew specific names of such drugs while rest 55.42% didn’t know their names but were aware about existence and use of such drugs. Among those who knew the name of drugs, multiple names were reported (14.45%) followed by Sedatives and Hypnotics (10.84) however the specific names of drugs chiefly reported were mainly Alcohol (7.22%) followed by Barbiturates (4.81%) and Opioids (4.81%). This highlights the fact that the majority of would-be medical professionals may remain unaware & hence in cases of rape examination, the drug may go undetected. The awareness was found to be significantly linked with professional course of the subjects while it was not significantly linked with socio-economic status, residential background, school background & level of education. The predominant sources of information were movies (22%) and TV (21%) while newspaper constituted only 12.04%. Thus **electronic media** plays main role than printed media in creating awareness. The most common circumstance of use of such drug is Party (7.22%) followed by Bar (2.40%). Thus people engaged in partying and drinking are more prone to fall victim to drug assisted sexual assault. Institutional sex education is most preferred choice of preventive measure (31.78%) followed by Banning of drug (20%) and Electronic media exposure (14%).
Discussion

Southwest Wisconsin Youth Survey (SWYS) survey (Bev Doll, 2006)\(^6\) conducted by 15 school districts and more than 3700 students reflected an awareness level of 46% only. Over half (54\%) of southwest Wisconsin teens have never heard of GHB, which is commonly referred to as the date rape drug. Similarly the awareness level in our study was found to be 29.65\%. Thus the awareness is quite low in this particular area of Raipur.

Also in SWYS, older females are more aware of the drug, 29\% of 12\textsuperscript{th} grade females and 38\% of 11\textsuperscript{th} grade females have never heard of GHB. In contrast we found that the Education Level was not found to be significantly linked with the level of awareness (p-value: 0.5849).

Conclusion

The awareness level is very low among the girls. It is influenced by type of professional course and electronic media exposure chiefly Television and Movies. People engaged in partying and bar are more prone to fall victim such drugs. Among the preventive measures, Institutional sex education is accorded highest priority.

Recommendation

The low level of awareness calls for informative media exposure and promotion of institutional sex education.

References

The Dilemma of Enteral against Parenteral Nutrition for the Surgical Patient – A Review

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Abstract

Background: One of the perennial debates in the surgical field is that between enteral and parenteral nutrition. Current recommendations advocate enteral feeding in the event that the gastrointestinal tract is functioning because it is safer, less expensive and more physiological. Delivery of nutrients to the gut may also help maintain gut barrier function and reduce postoperative complications. Parenteral nutrition, on the other hand, is indicated when nutritional support is required but effective enteral nutrition is not possible. This occurs when disease, dysfunction or resection of the intestinal tract results in inability to meet nutritional requirements by enteral means.

The safety and post-operative outcomes of patients offered either type of nutrition is still an ongoing dilemma. Although clinicians agree that the gastrointestinal tract is the preferable route for nutrient administration, patients are often provided total parenteral nutrition because of ease and reliability of administration. The gravity of the problem is highlighted by the plethora of research conducted to compare enteral feeding with parenteral feeding head to head. Such was the number of studies that 5 meta-analyses were conducted over the span of the last 20 years.

Aims and Objectives: The aim of this study is to present a comprehensive scientific review, addressing the conundrums faced in the aspect of nutrition in the surgical patient encountered by medical students and junior doctors. We seek to discuss the importance of perioperative nutrition in the surgical patient, and to expound on some of the ideas surrounding various routes of nutrition in surgical patients.

Methods: A retrospective review via MEDLINE, PUBMED and EMBASE was performed on scientific journals published within the last twenty years. These included meta-analyses, randomised trials, audits, original research and recent
guidelines published by Health Boards. Evidence-based medicine employed in clinical practice is emphasized.

**Results and Findings:** Several prospective randomised trials have been performed to compare the efficacy and safety between the routes of nutrition. One compared a group of major abdominal trauma patients undergoing laparotomy over a 28 month period. Their clinical study demonstrated that traditional protein markers such as albumin and transferrin were restored much better in the enteral group, reducing the incidence of septic complications in the stressed patient. Another randomised trial concluded that glucose metabolism was more physiological in the enterally fed group as they maintained normal insulin levels and had no fatty-acid deficiency. Patients given TPN, on the contrary, developed markedly elevated plasma insulin levels, driving excess glucose into the fat cells and increased lipolysis.

Notwithstanding a paucity of supporting literature for parenteral nutrition, some multi-centre studies have concluded that the use of pre-operative TPN can be used in patients who are severely malnourished. A recent meta-analysis of 27 randomized control trials also showed that TPN has no statistically significant effects on the overall mortality and morbidity of surgical patients.

**Study Limitations:** This review is limited by published data found on the databases as well as only those in the English language.

**Conclusion:** Principal lessons from these collective studies support that the enteral route should be used whenever possible, but should the enteral route not be available for more than one week, early administration of TPN should be considered. The NICE (2006) guidelines advocates that surgical patients who are malnourished through inadequate or unsafe oral intake, but have an accessible gastrointestinal tract or are due to undergo major abdominal procedures should be considered for pre-operative enteral tube feeding.

**Keywords:** Parenteral Nutrition, Enteral Nutrition, Nutrition, Surgical Nutrition, Pre-operative Feeding

**Introduction**

One of the perennial debates in the surgical field is that between enteral and parenteral nutrition. Current recommendations advocate enteral feeding in the event that the gastrointestinal tract is functioning because it is safer, less expensive and physiological. Delivery of nutrients to the gut may also help maintain gut barrier function and reduce postoperative complications (Thomson, 2008). Parenteral nutrition is derived from the Greek words “para” which means beside, and “enteron” meaning intestine. It involves the administration of nutrients in a route other than that of the digestive tract, such as intravenous injection. Parenteral nutrition is indicated when nutritional support is required but effective enteral nutrition is not possible. This occurs when disease, dysfunction or resection of the intestinal tract results in inability to meet nutritional requirements by enteral means (Burkitt, Quick, & Reed, 2007; O'Connell, Russell, Williams, Bulstrode, & Bailey, 2008). Some of the specific
indications for parenteral nutrition include proximal intestinal fistula, inflammatory bowel disease, massive intestinal resection, ileus and severe pancreatitis (O'Connell et al., 2008).

The safety and post-operative outcomes of patients offered either type of nutrition is still an ongoing dilemma. Although clinicians agree that the gastrointestinal tract is the preferable route for nutrient administration, patients are often provided total parenteral nutrition because of ease and reliability of administration (Kudsk et al., 1992). The gravity of the problem is highlighted by the plethora of research conducted to compare enteral feeding with parenteral feeding head to head. Such was the number of studies that 5 meta-analyses were conducted over the span of the last 20 years (Thomson, 2008).

The aim of this study is to present a comprehensive scientific review, addressing the conundrums faced in the aspect of nutrition in the surgical patient encountered by medical students and junior doctors. We seek to discuss the importance of perioperative nutrition in the surgical patient, and to expound on some of the ideas surrounding various routes of nutrition in surgical patients.

**History of Nutrition in Surgery**

Nutrition in surgery has seen many eminent founding fathers in its ranks, devising ways for aiding patients who were afflicted with disease. John Hunter, a distinguished Scottish surgeon, attended to King George III and pioneered the use of nasoenteric tube-feeding in London. He was famed for his astute skills of observation and keen scientific mind. In 1973, Using an eel-skin over whale-bone, he managed to successfully feed a patient whose muscles of glutition were paralysed by passing it down to the oesophagus (Deitel, 1985).

In 1831, a cholera epidemic in England became a stimulus to the development of intravenous infusions techniques. Cholera induced fluid losses from vomiting and diarrhoea, leading to fatal dehydration. Hence, the administration of fluid by mouth or rectum was impossible. Thomas Latta, also a Scottish doctor, managed to successfully infuse saline solutions into his patients. His research was based on ‘diluting’ patients’ blood with water and salt, which was initially thick, black and cold. By selecting a patient who was at terminal stages, he injected a large amount of saline solutions into her antecubital vein, managing to quickly restore her to health (Deitel, 1985).

These examples illustrate the humble beginnings of the importance of nutrition in surgery and medicine. Research and creativity allowed these doctors to save many lives. The techniques of artificial feeding were further refined and developed until today, but the principles of improving the health of the patients they treated remains the same.

**Nutrition in Surgery – Why is it important?**
Nutrition in surgical patients is an important issue. A nutritionally depleted patient undergoing surgery can lead to higher incidences of postoperative morbidity and mortality (Howard & Ashley, 2003). Malnutrition is defined as a wasting condition resulting from energy and protein deficiency, occasionally with vitamin and trace element deficiency as well (Burkitt et al., 2007). Malnutrition may be present in close to 50% of patients admitted to surgical wards, and the prompt assessment of nutritional needs with appropriate management plans remains a crucial component of surgical care (O'Connell et al., 2008). Whilst the adequately nourished patient may tolerate major surgery well with rapid recovery, the severely malnourished patient may suffer from impaired wound healing, infections or even multiorgan failure should malnutrition be severe (Howard & Ashley, 2003). Hence, the aim of nutritional support is to identify patients in need and to ensure that their nutritional requirements are met by the most appropriate route, and in a manner that minimizes the risk of complications.

The metabolic response to surgery

The physiological insult of bodily injury results in a surge of stresses on the body accompanied by a metabolic response (Ward, 2003). Injuries can encompass surgery, burns, dehydration, sepsis or acute medical illness. Although these changes are transient, a prolonged hypermetabolic state associated with a pronounced negative balance can ensue if adequate nutritional support is not rendered (Deitel, 1985; Hill, 1992). An example is excessive skeletal muscle proteolysis, which may occur with further depression of metabolism (O'Connell et al., 2008; Ward, 2003). Dr David Cuthbertson of Britain divided the metabolic response to injury into an early ‘ebb phase’ and a ‘flow phase’.

The ebb phase begins immediately after injury and lasts for typically 12-24 hours. It is characterized by hypovolaemia and a subsequent sympathetic and adrenal response, lasting until circulating blood volume has been replenished. The appearance of the pale, clammy and tachycardic patient visited by the surgeon soon after surgery is indicative of the ebb phase (Hill, 1992). A combination of pain, hypovolaemia and acidosis triggers the activity then of the sympatho-adrenal system. This is accompanied by the release of adrenocorticotrophic hormone (ACTH), growth hormone (GH) and glucagon. Hyperglycaemia during this phase results from hepatic glycogenolysis secondary to catecholamine release (Burkitt et al., 2007; Deitel, 1985; Hill, 1992).

The flow phase then ensues over the next 14 days where there is oxidation of muscle protein to provide glucose, which is an essential fuel for the brain and healing tissue and has become depleted. The release of cytokines such as interleukin-1 and interleukin-6 during this phase also contribute to the catabolic nature of this phase (Hill, 1992; Mizock, 2003). This stress response to injury represents a complex interaction between the neuroendocrine and cytokine systems (Mizock, 2003). The cumulative effects of the body’s response can result in extreme changes in fluid balance and electrolyte concentrations. The flow phase eventually merges into the anabolic phase, where protein and energy stores lost during the post-injury period are
repleted. The use of perioperative nutrition such as enteral and parenteral feeding seeks to reduce the harmful catabolic sequelae and to hasten the anabolic process of healing.

**Benefits of Good Nutrition to the Surgical Patient**

Nutritional support, both enterally and parenterally, has led to improved nutritional status and clinical outcomes in the malnourished patient and is largely supported by literature (Ward, 2003). Postoperative nutritional support in patients has also shown to significantly reduce morbidity and length of hospital stay (Askanazi et al., 1986). To determine the relationship between nutritional status of the patient to length of stay and hospital charges, a prospective audit was conducted on 100 patients. Their results showed that a patient’s good nutritional status translated into reduced costs associated with the length of hospital stay and morbidity, allowing an improved quality of life (Robinson, Goldstein, & Levine, 1987). Conversely, poor nutritional support leading to weight loss associated with organ impairment is a significant surgical risk factor in modern practice (Windsor & Hill, 1988). Adequate body protein stores are essential for normal body function and the prevention of postoperative complications which include sepsis, pneumonia, psychologic, respiratory and skeletal muscle dysfunction (Hill, 1992; Ward, 2003; Windsor & Hill, 1988).

**Assessing the Nutritional Status in Surgical Patients**

Although severe malnutrition, such as wasting of proximal limb muscles, is easy to detect, more subtle degrees of nutritional impairment are often overlooked (Salvino, Dechicco, & Seidner, 2004). In general, the severity of malnutrition is proportional to the amount of surgical risk involved (Burkitt et al., 2007; Salvino et al., 2004). The aim of nutritional assessment is to identify patients who are at increased risk of postoperative complications due to malnutrition, and where possible, to improve nutritional status through interventions (Salvino et al., 2004). Table 1 highlights the basis of assessment, which is broadly based on clinical assessment, anthropometric assessment and blood indices, of which clinical assessment is the most accurate.

**Basic Principles of Surgical Nutrition**

**A) Enteral Nutrition**

Enteral nutrition may be administered orally or through feeding tubes. A variety of nutrient formulations are available for enteral feeding, varying in terms of energy content, osmolarity, fat, nitrogen content and nutrient complexity. Most contain 1-2kcal and up to 0.6g of protein per millilitre. Polymeric feeds contain intact protein and thus requiring digestion, whereas monomeric feeds contain nitrogen in its peptide or free amino acid form (Deitel, 1985; Thomson, 2008).

Feeding tubes are appropriate when spontaneous oral intake is not adequate for nutritional requirements. They are inserted into the stomach or small intestine via the
nose or the abdominal wall. If a patient is able to eat and does not have dysphagia, sip feeds containing easily absorbed calories, protein, minerals and vitamins are encouraged (Burkitt et al., 2007). Tube feeds are indicated in patients suffering from swallowing difficulties, including overspills and lack of cooperation. Even if the patient is unable to swallow due to reasons such as bulbar palsy, unconsciousness or facial fractures, complete enteral nutrition may still be delivered through a fine-bore nasogastric tube. These tubes can be negotiated into the jejunum endoscopically or radiologically such as a naso-jejunal tube (O'Connell et al., 2008).

Feeding tubes can also be placed percutaneously into the stomach or jejunum either at operation or with endoscopic and laparoscopic help. Known as gastrostomies, they are often used in patients after stroke, obstructing lesions or in those with an upper gastrointestinal anastomoses. The technique employed is usually by percutaneous endoscopic gastrostomy (PEG) which is an endoscopic procedure. PEG tubes, however, are contraindicated in peritonitis, ascites and prolonged ileus (Burkitt et al., 2007).

B) Parenteral Nutrition

Total parenteral nutrition (TPN) is defined as the intravenous provision of all nutritional requirements, without the use of the gastrointestinal tract (O'Connell et al., 2008). Parenteral nutrition has a very recent history, first described by Dudrick et al in the late 1960s (Dudrick, Wilmore, Vars, & Rhoads, 1968). Jeejeebhoy subsequently showed in his clinical work that through the use of parenteral nutrition, his patients managed to rehabilitate much faster within 23 months and without complications (Jeejeebhoy et al., 1973). This led to the its more accepted and widespread use, with more clinicians beginning to adopt TPN in their practice (Kudsk et al., 1992). Parenteral nutrition, however, should be reserved for appropriate cases of intestinal failure, where the amount of functioning gut is below the minimum required for adequate digestion and absorption of nutrients (Burkitt et al., 2007).

TPN formulations consist primarily of a mixture of glucose, amino acids, lipids, minerals and vitamins. Its aim is to provide sufficient nitrogen and energy to counter the catabolic demands of surgery, trauma and its complications, as well as to compensate for pre-existing malnutrition (Deitel, 1985; Hill, 1992).

It is delivered mostly via the superior vena cava into the internal jugular or subclavian vein. This allows the high venous flow to rapidly dilute the hyperosmolar TPN solution, and minimizes the risk of thrombosis. The Groshong line, a tunnelled line with the skin access point remote from the venous entry point, is adopted when long periods of nutritional support are anticipated. Current NICE (National Institute for Health and Clinical Excellence) guidelines recommends its use when more than 30 days of bedstay is required post-surgery. This is to reduce the complications of line infection (NICE, February 2006).

Discussion
The decision to use enteral or parenteral nutrition for surgical patients, although supplemented by myriads of literature, is one that is fraught with conundrums. Discussed herewith are some of the landmark papers describing previous clinical research. “When the gut works use it” is the common dictum expressed by proponents of the enteral route (Kudsk et al., 1992). Enteral nutrition is the preferred route of administration in surgical patients, as it is safer, less expensive and more physiological as compared to the parenteral route (Thomson, 2008). The normal well-fed intestine absorbs nutrients whilst maintaining an effective barrier against intraluminal toxins and bacteria (Kudsk et al., 1992; O'Connell et al., 2008). Nutrients delivered enterally may therefore be used more efficiently through reaching the liver via the portal circulation rather than by vein (O'Connell et al., 2008). Animal research has also shown that by maintenance of peristalsis, increasing secretory immunoglobulin A and mucin, normal gut motility is promoted having a protective role in preventing infections (Baker, Deitch, Li, Berg, & Specian, 1988; Saito et al., 1987).

Several prospective randomised trials have been performed to compare the efficacy and safety between the routes of nutrition. One of which, conducted by Moore et al, compared a group of major abdominal trauma patients undergoing laparotomy over a 28 month period (Moore, Moore, Jones, McCroskey, & Peterson, 1989). Their clinical study demonstrated that traditional protein markers such as albumin and transferrin were restored much better in the enteral group, reducing the incidence of septic complications in the stressed patient. A randomised trial also concluded that glucose metabolism was more physiological in the enterally fed group as they maintained normal insulin levels and had no fatty-acid deficiency. Patients given TPN, on the contrary, developed markedly elevated plasma insulin levels, driving excess glucose into the fat cells and increased lipolysis (McArdle, Palmason, Morency, & Brown, 1981).

Moreover, the capacity to administer TPN peripherally is limited by the development of thrombophlebitis and venous thrombosis, a consequence of high osmolarity and low pH of feeding solutions. Catheter-related complications were also found to have a high incidence due to its invasive nature, illustrated by a prospective randomised study (Dudrick et al., 1968; Ryan et al., 1974). Their study described a high proportion of patients having catheter infections after being given TPN as compared to Enteral feeding. Other complications which were commonly exhibited included complications related to the feeding regimen, such as electrolyte abnormalities, hyperinsulinaemia and hypertriglyceridaemia (Ryan et al., 1974).

However, enteral nutrition is not without its critics. In enteral nutrition, complications can be divided into those resulting from intubation of the GI tract and those related to nutrient delivery (O'Connell et al., 2008). Catheter-related complications, as reported in a review by Thomson et al, involve perforation of the intestine and the inadvertent introduction of the feeding tube into the tracheobronchial tree. This can lead to aspiration of feed and perforation of the respiratory tract, introducing the feed into the pleural cavity (Thomson, 2008). Complications related to nutrient delivery include diarrhoea, intolerance causing flatulence and hyperglycemia. Moreover, in the intensive care unit, it is easier to infuse nutrition through an existing indwelling central line than to deal with diarrhoea, bloating and interruptions to feeds (Kudsk et al., 1992).
Notwithstanding a paucity of supporting literature for parenteral compared to enteral nutrition, some multi-centre studies such as the one by the Veterans Affairs TPN Cooperative Study Groups have concluded that the use of pre-operative TPN can be used in patients who are severely malnourished. Another prospective randomized study performed by Bozzetti et al showed that 10 days of preoperative TPN continued postoperatively is able to reduce the complication rate by approximately one third and was able to prevent mortality in severely malnourished patients with gastrointestinal cancer (Bozzetti et al., 2000; Ward, 2003). A recent meta-analysis of 27 randomized control trials concludes that TPN has no statistically significant effects on the overall mortality and morbidity of surgical patients (Heyland et al., 2001).

**Current Guidelines**

Hence, with the relatively contradictory evidence, there are often dilemmas amongst medical students and junior doctors. Clinical guidelines, based on the best available scientific evidence, are produced to aid healthcare professionals and patients in making informed decisions about appropriate healthcare. Enteral tube feeding and parenteral feeding are considered if there is inadequate spontaneous oral intake, or the problem of dysphagia in the patient. The current NICE guidelines (2006) recommend the following: A) That surgical patients who are malnourished through inadequate or unsafe oral intake, but have an accessible gastrointestinal tract or are due to undergo major abdominal procedures should be considered for pre-operative enteral tube feeding. B) General surgical patients should not have enteral feeding within 48 hours post-surgery unless they are malnourished or at risk of. They should have an inadequate oral intake and possess a functional and accessible gastrointestinal tract (NICE, February 2006).

Supplementary peri-operative parenteral nutrition should be indicated in malnourished surgical patients who have an inadequate or unsafe oral and enteral nutritional intake. A non-functional, inaccessible, or perforated gastrointestinal tract also supports its use. Should intestinal intolerance persistently limit enteral tube feeding in surgical or critical care patients, parenteral nutrition should be used to supplement or replace enteral tube feeding (NICE, February 2006). The latest ESPEN (European Society for Clinical Nutrition and Metabolism) 2009 guidelines also reinforce that post-operative parenteral nutrition is beneficial in patients with postoperative complications impairing gastrointestinal function, who are unable to receive and absorb adequate amounts of oral/enteral feeding for at least 7 days (Braga et al., 2009).

Refeeding problems are a dangerous and life threatening complication of incorrect treatment. This arises when at first, malnourishment reduces carbohydrate intake leading to catabolism of fat and protein instead of carbohydrate. Intracellular electrolytes, in particular phosphate which is essential for vital phosphorylation reactions, are depleted in the process. Giving nutrients and fluid to these malnourished patients reverses fat to carbohydrate metabolism. As a result, insulin secretion rises and cellular uptake of glucose, phosphate, potassium and water increases (Burkitt et al., 2007; Deitel, 1985; Hill, 1992). It is recommended that these patients are assessed carefully for risk factors of refeeding problems, seen in Table 2. For these patients at risk, the NICE guidelines recommends the ‘start low go slow’ rule where nutrition
support at a maximum of 10 kcal/kg/day slowly increasing to meet or exceed full needs by 4-7 days.

Looking to the Future

Amidst ongoing studies that seek to validate the roles and benefits of the various routes of delivery, interest in immunonutrition, a relatively new regimen, is developing. Immune-enhancing formulae are intended to boost the function of the immune system of patients suffering from the stresses of surgery and acute illness (Salvino et al., 2004; Ward, 2003). Glutamine is actively involved in antioxidant defence mechanisms through the influence of glutathione synthesis. It has an essential role in nitrogen transport and acid-base homeostasis. During severe stress and nutritional depletion, the demand for glutamine may exceed its production. Other studies have shown that the incorporation of glutamine to parenteral nutrition regimens, given to patients post abdominal surgery results in improved nitrogen balance and a quicker lymphocyte recovery. This translated into decreased length of stay and morbidity (Mertes et al., 2000; Morlion et al., 1998; Ward, 2003). There is also reduced complications such as infections and wound complications in patients treated with immunonutrition as compared to standard enteral nutrition (Braga et al., 2009).

Conclusion

In conclusion, principal lessons from these collective studies support that the enteral route should be used whenever possible, but should the enteral route not be available for more than one week, early administration of TPN should be considered.

In the ethos of holistic and patient-centred care, the safety and well-being of the patient should be the prime concern of surgeons and doctors alike. Understanding the various viewpoints of authors allows us to craft a better picture of how to better manage the malnourished patient undergoing surgery. The importance of nutrition in surgical patients cannot be over-emphasized. It is important to adopt and inculcate good clinical practice guidelines based on evidence-based medicine.

References


NICE. (February 2006). Nutrition support in adults Oral nutrition support, enteral tube feeding and parenteral nutrition., from www.rcseng.ac.uk


Tables

Table 1.1: Assessments for identification of the patient at risk

<table>
<thead>
<tr>
<th>A) CLINICAL</th>
<th>B) ANTHROPOMETRIC</th>
<th>C) BLOOD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malnutrition seen in the following:</td>
<td>- Reduced Tricep skin fold thickness, which shows body density and overall fat content</td>
<td>- Low serum albumin levels of &lt; 35g/L is associated with a 5-fold increase in complications and 10-fold increase in death rate.</td>
</tr>
<tr>
<td>- body mass index (BMI) of less than 18.5 kg/m²</td>
<td>- Reduced Mid-arm circumference</td>
<td>- Reduced plasma prealbumin</td>
</tr>
<tr>
<td>- unintentional weight loss greater than 10% within the last 3–6 months is a poor prognostic outcome</td>
<td>- Weak Hand grip strength: This is easy to perform but lacks reproducible baseline data</td>
<td>- Reduced lymphocyte count</td>
</tr>
<tr>
<td>- a BMI of less than 20 kg/m² and unintentional weight loss greater than 5% within the last 3–6 months.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Lack of nutritional intake for 5 days or more</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: NICE Criteria for determining people at high risk of developing refeeding problems

Patient has one or more of the following:
- BMI less than 16 kg/m²
- Unintentional weight loss greater than 15% within the last 3–6 months
- little or no nutritional intake for more than 10 days
- low levels of potassium, phosphate or magnesium prior to feeding.

Or patient has two or more of the following:
- BMI less than 18.5 kg/m²
- unintentional weight loss greater than 10% within the last 3–6 months
- little or no nutritional intake for more than 5 days
- a history of alcohol abuse or drugs including insulin, chemotherapy, antacids or diuretics.
Pulmonary Lung Functions in Sugarcane harvesters who Smoke

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Mahagaonkar AM

Abstract

Background

In India smoking is a common habit prevalent in both urban and rural areas. Cigarette and bidi (lower unrefined form of cigarette without any filter) smoking has extensive effects on respiratory function and is clearly implicated in the etiology of a number of respiratory diseases.

Objectives

1. To study and compare the pulmonary function tests among smokers in sugarcane harvesters in a rural area.
2. To study the role of possible associated factors and relation of type, quantity and duration of smoking on the pulmonary function tests.

Methods

Setting: Pravara Rural Hospital, Loni, District- Ahmednagar, Maharashtra.

Study design: Cross sectional study.

Materials & Methods: The pulmonary function tests were assessed on computerized spirometer in 400 male subjects comprising of 200 smokers and 200 non smokers and results were compared.

Statistical analysis: was done using SPSS Statistical Software 15.0.
Results

Almost all the pulmonary function parameters were significantly reduced in smokers and obstructive pulmonary impairment was commonest. Thus, by spirometry a spectrum of lung disorders may be detected at an early stage and subsequent morbidity can be minimized.

Conclusion

The present study reveals the effect of type, duration and pattern of smoking on the pulmonary functions in smokers. Bidi smoking was most common as the study setting was in rural India. Almost all the pulmonary function parameters were significantly reduced in smokers as compared to non-smoker controls and obstructive pulmonary impairment was commonest in smokers. By screening smokers, by computerized pulmonary function testing, the early changes in airflow obstruction may be detected.

Keywords: Smoker, Spirometry, Pulmonary functions, rural area

Introduction

Cigarettes kill an estimated 5 million people annually worldwide\(^1\). The World Health Organization reported that tobacco smoking killed 100 million people worldwide in the 20th century and warned that it could kill one billion people around the world in the 21st century\(^2\). By the early 2030, tobacco related death would increase to about 10 millions a year\(^3\). Tobacco smoking rates have decreased in industrialized countries since 1975, but there has been a corresponding 50% increase in smoking rates in low-income countries\(^4\).

In India smoking is a common habit prevalent in both urban and rural areas irrespective of mode of smoking i.e. cigarettes, bidis, pipes, cigar, hookah etc. In India, tobacco is consumed mainly in the form of bidis (54%), followed by smokeless tobacco (27%) and cigarettes (9%)\(^5\).

Bidi smoke may be more injurious because bidi contains unrefined form of tobacco as compared to cigarettes\(^6,7\). Cigarette smoking has extensive effects on respiratory function and is clearly implicated in the etiology of a number of respiratory diseases, particularly chronic bronchitis, emphysema, and bronchial carcinoma\(^8\).

Materials and Methods

The present cross sectional study was conducted in Pravara Rural Hospital of Rural Medical College, PIMS, Loni, in district Ahmednagar, Maharashtra from January 2007 to August 2008.
Sample Size: The study population included 400 male subjects comprising of 200 smokers and 200 non smoker controls aged between 30-60 years.

Sampling was done as per the inclusion & exclusion criteria.

**Inclusion criteria**

- Individuals with history of smoking cigarettes / bidis, daily for at least one year, were considered as smokers.\(^9\)

**Exclusion criteria**

- Ex-smokers or past smokers were excluded from the study.
- Those with chronic disease or requiring hospital admission or having serious illness 2 weeks prior to the start of the study were excluded.

**Control**

For the control group, 200 healthy non smokers of almost same age and matching other characteristics were selected. The materials used in the study were a computerized RMS Med-spirometer, weighing machine, measuring tape and Blood Pressure set. To evaluate dose and duration response relationship, quantification of tobacco smoking was performed by calculating smoking index for smokers.

**Smoking Index**: It is equal to multiplication of the average number of cigarettes/bidis smoked per day and duration (in years) of tobacco smoking\(^10,11\).

<table>
<thead>
<tr>
<th>Habit</th>
<th>Smoking Index (Frequency x duration)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-smokers</td>
<td>0</td>
</tr>
<tr>
<td>Light smokers</td>
<td>1-100</td>
</tr>
<tr>
<td>Moderate smokers</td>
<td>101-200</td>
</tr>
<tr>
<td>Heavy smokers</td>
<td>more than 200</td>
</tr>
</tbody>
</table>

The observations of the study were analyzed by statistical methods like percentages, chi square test and t-test of significance.

**Results**

In the present study it was observed that there was no significant difference in the mean physical parameters like age, height, weight, body mass index and body surface
area by calculating mean and standard deviation in smokers and non-smokers (Table 1). Most of the smokers smoked only bidi (62.0%) followed by both cigarette and bidi (mixed) (24.0%) and only cigarettes. (14.0%) (Table 2) Most smokers were light smokers (54.0%) followed by moderate smokers (30.0%) and heavy smokers (16.0%) based on the criteria of smoking index (Table 3). Majority of the light smokers were in the age group of 41-50 years (51.85%), moderate smokers in 51-60 years (46.66%) and heavy smokers, 51-60 years (75.0%) (Table 4).

All Pulmonary function parameters like FVC, FEV1, FEV1/FVC, PEFR, FEF25-75% and MVV showed statistically highly significant association between smokers and non-smokers by applying unpaired t-test of significance (p < 0.001) (Table 5). The association between smoking and impaired PFT was statistically highly significant. The smokers had 17.3 times more risk of having impaired pulmonary functions as compared to non-smokers (Table 6). The obstructive lung changes were most common and were observed predominantly in bidi smokers. (72.22%) (Table 7)
Table 1: Physical Characteristics of Smokers and Non-Smokers.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Smokers Mean ± 2 S.D.</th>
<th>Non-smokers Mean ± 2 S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.26 ± 10.09</td>
<td>48.10 ± 10.54</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.66 ±0.11</td>
<td>1.67 ± 0.12</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>65.4 ± 8.8</td>
<td>64.4 ± 11.5</td>
</tr>
<tr>
<td>Body Mass Index (BMI)</td>
<td>23.52 ± 3.20</td>
<td>23.80 ± 3.37</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>1.71 ± 0.06</td>
<td>1.74 ± 0.14</td>
</tr>
</tbody>
</table>

S.D. = Standard Deviation

Table 2: Type of Tobacco Smoking in Smokers.

<table>
<thead>
<tr>
<th>Type of smoking</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only Bidi</td>
<td>124</td>
<td>62.0</td>
</tr>
<tr>
<td>Both cigarette &amp; bidi (mixed)</td>
<td>48</td>
<td>24.0</td>
</tr>
<tr>
<td>Only Cigarette</td>
<td>28</td>
<td>14.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 3: Distribution of Grade of Smoking in Smokers.

<table>
<thead>
<tr>
<th>Grade of smoker</th>
<th>Number of smokers</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light smoker</td>
<td>108</td>
<td>54.0</td>
</tr>
<tr>
<td>Moderate smoker</td>
<td>60</td>
<td>30.0</td>
</tr>
<tr>
<td>Heavy smoker</td>
<td>32</td>
<td>16.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>200</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 4: Age Wise Distribution of Grade of Smoking.

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Light Smoker No. (%)</th>
<th>Moderate smoker No. (%)</th>
<th>Heavy smoker No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>31-40</td>
<td>28 (25.92)</td>
<td>8 (13.33)</td>
<td>0 (0.0)</td>
<td>36 (18.0)</td>
</tr>
<tr>
<td>41-50</td>
<td>56 (51.85)</td>
<td>24 (40.0)</td>
<td>8 (25.0)</td>
<td>88 (44.0)</td>
</tr>
<tr>
<td>51-60</td>
<td>24 (22.22)</td>
<td>28(46.66)</td>
<td>24(75.0)</td>
<td>76 (38.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>108 (100.0)</td>
<td>60 (100.0)</td>
<td>32 (100.0)</td>
<td>200 (100.0)</td>
</tr>
</tbody>
</table>
Table 5: Pulmonary Function Tests among Smokers and Non-Smokers.

<table>
<thead>
<tr>
<th>Pulmonary Function Tests (PFTs)</th>
<th>Smokers Mean ± 2 S.D</th>
<th>Non-smokers Mean ± 2 S.D**</th>
<th>Significance p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>2.98 ± 1.06</td>
<td>3.13 ± 0.98</td>
<td>0.03242 (S)</td>
</tr>
<tr>
<td>FEV₁</td>
<td>2.48 ± 1.02</td>
<td>2.81 ± 0.86</td>
<td>0.000692 (HS)</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>83.93 ± 23.98</td>
<td>89.49 ± 10.54</td>
<td>0.003808 (HS)</td>
</tr>
<tr>
<td>PEFR</td>
<td>5.30 ± 3.46</td>
<td>6.80 ± 3.44</td>
<td>0.000034 (HS)</td>
</tr>
<tr>
<td>FEF₂₅-₇₅%</td>
<td>2.99 ± 2.02</td>
<td>3.59 ± 1.74</td>
<td>0.00196 (HS)</td>
</tr>
<tr>
<td>MVV</td>
<td>86.1 ± 44.22</td>
<td>103.6 ± 33.66</td>
<td>0.00002 (HS)</td>
</tr>
</tbody>
</table>

Significance has been calculated by unpaired t test (p < 0.001).

Table 6: Interpretation of PFT results in smokers and non-smokers.

<table>
<thead>
<tr>
<th>PFT Results</th>
<th>Smokers No. (%)</th>
<th>Non-smokers No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive</td>
<td>72 (36.0)</td>
<td>8 (4.0)</td>
<td>80 (20.0)</td>
</tr>
<tr>
<td>Restrictive</td>
<td>4 (2.0)</td>
<td>0 (0.0)</td>
<td>4 (1.0)</td>
</tr>
<tr>
<td>Mixed</td>
<td>8 (4.0)</td>
<td>0 (0.0)</td>
<td>8 (2.0)</td>
</tr>
<tr>
<td>Normal</td>
<td>116 (58.0)</td>
<td>192 (96.0)</td>
<td>308 (77.0)</td>
</tr>
<tr>
<td>Total</td>
<td>200 (100.0)</td>
<td>200 (100.0)</td>
<td>400 (100.0)</td>
</tr>
</tbody>
</table>

Chi square value = 20.84, p < 0.001, highly significant. (Odds’ ratio = 17.3)

Table 7: Relation of Type of smoking with Pulmonary Function tests

<table>
<thead>
<tr>
<th>Type of smoking</th>
<th>PFT interpretation</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obstructive</td>
<td>Restrictive</td>
</tr>
<tr>
<td>Only Bidi</td>
<td>52 (72.22)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Both cigarette/ bidi</td>
<td>16 (22.22)</td>
<td>4 (100.0)</td>
</tr>
<tr>
<td>Only Cigarette</td>
<td>4 (5.55)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Total</td>
<td>72 (100.0)</td>
<td>4 (100.0)</td>
</tr>
</tbody>
</table>

Discussion

In the present study it was observed that there was no significant difference in the mean physical parameters like age, height, weight, body mass index and body surface area thereby showing proper matching of smokers and non-smokers (Table 1). None of individuals smoked tobacco in any form other than bidis or cigarettes. Most smokers were bidi smokers. (62.0%) (Table 2) Also the cigarette smokers usually smoked non-filter cigarettes since they are cheap and easily available in rural areas. In the present study most smokers were light smokers (Table 3) in the age group of 41-50 years (51.85%). Similarly, Burrows et al12 reported that there is quantitative significant relationship between impaired ventilator function and duration and
frequency of smoking (Table 4). All Pulmonary function parameters showed statistically highly significant association between smokers and non-smokers by applying unpaired t-test of significance (p < 0.001). Similar, observations showing lung function impairment in smokers were reported by Burrows et al\textsuperscript{12}, Pandya et al\textsuperscript{13}, and Gupta et al\textsuperscript{14}.

However, several researchers like Angelo\textsuperscript{15} and Mahajan et al\textsuperscript{16} observed no change in FVC in smokers and non-smokers (Table 5). The association between smoking and impaired PFT was statistically highly significant. The smokers had 17.3 times more risk of having impaired pulmonary functions as compared to non-smokers (Table 6). The fall in FEV\textsubscript{1}, PEFR and other flow rates indicate obstructive lung changes and fall in FVC indicates restrictive lung changes. Padmavathy\textsuperscript{17} in a study concluded that the pulmonary function tests are more affected in bidi smokers than in cigarette smokers (Table 7).

**Study Limitation**

Pravara Rural Hospital (PRH) being in a Rural area of Loni, we could not take into consideration the sugarcane harvesters of urban areas. Also not all the sugarcane harvesters of rural area could be taken into consideration due to paucity of time & finances. Also a Chest radiograph & other investigations to rule out various pulmonary diseases was not done.

**Conclusion**

The pulmonary function tests were assessed on a computerized spirometer in 400 male subjects comprising, 200 smokers and 200 non smoker controls. The present study reveals the effect of type, duration and pattern of smoking on the pulmonary functions in smokers. Bidi smoking was most common as the study setting was in rural India. Almost all the pulmonary function parameters were significantly reduced in smokers as compared to non smoker controls and obstructive pulmonary impairment was commonest in smokers. By screening smokers, by computerized pulmonary function testing, the early changes in airflow obstruction may be detected and special emphasis is to be recommended on smoking cessation strategies.

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8. WHO; World tobacco epidemic; 1993; 2nd Edition; p-47.


Influence of Protease Inhibitors on the Pharmacodynamics of Gliclazide in Rats

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Abstract

Background: Type 2 diabetes may occur as a result of HIV-infection and/or its treatment with protease inhibitors. Indinavir, ritonavir and atazanavir are widely used protease inhibitors for the treatment of HIV-infection. Gliclazide is a widely used drug for the treatment of type 2 diabetes. So there is every possibility for the combined use of protease inhibitors with gliclazide in chronic diabetics with HIV-infection. But there is no report on the safety and effectiveness of the combination.

Aims & Objectives: The objective of this study was to investigate the effect of protease inhibitors (indinavir, ritonavir and atazanavir) on the pharmacodynamics of gliclazide in normal and diabetic rats with respect to safety and effectiveness of the combination. The parameters considered for this study include blood glucose, insulin, total hemoglobin, glycosylated hemoglobin, insulin resistance index, beta cell function, insulin sensitivity index and body weight.

Methods/Study Design: Studies in normal and alloxan-induced diabetic rats were conducted with oral dose of gliclazide, interacting drug and their combination with adequate washout in between treatments. After single dose interaction study, the same group was continued with the daily treatment of interacting drug for the next eight days (multiple dose interaction study) with regular feeding. Later after 18 h fasting they were again given the combined treatment on the ninth day. Blood samples were collected in rats from retro orbital puncture to estimate the blood glucose, insulin, total hemoglobin and glycosylated hemoglobin. Blood samples were analyzed for blood glucose by GOD/POD method and plasma insulin concentrations were determined by radioimmunoassay method. Insulin resistance index, insulin sensitivity and percent beta cell function were determined by homeostasis model assessment (HOMA) model.

Results/Findings: Gliclazide produced biphasic hypoglycemic/antidiabetic activity in normal and diabetic rats with peak activity at 2 h and 8 h. Indinavir and ritonavir significantly elevated the blood glucose, insulin and glycosylated hemoglobin values,
whereas the total hemoglobin and body weights were decreased in normal and diabetic rats. The alterations associated with indinavir are more compared to ritonavir treated rats. Atazanavir alone has no significant effect on any parameter, except increase in body weight in normal and diabetic rats.

When given in combination, indinavir significantly reduced the effects of gliclazide in normal and diabetic rats following single and multiple dose treatments of indinavir and it confirms the pharmacodynamic interaction of indinavir with gliclazide. In combination ritonavir and atazanavir significantly enhanced the effects of gliclazide in rats (normal and diabetic) and it confirms the possibility of pharmacokinetic interaction with gliclazide.

**Limitations:** Present study is limited to describe the exact mechanism of action(s) behind these interactions and these have to be confirmed by conducting pharmacokinetic interaction studies. However the present study warrants further studies to find out the relevance of these interactions in other species/human beings and to know the exact mechanism of action(s) behind these interactions.

**Conclusion:** Since the interactions were seen in normal and diabetic rats following single dose and multiple dose administration, they are likely to occur in humans, also leading to decreased or increased activity of gliclazide, which may need dosage adjustment. Hence care should be taken when the combination is prescribed for their clinical benefit in diabetic patients.

**Keywords:** Protease inhibitors, Gliclazide, Diabetes, HIV-infection, Pharmacodynamics, Pharmacokinetics

**Introduction**

The study of mechanisms of drug interactions has profound value for the selection of drug concentrations to provide rational therapy. The drug interaction studies presume much importance especially for drugs which have narrow margin of safety and used for chronic period of time. Diabetes mellitus is such metabolic disorder that needs treatment for chronic period and maintenance of normal blood glucose level is very important in this condition, since both hyperglycemia and hypoglycemia are unwanted phenomenon (Satyanarayana et al, 2006).

Diabetes mellitus is a chronic metabolic disorder characterized by elevated blood glucose levels and disturbances in carbohydrate, fat and protein metabolism with micro and macrovascular complications that result in a significant morbidity and mortality (Saely et al, 2004). Type-1 diabetes is due to decrease in the synthesis of insulin and type-2 diabetes is characterized by hyperglycemia in the context of insulin resistance and relative insulin deficiency. The number of people suffering from diabetes mellitus worldwide is increasing and estimated to 366 million by the year 2030 (Wild et al, 2004).
Type 2 diabetes may occur as a result of HIV-infection and/or its treatment. Highly active antiretroviral therapy (HAART), a combination of non-nucleoside reverse transcriptase inhibitors (NNRTIs), nucleoside reverse transcriptase inhibitors (NRTIs), and protease inhibitors (PIs), is widely used to control HIV-infection and the development of AIDS. Among the many metabolic perturbations that occur as a result of HIV-infection and its treatment, alterations in normal glucose homeostasis remain a particularly prevalent and alarming clinical change in affected patients (Hruz, 2006). HAART has been associated with a spectrum of metabolic abnormalities including ranging from insulin resistance to impaired glucose tolerance and diabetes mellitus, dyslipidemia, and alterations in body fat distribution (Leow et al, 2003), especially with PIs (Dube, 2000). Much of concern is due to the recognition of the long-term complications of insulin resistance and hyperglycemia and understood is the context of the growing worldwide epidemic of type 2 diabetes mellitus (Zimmet, 2001). The widely used PIs include ritonavir, atazanavir and indinavir.

Oral hypoglycemic agents are used in the treatment of type-2 diabetes, among which gliclazide; a second generation sulphonylurea derivative is preferred in therapy because of its antidiabetic activity, low incidence of producing severe hypoglycemia, antioxidant property, and other haemobiological effects (Mastan et al, 2009).

Regulation of glucose metabolism is a key aspect of metabolic homeostasis and insulin is the predominant hormone influencing this regulatory system. Insulin plays a key role in the maintenance of glucose homeostasis and provides the major modulator of glucose storage and utilization. Glucose was measured as a metabolic control of insulin action. The impairment of glucose homeostasis and increase in plasma glucose level are associated with diabetes. Insulin resistance (IR) is a state where normal or elevated insulin level produces a reduced biological response (Cefalu, 2001) and refers to impaired sensitivity to insulin mediated glucose disposal (Reaven, 2004). So it is of greatest importance to study the glucose-insulin homeostasis, in order to have better understanding of the pathological process/mechanisms of insulin resistance to evaluate the safety and effectiveness of the drug combinations. The homeostatic model assessment (HOMA) is more reliable and validated method to measure insulin resistance, insulin sensitivity and β-cell function from fasting glucose and insulin. Quantifying total hemoglobin, glycosylated hemoglobin and body weight could give more reliable findings in this task.

In our previous studies (Mastan et al, 2009), we investigated the effect of antiretroviral drugs on the pharmacodynamics of gliclazide in animal models with respect to few parameters. However, there is no much evidence on the effect of antiretroviral drugs on the activity of gliclazide with respect to multiple parameters, which will substantiate the actual facts of the interactions. So the present study was planned to investigate the effect of protease inhibitors in rats (normal and diabetic) to evaluate the safety and effectiveness of the combination.

Material and Methods

Drugs and Chemicals
Gliclazide and protease inhibitors (indinavir, ritonavir and atazanavir) are the gift samples from Micro Labs (Bangalore, India) and Aurobindo Pharma Ltd (Hyderabad,
India), respectively. Alloxan monohydrate was purchased from LOBA Chemie (Mumbai, India). Glucose kits (Span diagnostics) were purchased from local pharmacy. All other reagents/chemicals used were of analytical grade.

**Animals**

Albino rats of either sex of 6 to 8 weeks of age, weighing between 250-320 g were used in the study. They were procured from National Institute of Nutrition, Hyderabad, India. They were maintained under standard laboratory conditions at an ambient temperature of 25 ± 2°C and 50 ± 15% relative humidity with a 12-h light/12-h dark cycle. Animals were fed with a commercial pellet diet (Rayan’s Biotechnologies Pvt Ltd., Hyderabad, India) and water *ad libitum*. They were fasted for 18 h prior to the experiment and during the experiment they were withdrawn from food and water. The animal experiments were performed after prior approval of the study protocol by the Institutional Animal Ethics Committee (Reg. No. 516/01/A/CPCSEA). The study was conducted in accordance with the guidelines provided by Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

**Selection of doses and preparation of oral test solution/suspension**

In clinical practice, protease inhibitors in therapeutic dose will be administered orally. Hence, human oral therapeutic doses of the respective drugs were extrapolated to rat based on body surface area (Lawrence et al, 1964) But the dose of gliclazide was selected as 2 mg/kg bd. wt based on the influence of dose-effect relationship of gliclazide on blood glucose in normal rats. Indinavir, ritonavir and atazanavir were orally administered in the dose of 72, 18 and 36 mg/kg bd. wt. to normal and diabetic rats. PIs were suspended in CMC for oral administration (Yamaji et al, 1999; Shibata et al, 2002). Gliclazide solution was prepared by dissolving it in a few drops of 0.1N NaOH then made up to the volume with distilled water. All the drugs were administered to the respective groups by oral gavage.

**Experimental Design**

The study consists of three phases.

Phase-I: dose-effect relationship of gliclazide in normal rats
Phase-II: interaction study of protease inhibitors with gliclazide in normal rats
Phase-III: interaction study of protease inhibitors with gliclazide in diabetic rats

Each phase of II and III consists of three groups (N = 6) for the interaction study of 3 respective protease inhibitors with gliclazide (single dose study followed by multiple dose study).

**Dose-effect relationship of gliclazide in rats**

A group of six normal rats was administered with 1 mg/kg bd. wt of gliclazide, orally. The same group was administered with gliclazide 2 mg/kg bd. wt., orally and 4 mg/kg bd. wt of gliclazide, orally. One week washout period was maintained between treatments.
Interaction study of protease inhibitors with gliclazide in normal rats

Each group of six rats was administered with gliclazide, orally. The same group was administered with interacting drug (Indinavir or ritonavir or atazanavir) and the combination of respective interacting drug and gliclazide. One week washout period was maintained between treatments. After this single dose interaction study the same group was continued with the daily treatment of respective interacting drug for the next eight days with regular feeding. Later after 18 h fasting they were again given the combined treatment on the ninth day.

Interaction study of protease inhibitors with gliclazide in diabetic rats

Diabetes was induced in rats by the administration of alloxan monohydrate in two doses, i.e. 100 mg and 50 mg/kg bd. wt intraperitoneally for two consecutive days (Heikkila, 1977). After 72 h, samples were collected from rats by orbital puncture of all surviving rats and the serum was analyzed for glucose levels. Rats with blood glucose levels of 200 mg/dl and above were considered as diabetic and selected for the study. The same treatment (single dose interaction study followed by multiple dose interaction study) as described in the study in normal rats was performed with a group of six alloxan-induced diabetic rats.

Blood sampling and determination of biochemical parameters

Blood samples were withdrawn from retro orbital plexus (Riley, 1960) of each rat at 2 and 8 h. The blood samples were analyzed for blood glucose by GOD/POD method (Trinder, 1969) using commercial glucose kits, and plasma insulin was measured by Radio Immuno Assay method. Total hemoglobin was estimated by the cyanomethaemoglobin method (Drabkin, 1932) and glycosylated hemoglobin (HbA1C) was estimated by the modified method (Nayak et al, 1981; Bannon, 1982).

Determination of insulin resistance index and β-cell function

The insulin resistance index and β-cell function were assessed by homeostasis model assessment as follows (Matthews et al, 1985; Bonora et al, 2000). Insulin sensitivity was obtained by using the program HOMA Calculator v 2.2.2 (http://www.dtu.ox.ac.uk).

\[
\text{Insulin resistance} = \frac{\text{FPI} \times \text{FPG}}{22.5}
\]

\[
\text{β-cell function} = \frac{(20 \times \text{FPI})}{(\text{FPG} - 3.5)}
\]
Where FPI is fasting plasma insulin concentration (µu/ml) and FPG is fasting plasma glucose (mmol/l).

**Data and statistical analysis**
Data were expressed as mean ± SEM. The significance was determined by applying Student’s paired ‘t’ test.

**Results**

**Dose-effect relationship of gliclazide in rats**

Dose-dependent response of gliclazide was observed with the three oral doses. The 2 mg/kg bd. wt of gliclazide was selected based on ideal blood glucose reduction which is about 35%. The gliclazide produced hypoglycemic activity with maximum biphasic reduction of 26.77 ± 1.13% & 28.91 ± 2.53%, 38.59 ± 1.58% & 40.50 ± 1.40% and 46.28 ± 1.67% & 50.65 ± 1.46% at 2 h and 8 h with 1 mg/kg bd. wt, 2 mg/kg bd. wt and 4 mg/kg bd. wt of gliclazide, respectively (Figure 1).

![Figure 1: Dose effect relationship of gliclazide in normal rats (N=6)](image)

**Effect of indinavir on the activity of gliclazide**

The levels of biochemical parameters following gliclazide, indinavir and their combination (single dose and multiple doses) were represented in Table 1. Indinavir alone produced significant increase in glucose, insulin, glycosylated hemoglobin, insulin resistance index and decrease in total hemoglobin, β-cell function and insulin sensitivity.
Table 1: Effect of indinavir on the activity of gliclazide in normal and diabetic rats (N = 6)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gliclazide</th>
<th>Indinavir</th>
<th>Indinavir + Gliclazide (SDA)</th>
<th>Indinavir + Gliclazide (MDA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 h</td>
<td>8 h</td>
<td>2 h</td>
<td>8 h</td>
</tr>
<tr>
<td><strong>Normal rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>53.83±0.54</td>
<td>55.67±0.61</td>
<td>106.67±0.67</td>
<td>83.33±1.84</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>12.04±0.26</td>
<td>11.89±0.38</td>
<td>19.05±0.27</td>
<td>21.58±0.33</td>
</tr>
<tr>
<td>Insulin resistance†</td>
<td>0.16±0.04</td>
<td>0.16±0.05</td>
<td>0.05±0.02</td>
<td>0.04±0.06</td>
</tr>
<tr>
<td><strong>β-cell function†</strong></td>
<td>483.52±34.68</td>
<td>602.01±42.99</td>
<td>157.22±2.95</td>
<td>398.49±33.74</td>
</tr>
<tr>
<td>Insulin sensitivity†</td>
<td>44.97±0.92</td>
<td>46.97±0.84</td>
<td>35.33±0.62</td>
<td>35.33±0.62</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>236.46±2.46</td>
<td>240.64±1.16</td>
<td>96.34±0.48</td>
<td>94.86±2.21</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>78.34±0.34</td>
<td>76.84±1.26</td>
<td>98.36±0.64</td>
<td>94.28±2.38</td>
</tr>
<tr>
<td><strong>Diabetic rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>141.67±0.95</td>
<td>135.67±0.61</td>
<td>307.17±1.94</td>
<td>258.00±0.89</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>11.19±0.32</td>
<td>11.64±0.16</td>
<td>15.46±0.50</td>
<td>13.84±0.23</td>
</tr>
<tr>
<td>Insulin resistance†</td>
<td>03.91±0.10</td>
<td>03.90±0.06</td>
<td>11.72±0.34</td>
<td>08.82±0.13</td>
</tr>
<tr>
<td><strong>β-cell function†</strong></td>
<td>51.30±1.67</td>
<td>57.66±0.66</td>
<td>22.82±0.85</td>
<td>25.57±0.51</td>
</tr>
<tr>
<td>Insulin sensitivity†</td>
<td>30.22±2.34</td>
<td>31.20±0.38</td>
<td>20.84±1.66</td>
<td>21.68±3.01</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>116.34±1.34</td>
<td>120.46±2.38</td>
<td>76.24±2.35</td>
<td>72.34±3.64</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>84.64±1.21</td>
<td>86.28±1.38</td>
<td>99.28±1.34</td>
<td>98.66±2.96</td>
</tr>
</tbody>
</table>

SDA: Single dose administration; MDA: Multiple dose administration; Data was expressed as Mean ± SEM; †Calculated by homeostasis model assessment method; *Significant at P < 0.05 compared to gliclazide control
Table 2: Effect of ritonavir on the activity of gliclazide in normal and diabetic rats (N = 6)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gliclazide</th>
<th>Ritonavir</th>
<th>Ritonavir + Gliclazide (SDA)</th>
<th>Ritonavir + Gliclazide (MDA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 h</td>
<td>8 h</td>
<td>2 h</td>
<td>8 h</td>
</tr>
<tr>
<td><strong>Normal rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>53.00±0.45</td>
<td>54.67±0.42</td>
<td>97.33±1.52</td>
<td>96.00±0.89</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>12.35±0.24</td>
<td>12.55±0.12</td>
<td>18.01±0.20</td>
<td>18.11±0.23</td>
</tr>
<tr>
<td>Insulin resistance†</td>
<td>1.62±0.04</td>
<td>1.69±0.01</td>
<td>4.23±0.09</td>
<td>4.29±0.09</td>
</tr>
<tr>
<td>β-cell function†</td>
<td>449.85±22.85</td>
<td>548.63±23.52</td>
<td>190.65±8.12</td>
<td>197.93±2.92</td>
</tr>
<tr>
<td>Insulin sensitivity†</td>
<td>46.28±1.28</td>
<td>44.20±1.68</td>
<td>33.08±2.61</td>
<td>34.84±1.62</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>238.2±1.43</td>
<td>244.34±2.34</td>
<td>106.34±0.48</td>
<td>110.25±3.14</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>76.28±1.32</td>
<td>78.26±3.05</td>
<td>94.28±0.66</td>
<td>89.46±3.20</td>
</tr>
<tr>
<td><strong>Diabetic rats</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>142.67±1.23</td>
<td>140.00±1.03</td>
<td>274.00±3.14</td>
<td>279.00±2.52</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>11.79±0.21</td>
<td>12.13±0.28</td>
<td>15.56±0.46</td>
<td>15.36±0.24</td>
</tr>
<tr>
<td>Insulin resistance†</td>
<td>04.15±0.06</td>
<td>04.19±0.10</td>
<td>10.54±0.37</td>
<td>10.59±0.22</td>
</tr>
<tr>
<td>β-cell function†</td>
<td>53.40±1.46</td>
<td>56.76±1.42</td>
<td>26.55±0.70</td>
<td>25.61±0.36</td>
</tr>
<tr>
<td>Insulin sensitivity†</td>
<td>32.46±3.01</td>
<td>33.64±1.26</td>
<td>25.84±8.42</td>
<td>24.36±0.64</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>120.30±3.35</td>
<td>122.54±.68</td>
<td>80.20±2.32</td>
<td>82.36±1.21</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>86.02±2.24</td>
<td>85.32±2.24</td>
<td>95.22±0.32</td>
<td>94.22±0.10</td>
</tr>
</tbody>
</table>

SDA: Single dose administration; MDA: Multiple dose administration; Data was expressed as Mean ± SEM; †Calculated by homeostasis model assessment method; *Significant at P < 0.05 compared to gliclazide control
Table 3: Effect of atazanavir on the activity of gliclazide in normal and diabetic rats (N = 6)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gliclazide</th>
<th>Atazanavir</th>
<th>Atazanavir + Gliclazide (SDA)</th>
<th>Atazanavir + Gliclazide (MDA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 h</td>
<td>8 h</td>
<td>2 h</td>
<td>8 h</td>
</tr>
<tr>
<td>Normal rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>53.00±0.45</td>
<td>54.67±0.42</td>
<td>94.33±1.41</td>
<td>84.00±2.25</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>12.25±0.22</td>
<td>12.04±0.10</td>
<td>08.44±0.06</td>
<td>08.90±0.23</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>01.60±0.04</td>
<td>01.62±0.02</td>
<td>01.96±0.01</td>
<td>01.85±0.07</td>
</tr>
<tr>
<td>β-cell function†</td>
<td>446.02±21.50</td>
<td>527.64±27.87</td>
<td>98.09±04.73</td>
<td>162.44±17.50</td>
</tr>
<tr>
<td>Insulin sensitivity‡</td>
<td>44.16±2.24</td>
<td>45.62±2.20</td>
<td>56.28±1.12</td>
<td>58.46±2.24</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>234.16±0.24</td>
<td>240.16±1.16</td>
<td>240.16±2.24</td>
<td>242.14±2.10</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>74.18±1.22</td>
<td>76.04±1.06</td>
<td>54.34±2.38</td>
<td>58.34±4.10</td>
</tr>
<tr>
<td>Diabetic rats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>143.33±0.84</td>
<td>140.33±1.41</td>
<td>263.67±0.80</td>
<td>236.67±5.18</td>
</tr>
<tr>
<td>Insulin (µu/mL)</td>
<td>11.54±0.11</td>
<td>12.87±0.12</td>
<td>4.34±0.14</td>
<td>04.40±0.16</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>04.09±0.05</td>
<td>04.46±0.08</td>
<td>02.83±0.09</td>
<td>02.57±0.11</td>
</tr>
<tr>
<td>β-cell function†</td>
<td>51.75±0.57</td>
<td>59.98±0.74</td>
<td>07.79±0.26</td>
<td>09.15±0.39</td>
</tr>
<tr>
<td>Insulin sensitivity‡</td>
<td>34.10±2.01</td>
<td>35.42±1.46</td>
<td>42.26±1.16</td>
<td>43.34±0.26</td>
</tr>
<tr>
<td>Total hemoglobin (g/dL)</td>
<td>124.32±2.64</td>
<td>124.28±2.24</td>
<td>158.36±3.46</td>
<td>154.20±1.13</td>
</tr>
<tr>
<td>Glycosylated hemoglobin (%)</td>
<td>88.02±1.30</td>
<td>84.16±2.34</td>
<td>94.2±0.32</td>
<td>96.32±0.10</td>
</tr>
</tbody>
</table>

SDA: Single dose administration; MDA: Multiple dose administration; Data was expressed as Mean ± SEM; †Calculated by homeostasis model assessment method; *Significant at P < 0.05 compared to gliclazide control
When given in combination indinavir significantly (p<0.05) altered the pharmacodynamics of gliclazide in both normal diabetic rats following single and multiple dose treatments. This interaction was significantly reflected by increase in glucose, insulin, glycosylated hemoglobin and insulin resistance and decrease in β-cell function and insulin sensitivity. The reduction in gliclazide effect is more with the single dose treatment of indinavir than the multiple dose treatment.

**Effect of ritonavir on the activity of gliclazide**

The levels of biochemical parameters following gliclazide, ritonavir and their combination (single dose and multiple doses) were represented in Table 2. Ritonavir alone produced significant increase in glucose, insulin, glycosylated hemoglobin and insulin resistance index and decrease in total hemoglobin, β-cell function and insulin sensitivity. When given in combination ritonavir significantly (p<0.05) enhanced the pharmacodynamics of gliclazide in rats (normal diabetic) following single and multiple dose treatments. The enhancement in gliclazide effect is more with the multiple dose treatment of ritonavir than the single dose.

**Effect of atazanavir on the activity of gliclazide**

The levels of biochemical parameters following gliclazide, atazanavir and their combination (single dose and multiple doses) were represented in Table 3. Atazanavir alone has no significant effect on biochemical parameters. When given in combination atazanavir significantly (p<0.05) altered the pharmacodynamics of gliclazide in rats (normal diabetic) following single and multiple dose treatments. The enhancement in gliclazide effect is more with the multiple dose treatment of atazanavir than the single dose treatment.

**Discussion**

HIV-infected patients are likely to suffer with diabetes mellitus and hence frequently antiretroviral drugs are co-administered with oral antidiabetic drugs. HIV-infection and diabetes are chronic diseases that significantly affect lifestyle. When they intersect, the treatment required for both diseases can be overwhelming for patients. Several studies have reported a prevalence of diabetes as 2-7% among HIV-infected patients receiving protease inhibitors (Carr et al, 1999), and an additional 16% having impaired glucose tolerance (Samaras, 2009). The incidence of diabetes mellitus in HIV-infected patients has been estimated to range from 1-10% in various studies (Samaras, 2009). In our study we have studied the effect of widely used PIs on the activity of widely used antidiabetic drug, gliclazide.

Previously we have reported (Mastan et al, 2009) the effect of protease inhibitors on the activity of gliclazide with few parameters in animal models. But in our present study we investigated the effect of antiretroviral drugs on the activity of gliclazide with respect to multiple biochemical parameters. In the present study, the multiple dose effect of antiretroviral drugs on the gliclazide activity was studied for the influence of the chronic treatment with antiretroviral drugs since both are used for chronic period.

Drug interactions are usually seen in clinical practice and the mechanisms of interactions are evaluated usually in animal models. We studied the influence of PIs on the pharmacodynamics of gliclazide in normal and diabetic rats. The normal rat model served to quickly identify the interaction and diabetic rat model served to validate the same response in the actually used condition of the drug. Although animal models can never replace the need for comprehensive studies in human subjects, their use can
provide important insights to understand and to evaluate the potent interactions between drugs. Since small amount of blood was required for this study, the blood samples were collected by retro-orbital puncture as it was reported to be good method when small samples of blood was required. Diabetes was induced with alloxan monohydrate, since it was more economical and easily available.

Rats are known to be more sensitive to gliclazide response. So we have conducted the dose effect-relationship study of gliclazide to select the oral dose which produces approximately 35% of blood glucose reduction in rats. Consistent with our previous studies (Mastan et al, 2009) and literature (Satyanarayana et al, 2007), gliclazide produced maximum biphasic response (at 2 and 8 h) in rat model when administered alone, which may be due its biliary excretion and entero hepatic cycling. Gliclazide is known to produce hypoglycemic/ antihyperglycemic activity by pancreatic (stimulating insulin secretion by blocking K⁺ channels in the pancreatic β cells) and extra pancreatic (increasing tissue uptake of glucose) mechanisms (Mastan, 2009). The results obtained in our study are consistent with the available literature. Based on this background, in our study we have selected 2 and 8 h as blood sampling time points to measure the various biochemical parameters in rats.

The elevated insulin levels is the face of increased glucose levels suggest an insulin resistant state (Cefalu, 2001; Reaven, 2004). Diabetes associated glucose intolerance is characterized by an increase in insulin resistance and alterations in insulin clearance, insulin sensitivity of hepatic and peripheral tissues. In our study indinavir and ritonavir alone produced significant impact on glucose-insulin homeostasis with the contribution of insulin resistance and impaired in β-cell function in normal and diabetic rats, and these effects were more in diabetic condition, indicating the potency of these drugs towards exacerbation of existing diabetes mellitus. Decreased total hemoglobin content observed in indinavir and ritonavir treated rats might be due to increased formation of glycosylated hemoglobin. Generally total hemoglobin level is much below the normal level in diabetic condition and glycosylated hemoglobin level has been reported to be increased in patients with diabetes mellitus (Paulsen, 1973). It was reported that during diabetes mellitus, the excess of glucose present in the blood reacts with hemoglobin to form glycosylated hemoglobin (Koening et al, 1976). The level of glycosylated hemoglobin is always monitored as a reliable index of glycemic control in diabetes (Gabbaray, 1976). Elevated levels of glycosylated hemoglobin and reduced levels of total hemoglobin observed in indinavir and ritonavir treated rats reveal that these animals resembling the diabetes condition. In addition, ritonavir and indinavir treated animals shown decreased in body weights further indicating the alteration in metabolic pathways. But atazanavir alone has not shown any significant impact on these biochemical parameters. The results obtained from this study clearly indicate glucose-insulin homeostasis disorders associated with protease inhibitors are drug specific, but not in a class-specific manner. All these observations are consistent with our previous studies.12-15

In combination, the pharmacodynamics of gliclazide was significantly reduced in the presence of indinavir following single and multiple dose treatment in rat (normal and diabetic) model, and it confirmed the presence of potential interaction between gliclazide and indinavir. The possible mechanism of this potential pharmacodynamic interaction is due to the opposing effects of gliclazide and indinavir on insulin resistance, insulin release or tissue uptake of glucose, as reflected in our study.

Contrast to theoretical expectation and consistent with our previous studies, the pharmacodynamics of gliclazide were enhanced by ritonavir following single and multiple dose administration in rats, even though ritonavir alone has shown significant alterations in glucose-insulin homeostasis. Gliclazide is known to be metabolized by hepatic microsomal enzymes CYP2C9 primarily and partly by CYP3A4 (Mastan, 2009). Ritonavir is a well known potent CYP3A4 inhibitor12 and used to enhance the pharmacokinetic and anti-HIV activity profiles of the concomitantly administered PIs. Since ritonavir increased blood glucose and insulin levels on its own, the increase in the effect of gliclazide on blood glucose might be due to improved blood gliclazide level in the presence of ritonavir, as there is a possibility of pharmacokinetic interaction at metabolic level. Thus it clearly indicates the presence of potential pharmacokinetic interaction at metabolic level between gliclazide and ritonavir, rather than
pharmacodynamic interaction. However, it has to be confirmed by conducting pharmacokinetic studies in animal models. In combination, atazanavir also enhanced the pharmacodynamics of gliclazide with respect to glucose-insulin homeostasis, which is consistent with our previous study and confirms the pharmacokinetic interaction at metabolic level, as atazanavir inhibited CYP3A4 and CYP2C9-mediated drug metabolism leading to raised serum levels of gliclazide (Mastan, 2009). Thus our study has demonstrated the effect of various PIs on the activity of gliclazide with respect to multiple factors of glucose-insulin homeostasis. However, as metabolic complications arising from HIV-infection and/or antiretroviral therapy are multifactorial and complex, study of other possible factors and mechanism(s) behind these interactions couldn’t be ruled out.

**Conclusion**

Our study confirmed that glucose-insulin homeostasis disorders associated with protease inhibitors are drug specific. Since the interactions of PIs (indinavir, ritonavir and atazanavir) with gliclazide were seen in normal and diabetic condition, they are likely to occur in humans also, leading to increased/decreased activity of gliclazide, which may need dosage adjustment. Hence care should be taken when the combinations are prescribed for their clinical benefit in diabetic patients. However the present study warrants further studies to find out the relevance of these interactions in other species/human beings and to know the exact mechanism of action(s) behind this interaction(s) if any.

**References**


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Anaemia Prevalence & Socio-demographic Associates amongst Pregnant Women

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Rohilkhand Medical College & Hospital, India

Rubeena Bano
Department of Physiology
Rohilkhand Medical College and Hospital, India

Abstract

Background: Anaemia affects mainly the women in child bearing age group, young children and adolescent girls.

Objectives

1. To find out the prevalence of anemia amongst pregnant women of Rural Maharashtra.
2. To study and compare the socio-demographic profile of anemic pregnant women in a rural area.
3. To establish an association between anemia & abortion.

Methods

Setting: Pravara Rural Hospital, Loni, District- Ahmednagar, Maharashtra & the Primary Heath Care Center attached to it.

Study design: Cross sectional study.

The study was conducted amongst the rural pregnant women reporting to the Primary Health Centre attached to Rural Medical College as well as the Maternity OPD & Clinics of RMC, Loni, Maharashtra. A total of 100 pregnant women with gestational period between 12-20 weeks were registered for the study. The study variables included the blood haemoglobin level, age, education, religion, caste, income, type of family, gravida, and birth interval, number of abortions and history of abnormal bleeding.

Statistical analysis: Chi-Square test.

Results

A high prevalence (96.0 %) of iron deficiency anaemia (Hb <11 gm/dl) was observed. Majority of the anaemic women (56.25%) were in 20-24 years age group. The association of socio-demographic
characteristics like type of family, education and socio-economic status with the anaemic status was not statistically significant.

**Conclusion**

Considering the high-risk status of anaemia in pregnancy, there is a need to initiate intervention measures at all levels of health care delivery.

**Keywords:** Pregnant women, Anaemia, Rural area

**Introduction**

The importance of anemia as a major public health problem throughout the world is widely recognized. According to WHO, in developing countries, the prevalence of anaemia among pregnant women averages 56%, with wide variations in different regions of the world\(^1\). In India, anaemia is the second most common cause of maternal deaths, accounting for 20% of total maternal deaths\(^2\). Anaemia affects mainly the women in child bearing age group, young children and adolescent girls. The association of anaemia with adverse maternal outcomes such as puerperal sepsis, ante-partum haemorrhage, post-partum haemorrhage and maternal mortality is no longer a debatable subject\(^3\). Apart from the risk to the mother, it is also responsible for increased incidence of premature births, low birth weight babies and high perinatal mortality\(^4\). The National Nutritional Anaemia Prophylaxis Programme (NNAPP) was initiated in 1970 during fourth five year plan with the aim to reduce the prevalence of anaemia to 25 percent\(^5\). Since 1992, the daily dosage of elemental iron for prophylaxis and therapy has been increased to 100 mg and 200 mg, respectively under Child Survival and Safe Motherhood (CSSM) Programme. In view of the above, present study was carried out to find out the prevalence of anaemia amongst pregnant women and to study the factors associated with anaemia in pregnancy.

**Materials and Methods**

The present study was conducted in the Primary Health Center (PHC) & the Maternity Clinics of Rural Medical College, Loni. The rural pregnant women reporting to the Maternity Ward of RMC, Loni formed the study population. In the present study purposive sampling technique was applied. Based on the knowledge that about 50% pregnant women in the country are anaemic\(^6\), it was assumed that a sample size of 100 shall be adequate for a preliminary study.

**Inclusion criteria**

A total of 100 pregnant women with 12-20 weeks of gestation, reporting to Maternity ward & PHC attached to RMC, Loni, within three months i.e. Oct-Dec. 2008 were registered for the study.

**Exclusion criteria**

The women with multiple pregnancies and bleeding disorders were excluded from the study.
The pregnant women were informed about the study, consent form was filled and were interviewed using a pre-structured, pre-tested schedule. Haemoglobin estimation was done by Sahli's method. Anaemia was classified as per the WHO grading criteria. The typing of anaemia was done as per standard peripheral blood smear examination method. Modified BG Prasad classification was used for income classification.

**Statistical tests:** Chi-square and related tests were used as applicable.

### Results

Table I: Age-wise distribution of degree of anaemia

<table>
<thead>
<tr>
<th>Age (in years)</th>
<th>Mild No. (%)</th>
<th>Moderate No. (%)</th>
<th>Severe No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>6 (26.08)</td>
<td>11 (21.15)</td>
<td>2 (9.52)</td>
<td>19 (19.79)</td>
</tr>
<tr>
<td>20-24</td>
<td>13 (56.52)</td>
<td>32 (61.53)</td>
<td>9 (42.85)</td>
<td>54 (56.25)</td>
</tr>
<tr>
<td>25-29</td>
<td>4 (17.39)</td>
<td>8 (15.38)</td>
<td>7 (33.33)</td>
<td>19 (19.79)</td>
</tr>
<tr>
<td>30 and above</td>
<td>0 (0.0)</td>
<td>1 (1.92)</td>
<td>3 (14.28)</td>
<td>4 (4.16)</td>
</tr>
<tr>
<td>Total</td>
<td>23 (23.95)</td>
<td>52 (54.14)</td>
<td>21 (21.87)</td>
<td>96 (96.0)</td>
</tr>
</tbody>
</table>

In the present study 96.0% pregnant women were anaemic. 23.95% had mild, 54.14% moderate and 21.87% severe anaemia. Majority of anaemic women (56.25%) were in 20-24 years age group.

Table II: Association of anaemic status with socio-demographic factors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Anaemia No. (%)</th>
<th>Normal No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of family</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nuclear</td>
<td>15 (15.62)</td>
<td>0 (0.0)</td>
<td>15 (15.0)</td>
</tr>
<tr>
<td>Joint</td>
<td>21 (21.87)</td>
<td>2 (50.0)</td>
<td>23 (23.0)</td>
</tr>
<tr>
<td>Extended</td>
<td>60 (62.5)</td>
<td>2 (50.0)</td>
<td>62 (62.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96</td>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Educational status</th>
<th>No. (%)</th>
<th>No. (%)</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Illiterate</td>
<td>20 (20.83)</td>
<td>1 (25.0)</td>
<td>21 (21.0)</td>
</tr>
<tr>
<td>Just literate</td>
<td>34 (35.41)</td>
<td>0 (0.0)</td>
<td>34 (34.0)</td>
</tr>
<tr>
<td>Primary</td>
<td>26 (27.08)</td>
<td>0 (0.0)</td>
<td>26 (26.0)</td>
</tr>
<tr>
<td>Middle school</td>
<td>9 (9.37)</td>
<td>1 (25.0)</td>
<td>10 (10.0)</td>
</tr>
<tr>
<td>High school</td>
<td>4 (4.16)</td>
<td>1 (25.0)</td>
<td>5 (5.0)</td>
</tr>
<tr>
<td>Senior secondary</td>
<td>3 (3.12)</td>
<td>1 (25.0)</td>
<td>4 (4.0)</td>
</tr>
<tr>
<td>Graduate &amp; above</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>96</td>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Socio-economic status</th>
<th>No. (%)</th>
<th>No. (%)</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>
Class II 4 (4.16) 1 (25.0) 5 (5.0)
Class III 13 (13.54) 2 (50.0) 15 (15.0)
Class IV 32 (33.33) 0 (0.0) 32 (32.0)
Class V 47 (48.95) 1 (25.0) 48 (48.0)
Total 96 4 100

The association of socio-demographic characteristics like type of family, education and socio-economic status with anaemic status is shown in table II. In the present study majority of pregnant women belonged to extended or three generation family (62.0%). The association with anaemic status was statistically not significant (p>0.05). Most of women were just literates (34.0%). Only 9.0% were educated high school and above. The association with anaemic status was statistically not significant (p>0.05). Majority (80.0%) belonged to socio-economic class IV and V. The association with anaemic status was also statistically not significant (p>0.05).

Table III: Association of anaemia with number of abortions.

<table>
<thead>
<tr>
<th>No. of abortions</th>
<th>Anaemia No. (%)</th>
<th>Normal No. (%)</th>
<th>Total No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>80 (83.33)</td>
<td>3 (75.0)</td>
<td>83 (83.0)</td>
</tr>
<tr>
<td>1</td>
<td>12 (12.5)</td>
<td>1 (25.0)</td>
<td>13 (13.0)</td>
</tr>
<tr>
<td>2 or more</td>
<td>4 (4.16)</td>
<td>0 (0.0)</td>
<td>4 (4.0)</td>
</tr>
<tr>
<td>Total</td>
<td>96</td>
<td>4</td>
<td>100</td>
</tr>
</tbody>
</table>

The association of anaemia with number of abortions is shown in table 2. In the present study 83.0% pregnant women had no history of abortions however 83.33% of them were anaemic. The association between anaemia and abortion was statistically not significant (p>0.05). All the pregnant women with past history of abnormal bleeding (11.4%) were anaemic and (76.93%) had moderate or severe anaemia.

Discussion

A total of 100 pregnant women reporting to a rural health care facility were studied. In the present study a high prevalence of anaemia (96.0%) among pregnant women was observed. Majority (54.14%) had moderate anaemia. Most of the anaemic pregnant women were between 20 and 24 years of age (56.25%), followed by equal distribution in less than 20 years (19.79%) and 25-29 years (19.79%), and only (4.16%) in 30 years and above. (Table I). Majority of pregnant women were Hindus (91.2%), followed by Muslims (6.1%) and Sikhs (2.6%). Normocytic hypochromic and microcytic hypochromic type of blood picture, a characteristic of iron deficiency anemia was observed. The prevalence of anaemia was not significantly related with age, type of family, income, religion, caste, birth interval and number of abortions (Tables I, II and III). There was a trend of low severity of anaemia with high per capita income. Women with gravida >2 more often had severe anaemia. However, these trends were statistically not significant. The observed very high prevalence of anaemia and its severity in the current study although is similar to earlier studies10, 11. Since haemoglobin estimation was done at 12-20 weeks of gestation, e.g., before maximum haemodilution, the observed status reflects pre-pregnant levels, which calls for widening the scope of programme for prevention and control of nutritional anaemia, so as to cover adolescent girls also. As in other studies, the severity of anaemia was inversely related to educational status12 and income13.
Study Limitation

Not all the pregnant women of the rural area of Loni were taken into consideration. Hence the results of the study cannot be generalized.

Conclusion

A very high prevalence of anaemia (96.0%) early in pregnancy i.e. 12-20 weeks of gestation is indicative of the status of pre-pregnant levels. It calls for studies on anaemia among adolescent girls and a strategic shift in a programme focussed on pregnant women alone to broaden the coverage so as to include adolescent girls also for control of anaemia. As normocytic hypochromic and microcytic hypochromic blood pictures were predominant, it indicates deficient iron intake/absorption irrespective of age, type of family, caste, religion or number of children as the prevalence was equally high in all groups in this population.

References

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White Phosphorus Burn: Case Report

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Introduction

White phosphorus burn is a special subtype of chemical burns, rarely encountered and is very limited in literature.

Case Presentation

On January 11, 2009, an 18-year-old male was transferred to the Emergency room (ER) due to exposure to military attack with White Phosphorus shell with multiple scattered patches of full thickness burn surrounded by sloughed tissue, involving 30% of his body surface area, distributed in both upper and lower limbs and right shoulder, a clinical diagnosis of white phosphorus burn was made. Airway was secured, without signs of inhalation burns; fluid resuscitation was initiated, irrigation with diluted sodium bicarbonate solution and wet dressing were done.

In the Burn Unit, White smoke was noticed coming up from the wounds which became deeper, with extensive necrotic tissue, apparent localized injuries weren’t correlated with underlying severe deep destruction (Figure 1).

In the operation room, debridement and excision for dead tissues and removing phosphorus particles was accomplished, transferred to ICU for monitoring of vital signs, electrolyte disturbance and ECG changes where he was managed accordingly.

After 8 days of hospitalization, the patient was relatively well, and discharged without manifestations of systemic complication of white phosphorus burn.
Discussion

White phosphorus is a transparent combustible substance (KG., 2002), associated with extensive full thickness burn injury with delayed wound healing (Irizarry, 2007).

In our case, the management include irrigation by diluted sodium bicarbonate solution at ER, whereas, only water have been proved to prevent deaths (KG., 2002) (Eldad A, Simon GA., 1991) (Eldad A, Wisoki M, Cohen H, Breiterman S, Chaouat M, Wexler MR, Ben-Bassat H., 1955) (Chou TD, Lee TW, Chen SL, Tung YM, Dai NT, Chen SG, Lee CH, Chen TM, Wang HJ., 2001), early excision and massive debridement of particles was accomplished, electrolyte disturbance was noticed as a complication.

References


The Role of Anthocyanin and Flavonoides in Patient with Diabetes Mellitus - Type II

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Republic of Kosovo

Abstract

Background: Diabetes Mellitus Type 2 also called non-insulin-dependent diabetes mellitus (NIDDM) is a disorder that is characterized by high blood glucose in the context of insulin resistance and relative insulin deficiency. The aim of study was to see if Cranberries (Vaccinium macrocarpon - Cornus Mas) have really had an impact on patient’s health state.

Materials and Methods: A female patient N.N. 67 years old with Diabetes Mellitus Type II was monitored for about two years. Laboratory analyses reports (endocrinology and biochemistry) as well as reports from Specialities (endocrinologist, cardiologist, nephrologists and ophthalmologist).

We used a questionary asking the patient to evaluate the improvement for the disease symptoms with points from 1-5 (1-bad, 2-fair, 3-good, 4-very good, 5-excellent) every month and also manner based on laboratory analyses (hematology and biochemistry) every two months and also based on medical reports every six month.

Results: Before starting this research we showed Glucose level about 8.5 mmol/L or 153 mg/dl.

After stopping to use Cornus Mas, an evaluation of Glucose which was slow in the beginning but rapid later, was noticed, with average 16.5 mmol/L or 297 mg/dL. Medical reports were showing an aggravation in the condition was with total of 2.3 points average.

It was found that after starting to use the fruits, Glucose value has started to fall, first slowly and then for about 2 months the value obtained was 9.5 mmol/L or 171 mg/dL. Subjective evaluation of the symptoms of disease was with average of total points 3.5.

Conclusion: This study puts Highlights three dilemmas:
• If oral antidiabetic therapy use for oral therapy should be or not to Non Insulin Diabetes Patients.

• Use of any drug containing these two substances Anthocyanin and Flavonoides as an antioxidant with an unknown mechanism will be a goal of therapy for Non Insulin Diabetes Patients in the future.

• Dedication of particular importance to products with natural content in the future by Scientists.

**Keywords:** Diabetes Mellitus, Cranberry - Cornus Mas

**Acknowledgements:** This study was supported by Hasan Kutllovc MD, Institute of Occupational Medicine – Prishtina, Republic of Kosova

**Case Report**

A female Patient N.N. 67 years old with Diabetes Type II asked to be an object of study, because her health state improved a lot after using a fruit Cranberries (Cornus Mas) and this was supported by laboratory analyses reports (endocrinologist and biochemistry) as well as specialistic reports (endocrinologist, cardiologist, nephrologists and ophthalmologist)

The patient was on Oral Antidiabetic Therapy and on very strict Antidiabetic diet.

The aim of study was to see if these fruits Cranberries (Cornus Mas) really had an impact on patient’s health state. This is why research was oriented in two ways: Patient and Cranberries (Cornus Mas)

**Patient:**

The patient was monitored about two years.

Before the beginning of the experiment, medical reports from laboratory (hematologic and biochemistry) and specialistic (endocrinology, cardiology, nephrology and ophthalmology) done from the moment when a patient started to use the fruit were collected and then the condition of the patient until the moment of research was evaluated.

The values of Glucose from the reports collected before the beginning of the experiment were about 8.5 mmol/L or 153 mg/dl (average). Specialistic reports showed a great improvement of her health condition including the condition of cardio-vascular system, kidney and eyes.

The use of fruit was stopped for one year and the patient condition was again evaluated in subjective manner asking the patient to evaluate the improvement of the diseases symptoms through questionary every month, and in objective manner based on laboratory analyses (hematology and biochemistry) every two months and also based on specialistic reports (endocrinologist, cardiologist, nephrologists and ophthalmologist).

After quitting the use of Cranberries (Cornus Mas) an elevation of Glucose which was slow in beginning but rapid later, was noticed with average 16.5 mmol/L or 297 mg/dL blood
Glucose. Questionary and Specialistic reports showed an aggravation in the condition was with total of 2.3 points average.

The patient was again directed to continue using the fruits Cranberries (Cornus Mas) and her condition was evaluated in two ways: In subjective manner asking the patient to evaluate the improvement of the diseases symptoms through questionary every month, and in objective manner based on laboratory analyses (hematology and biochemistry) every two months and also based on specialistic reports (endocrinologist, cardiologist, nephrologists and ophthalmologist).

After restarting to use the fruit Glucose value had started to fall, first slowly and then for about two months the value obtained was 9.5 mmol/L or 171 mg/dL. Questionary was with total 3.5 in average. Specialistic reports were showing an amelioration of cardio-vascular system, kidney and eyes.

**Fruit:**

Cranberry (Cornus Mas) is a plant which grows in South Europe but also in Republic of Kosova and it’s name is “The Europian Corneal”

Laboratory analyses showed that Cranberries (Cornus Mas) are source of Flavaonoides and Phenolic Ac. known with a name Polyphenole with great antioxidant characteristics. They also contain the substance called Anthocyanin which is an important pigment for the color of this fruit.

Flavonoides accomplish their activity by lowering the oxidation of the lipids and by decreasing the glucolisation of proteins by acting on lowering of glucose and lipid value.

Anthocyanin lowers the glucose level by increasing the Insulin level in the blood using an unknown mechanism.

**References**


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QUESTIONARY FOR DIABETES MELLITUS

Name(Initials): _________________________          Today's date: _______________
Address:           _________________________
City, state, zip: ___________________________
Telephone: home ( ) _________- _____________            Date of birth: ______________
work ( ) _________- _____________              Sex:              Female  Male

Background

1. Ethnic origin (check only one):
   White Albanian          Serbian             Bosnian            Romes             Egyptian
   Other: __________________________

2. Please circle the highest year of school completed:
   1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18  19  20  21  22  23+
   (primary)                 (high school)        (college/university)       (graduate school)

3. Are you currently (check only one):
   married      separated          widowed           single           divorced

4. Please indicate below which chronic condition(s) you have:
   Diabetes type 2  Diabetes type 1  High cholesterol  High blood pressure
   Heart disease Type of heart disease: _________________________________
   Lung disease Type of lung disease: _________________________________
   Other chronic condition Specify:     _________________________________

General Health

1. In general, would you say your health is:   (Circle one)
Excellent..........................5
Very good...........................4
Good........................................3
Fair..........................................2
Poor..........................................1

Symptoms

How much time during the past month...

<table>
<thead>
<tr>
<th>None</th>
<th>A little</th>
<th>Some</th>
<th>A good</th>
<th>Most</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>of the</td>
<td>of the</td>
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</table>

1. Were you discouraged by your health problems?........................... 5 4 3 2 1 0

2. Were you fearful about your future health?.............................. 5 4 3 2 1 0

3. Was your health a worry in your life?.5 4 3 2 1 0

4. Were you frustrated by your health problems?.................................... 5 4 3 2 1 0

In the PAST WEEK, did you ever have any of the following symptoms…

Increased thirst? .............................................................. No Yes Don’t know
Dry mouth? ..............................................................  No  Yes  Don’t know

Decreased appetite? ......................................................  No  Yes  Don’t know

Nausea or vomiting? ..........................................................  No  Yes  Don’t know

Abdominal pain? ..............................................................  No  Yes  Don’t know

Frequent urination at night? Do you have
to get up to urinate 3 or more times a night? .......................  No  Yes  Don’t know

Severely high blood sugar
(blood glucose readings of 300 mg or higher?) .......................  No  Yes  Don’t know

Morning headaches? ..........................................................  No  Yes  Don’t know

Nightmares? ............................................................................  No  Yes  Don’t know

Night sweats? .............................................................................  No  Yes  Don’t know

Lightheadedness? .................................................................  No  Yes  Don’t know

Shakiness or weakness? .........................................................  No  Yes  Don’t know

Intense hunger? ..........................................................  No  Yes  Don’t know

Times when you passed out fainted or lost
consciousness, even for a short time? .................................  No  Yes  Don’t know
**Daily Activities**

During the past 4 weeks, how much... (Circle one)

<table>
<thead>
<tr>
<th>Not at all</th>
<th>Slightly</th>
<th>Moderately</th>
<th>a bit</th>
<th>totally</th>
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</thead>
</table>

1. Has your health interfered with your normal social activities with family, friends, neighbors or groups? 
   5 4 3 2 1

2. Has your health interfered with your hobbies or recreational activities? 
   5 4 3 2 1

3. Has your health interfered with your household chores? 
   5 4 3 2 1

4. Has your health interfered with your errands and shopping? 
   5 4 3 2 1

**Your Glucose Testing**

1. Do you have a machine to measure your blood sugar (glucose) level? Yes No

2. On how many days in the last week did you test your blood sugar level? (If you were sick in the last week, think of the most recent 7 days when you were NOT sick) 
   _______ days

3. On days that you test your blood sugar, how many times do you test on average? 
   _______ times
### Physical Activities

During the past week, even if it was not a typical week for you, how much total time (for the entire week) did you spend on each of the following? (Please circle one number for each question.)

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<thead>
<tr>
<th></th>
<th>less than</th>
<th>30-60</th>
<th>1-3 hrs</th>
<th>more than</th>
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<tr>
<td></td>
<td>none</td>
<td>30 min/wk</td>
<td>min/wk</td>
<td>per week</td>
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1. Stretching or strengthening exercises
   (range of motion, using weights, etc.)
   [5 4 3 2 1]

2. Walk for exercise
   [5 4 3 2 1]

3. Swimming or aquatic exercise
   [5 4 3 2 1]

4. Bicycling (including stationary exercise bikes)
   [5 4 3 2 1]

5. Other aerobic exercise equipment
   (Stairmaster, rowing, skiing machine, etc.)
   [5 4 3 2 1]

6. Other aerobic exercise
   Specify __________________________
   [5 4 3 2 1]

### Confidence About Doing Things

For each of the following questions, please circle the number that corresponds with your confidence that you can do the tasks regularly at the present time.

<table>
<thead>
<tr>
<th>1. How confident do you feel that you can eat your meals every 4 to 5 hours every day, including breakfast every day?</th>
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<tbody>
<tr>
<td>Not at all</td>
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### 2. How confident do you feel that you can follow your diet when you have to prepare or share food with other people who do not have diabetes?

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### 3. How confident do you feel that you can choose the appropriate foods to eat when you are hungry (for example, snacks)?

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### 4. How confident do you feel that you can exercise 15 to 30 minutes, 4 to 5 times a week?

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### 5. How confident do you feel that you can do something to prevent your blood sugar level from dropping when you exercise?

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### 6. How confident do you feel that you know what to do when your blood sugar level goes higher or lower than it should be?

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### 7. How confident do you feel that you can judge when the changes in your illness mean you should visit the doctor?

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### 8. How confident do you feel that you can control your diabetes so that it does not interfere with the things you want to do?

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### Your Diet

1. How many times last week did you eat breakfast when you got up? ____ times last week

2. This morning, did you eat any of the following foods for breakfast? (Please check all that apply)

- [ ] milk (½ cup)
- [ ] cheese
- [ ] yogurt
eggs                                meat, poultry, or fish           beans
If you ate anything else, please write here: _____________________________________

**Medications**

1. In the past week did you take pills for diabetes?................. No  Yes  Don’t know
   Please specify the name(s) of the diabetes pills you took: ______________________________

2. In the past week did you get insulin injections?............... No  Yes  Don’t know

3. In the past week did you take pills for high blood pressure?........................................... No  Yes  Don’t know
   Please specify the name(s) of the blood pressure pills you took: ______________________________

4. In the past week did you take pills for cholesterol?........... No  Yes  Don’t know
   Please specify the name(s) of the cholesterol pills you took: ______________________________

**Medical Care**

1. When you visit your doctor, how often do you do the following (please circle one number for each question):

   Never    Almost never    Sometimes    Fairly often    Very often    Always

   a. Prepare a list of questions
   for your doctor.............................. 5    4    3    2    1    0

   b. Ask questions about the things you
      want to know and things you don’t
      understand about your treatment.... 5    4    3    2    1    0
c. Discuss any personal problems that may be related to your illness........5 4 3 2 1 0

2. In the past 6 months, how many times did you visit a physician?
Do not include visits while in the hospital or the hospital emergency department


3. In the past 6 months, how many times did you go to a hospital emergency department?


4. In the past 6 months, how many TIMES were you hospitalized for one night or longer?

a. How many total NIGHTS did you spend in the hospital in the past 6 months?

b. Were any of these hospitalizations at a skilled nursing facility, convalescent hospital, or other minimum care facility? Yes No

5. When was the last time you had your eyes examined?
(example: for glaucoma or any other problem)

Month Year

6. How many times did the doctor or nurse examine your feet in the last 6 months?


ILIZAROV FOR PELVIC FRACTURES

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Email: ilizarov2007@gmail.com

Abstract

Aim of the study: We aim to use ilizarov method to correct the displacement of fragments in pelvic fractures in patients who are not fit for anaesthesia. As the procedure requires only local anaesthesia, it can be performed even at any peripheral centers.

Materials and Methods:

Total number of patients - 42

Male patients - 39

Female patients - 3

A - O External fixator set with six shanz pin and connecting elements

Ilizarov set consisting two half rings, long threaded rods, hinges, rancho cubes, bolts and nuts

As the patient arrives at the emergency department a general assessment is made. If decided for application of external fixator, a conventional external fixator is applied over the both iliac crests. If possible three shanz pins are used on each iliac crest; especially when we require multi directional correction of pelvic bones.

Most of the following types of fractures can be corrected with application of Ilizarov method

a) Open book type pelvic fractures
b) Closed book type pelvic fractures
c) Vertical shear fractures
d) Rotational malalignment of iliac wing
e) Multi directional displacements

Usually the patient will not be fit for anaesthesia due to poly trauma, associated chest injuries and hypo tension. The patient will be under shock. In order to save the life of the patient and save time we prefer to apply the shanz pins under local anaesthesia.
DAY 1 – At emergency room – Resuciation, bladder care, External fixation

It is highly advisable to apply the frame with a time frame of 5 to 30 minutes.

After the application of the frame a minimal correction can be performed if the patient is stable. If not the corrections can be done later. The advantage of ilizarov method is further corrections can be done gradually, under image control and without anaesthesia.
Few days after injury conversion to ilizarov frame

Gradual correction of pubic bone and vertical shear under image intensifier
Gradual correction of sacro iliac joint under image intensifier

After correction
Limitations and Contra indications:
This method has the following limitations:
1) Fractures involving iliac crest
2) Complexity of the frame
3) Acceptance by the patient as the frame is bulky and needs uncomfortable postures during the treatment period.
4) Social and cosmetic reasons can make the patient prefer for internal fixation
5) Associated visceral injuries
6) Need of ilizarov trained person (once the patient is stable with conventional frame the patient can be referred to an Ilizarov surgeon at nearby centers)

Results:
- A better selection of patients will give a better result. Knowledge of Ilizarov principle is not an indication
- We selected patients whom we felt the correction can be achieved by ilizarov apparatus. The remaining patients we subjected for open reduction and internal fixation
- All of our patients had a reasonable reduction except for one patient with posterior instability. We had to do an additional posterior fixation. We preferred hybrid fixation for posterior instability as the frame application over the posterior aspect will be uncomfortable for the patient
- All our patients were able to walk approximately 6 weeks after surgery
- Four of our patients were complaining of vague pain which cannot be localized. But the pain subsided spontaneously over a period of 6 months.
- No patients had limb length discrepancies

Conclusion:
As the pelvic bone is a cancellous bone it tends to unite over a period of three weeks. So it is the surgeon’s duty to achieve maximum possible correction within three weeks. A delay in this reduction will lead to malunion of fragments. Further management will lead a complicated osteotomies and blood transfusions.
Advantages:
- Bloodless surgery
- Scarless surgery
- No need of Major anaesthesia
- No need of major surgical procedures
- Incidence of malunion of pelvic bones can be prevented
- Can be performed even in under equipped peripheral centers
- Multiple corrections can be done as required gradually with the image intensifier
- Gradual corrections are usually painless
- An early correction of the displaced pelvic bones can be achieved in poly trauma patients and in patients who are having problems for anaesthetic fitness due to chest injury, spine injuries, visceral injuries etc.
Study of Psychiatric Morbidity among Pulmonary Tuberculosis Patients

Jagpal Singh Klair
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Baba Farid University of Health Sciences, Faridkot, PUNJAB, India
Email: klairjagpal@yahoo.com

Introduction

Pulmonary Tuberculosis is a specific infectious disease caused by Mycobacterium tuberculosis. The disease is usually chronic with varying clinical manifestations, usually manifesting as onset of respiratory and constitutional symptoms. Haemoptysis (blood tinged sputum) is the most frightening symptom and often leads the patient to seek treatment.

Pulmonary Tuberculosis is the most common cause of morbidity and mortality due to single infectious agent in adults and accounts for over a quarter of the avoidable deaths worldwide. According to conservative estimates of World Health Organisation, there are 15-20 million cases of infectious TB in the world. There are about 8 million new cases and 3 million deaths each year due to tuberculosis. 95% of the tuberculosis cases and 98% of the tuberculosis deaths occur in developing countries. Pulmonary TB is the India’s biggest public health concern. About 30% of total population is infected with Mycobacterium tuberculosis and 1.5% of population suffers from radiologically active pulmonary tuberculosis. Pulmonary tuberculosis especially the multidrug resistant tuberculosis is characterized by prolonged and distressing symptoms like haemoptysis (Govt. of India, Annual Report, 1993-94, DGHS, New Delhi).

The problem is further complicated by relentless spread of human immunodeficiency virus which causes acquired immunodeficiency syndrome (AIDS) pandemic and the emergence of multi-drug resistant strains. The immune defects produced by HIV increases the predisposition to tuberculosis. The incidence of tuberculosis in HIV infected patients is about a hundred fold than that in general population (Small, 1991) and 40% develop active tuberculosis within few months following infection.

Psychological distress may become manifest in disrupted breathing as in the tachypnea seen in anxiety disorders or sighing respirations in the depressed or anxious patients. The interaction of psychic and somatic influences becomes more complex when one considers the etiology and maintenance of symptoms of pulmonary disorders. For example self-destructive or depressive feeling may generate or give momentum to a smoking habit which would increase the incidence of pulmonary tuberculosis.

Pulmonary tuberculosis besides the specific clinical manifestations, can also cause the appearance of social, emotional and sexual problems. (Ibanez et al, 2001) in an interview based study which evaluated the perception of sexual difficulties and changes in communication with patients and their wives showed 67% of patients and 94% of their wives had some type of sexual problems like decreased desire or impotence. The latter problems appear in advanced lung disease. It had been observed that deterioration of pulmonary function is related to organic erectile dysfunction. Besides, hypoxaemia has been shown to reduce level of testosterone and also suppresses hypothalamic-pituitary-testicular axis.

Dudley et al. (1985) observed that when patients and physicians face chronic disease, they may feel helpless. The patient may be viewed by others as weak and lacking motivations. Physicians may be seen as lacking clinical competence when a patient can’t be cured. The patient and family may be angry and frustrated that this illness cannot be fixed. Patient may feel guilty if smoking was one of the
factors resulting in the disease. They may feel like a burden to their spouses and families. Patients may avoid strong emotions to minimize the demands on the lungs. Denial, suppression of affect, repression and isolation frequently are used as coping strategies in these patients. Consequently, the patients spouse or family may feel that the patient is emotionally distant and unavailable. They may view the patient as unwilling to address issues that they bring up, not recognizing that this strategy is viewed by the patient as necessary for survival. Family members may experience the patients rigid avoidance of affect and conflict as rejection of them. This may perpetuate a cycle of confrontation and avoidance, leading to unresolved anger and despair because neither the needs of the patients nor those of the family are met. Patients may fear loss of control or loss of independence. They may have many losses to contend with because of their pulmonary tuberculosis, such as loss of their job, social status, role in family, or changes in appearance. Despite the availability of inexpensive and effective anti-tuberculosis medicines, non-adherence to medication by patients due to depression is the principal obstacle in the treatment of tuberculosis.

Though there are a number of studies showing high prevalence of psychiatric morbidity among patients of chest disease like COPD and asthma, there is paucity of studies regarding prevalence of psychiatric morbidity in patients of pulmonary tuberculosis.

This present study intends to have an insight into prevalence of psychiatric morbidity among Indian patients with pulmonary tuberculosis.

**Review of Literature**

Research suggest that psychic forces affect the clinical expression of chronic chest diseases in several ways altered awareness of airway resistance, suggestibility to airway constrictions, co-morbidity with anxiety, panic disorders and depression (Kikochi et al, Spinhoven P Van et al, Stone C et al 1994, 1997). Psychiatric issues impinge on many facets of the cause of chronic respiratory diseases like pulmonary tuberculosis, from etiology to ongoing symptoms and appearance of related respiratory syndrome as well as psychiatric morbidity. Number of studies have evaluated have higher prevalence of psychiatric morbidity among patients with chronic chest diseases compared with general population (Karjesh, 1990; Pollach, 1996; Wells, 1998).

Wells (1998) demonstrated the sex and age adjusted prevalence of any psychiatric disorder in the proceeding six months was 24.7% and of life time psychiatric disorder was 42.2% among persons with one or more medical conditions (which include lung disease) compared to 17.5% and 33.0% respectively for persons with no medical condition.

In a study by Ayden et al. (2001) depression and anxiety (as assessed by Intervention Diagnostic Interview) composite among TB patients was 19% in recently diagnosed TB, 21.6% in defaulters TB and 25.6% in MDR-TB patients.

Tuberculosis remains a leading infectious cause of mortality worldwide, with 3/4th of patients in developing countries. The management of pulmonary tuberculosis is further complicated by dual infection of HIV and TB and the emergence of multidrug resistant TB. Psychiatric complications present challenge in the treatment of patient with MDR-TB. A recently published study by (Peru, 2004) showed prevalence of baseline depression and anxiety 52% and 8.7% in a cohort of MDR-TB patients. The incidence of depression, anxiety and psychosis during MDR-TB treatment was 13.3%, 12% and 12% respectively. While the majority of individuals with depression, anxiety and psychosis required treatment, cycloserine administration with known neuropsychiatric side effects was successfully continued in all cases (Vega et al, 2004).
In another study by Mohammed O Husain, Sam P Dearman, Imran B Chaudhry, Nadeem Rizvi, and Waquas Waheed (2008) on the relationship between anxiety, depression and illness perception in tuberculosis patients in Pakistan it was found that out of 108 patients, 50 (46.3%) were depressed and 51 (47.2%) had anxiety. Raised depression and anxiety scores were associated with an increase in the number of symptoms reported, more serious perceived consequences, and less control over their illness.

A study was carried out on psychiatric morbidity, patients’ perspectives of illness and factors associated with poor medication compliance among the tuberculosis in Vellore, South India by E. Manoharam, John, Joseph and Jacob (2001). In this study of the 52 subjects recruited for the study, 45 (86.5%) had pulmonary tuberculosis. In all, 9(17.3%) subjects satisfied the International Classification of Diseases 10 Primary Care Criteria for psychiatric disorders. Depression was the commonest disorder. The majority of subjects knew the name of their disease (87.7%), believed its infectious nature (51.9%), feared incapacitation (21.2%) and death (59.6%), wanted symptomatic relief (40.4%) and were satisfied with their treatment (82.7%). A total of 48 subjects were followed up for 6 months, till the course of anti-tuberculosis treatment was completed; 32(66.7%) subjects completed their treatment. Only smoking was found to be associated with poor compliance in univanate analysis.

Similar study was carried out on illness behaviour of tuberculosis patients undergoing DOTS therapy: a case-control study by (S.K.Bhasin, Atul Mittal, O.P.Aggarwal, and R.K.Chadha, 2001) in which Illness Behaviour Questionnaire (IBQ), a self-report instrument was administered to 103 tuberculosis cases and a similar number of age, sex matched controls to find out the difference in illness behaviour profile of the two groups. The tuberculosis patients were receiving treatment from two DOTS centres in East Delhi and the controls were from the same locality. The tuberculosis patients exhibited features pertaining to general hypochondrasis (GH), affective inhibition (AI) and affective disturbance (AD) more than the controls and the differences between the two groups were statistically significant. However, denial of problem (D) was seen more in controls compared to tuberculosis patients.

Bhatia, Bhasin and Dubey (2000) carried out research on Psychosocial dysfunction in tuberculosis patients. The sample consisted of 50 patients with the mean age of 28.3 years (age range 11-55 years). There were 38 males (76%) and 12 females (24%). The marital status was 26 married (52%) and 24 unmarried (48%). 21 patients (42%) were illiterate, 18 (36%) were studied upto primary class, 6(12%) were literate upto high school, 5 patients studied above high school. Various occupational groups were Housewives - (16%), students 12 (24%), skilled workers - 6 (12%), clerical employees - 8 (16%), small scale businessmen - 6 (12%) and unskilled workers - 10 (20%). 26 patients (52%) lived in joint families and 24 patients (48) had a nuclear family. The average monthly income was Rs. 1500. On Neuroticism scale, 39 patients (78%) scored significantly (i.e. above 9). Mean score was 16.6 (±3.2). The degree of neuroticism correlated significantly with scores on subscales of DAQ. Higher neuroticism showed higher psychosocial dysfunctioning.

Aims and Objectives

1. To find out psychiatric morbidity in patients of pulmonary tuberculosis.
2. To correlate psychiatric morbidity with gradation of sputum examination, radiological extent of the disease and socio-economic factors.
3. To evaluate the effect of pulmonary tuberculosis on quality of life.

Material and Methods
1. Sample Size

In the present study the patients with Pulmonary Tuberculosis were screened from TB and Chest Hospital, Govt. Medical College, Patiala. Patients of Pulmonary Tuberculosis were contacted. The diagnosis and type of Pulmonary Tuberculosis was determined with consultation of Professor of TB and Chest Diseases department.

2. Patient inclusion criteria

(a) Patients of adult age group (18 years and above)

(b) Both male and female were examined.

(c) Patients diagnosed and confirmed by histo-pathological examination for lung cancer.

3. Patient exclusion criteria

(a) Patient with any history of alcohol or substance abuse.

(b) Patient with any other chronic medical illness or epilepsy.

(c) Patients having mental retardation.

(d) Those who refused to give informed consent.

(e) Pregnant women diagnosed with chronic chest disease.

(f) Patients previously diagnosed with psychiatric disorder.

**Personal Biodata Proforma (including Medical background data)**

This proforma included items or variables to study the sociodemographic profile of the patients. The variables included age, marital status, domicile, education and occupation. Information regarding attributes of Pulmonary Tuberculosis like time since diagnosis, duration since onset of disease, diagnosis and types of Pulmonary Tuberculosis, treatments received, symptoms associated with treatment and previous lab investigations were included from the patient's reports in the medical records at the time of clinical assessment.

The following instruments were applied for the purpose of the study:

- Symptom check list (SCL)-80
- Quality of life (QOL) scale - 16 item number scale as adapted for patients with chronic illness (Burckhardt and colleagues).
- Clinical diagnosis of psychiatric disorders will be made as per rCD criteria.
Symptom Check List-80

It consists of 80 items. These 80 items are further divided into nine subscales namely:

1. Somatization subscale (12)
2. Depression subscale (13)
3. Paranoid ideation subscale (6)
4. Interpersonal sensitivity subscale (9)
5. Phobic anxiety subscale (7)
6. Anxiety subscale (10)
7. Obsessive compulsive neurosis subscale (10)
8. Anger hostility subscale (6)
9. Additional symptoms subscale (7)

The items included in each subscale are listed in the scoring key. Each item had a maximum score of four, depending upon the severity of symptom. The score one was given when patients complained of a little bit of symptom, score four for extremely severe.

The severity of symptoms in each subscale was divided into:

1. Absent
2. Mild
3. Moderate
4. Severe

The total score obtained by a given patient in the said subscale was added up. Depending upon the score, the maximum score obtained by any given subject was taken into consideration. If the score of the given subject was between 0-25% of the maximum score, he/she was placed in the category of the absent, if the score was between 25-50% of maximum score, he/she was placed in category of mild, if the patient scored between 50-75% of the maximum score, he/she was placed in category of moderate he/she scored between 75-100% of the maximum score, he/she was placed in the category of severe.

Quality of Life Scale (QOLS)-adapted by Burchardt and colleagues for chronic illness

The Quality of Life Scale (QOLS) was originally created by American Psychologist John Flanagan in 1970's. The QOLS is now called the "Adapted Quality of Life Scale" or "Flanagan Quality of Life Scale." In this thesis, it will be called simply the QOLS and always refer to the 16-item scale as adapted by Burchardt and colleagues for persons with chronic illness.
Measurement by Quality of Life Scale (QOLS)

The instrument measures domains that diverse patient groups with chronic illness define as quality of life and has low to moderate correlations with physical health status and disease measures. The QOLS is a valid instrument for measuring quality of life across patient groups and cultures and is conceptually distinct from health status or other causal indicators of quality of life. Use in chronic illness populations, including a small group of cancer patients with ostomies, has been validated.

The QOLS was originally a 15-item instrument that measured 5 "conceptual domains of quality of life":

- Material and physical well being
- Relationships with other people
- Social, community and civic activities
- Personal development and fulfillment
- Recreation

The instrument was expanded to include one more item: "Independence, the ability to do for yourself". It has 16 items rather than the 15 found in the original Flanagan version.

Item Scaling

A 7-point delighted terrible scale has been used to measure satisfaction with each item for a broad range of affective responses to QOL items. The seven responses were "delighted" (7), "pleased" (6), "mostly satisfied" (5), "mixed" (4), "mostly dissatisfied" (3), "unhappy" (2), "terrible" (0). (Andrews and Crandall, 1976).

Scoring and Interpretation of QOLS

The QOLS is scored by adding up the score on each item to yield a total score for the instrument. Scores can range from 16 to 112. The QOLS scores are summed so that a higher score indicates higher quality of life. Average total score for healthy populations is about 90. Means for various chronic conditions come from descriptive studies or experimental pretest data e.g. Average total scores for other conditions range from 61 for patients with post-traumatic stress disorder, to 83 for rheumatoid arthritis, to 84 for systemic lupus erythematosus, to 87 for osteoarthritis. And like many QOL instruments, the means tend to be quite negatively skewed with most patients reporting some degree of satisfaction with most domains of their lives.

This scale can be used with confidence in chronic illness groups. In the current study, it is used for the purpose of Pulmonary Tuberculosis.
Data Collection

All the scales and analyses were administered personally to the subjects. All queries regarding the study were also explained. At the beginning, written consent was taken and information about the study was provided to the patient. A detailed history of illness was recorded from the patients with the various socio-demographic variables and details of Pulmonary Tuberculosis on Proforma.

Using the inclusion and exclusion criteria of the Pulmonary Tuberculosis, 27 patients were excluded from study, 10 patients due to diabetes mellitus, 8 due to ischaemic heart disease, 7 due to history of alcohol/substance abuse and 2 patients excluded due to pregnancy. Patients who refused to give the informed consent were excluded from the present study.

All the selected cases were screened in detail, were interviewed and psychiatric symptoms were elicited on the basis of SCL-80 and clinical interviews conducted in consultation with consultant psychiatrist. QOLS were used to assess the Quality of Life (QOL). The diagnosis of psychiatric morbidity were made according to clinical description and diagnostic criteria for ICD-10, on the basis of which patients were classified.

Out of the total patients screened, 50 patients were diagnosed as the patients of Pulmonary Tuberculosis with psychiatric morbidity. Such patients were enrolled in Group A. The Attendants of these patients serving as control were enrolled in Group B.

Statistical Methods

Substitution of missing values on questionnaires scales (QOLS) was made if the patient had responded at least half of the items in a specific subscale. The missing value was replaced by the mean of completed items in that scale for each patient. If more than half of the scale items were incomplete, the scale score was treated as missing data.

The data collected was subjected to statistical analysis and chi-square and t test were applied to test the statistical significance of the various factors that contributed to psychiatric morbidity.

OBSERVATIONS

Table 1: Number Of Patients

<table>
<thead>
<tr>
<th>Description</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients Excluded</td>
<td>27</td>
</tr>
<tr>
<td>Group A Number of patients of Pulmonary Tuberculosis with psychiatric morbidity</td>
<td>50</td>
</tr>
<tr>
<td>Group B Attendants (Control) of Group A patients</td>
<td>50</td>
</tr>
<tr>
<td>Number of Attendants (Control) with psychiatric morbidity</td>
<td>6</td>
</tr>
<tr>
<td>Prevalence of psychiatric morbidity among patients of Pulmonary Tuberculosis</td>
<td>51.55%</td>
</tr>
<tr>
<td>Prevalence of psychiatric morbidity among the Attendants (Control)</td>
<td>12%</td>
</tr>
</tbody>
</table>

Table 1 shows that 124 patients with Pulmonary Tuberculosis were screened to get 50 patients of Pulmonary Tuberculosis with psychiatric morbidity (Group A). Out of these 124 patients 27 patients
were excluded initially. So the prevalence of psychiatric morbidity among patients of Pulmonary Tuberculosis is 51.55%.

50 Attendants of the 50 patients of Pulmonary Tuberculosis with psychiatric morbidity (Group A) were taken as Control (Group B). Out of these 50 Attendants (Control), 6 had psychiatric morbidity. So the prevalence of psychiatric morbidity among the Attendants (Control) is 12%.

Table 2: Socio-Demographic Attributes of Patients

<table>
<thead>
<tr>
<th>Socio-demographic attributes</th>
<th>Group A</th>
<th>Group B</th>
<th>X2</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>36</td>
<td>72</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>14</td>
<td>28</td>
<td>18</td>
</tr>
<tr>
<td>Marital Status</td>
<td>Married</td>
<td>41</td>
<td>82</td>
<td>35</td>
</tr>
<tr>
<td></td>
<td>Unmarried</td>
<td>9</td>
<td>18</td>
<td>15</td>
</tr>
<tr>
<td>Education</td>
<td>Illiterate</td>
<td>33</td>
<td>66</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Primary</td>
<td>13</td>
<td>26</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>4</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Domicile</td>
<td>Urban</td>
<td>10</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Rural</td>
<td>40</td>
<td>80</td>
<td>38</td>
</tr>
<tr>
<td>Occupation</td>
<td>Housewifes</td>
<td>9</td>
<td>18</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Labourers/Farmers</td>
<td>31</td>
<td>64</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Govt. Employes</td>
<td>8</td>
<td>14</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Professional</td>
<td>2</td>
<td>4</td>
<td>3</td>
</tr>
</tbody>
</table>

Table 2 shows that the number of male and female patients in both groups did not differ significantly. The patients were almost similar on other variables like marital status, domicile and occupation. The difference in number of illiterate patients in both groups was significant.
Pie diagram showing Distribution of Patients according to Sex in Group A

Pie diagram showing Distribution of Patients according to Sex in Group B

Pie diagram showing Distribution of Patients according to Marital Status in Group A
Pie diagram showing Distribution of Patients according to Marital Status in Group B

Pie diagram showing Distribution of Patients according to Education in Group A

Pie diagram showing Distribution of Patients according to Education in Group B
Pie diagram showing Distribution of Patients according to Domicile in Group A

Pie diagram showing Distribution of Patients according to Domicile in Group B

Pie diagram showing Distribution of Patients according to Occupation in Group A
Pie diagram showing Distribution of Patients according to Occupation in Group B

Table 3: Age of Patient

<table>
<thead>
<tr>
<th>Age Group (in years)</th>
<th>Group A (n = 50)</th>
<th>Group B (n = 50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>%</td>
<td>Number</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>30 – 50</td>
<td>24</td>
<td>26</td>
</tr>
<tr>
<td>&gt; 50</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Range (yrs)</td>
<td>24 – 68</td>
<td>21 – 59</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>42.06±12.13</td>
<td>38.8±11.018</td>
</tr>
<tr>
<td>Df</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>'t' &amp; ‘p’ value</td>
<td>1.402, p=.163</td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

The table shows age distribution of patients in Group A and Group B. Mean Age (±SD) for Group A was 42.06±12.13 and that for Group B was 38.8±11.018. The Mean Age of Group A is more than that of Group B but the difference is NS.

Table 4: Showing Smoking Status In Patients of Pulmonary Tuberculosis

Bar diagram showing Age of Patients
<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group B</th>
<th>Chi-sq</th>
<th>X2</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current smokers</td>
<td>28</td>
<td>12</td>
<td>10.67</td>
<td>0.001**</td>
<td></td>
</tr>
<tr>
<td>Past smokers</td>
<td>13</td>
<td>28</td>
<td>9.30</td>
<td>0.002**</td>
<td></td>
</tr>
<tr>
<td>Non smokers</td>
<td>9</td>
<td>10</td>
<td>0.06</td>
<td>0.80</td>
<td></td>
</tr>
</tbody>
</table>

There was no difference in number of smokers (current and past) and non-smokers in both the groups; however there were significantly higher number of current smokers in Group A compared with Group B (p=0.001**). The difference in the number of past smokers in Group A compared with Group B was also highly significant (p=0.0002**).

Bar diagram showing Smoking Status in Patients of Pulmonary Tuberculosis

Table 5: SCL-80 SCORE

<table>
<thead>
<tr>
<th>SCL Score</th>
<th>Group A</th>
<th>Group B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>&lt; 20</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>21 – 40</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>41 – 60</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>61 – 80</td>
<td>13</td>
<td>26</td>
</tr>
<tr>
<td>81 – 100</td>
<td>19</td>
<td>38</td>
</tr>
<tr>
<td>101 – 120</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>&gt; 120</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Range</td>
<td>26 – 116</td>
<td>11 – 54</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>78.2400±21.36138</td>
<td>22.9400±11.10508</td>
</tr>
<tr>
<td>df</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>'t' value</td>
<td>16.242</td>
<td></td>
</tr>
<tr>
<td>'p' value</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Significance</td>
<td>HS</td>
<td></td>
</tr>
</tbody>
</table>

The above table shows that the scores as measured on SCL-80 were more in Group A Mean (±SD) 78.2400±21.36138 compared with Group B Mean (±SD) 22.9400±11.10508 and the difference was highly significant (HS) (p<0.001).
Table 6: Scores on Individual SCL-80 Sub Scale

<table>
<thead>
<tr>
<th>SCL Sub Scale</th>
<th>Group A</th>
<th>Group B</th>
<th>Chi-sq</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Somatization</strong></td>
<td>Absent 0-12</td>
<td>23 46</td>
<td>48 96</td>
<td>27.27</td>
</tr>
<tr>
<td></td>
<td>Present 13-48</td>
<td>27 54</td>
<td>2 4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>19.06±13.91286</td>
<td>7.30±4.14163</td>
<td></td>
</tr>
<tr>
<td><strong>Depression</strong></td>
<td>Absent 0-13</td>
<td>21 42</td>
<td>46 92</td>
<td>26.05</td>
</tr>
<tr>
<td></td>
<td>Present 14-52</td>
<td>29 58</td>
<td>4 8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>20.5±15.00238</td>
<td>6.70±4.33425</td>
<td></td>
</tr>
<tr>
<td><strong>Paranoid</strong></td>
<td>Absent 0-6</td>
<td>46 92</td>
<td>50 100</td>
<td>2.34</td>
</tr>
<tr>
<td></td>
<td>Present 7-24</td>
<td>4 8</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>4.02±2.14276</td>
<td>3.42±1.56609</td>
<td></td>
</tr>
<tr>
<td><strong>I/P Sensitivity</strong></td>
<td>Absent 0-9</td>
<td>47 94</td>
<td>50 100</td>
<td>1.37</td>
</tr>
<tr>
<td></td>
<td>Present 10-36</td>
<td>3 6</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>5.50±3.05894</td>
<td>5.20±2.12852</td>
<td></td>
</tr>
<tr>
<td><strong>Phobia</strong></td>
<td>Absent 0-7</td>
<td>40 80</td>
<td>50 100</td>
<td>9.00</td>
</tr>
<tr>
<td></td>
<td>Present 8-28</td>
<td>10 20</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>6.04±4.91545</td>
<td>4.18±1.98659</td>
<td></td>
</tr>
<tr>
<td><strong>Anxiety</strong></td>
<td>Absent 0-10</td>
<td>41 82</td>
<td>50 100</td>
<td>7.81</td>
</tr>
<tr>
<td></td>
<td>Present 11-40</td>
<td>9 18</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>7.90±6.90534</td>
<td>5.90±2.61276</td>
<td></td>
</tr>
<tr>
<td><strong>OCN</strong></td>
<td>Absent 0-10</td>
<td>41 82</td>
<td>50 100</td>
<td>7.81</td>
</tr>
<tr>
<td></td>
<td>Present 11-40</td>
<td>9 18</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>9.16±6.73510</td>
<td>5.90±2.63609</td>
<td></td>
</tr>
<tr>
<td><strong>Anger/Hostility</strong></td>
<td>Absent 0-6</td>
<td>43 86</td>
<td>50 100</td>
<td>5.53</td>
</tr>
<tr>
<td></td>
<td>Present 7-24</td>
<td>7 14</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>4.54±3.40594</td>
<td>3.38±1.51037</td>
<td></td>
</tr>
<tr>
<td><strong>Additional</strong></td>
<td>Absent 0-7</td>
<td>31 62</td>
<td>49 98</td>
<td>18.06</td>
</tr>
<tr>
<td></td>
<td>Present 8-24</td>
<td>19 38</td>
<td>1 2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>8.48±7.45665</td>
<td>3.58±2.16738</td>
<td></td>
</tr>
</tbody>
</table>
This table shows that on the basis of SCL-80 scores, Group A patients had significantly higher mean score for all the parameters except Paranoid and I/P sensitivity subscales as compared to Group B subjects.

The difference in the scores of parameters Somatization, Depression, Phobia, Anxiety, OCN and Additional were highly significant (HS) (p<0.001) and was significant (S) (p<0.05) for Anger/Hostility.

Bar diagram showing Mean Scores of Individual SCL-80 Sub scale

Table 7: Severity of Symptoms on Individual SCL-80 Sub Scale

<table>
<thead>
<tr>
<th>SCL Sub Scale</th>
<th>Group A</th>
<th>Group B</th>
<th>Chi Sq</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%</td>
<td>Number</td>
<td>%</td>
</tr>
<tr>
<td>Somatization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0-12</td>
<td>23 46</td>
<td>48 96</td>
<td>27.97</td>
</tr>
<tr>
<td>Mild</td>
<td>13-24</td>
<td>9 18</td>
<td>2 4</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>25-36</td>
<td>11 22</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>37-48</td>
<td>7 14</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>19.06±13.91286 7.3000±4.14163</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0-13</td>
<td>21 42</td>
<td>47 94</td>
<td>28.72</td>
</tr>
<tr>
<td>Mild</td>
<td>14-26</td>
<td>11 22</td>
<td>3 6</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>27-39</td>
<td>11 22</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>40-52</td>
<td>7 14</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>20.50±15.00238 6.7000±4.33425</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paranoid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0-6</td>
<td>46 92</td>
<td>50 100</td>
<td>2.34</td>
</tr>
<tr>
<td>Mild</td>
<td>7-12</td>
<td>4 8</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>13-18</td>
<td>- -</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>19-24</td>
<td>- -</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>4.0200±2.14276 3.4200±1.56609</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I/P Sensitivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0-9</td>
<td>47 94</td>
<td>50 100</td>
<td>1.37</td>
</tr>
<tr>
<td>Mild</td>
<td>10-18</td>
<td>3 6</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>19-27</td>
<td>- -</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>28-36</td>
<td>- -</td>
<td>- -</td>
<td></td>
</tr>
<tr>
<td>Mean±SD</td>
<td>5.5000±3.05894 5.2000±2.12852</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Phobia Absent 0-7 40 80 50 100 9.00 0.003**  
Mild 8-14 7 14 - -  
Moderate 15-21 2 4 - -  
Severe 22-28 1 2 - -  
Mean±SD 6.0400±4.91545 4.1800±1.98659  
Anxiety Absent 0-10 41 82 50 100 7.81 0.005**  
Mild 11-20 5 10 - -  
Moderate 21-30 3 6 - -  
Severe 31-40 1 2 - -  
Mean±SD 7.9000±6.90534 5.9000±2.61276  
OCN Absent 0-10 41 82 50 100 7.81 0.005**  
Mild 11-20 5 10 - -  
Moderate 21-30 4 8 - -  
Severe 31-40 1 2 - -  
Mean±SD 9.1600±6.73510 5.9000±2.63609  
Anger/Hostility Absent 0-6 43 86 50 100 5.53 0.0187*  
Mild 7-12 5 10 - -  
Moderate 13-18 2 4 - -  
Severe 19-24 - - - -  
Mean±SD 4.5400±3.40594 3.3800±1.51037  
Additional Absent 0-7 31 62 49 98 18.06 0.001**  
Mild 8-14 7 14 1 2  
Moderate 15-21 9 18 - -  
Severe 22-28 3 6 - -  
Mean±SD 8.4800±7.45665 3.5800±2.16738  

The above table shows significantly severe symptoms on all subscales except Paranoid and I/P sensitivity. The difference in the severity of Somatization, Depression, Phobia, Anxiety, OCN and Additional were highly significant (HS) (p<0.001) and was significant (S) (p<0.05) for Anger/Hostility.

Table 8: Clinical Diagnosis according to ICD-10 Criteria

<table>
<thead>
<tr>
<th>ICD-10 Diagnosis</th>
<th>Number of patients</th>
<th>%age of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression (F-32)</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>Mild</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Severe</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Generalised anxiety disorder (F-41)</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Phobia (F-40)</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Somatization (F-45)</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>38</td>
<td>76</td>
</tr>
</tbody>
</table>

This table shows as per ICD-10 criteria, Depression was most common psychiatric diagnosis followed by generalized anxiety disorder, somatisation and phobia. Out of 20 patients (40%) in Group A who satisfied the criteria for depression, 5 patients (10%) were of mild depression, 12 (24%) were of moderate depression and 3 (6%) were of severe depression. There were 9 patients (18%) of generalized anxiety disorder, 4 patients (8%) of phobia and 5 patients (10%) were diagnosed having somatisation.
### Table 9: Quality Of Life Scale (QOLS) Scores in Groups of Patients of Pulmonary Tuberculosis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean SD A</th>
<th>Mean SD B</th>
<th>T</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Material comforts home, food, conveniences, financial security</td>
<td>3.27 ±1.285</td>
<td>3.97 ±1.189</td>
<td>-2.191</td>
<td>.033 &lt;.05 (S)</td>
</tr>
<tr>
<td>Health – being physically fit and vigorous</td>
<td>3.17 ±1.367</td>
<td>4.27 ±1.507</td>
<td>-2.961</td>
<td>.004 &lt;.05 (S)</td>
</tr>
<tr>
<td>Relationships with parents, siblings &amp; other relatives – communicating, visiting, helping</td>
<td>3.60 ±1.453</td>
<td>4.30 ±1.442</td>
<td>-1.873</td>
<td>.066 &gt;.05 (NS)</td>
</tr>
<tr>
<td>Having and rearing children</td>
<td>2.97 ±1.159</td>
<td>3.87 ±1.137</td>
<td>-3.036</td>
<td>.004 &lt;.05 (S)</td>
</tr>
<tr>
<td>Close relationships with spouse or significant other</td>
<td>3.50 ±1.383</td>
<td>4.03 ±1.402</td>
<td>-1.483</td>
<td>.143 &gt;.05 (NS)</td>
</tr>
<tr>
<td>Close friends</td>
<td>3.87 ±1.432</td>
<td>4.67 ±1.373</td>
<td>-3.769</td>
<td>.031 &lt;.05 (S)</td>
</tr>
<tr>
<td>Helping and encouraging others, volunteering, giving advice</td>
<td>3.27 ±0.907</td>
<td>4.23 ±1.073</td>
<td>-3.769</td>
<td>&lt;.001 (HS)</td>
</tr>
<tr>
<td>Participating in organizations and public affairs</td>
<td>3.63 ±1.377</td>
<td>4.27 ±1.507</td>
<td>-1.699</td>
<td>0.095 &gt;.05 (NS)</td>
</tr>
<tr>
<td>Learning – attending school, improving understanding, getting additional knowledge</td>
<td>3.53 ±1.167</td>
<td>3.87 ±1.224</td>
<td>-1.080</td>
<td>0.285 &gt;.05 (NS)</td>
</tr>
<tr>
<td>Understanding yourself – knowing your assets and limitations – knowing what life is about</td>
<td>3.57 ±1.382</td>
<td>4.47 ±1.383</td>
<td>-2.522</td>
<td>0.014 &lt;.05 (S)</td>
</tr>
<tr>
<td>Work job in home</td>
<td>3.40 ±1.070</td>
<td>4.13 ±1.137</td>
<td>-2.573</td>
<td>0.013 &lt;.05 (S)</td>
</tr>
<tr>
<td>Expressing yourself creatively</td>
<td>2.83 ±0.874</td>
<td>3.60 ±1.037</td>
<td>-3.096</td>
<td>0.003 &lt;.05 (S)</td>
</tr>
<tr>
<td>Socializing – meeting other people, doing things, parties etc.</td>
<td>3.43 ±1.331</td>
<td>4.57 ±1.406</td>
<td>-3.206</td>
<td>0.002 &lt;.05 (S)</td>
</tr>
<tr>
<td>Reading, listening to music, or observing entertainment</td>
<td>2.90 ±1.094</td>
<td>3.87 ±1.106</td>
<td>-3.404</td>
<td>&lt;.001 (HS)</td>
</tr>
<tr>
<td>Participating in active recreation</td>
<td>2.77 ±0.817</td>
<td>3.80 ±1.448</td>
<td>-3.404</td>
<td>&lt;.001 (HS)</td>
</tr>
<tr>
<td>Independence, doing for yourself</td>
<td>2.53 ±0.973</td>
<td>3.53 ±1.479</td>
<td>-3.093</td>
<td>0.003 &lt;.05 (S)</td>
</tr>
<tr>
<td>QLY of Life Total</td>
<td>52.23 ±7.276</td>
<td>65.43 ±13.146</td>
<td>-4.812</td>
<td>&lt;.001 (HS)</td>
</tr>
</tbody>
</table>

This table shows that quality of life score was highly significant (HS) (p<0.001)
In Group A the mean value of quality of life is 52.23 ± 7.276 and in Group B the mean value of quality of life is 65.43 ± 13.146. In both Groups A & B the item with highest rate of satisfaction was Close friends and Independence, doing for yourself received the lowest satisfaction rate.

### Conclusions

- Among the hospitalized patients Of Pulmonary Tuberculosis in the Chest and Tuberculosis ward, 51.55 % were having psychiatric morbidity as assessed on SCL-80 scale. Among the 50 Attendants (Control), 12% were having psychiatric morbidity.
- The comparison of Group A with B on the basis of SCL-80 scores subscale shows significantly severe symptoms on all subscales except Paranoid and I/P sensitivity sub-scales. The difference in
the scores of parameters Somatization, Depression, Phobia, Anxiety, OCN and Additional were highly significant (HS) (p<0.001) and was significant (S) (p<0.05) for Anger/Hostility.

- 76% patients met ICD-10 criteria for diagnosis of psychiatric disorders. Most common psychiatric disorder in patients with Pulmonary Tuberculosis was depression followed by generalized anxiety disorder, somatisation and phobia.

- Pulmonary Tuberculosis with psychiatric morbidity occurred more frequently among current smokers.

- The quality of life was poorer as shown by a lower mean value of quality of life score (52.23 ± 7.276) in patients with psychiatric morbidity as compared to that of other group of their Attendants (65.43 ± 13.146)

References


Small PM, Schecter GF, Goodman PC, Sande Ma et al. treatment of patients with advanced human immunodeficiency virus infection; NEJM 1991;324:289-94.


Study of Sleep disturbances after Minor Head Injury

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Abstract

Head injuries are very common in a country like India. My study is aimed to measure the long term sleep disturbances in adults who had past history of minor head injury. As sleep disturbances in the form of parasomnias and disturbed sleep rhythm affects the general functionality of the person. It is important to study the co relation between minor head injury and the sleep disturbances. The study was prospective questionnaire based including medical history, details of the MHI event, sleep habits and sleep disturbances. 40 patients who had suffered MHI three years before the study were selected as study group and completed the sleep questionnaire. 40 people with no history of MHI participated in the study and were considered as control group. Those patients who were ever treated or diagnosed with any psychiatry disorder, who had any sleep disturbances before the head injury instance were excluded from the study group. Among 40 participants 32 were males. 63% had significant amnesia regarding the MHI event. 74% had learning and concentration difficulties. 37% (study group) v/s none (control group) experienced early morning awakenings. 68% (study group)v/s 31%(control group) complained of daytime sleepiness and 63% (study group) v/s 44% (control group) reported restless sleep two or more times a week. Parasomnia were also relatively common with 42 % (study group) v/s 20% (control group) reporting sleep talking two or more times a week. 20 %( study group) v/s none reported sleep enuresis. 42 % (study group) v/s 5 % (control group) complained of bruxism. 42% of the study group patients experienced fears of going to sleep, 62% reported fearful awakenings from sleep and 58% experienced frightening dreams two or more times a week.

Keywords: Minor Head Injury, Long term effects, Sleep Disturbances, General functionality, Parasomnias, Somnambulism

Introduction

Head injuries are very common in a country like India. Minor head injury (MHI) is characterized as a brain concussion that can cause a transient loss or impairment of consciousness (for less than 30 minutes), vomiting, and a short anterograde or retrograde amnesia. In MHI the Glasgow Coma Scale (GCS) score is 13 or higher [1]. These are left unnoticed as the neurological evaluation, including computed tomography (CT) and magnetic resonance imaging (MRI) scans, electroencephalogram (EEG) is normal or reveals minor transient abnormalities [1].

However, although considered a benign event, MHI may have long-term effects generally termed postconcussive syndrome, or, in less-frequent cases, may result in posttraumatic stress disorder
Postconcussive syndrome includes headaches, memory and concentration impairments, anxiety, mood disorders, and sleep disorders [1]. There is some overlap with symptoms found in PTSD, which is a mental disorder consisting of flashbacks, nightmares, and an inability to cope with daily life events. The syndrome primarily affects adults and includes two types of sleep disturbances as part of the diagnostic criteria (based on the DSM-IV): re-experiencing events (nightmares, Criteria B) and a hyperarousal state (difficulty initiating and maintaining sleep, Criteria D). There is controversy as to whether MHI can cause PTSD because of the loss of consciousness and the posttraumatic amnesia, which occur in the event [2]. Adolescents and young adults who have undergone MHI may suffer from sleep disorders without necessarily having other symptoms of the postconcussive syndrome or PTSD. Subjective evaluation of individuals after MHI revealed complaints of difficulties in initiating and maintaining sleep, early morning awakenings, decreased daytime performance, and a generally decreased sleep quality [3, 4]. Few studies have attempted to objectively measure sleep behavior after MHI. In the acute phase after head injury in children, Lenard and Pennigstroff [5] found an increase in stage 2 (“light sleep”) and a decrease in stages 3-4 (“deep sleep”) with no consistent changes in percentage of rapid eye movement (REM) sleep. They also found more spindle activity in stages 2-3 and increased REM density. In contrast, Harada et al. [6] found a decrease in spindles and K-complexes during NREM sleep and decreased REM activity. Enomoto et al. [7] reported EEG changes in 42.5% of 280 children under 15 years of age in the acute phase after MHI. EEG abnormalities included an increase in slow-wave activity (associated with deep sleep) that had resolved during follow-up examinations.

All of the above-mentioned findings refer to the effects of MHI on sleep in the acute phase. The long-term effects of MHI on sleep have not yet been studied consistently. Thus the purpose of our study was to characterize subjective sleep abnormalities of adults who had experienced MHI and consequently complained of sleep disorders at the chronic phase after the injury.

Aims and Objectives

The purpose of the study is to characterize subjective sleep abnormalities and general functionality of adults who had experienced Minor Head Injury and complained of sleep disorders at the chronic phase after the injury.

Method

This is a study conducted in Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital (A.V.B.R.H.), a 909 bedded tertiary teaching hospital of Datta Meghe Institute of Medical Sciences University (NAAC Accredited Grade A).

Approved from the Institutional Ethical Committee of Datta Meghe Institute of Medical Sciences University.

Study Protocol

The study was prospective a detailed questionnaire, including medical history, details of the MHI event, sleep habits, and sleep disturbances.

Study Group

A list was formed of all admissions above 18 years of age who had been admitted to the hospital between the years 2003 and 2005 for Minor Head Injury (ICD-10 code S06.0) with a GCS of 13 or
above on admission to the emergency department. Out of these, contact details of the patients like address and telephone numbers were derived. Then with the help of local social health worker and volunteers the patients were approached.

Patients were explained the purpose of the study and were requested to participate. Those who gave their consent were included in the study. Others, who left the interview and examination halfway for various reasons, and those who had any past medical history of neurological or psychiatric illness, any emotional stress or any other cause of sleep disturbance were excluded from the study. Rapport was developed with the participants. They were asked to fill the questionnaire which was in their vernacular language. The data was collected using a structured interview schedule and experienced evaluators. Each interview and questionnaire completion lasted for at least 30-45 minutes per participant. At the end of the interview and examination the questionnaire was checked for completeness and the interviewer thanked the responder.

**Control group**

The control group for study was composed of 40 sample of the same age group of above 18 as the control subjects.

**Statistical Analysis**

The collected data was depicted in tabular form and interpreted statistically and analyzed. The collected data was statistically analyzed by using the standard tests to ascertain the clinical relevance of the present study. Software used is SPSS 14.0 version.

**Results**

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amnesia of events after the head injury</td>
<td>15</td>
<td>02</td>
<td>06</td>
<td>09</td>
<td>08</td>
</tr>
<tr>
<td>Learning and concentration difficulties</td>
<td>10</td>
<td>10</td>
<td>14</td>
<td>04</td>
<td>02</td>
</tr>
<tr>
<td>Fears before the head injury</td>
<td>17</td>
<td>06</td>
<td>02</td>
<td>09</td>
<td>06</td>
</tr>
<tr>
<td>Fears after the head injury</td>
<td>19</td>
<td>06</td>
<td>02</td>
<td>01</td>
<td>12</td>
</tr>
<tr>
<td>Headaches before the head injury</td>
<td>35</td>
<td>04</td>
<td>01</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Headaches after the head injury</td>
<td>08</td>
<td>02</td>
<td>02</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Difficulty sleeping away from home</td>
<td>09</td>
<td>08</td>
<td>14</td>
<td>04</td>
<td>05</td>
</tr>
</tbody>
</table>

Numbers represent the number of patients who answered in each scoring category. Scores ranged from 0 - none to 4 - extremely severe.
Table 2: Questionnaire results of our study group (n = 40, mean age = 25.53 ± 1.68, 32 males, 8 females) to questions regarding their sleep habits and disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falling asleep within 20 minutes of “lights out”</td>
<td>08</td>
<td>07</td>
<td>09</td>
<td>16</td>
<td>00</td>
</tr>
<tr>
<td>Early awakenings</td>
<td>17</td>
<td>08</td>
<td>07</td>
<td>04</td>
<td>04</td>
</tr>
<tr>
<td>Difficulty awakening in the morning</td>
<td>05</td>
<td>04</td>
<td>09</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>09</td>
<td>04</td>
<td>10</td>
<td>15</td>
<td>02</td>
</tr>
<tr>
<td>Restless sleep</td>
<td>06</td>
<td>09</td>
<td>02</td>
<td>09</td>
<td>14</td>
</tr>
<tr>
<td>Somnambulism</td>
<td>34</td>
<td>04</td>
<td>00</td>
<td>02</td>
<td>00</td>
</tr>
<tr>
<td>Somniloquence</td>
<td>11</td>
<td>12</td>
<td>11</td>
<td>06</td>
<td>00</td>
</tr>
<tr>
<td>Bruxism</td>
<td>23</td>
<td>11</td>
<td>04</td>
<td>02</td>
<td>00</td>
</tr>
<tr>
<td>Nocturnal enuresis</td>
<td>32</td>
<td>04</td>
<td>04</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Fear of going to sleep</td>
<td>23</td>
<td>06</td>
<td>03</td>
<td>04</td>
<td>04</td>
</tr>
<tr>
<td>Fearful awakenings from sleep</td>
<td>15</td>
<td>09</td>
<td>08</td>
<td>08</td>
<td>00</td>
</tr>
<tr>
<td>Frightening dreams</td>
<td>07</td>
<td>10</td>
<td>15</td>
<td>06</td>
<td>02</td>
</tr>
</tbody>
</table>

Numbers represent the number of adults who answered in each scoring category (0 = never; 1 = once monthly or less; 2 = two to four times weekly; 3 = 5 or more times weekly; 4 = every night).

Table 3: Questionnaire results of our control group (n = 40, mean age = 23.31 ± 1.09, 34 males, 6 females) to questions regarding their sleep habits and Disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Falling asleep within 20 minutes of “lights out”</td>
<td>00</td>
<td>03</td>
<td>09</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Early awakenings</td>
<td>24</td>
<td>16</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Difficulty awakening in the morning</td>
<td>04</td>
<td>09</td>
<td>16</td>
<td>06</td>
<td>05</td>
</tr>
<tr>
<td>Daytime sleepiness</td>
<td>12</td>
<td>16</td>
<td>12</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Restless sleep</td>
<td>12</td>
<td>10</td>
<td>07</td>
<td>07</td>
<td>04</td>
</tr>
<tr>
<td>Somnambulism</td>
<td>32</td>
<td>08</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Somniloquence</td>
<td>18</td>
<td>14</td>
<td>04</td>
<td>04</td>
<td>00</td>
</tr>
<tr>
<td>Bruxism</td>
<td>38</td>
<td>02</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Nocturnal enuresis</td>
<td>40</td>
<td>00</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Fear of going to sleep</td>
<td>33</td>
<td>07</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Fearful awakenings from sleep</td>
<td>29</td>
<td>11</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
<tr>
<td>Frightening dreams</td>
<td>15</td>
<td>21</td>
<td>04</td>
<td>00</td>
<td>00</td>
</tr>
</tbody>
</table>
Numbers represent the number of adults who answered in each scoring category (0 = never; 1 = once monthly or less; 2 = two to four times weekly; 3 = 5 or more times weekly; 4 = every night).

Table 1 lists the responses (ranging from 0 = “none” to 4 = “extremely severe”) of our patients to questions related to the post concussive syndrome. Results ranging from 2-4 were considered moderate to extremely severe and were therefore significant. Sixty-three percent of the subjects complained of significant amnesia regarding the MHI event but fewer complained about retrograde amnesia or amnesia of events after the head injury. Seventy-four percent of the subjects complained of significant learning and concentration difficulties, and most subjects reported more fears and headaches since the time of MHI. Finally, 58% of the subjects complained of a significant difficulty sleeping away from home.

Tables 2 and 3 present the questionnaire results of the study and control groups, respectively. As expected, because of the selection criteria, there was a higher frequency of sleep disturbances reported in the study group than in the control group. The cut-off for most results presented in this part of the questionnaire is two, except for three questions that represent parasomnia, which are considered relatively rare. In these three questions regarding somnambulism, bruxism, and nocturnal enuresis the cut-off was one.

1. In the question ‘Falling asleep within 20 minutes of light out’, 63% of the study group fall asleep within 20 minutes of lights out, as compared to 94% of the control group.

![Bar chart showing percentage of subjects who fell asleep within 20 minutes of lights out.](image)

Mean Knowledge score for the question “Falling within 20 minutes off” was 1.82±1.17 in study group and 3.07±0.99 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=4.46, p=0.000)

2. In the question ‘early morning awakenings’, 37% percent of the study group experienced early morning awakenings, whereas none of the control group had this complaint.
Mean Knowledge score for the question “Early morning awakenings” was 1.22±1.36 in study group and 0.40±0.49 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=2.65, p=0.008)

3. In the question ‘Difficulty awakening in morning’, 79% in study group and 69% in control group had difficulty waking up in the morning.

Mean Knowledge score for the question “Difficulty awakening in morning” was 2.45±1.31 in study group and 1.97±1.14 in control group. By using Mann Whitney U test no statistical significant difference is found in both groups (z=1.90, p=0.057)

4. In the question Daytime sleepiness, 68% in study group and 31% in control group complained of daytime sleepiness.
Mean Knowledge score for the question “Daytime sleepiness” was 1.92±1.26 in study group and 1.00±0.78 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=3.51, p=0.000).

5. In the question ‘Restless Sleep’, 63% in study group and 44% in control group complained of Restless Sleep.

Mean Knowledge score for the question “Restless Sleep” was 2.40±1.53 in study group and 1.52±1.35 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=2.60, p=0.009).

6. In the question ‘sleep talking’, 42% in study group and 20% in control group complained of sleep talking.
Mean Knowledge score for the question “sleep talking” was 0.27±0.71 in study group and 0.20±0.40 in control group. By using Mann Whitney U test no statistical significant difference is found in both groups (z=0.17,p=0.865).

7. In the question ‘sleep enuresis’, 20% in study group and no one in control group complained of sleep enuresis.

Mean Knowledge score for the question “sleep enuresis” was 1.30±1.04 in study group and 0.85±0.97 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=2.02,p=0.043).

8. In the question ‘bruxism’, 42 % in study group and 5 % in control group complained of bruxism.
Mean Knowledge score for the question “bruxism” was 0.62±0.86 in study group and 0.05±0.22 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=3.96,p=0.000).

9. In the question Somnambulism, 16% in study group and 20% in control group complained of Somnambulism.

Mean Knowledge score for the question “Somnambulism” was 0.30±0.64 in study group and 0.00±0.00 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=2.95,p=0.003).

10. In the question ‘fears of going to sleep’, 42% in study group and 17% in control group complained of fears of going to sleep.
Mean Knowledge score for the question “fear going to sleep” was 1.00±1.41 in study group and 0.17±0.38 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=2.84,p=0.004).

11. In the question ‘fearful awakenings from sleep’, 62% in study group and 27 % in control group complained of fearful awakenings from sleep.

Mean Knowledge score for the question “fearful awakenings from sleep” was 1.22±1.16in study group and 0.27±0.45 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=3.92,p=0.000).

12. In the question ‘frightening dreams’, 58 % in study group and 10 % in control group complained of frightening dreams.
Mean Knowledge score for the question “frightening dreams” was 1.65±1.09 in study group and 0.62±0.49 in control group. By using Mann Whitney U test statistical significant difference is found in both groups (z=4.56,p=0.000).

Summary of Mean Knowledge score:

Discussion

This study demonstrates that 3 years after a MHI without any important known clinical consequence, patients complained of significant sleep disturbances. Despite their sleep complaints and their disrupted sleep, most of our patients manage to function quite normally in everyday life. Even so, some of our patients complained of serious difficulties in functioning because of increased daytime somnolence that prevented them from going to school and led to learning and concentration difficulties, fears, and headaches. Some of the patients had even sought medical care. Presently, health professionals view MHI as transient minor injury that does not cause any permanent damage. EEG, CT scan, or MRI is usually normal, and patients are commonly discharged from the emergency department with no more than one additional follow-up appointment. Whatever the etiology might be, it is important to recognize that although MHI appears to be a “benign” event with no long-term
effects, morbidity after MHI can have a serious impact. Even if the subjective complaints are more impressive than the objective findings, underlying them is a substantial disorder that might influence daily functioning and thus should be addressed and treated properly. Management steps, including psychotherapy, should be taken in time to prevent sleep disorder-induced behavioral impairment that may result in learning disabilities and impaired physical and emotional development.

Study Limitations

1. Recall bias as study based on subjective basis.
2. Response rate less (40 cases out of 64 cases) as lack of contact details / mobilisation.
3. Confounding bias due to other confounding factors causing sleep disturbances.

References


Seroprevalence of Hepatitis B and C among Blood Donors and a Profile of Hepatitis B Seropositive Blood Donors

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Abstract

Background: Hepatitis B and C are global health problems, serological surveys of blood donors helps in estimating the prevalence of HBV infection among adults in general population. Socio demographic profile of seropositive blood donors gives epidemiological determinants of susceptibility and risk factor estimation gives dynamics of disease transmission. Evaluating knowledge of Hepatitis B helps streamlining educational methods.

Aims and Objectives: To determine the prevalence of serological markers of Hepatitis B and Hepatitis C virus among blood donors using Blood bank records.

To know the socio-demographic profile, risk factors and knowledge of disease and vaccination among Hepatitis B positive blood donors in Visakhapatnam using interviews.

Methodology and Materials: This is a descriptive type of study. Serological data of blood donors between January 2009 and June 2009, obtained from five blood banks in Visakhapatnam, a medical hub situated in north coastal Andhra Pradesh (India) catering to people of surrounding three districts with a total population of about 8 million. Screening for HBsAg and Anti HCV anti-bodies was done using enzyme immunoassays (ELISA) and rapid ELISA techniques. Through simple random sampling 55 Hepatitis B positive blood donors were interviewed for socio demographic characteristics, risk factors and knowledge of Hepatitis B after informed consent.

Results: Of the 23,677 blood donors (voluntary 14,086 and replacement 9,591) 502 (2.12%) donors [239(1.70%) voluntary and 263(2.74%) replacement donors] tested positive for Hepatitis B and 58 (0.24%) donors [24(0.17%) voluntary and 34(0.35%) replacement donors] tested positive for Hepatitis C. Mean age of Hepatitis B seropositives was 27.4, with 30.9% from urban and 69.1% from rural areas, all are literate, 25(45.5%) are dependant financially, 10(18.2%) belong to low income group. 38 seropositives heard of Hepatitis B of which 9(16.4%) know it to be infectious with 3(5.5%) naming 4 routes of transmission. 5(9.1%) seropositives heard of complications of Hepatitis B, 26(47.3%) are aware of the existence of vaccine for Hepatitis B but only 7(12.7%) took vaccine. 6(10.9%) seropositives gave history of multiple sexual partners, 3(5.4%) had previous blood transfusions, 13(23.6%) had previous surgeries and 12(21.8%) had a relative at residence with jaundice in the past.

Discussion: Seroprevalence of Hepatitis B is 2.12%, which is in the range of published prevalence data of 1 -13% but less than published average prevalence of 4.7% in India. Seroprevalence of Hepatitis C is 0.24%. Prevalence is more among replacement than voluntary donors, more in rural than urban donors. Majority of the donors have inadequate knowledge of Hepatitis B disease and vaccination. 23.6% seropositives had history of surgeries and 69.1% are from rural background with poor sterilisation techniques, 21.8% had a family member at home with jaundice, which is in
In accordance with published data of transmission routes as unsterilized needles and horizontal transmission in childhood.

**Limitations:** Recall bias during interviews.

**Conclusion:** The findings suggest prevalence of viral hepatitis among blood donors and risk of susceptibility among recipients, hence a need for improving sensitivity of screening techniques. There is also a need for intimating blood donors if tested positive and proper counselling is required. High prevalence in rural areas and poor knowledge of Hepatitis B highlights the need for educating masses of the routes of transmission, complications of Hepatitis B and availability of vaccination especially to high risk individuals.

**Keywords:** Prevalence, Hepatitis B and C, Blood Donors, Profile

**Introduction**

Hepatitis is a term meaning the inflammation of Liver and can be caused by a variety of viruses such as Hepatitis A, B, C, D, E and G. Hepatitis B infection is a challenging global health problem with approximately 30% of the world’s population, i.e. about 2 billion people having serological evidence of infection with Hepatitis B virus (HBV). It is estimated that 400 million of them have chronic HBV infection, about a million of whom die each year from chronic liver disease. Various studies conducted in India show the Hepatitis B surface antigen (HBsAg) carrier rate to range between 1% and 13%, with a national average of 4.7%, placing India in a meso-endemic area (≥2-7%).

Risk of chronic hepatitis B after an exposure varies between 90% and 10% for different age groups. 15-25% of Chronically affected individuals will die due to Hepatitis B disease, 68% of Cirrhosis and 80% of Hepatocellular carcinoma in India is due to Hepatitis B infection. Vaccination against Hepatitis B is available since 1982 and Chronic Hepatitis B can be managed by giving Interferon alfa 2b or nucleoside and nucleotide analogues like Lamivudine, Adefovir dipivoxil and Entecavir.

Hepatitis C is caused by Hepatitis C Virus (HCV) and has a prevalence of 3% of world population. About 50% of the cases are asymptomatic and rate of chronification is 75-85%. No vaccine is available and drug therapies include Interferon alfa 2b and Ribavarin.

Hepatitis B and Hepatitis C have similar risk factors, transmission routes and complications. Estimation of Seroprevalence of viral Hepatitis and profile of Hepatitis B positive individuals helps in estimating the burden of disease in society and provides an insight into epidemiological determinants of disease transmission. Conducting longitudinal studies in general population is demanding and estimating the prevalence of Hepatitis B serological markers in unpaid blood donors offer the most useful means of estimating the prevalence of HBV infection among adults in the general population. Socio demographic profile of seropositive blood donors gives epidemiological determinants of susceptibility and risk factor estimation gives dynamics of disease transmission. Evaluating knowledge of Hepatitis B helps streamlining educational methods.

**Materials & Methods**

**Study Type**

This is a blood bank based descriptive study conducted between 1-1-2009 and 30-6-2009.
General Methods

During the study period, awareness was created to all blood donors attending blood banks and blood donation camps in Visakhapatnam, about Hepatitis B and Hepatitis C and the importance of Hepatitis B vaccination using posters at blood banks and lectures at blood donation camps by

1-Blood bank, King George Hospital
2-Blood bank, Victoria Government Hospital
3-A.S.Raja Blood bank
4-Red Cross Society Blood bank
5-Rotary Blood bank

Visakhapatnam is a medical hub situated in north coastal Andhra Pradesh catering to people of surrounding three districts with a total population of about 8 million as a tertiary health care centre.

Stage 1 Preliminary data was collected from the Blood Banks regarding the total number of blood donors with details on voluntary and replacement type of donors, male and female among them. Hepatitis B and Hepatitis C test status of blood donors was obtained from blood bank records. All blood donors who were HBsAg positive when tested by ELISA using HBsAg ELISA kit (either second generation or third generation kits) and repeated with Rapid ELISA test were considered as Hepatitis B seropositive individuals. Those blood donors who were Anti HCV anti-bodies positive when tested by ELISA (either second generation or third generation kits) were considered as Hepatitis C seropositive individuals, also repeated with Rapid ELISA test.

Stage 2 Through simple random sampling 60 Hepatitis B positive individuals were summoned to Blood Banks to explain their seropositive status and 55 of them volunteered to participate in the study. Informed consent was obtained and a total of around 15 minutes was spent on each individual educating various aspects of Hepatitis B such as modes of spread, complications, methods of prevention, follow up etc. After establishment of rapport with the individual, they were interviewed and a pre tested questionnaire was employed to collect information on socio demographic characteristics, exposure to known and potential risk factors, immunisation history, knowledge of Hepatitis B prior to awareness program etc. At all stages of study, privacy and confidentiality was maintained. Following the interview the subject was referred to our Institute’s Gastroenterology Department for further evaluation. Data was analysed using Excel sheet and results are presented in proportions.

Results

Of a total of 23,677 blood donors; 14,086 were voluntary donors and 9,591 were replacement donors.502(2.12%) donors tested positive for hepatitis B of which 239(1.70%) were voluntary donors and 263(2.74%) were replacement donors. 58 (0.24%) donors tested positive for Hepatitis C of which 24(0.17%) were voluntary donors and 34(0.35%) were replacement donors.
Table 1: Prevalence of Hepatitis B and Hepatitis C among Voluntary and Replacement donors

<table>
<thead>
<tr>
<th></th>
<th>Voluntary Donors</th>
<th>Replacement Donors</th>
<th>Total Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Prevalence</td>
<td>Number</td>
</tr>
<tr>
<td>HEPATITIS B SEROPOSITIVE</td>
<td>239</td>
<td>1.70%</td>
<td>263</td>
</tr>
<tr>
<td>HEPATITIS C SEROPOSITIVE</td>
<td>24</td>
<td>0.17%</td>
<td>34</td>
</tr>
</tbody>
</table>

Fifty five (55) Hepatitis B seropositive males were interviewed and their mean age was 27.4 years (range 18-56 years) with majority, 38 (69.1%) of them from urban areas and 17 (30.9%) from rural areas. All the subjects were literate and 25 (45.5%) were financially dependent on their families. 10 (18.2%) subjects belonged to low income group.

Table 2: Education and Income of Interviewed donors

<table>
<thead>
<tr>
<th></th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDUCATION</td>
<td></td>
<td></td>
</tr>
<tr>
<td>UPTO HIGH SCHOOL</td>
<td>13</td>
<td>23.64%</td>
</tr>
<tr>
<td>GRADUATE</td>
<td>31</td>
<td>56.36%</td>
</tr>
<tr>
<td>POST GRADUATE</td>
<td>11</td>
<td>20%</td>
</tr>
<tr>
<td>FAMILY INCOME</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5,000 RUPEES/MONTH</td>
<td>10</td>
<td>18.18%</td>
</tr>
<tr>
<td>5,000 to 10,000 RUPEES/MONTH</td>
<td>22</td>
<td>40%</td>
</tr>
<tr>
<td>&gt;10,000 RUPEES/MONTH</td>
<td>23</td>
<td>41.82%</td>
</tr>
</tbody>
</table>

Figure 1: Age and Place Distribution of Interviewed Donors
Three (5.45%) of the interviewed subjects had a prior knowledge of their infectious status by a previous screening test but were not advised to discontinue blood donation while 52(94.55%) were never knew of their Hepatitis B status though 23(44.23%) of them donated blood previously. On assessment of their knowledge of Hepatitis B prior to awareness program, it was seen that 17(30.9%) of them never heard of Hepatitis B while 38(69.1%) were aware of existence of Hepatitis B disease. Only 9(16.45%) of the subjects knew Hepatitis B was infectious and 8 (14.55%) of them could give at least one route of transmission. 50(90.9%) of the subjects were not aware of any consequence of Hepatitis B infection while 26(47.27%) of the subjects were aware of the availability of effective vaccination against Hepatitis B.

Seven (12.73%) of the interviewed subjects gave prior history of immunisation for Hepatitis B of whom 3(42.85%) were incompletely immunised. 48(87.27%) were not previously immunised for Hepatitis B and 29(60.42%) of them gave the main reason as being unaware of the vaccine while 19(39.58%) of them considered the vaccine unnecessary for them.

On interviewing for potential risk factors and prior exposure risks, 18(32.73%) of them gave history of surgeries for various conditions, 3(5.45%) of them had previous blood transfusions, 6(10.9%) of them donated blood more than five times previously, 6 (10.9%) gave history sexual exposure with multiple partners and 12(21.82%) of them had an acquaintance at residence with jaundice.

Figure 2: Immunization status against Hepatitis B
Figure 3: Knowledge of Hepatitis B status prior to Blood donation

Table 3: Knowledge of Hepatitis B of Interviewed Donors

<table>
<thead>
<tr>
<th>Question</th>
<th>NUMBER</th>
<th>PERCENTAGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Heard about Hepatitis B disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>38</td>
<td>69.1%</td>
</tr>
<tr>
<td>NO</td>
<td>17</td>
<td>30.9%</td>
</tr>
<tr>
<td>b) Knows Hepatitis B to be infectious</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>9</td>
<td>16.4%</td>
</tr>
<tr>
<td>NO</td>
<td>46</td>
<td>83.6%</td>
</tr>
<tr>
<td>c) Routes of transmission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>at least 4 routes</td>
<td>3</td>
<td>5.5%</td>
</tr>
<tr>
<td>at least 3 routes</td>
<td>2</td>
<td>3.6%</td>
</tr>
<tr>
<td>at least 2 routes</td>
<td>2</td>
<td>3.6%</td>
</tr>
<tr>
<td>at least 1 route</td>
<td>1</td>
<td>1.8%</td>
</tr>
<tr>
<td>d) Heard of complications of Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>5</td>
<td>9.1%</td>
</tr>
<tr>
<td>NO</td>
<td>50</td>
<td>90.9%</td>
</tr>
<tr>
<td>e) Aware of vaccination for Hepatitis B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>YES</td>
<td>26</td>
<td>47.3%</td>
</tr>
<tr>
<td>NO</td>
<td>29</td>
<td>52.7%</td>
</tr>
</tbody>
</table>
Table 4: Risk Factors among Hepatitis B Positive Blood Donors

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple sexual partners</td>
<td>6</td>
<td>10.9%</td>
</tr>
<tr>
<td>History of Blood transfusion</td>
<td>3</td>
<td>5.4%</td>
</tr>
<tr>
<td>More than 5 previous Blood donations</td>
<td>6</td>
<td>10.9%</td>
</tr>
<tr>
<td>History of Surgery/ies</td>
<td>18</td>
<td>32.7%</td>
</tr>
</tbody>
</table>

Discussion

This study gives the Seroprevalence of Hepatitis B among blood donors as **2.12%** which is in the range of published general population prevalence data of 1 -13% but less than published average prevalence of 4.7%³ in India. Studies conducted on blood donors in India gave a Seroprevalence of Hepatitis B in the range of 1.2-2.8%¹¹ and this study’s Seroprevalence of 2.12% is close to 2.11% by Mohite et al (1998) and 3% by Kothari et al (2002). This study also shows that Seroprevalence of Hepatitis B was more among replacement blood donors at 2.74% compared to voluntary blood donors at 1.70%.

The Seroprevalence of Hepatitis C among blood donors was **0.24%** and it was more among replacement blood donors at 0.35% compared to voluntary donors at 0.17%. Prevalence of Hepatitis B in India varies from place to place due to various factors, it is as low as 0.97% in Chandigarh⁶ and 5.5% in Chennai⁶, there is variation in different communities seen as ranging from 1.86% among the tribes of Kolli Hill in Tamilnadu to 65.60% among the Jarawas in Andamans¹².

Table 5: Hepatitis B Seroprevalence among Blood donors of various countries¹³,¹⁴

<table>
<thead>
<tr>
<th>Country</th>
<th>Hepatitis B Prevalence Among Blood Donors</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>4.7%</td>
</tr>
<tr>
<td>China</td>
<td>10.3%</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2.2%</td>
</tr>
<tr>
<td>Nepal</td>
<td>0.82-0.92%</td>
</tr>
<tr>
<td>Egypt</td>
<td>4.3%</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>1.5%</td>
</tr>
<tr>
<td>Turkey</td>
<td>1.38%</td>
</tr>
<tr>
<td>Myanmar</td>
<td>8-10%</td>
</tr>
<tr>
<td>Indonesia</td>
<td>5%</td>
</tr>
<tr>
<td>Korea</td>
<td>12%</td>
</tr>
<tr>
<td>Japan</td>
<td>1-3%</td>
</tr>
</tbody>
</table>
Table 6: Hepatitis B among various population groups in INDIA

<table>
<thead>
<tr>
<th>Group</th>
<th>Seroprevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Donors</td>
<td>1.2-2.8%&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>2.5-3%&lt;sup&gt;15&lt;/sup&gt;</td>
</tr>
<tr>
<td>Doctors</td>
<td>3.33%&lt;sup&gt;11&lt;/sup&gt;</td>
</tr>
<tr>
<td>Nurses</td>
<td>1.41%&lt;sup&gt;16&lt;/sup&gt;</td>
</tr>
<tr>
<td>Eye Donors</td>
<td>3.52%&lt;sup&gt;17&lt;/sup&gt;</td>
</tr>
<tr>
<td>I V Drug Users</td>
<td>23.6%&lt;sup&gt;18&lt;/sup&gt;</td>
</tr>
<tr>
<td>Csw</td>
<td>8.3-24%&lt;sup&gt;19&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hiv Co Infection</td>
<td>9.9%&lt;sup&gt;20&lt;/sup&gt;</td>
</tr>
<tr>
<td>Std Clinics</td>
<td>8.8-13.6%&lt;sup&gt;21,22&lt;/sup&gt;</td>
</tr>
<tr>
<td>Urban Slum</td>
<td>10.3%&lt;sup&gt;23&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

All the 55 Hepatitis B seropositive subjects picked up for interviewing, by simple random sampling were males and mostly from urban and semi urban areas. All the subjects were literate and were from different income groups. Three (5.45%) of the subjects had prior knowledge of their infective status by previous screening procedures but were unaware of the routes of transmission. They were never counselled or advised for referral. The remaining 52 subjects never knew of their Hepatitis B positive status though 23(44.23%) of them donated blood previously and was screened for Hepatitis B. This is due to inconsistent intimation and counselling protocol in our over burdened and under manpowered blood banks.

The knowledge of the interviewed sample subjects about Hepatitis B was very poor with only 38(69.1%) of them being aware of existence of Hepatitis B disease while the rest 17(30.9%) of them never heard of Hepatitis B. As was seen in this study, 46(83.64%) did not know Hepatitis B was infectious or that it can spread from person to person and only 8 (14.55%) of the counselled subjects could give at least one route of transmission. The majority 50(90.9%) were not aware of any consequence of Hepatitis B infection. This may be due to nonexistent health education on Hepatitis B compared to HIV in India, though India harbours 30 million carriers and around 100,000 people die each year due to consequences of Hepatitis B infection<sup>24</sup>.

Vaccination coverage among the subjects was also low with only 7(12.73%) of the interviewed subjects giving a prior history of immunisation for Hepatitis B and 3(42.85%) of them did not complete the prescribed doses in schedule. The vaccination coverage even among Indian children is low at around 35% in urban areas, 5.6% in urban slums and 2.7% in rural areas<sup>25</sup> though Hepatitis B vaccine is included in the immunisation program. 48(87.27%) of the counselled subjects were not previously immunised for Hepatitis B though many of them were in high risk category. Vaccination though not recommended for all general population, it is recommended for infants and high risk category such as health care workers, patients requiring recurrent blood transfusion or haemo dialysis, family members of Hepatitis B individuals, clients and staff of institutions for the developmentally disabled, injecting drug users, men who have sex with men, and persons with multiple sex partners<sup>4</sup>. The main reason given for not being vaccinated, by 29(60.42%) of them was being unaware of the vaccine while 19(39.58%) of them considered the vaccine unnecessary for them.

Hepatitis B is 100 times more infectious than HIV with 0.0001 ml of infected blood capable of transmitting infection and virus can stay active on environmental surfaces for up to 7 days. Major routes of transmission are from mother to child (perinatal), contact with an infected person (horizontal), sexual contact and exposure to infected blood and body fluids<sup>2</sup>. 18(32.73%) of subjects gave history of minor or major interventional surgeries and in India indiscriminate use of interventional procedures and inadequate sterilisation is considered a major mode of transmission.
3(5.45%) of the subjects gave history of previous blood transfusions though individuals with history of transfusions are not routinely accepted for blood donation. 6(10.9%) of subjects donated blood more than five times previously though professional blood donation is banned in India, most of them were from low socio economic group.

Six (10.9%) of the subjects gave history of sexual exposure with multiple partners which is common mode for adult acquired infection especially in meso endemic and low endemic areas. 12(21.82%) of them had an acquaintance at residence with history of jaundice or succumbed due to an unknown condition associated with jaundice and as was mentioned, most of the infections in India are horizontally acquired in childhood from close contacts. 7(12.73%) of the subjects gave history of jaundice in themselves which is lower than 30-50% expected jaundice rates in infected individuals.

**Conclusion**

The epidemiology and risk factors of viral hepatitis from a population base should aid in prioritising preventive measures by identifying the at-risk populations. This will allow for the most appropriate use of available resources. Accordingly, the appropriate precautions can be implemented to decrease the prevalence of this infection.

Screening should be made compulsory in hyper endemic areas, family members of positive individuals, pregnant women, dialysis patients, injection drug users, HIV positive individuals, homosexual men.

Effective child immunisation program will reduce burden of infection in country but sterile injection practice, education, awareness, improved screening protocol and technology will help in quickening the process. The routine vaccination of infants rapidly reduces the transmission of HBV but in countries like India substantial disease burden from chronic infections acquired by older children, adolescents and adults is considerably large hence, vaccinating infants alone may not substantially lower the incidence of the disease for decades, and catch-up strategies targeted on these older age groups, in addition to routine infant vaccination, may be desirable like age-specific cohorts and persons with risk factors for acquiring HBV infection. Hepatitis B immunisation can be recommended to mothers at child birth giving first dose immediately after delivery and second, third doses coinciding with child’s first and second immunisation doses as is being suggested in Saudi Arabia. China reduced incidence among young children from 9.4% to 0.9% within 4 years. Public awareness programs and legislations reduced incidence in USA by 89% in a decade. Pentavalent vaccine recently introduced in India is a welcoming step.

Counselling procedure for seropositives should be improved with properly trained counsellors as is being done in Voluntary Counselling and Testing Centres in India, also a proper protocol and machinery for intimating seropositive donors must be introduced. This will eliminate seropositive individuals from blood donation pool. New technology for screening procedures should be introduced such as third generation ELISA and cassette testing, to reduce window period and improve sensitivity thereby making blood safer.

There is a gross deficit of blood at blood banks in India with only 50% being currently met, thereby increasing illegal professional donors; hence voluntary blood donation must be encouraged.

**References**

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8. WHO Hepatitis C Factsheet No-164.


25. Table I, Hepatitis B Vaccine coverage among children (2000), Indian Journal of Medical Sciences. 54(8).


Very late recurrence of Ewing's Sarcoma – a worthy challenge

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Introduction

Ewing's sarcoma is a malignancy of the bones mainly affecting young adults, with a peak incidence in the second decade of life. It has a good prognosis for localized disease when treated aggressively with combination chemotherapy, surgery and radiotherapy. Studies have found that it has the highest survival at 20 years of all the paediatric cancers. Recurrence is rare but has a worse prognosis, with the majority of these cases occurring in the first two years. Yet, there are case reports of patients who have had late recurrences up to 19 years after the first diagnosis. We present a case of a patient originally diagnosed with Ewing’s Sarcoma at the age of 19 and who was treated successfully, but has since had two late recurrences of his disease at 10 and 15 years from diagnosis. We present this case to highlight an unusual pattern of recurrence of a rare cancer (Ewing’s sarcoma), with long intervals between recurrences. The excellent response to treatment adds a further uniqueness to the case. Yet this case emphasises the lack of data on late recurrence of rare cancers, and the difficulties in decision-making on the aggressiveness of treatment in a metastatic setting. It also serves to re-affirm the practise of managing the teenage and young adult cancers at multi-disciplinary specialist centres to achieve better outcomes.

Case report

This previously fit 19 year old male presented with persistent right hip and leg pain which defied diagnosis for 6 months. A mass was eventually demonstrated in connection with the right iliac bone for which he underwent a biopsy. During the biopsy he began to haemorrhage and required 35 units of blood before being transferred to a specialist orthopaedic centre for a de-bulking operation. The histology from this biopsy initially suggested Malignant Haemangiopericytoma but a second opinion advised that a differential of Ewing's Sarcoma family of tumours should be considered. Following the operation he had multi-agent chemotherapy followed by radiotherapy which he tolerated well and had a good response to the treatment. Over the coming years our patient continued to do well and was considered effectively cured at five years. 10 years after treatment though, a chest X-Ray at routine follow up revealed a lung mass. This
was resected, the histology of which was compared to the original biopsy and found to be identical. He had a resection with no lymph node involvement and post-operative chemotherapy was offered but this was refused by the patient.

For five more years, our patient again continued to lead a full life until he started to develop worsening breathlessness. He was found to have a large pericardial effusion from which 2 litres of blood stained fluid was removed. Further investigation revealed a mediastinal mass surrounding the pericardium and a recurrence of the effusion. A pericardial window was performed and histology from the operation showed this was a recurrence of the Ewing's sarcoma.

He received 6 cycles of combination chemotherapy with Vincristine, Ifosphamide, Doxorubicin and Etoposide (VIDE). Having received the maximum cumulative dose of Anthracyclines at initial diagnosis, his chemotherapy was combined with Dexrazoxane to protect the heart.

In spite of poor prognosis related to the recurrence and the presentation of his disease, he responded well to the treatment with the mediastinal mass shrinking and pericardial effusion not returning. His echocardiogram did not show any acute cardiac toxicity from chemotherapy. However, his treatment was complicated by recurrent episodes of severe neutropenic sepsis, at times requiring ICU admission, despite the addition of GCSF. This was due to a complicated rectal abscess which required consideration for a colostomy. Even with the severe complications our patient suffered, it was decided after discussion between the patient, his family and medical staff to continue with the aggressive treatment according to the Euro-Ewing’s 99 protocol.

**Discussion**

Ewing's Sarcoma is a tumour of the bones that was first described by James Ewing in 1921. It is histologically similar to the peripheral primitive neuroectodermal tumour, neuroepithelioma, atypical Ewing's sarcoma and Askin tumor. These tumours are collectively known as the Ewing's sarcoma family of tumours. It is a rare condition affecting approximately 30 patients per year in the UK.

The majority of cases present with localised disease mainly affecting the long bones, pelvis and ribs. A fifth of patients will present with metastases, the main sites being the lungs, bone and bone marrow, with a markedly reduced survival rate compared to localised disease. In fact, the five year survival for patients with localised disease is approaching 70-75%, with metastatic disease only 20-25%.

Treatment of Ewing's sarcoma is dependant on whether the disease is localised or metastatic. The current protocol in use is the Euro-Ewing's 99 which involves a multi-agent chemotherapy regime consisting of VIDE which can be combined with surgery and/or radiotherapy.

Recurrence of Ewing's sarcoma is rare but unfortunately does occur. The majority of these occur in the first two years although can occur late. The prognosis for patients with a recurrence of Ewing's sarcoma is greatly reduced with a five year survival of only 15.2%. Further relapse, as in our case, is an even rarer phenomenon but not unknown. One study suggests that the prognosis is further reduced for a second relapse, with an overall survival of only 13.8% at 5 years, with a better prognosis for those patients whose first relapse was later than 2 years post initial treatment.

Even with this poor prognosis in recurrence of disease and with second relapse, it can be considered a curable cancer and for this reason it is treated aggressively. The treatment our patient is undergoing is now causing serious and frequent life threatening neutropenic sepsis. Yet we do not have robust evidence in favour of stopping this aggressive treatment, and hence he continues with a very small potential for cure, but in all likelihood, non-curatively.
In previous case reports and with our patient, these late recurrences have been diagnosed when the patient has been considered effectively cured\(^3\). Our case serves to further highlight the need for long term, even life long follow up for patients with Ewing's sarcoma.

This case illustrates the lack of data available and therefore reaffirms our belief in the continued treatment in the hope that he responds favourably as he has in the past.

The complexity of management involved with late recurrence raises the question of whether these patients should only be managed in specialist centres to improve outcomes and again this is an area that needs further research.

References


Tuberculous Pericarditis – A Case Report and Review of Literature

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Abstract

Tuberculous pericarditis is a rare, but life threatening form of extra-pulmonary tuberculosis and accounts for approximately 4% of acute pericarditis and 7% of cardiac tamponade cases. Mortality due to tuberculous pericarditis can reach up to 40%. High index of suspicion amongst the treating clinicians supplemented with prompt diagnosis and treatment can reduce the high mortality associated with this disease. We report a case of a young adult male patient who presented with a 2 month history of productive cough and breathlessness of recent onset. Preliminary diagnosis of tuberculous pericarditis based on his clinical and radiological findings was confirmed with Ziehl-Neelsen’s stain for acid fast bacilli and culture of the pericardial fluid aspirate. The patient responded well to pericardiocentesis and subsequent anti-tuberculous chemotherapy.

Keywords: Tuberculosis, Pericarditis, Acid fast bacilli, Culture, Anti-tuberculous chemotherapy

Introduction

Although there has been a significant decline in tuberculosis caused by *Mycobacterium tuberculosis* in wealthy industrialized countries over the past 100 years, the estimated number of new cases worldwide has increased steadily mainly in the developing world.1 Extra pulmonary tuberculosis occurs in 20% of patients with pulmonary tuberculosis. Tuberculous pericarditis caused by *Mycobacterium tuberculosis* accounts for about 1% of all autopsied cases of tuberculosis and 1-2% instances of pulmonary tuberculosis.2 Rapid and accurate diagnosis which is often difficult is essential for effective treatment which prove to be life saving3. We here-with report a case of tuberculous pericarditis in a young adult male patient.
Case Report

A 25 year old male patient without any prior significant medical illness presented with a history of productive cough with mucoid sputum of 3 months duration and gradually progressive breathlessness since 15 days. He had a significant loss of body weight in the past 3 months. On examination, he was afebrile, pulse rate of 140/min and blood pressure of 116/80 mm Hg. Jugular venous pressure was raised. There was bilateral pedal edema. On systemic examination cardiac dullness was obliterated, apex was not palpable and a pericardial rub was appreciated. Other systemic examination revealed no abnormalities. Routine biochemical and hematological investigations were within normal limits, except for a slight increase in total leucocyte count (11,700 cells/cumm) and serum lactate dehydrogenase (LDH) was 739 U/L. Electrocardiogram (ECG) showed sinus tachycardia, low voltage complexes and diffuse T wave inversions. Echocardiography revealed massive pericardial effusion with normal left ventricular function (ejection fraction – 72%). His clinical diagnosis at this stage was pericardial effusion with tamponade.

In view of his clinical findings and radiological investigations, pericardiocentesis was done and 300 ml of hemorrhagic fluid was tapped. Following which, the patient improved symptomatically with reduced dysnoea. Pericardial fluid analysis showed; glucose – 23 mg/dl, protein 5.3 g/dl, albumin – 1.9 g/dl, LDH – 5038 U/L and adenosine deaminase (ADA) – 213 U/L. Fluid total leucocyte counts were elevated (8700 cells/cu mm). Pericardial fluid protein to serum protein ratio was 0.73 and pericardial fluid LDH to serum LDH ratio was 6.82, which identified the exudative nature of the fluid. Ziehl-Neelsen’s stain of the fluid was positive for acid fast bacilli (AFB 1+). Routine bacterial culture of the fluid was sterile. The patient was started on Antituberculous chemotherapy (ATT) with four drugs – isoniazid (300 mg), rifampicin (450 mg), ethambutol (800 mg) & pyrazinamide (1500 mg) and steroids, with which he improved significantly with no recollection of effusion and was discharged from the hospital. His ATT was continued and the steroids tapered. Later culture of the pericardial fluid in automated system (M-BacT/Alert, Biomerieux) detected the growth of *Mycobacterium tuberculosis* which was confirmed by using DNA probe i.e, Accuprobe system (Gen-Probe incorporated, San Diego CA, USA). Anti-tubercular susceptibility testing was done by proportion method and the strain was resistant to isoniazid and streptomycin but sensitive to rifampicin, ethambutol and pyrazinamide. The patient improved with medications and was asymptomatic on regular follow up.

Discussion

Tuberculous pericarditis results from retrograde lymphatic spread of *M. tuberculosis* from peritracheal, peribronchial or mediastinal lymph nodes or by hematogenous spread from primary tuberculous infection from a focus in the lung, genitourinary tract, the skeletal system, or elsewhere. It is suggested that tuberculous pericardial effusions arise as a result of a hypersensitivity reaction orchestrated by the TH-1 lymphocytes against the protein antigens of tubercle bacillus. The pathological stages of tuberculous pericarditis include a fibrinous pericarditis with caseating necrosis and polymorphonuclear infiltrate which gives rise to an effusive phase with predominantly lymphocytic exudate along with monocytes and foam cells, and which is often voluminous and hemodynamically significant. An adhesive phase follows resolution of the effusion and eventuates in dense, calcific adhesions with clinical constriction in nearly 50 percent of patients.

Tuberculosis should be considered in the differential diagnosis of all cases of pericardial heart disease without a rapidly self-limited course. Tuberculous pericarditis has a variable clinical presentation and the affected individuals generally lack the typical symptoms and signs of pulmonary tuberculosis. Tuberculous pericarditis presents clinically in 3 forms, namely, pericardial effusion, constrictive pericarditis, and a combination of effusion and constriction. Fever, weight loss, and night sweats occur early; Symptoms of cardiopulmonary origin tend to occur later and include cough, dyspnea,
orthopnea, ankle swelling, and chest pain. The chest pain may occasionally mimic angina but usually is described as being dull, aching, and often affected by position and by inspiration.\(^5\) The most common physical findings arecardiomegaly and fever, followed by tachycardia, pulsus paradoxus, and hepatomegaly. A pericardial friction rub and distant heart sounds are common. Pleural effusion and peripheral edema may be evident, while Kussmaul's sign (inspiratory swelling of the neck veins) may be seen in patients with constrictive pericarditis.\(^4\)

Rapid diagnosis and treatment are crucial in reducing mortality and morbidity from pericardial disease.\(^7\) The diagnostic modalities include, chest radiograph which may reveal enlarged cardiac shadow in more than 90% of cases, features of active pulmonary TB in 30% of cases and pleural effusion in 40% to 60% of cases. The ECG is abnormal in virtually all cases of tuberculous pericardial effusion, usually in the form of nonspecific ST-T wave changes. The presence of microvoltages (ie, complexes <5 mm in limb leads and <10 mm in precordial leads) suggests a large pericardial effusion.\(^1\) Such changes were seen in the ECG of our patient. Echocardiogram showing a large pericardial effusion with frond-like projections, and thick “porridge-like” exudate is suggestive of an exudate but not specific for a tuberculous etiology. CT scan and/or MRI of the chest show evidence of pericardial effusion and thickening (>5 mm) and typical mediastinal and tracheobronchial lymphadenopathy (>10 mm, hypodense centers, matting), with sparing of hilar lymph nodes.\(^1\)

A definitive diagnosis can be obtained by pericardiocentesis under echocardiographic guidance.\(^8\) Pericardial fluid may be serosanguineous, or even grossly hemorrhagic.\(^4\) Tuberculous pericardial effusions are typically exudative with a high protein content and increased leukocyte count, with a predominance of lymphocytes and monocytes.\(^1\) Demonstration of tubercle bacilli in stained Ziehl-Neelsen smear (yield of 0 - 42%), a positive culture of pericardial fluid for \textit{M. tuberculosis} or caseating granulomata found on histological examination of pericardium with consistent clinical circumstances are convincing evidence of a tuberculous etiology.\(^1,2,6\) Evidence of pericarditis in a patient with tuberculosis demonstrated elsewhere in the body and/or a good response to antituberculosis chemotherapy makes a probable diagnosis of tuberculous pericarditis.\(^1\) Also elevated pericardial fluid adenosine deaminase (ADA - ≥35 U/L), Interferon-\(\gamma\) (>200 pg/L) and lysozyme (≥6.5 \(\mu\)g/dL) are suggestive of tuberculous pericarditis.\(^1\) Rapid diagnosis by Polymerase Chain Reaction can be an important diagnostic tool; however PCR has shown a low sensitivity in a study by Peter Cegielski et al.\(^7\) when compared with culture and histopathology. In the present case, definitive diagnosis was done based on demonstration of acid fast bacilli in stained smears from the aspirated effusion and later isolation of \textit{M. tuberculosis} in culture.

Prompt institution of antituberculosis chemotherapy increases survival dramatically in tuberculous pericarditis. A regimen consisting of rifampicin, isoniazid, pyrazinamide, and ethambutol for at least 2 months, followed by isoniazid and rifampicin (total of 6 months of therapy) has been shown to be highly effective in treating patients with extrapulmonary TB.\(^1\) Pericardiectomy may be necessary for recurrent cardiac tamponade.\(^5\) A course of glucocorticoid treatment is useful in the management of acute disease, reducing effusion, facilitating hemodynamic recovery, and thus decreasing mortality rates. Progression to chronic constrictive pericarditis, however, seems unaffected by such therapy.\(^8\)

**Conclusion**

Tuberculous pericarditis is a potentially lethal condition and should be considered in the evaluation of all cases of pericarditis.
References


Effect of alpha lipoic acid on oxidative stress and vascular cell adhesion molecule level in diabetes mellitus induced rats

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Abstract

Background: Alpha lipoic acid (ALA) is a unique antioxidant and has beneficial effects in fuel metabolism. The aim of the present study was to investigate the effect of ALA supplementation on biomarker of oxidative stress and vascular cell adhesion molecule (VCAM) level in streptozotocin (STZ) induced diabetes mellitus rats.

Method: A total of 40 (250-280g) Sprague Dawley rats were used and divided into four groups randomly. The diabetic rats were divided into two groups: supplemented with ALA (100mg/kg/day) and non-supplemented with ALA. STZ 45mg/kg was injected intravenously to induce diabetes mellitus. The non-diabetic rats were also divided into two groups: supplemented with ALA (100mg/kg/day) and non-supplemented with ALA. Following of four weeks of force feeding treatment, samples such of aorta and plasma were taken.

Results: The finding of this study showed that the level of malondealdehyde (MDA) of diabetes mellitus induced rat aorta treated with ALA decreased (32.92%) significantly (p<0.05) compared to untreated diabetic rats. The ascorbic acid levels were increased (434.05%) significantly (p<0.05) in aorta of diabetic mellitus treated rats compared to untreated diabetic rats. The glutathione peroxidase (GPx) levels were not significantly different between aorta of diabetes mellitus induced treated rat and untreated diabetic rats. The concentration of plasma VCAM of diabetes mellitus induced rat treated with ALA decreased (60.70%) significantly (p<0.05) compared to untreated diabetic rats. The concentration of plasma VCAM of control group treated with ALA also decreased (75.98%) significantly (p<0.05) compared to untreated control group.

Conclusion: This study suggested that ALA may be effective in reducing oxidative stress in aorta of STZ induced diabetic rats. It is also suggested that ALA may reduce VCAM level in diabetic condition.

Keywords: Lipoic acid, oxidative stress, atherosclerosis

Background

Diabetes mellitus is an endocrine disease characterized by hyperglycaemia. It causes long term complication involving eye, kidney, nerve and blood vessels (Ceriello 2000). Oxidative stress plays a vital role in pathogenesis of diabetic complications (Baynes & Thorpe 1999) especially cardiovascular complication. Studies show that lipid oxidation by free radicals is an essential factor in early atherosclerosis development (Ross 1999).
ALA is a short chain which has thiol groups (Vessal et al. 2003) and can be converted to dehydrodihydrothioic acid (DHLA), strong antioxidant. Both antioxidant forms scavenge radicals. Radicals play a vital role in development of atherosclerosis. Thus, antioxidant is analyzed to determine the effect of ALA supplementation on oxidative stress in aorta and VCAM of diabetic rats.

ALA occurs naturally in the human diet and is found in abundance in animal tissues with high metabolic activity such as heart, liver and kidney, and to a lesser extent in fruits and vegetables (Packer et al. 2001). The concentration of ALA from highest to lowest in nonanimal sources are: spinach, broccoli, tomato, garden pea, brussel sprouts and rice bran (Morikawa et al. 2001).

Methods

Animal preparation

40 Male Spraque Dawley rats, weighing 260-290 grams, were supplied by The Animal Unit of Universiti Kebangsaan Malaysia. All animals were maintained on a balanced diet and water without restriction. The study was approved by Universiti Kebangsaan Malaysia Animal Ethics Committee (UKMAEC) and the guidelines were followed.

Diabetes was induced by a single intravenous injection of STZ (45 mg/kg) (Sigma, St Louis, USA), freshly dissolved in normal saline, and administered after an overnight fast. The non diabetic rats received saline injection [NDMTx₀ (n=10) and NDMTx⁺ (n=10)] and acted as control groups. Three days following the STZ administration, glucose concentration was measured by a strip operated blood glucose sensor (Advantage II Roche Diagnostics, New Zealand) and rats with blood glucose levels >15.0 mmol/l were included in the study. Diabetic rats were divided into two groups which are supplemented with ALA (n= 10) (DMTx⁺) and not supplemented with ALA (DMTx₀) (n=10). ALA (Sigma, St Louis, USA) was administered orally at a dose of 100 mg/kg/day throughout the feeding period of four weeks. Meanwhile, the DMTx₀ and NDMTx₀ rats were left untreated.

Antioxidant Analysis

Following four weeks of supplementation, rats were fasted overnight and blood was collected by cardiac puncture under deep anaesthesia with diethyl ether and descending aorta was quickly excised for homogenization and stored at -70°C. Blood was kept on ice and centrifuged at 3000 rpm for 15 min at 4°C and the obtained plasma was stored at -50°C until analysis.

Aortic homogenate is used to analyze MDA using Stock et al. 1974 method, ascorbic acid using Lloyd et al. 1945 method and GPx using Paglia & Valentine 1967 method. VCAM plasma was evaluated using Quantikine sVCAM-1 Kit (R&D System, UK).

For analysis of MDA, 0.1 ml of sample was mixed to 0.4 ml of distilled water. The mixture was vortex-mixed and 2.5 ml of TCA/HCL was added. After 15 minutes, 1.5 ml of TBA/NAOH was added. The mixture was incubated for 30 minutes at 100°C. Then, 4ml of n-butanol was added to the mixture and vortex-mixed for 3 minutes. The mixture was centrifuged at 3000rpm for 10 minutes and the absorption of supernatant was read at 532 nm.

For analysis of ascorbic acid, 0.5 ml of sample and 2ml of metaphosphoric acid were vortex-mixed and centrifuged for 10 minutes, 2500rpm. 1.2 ml of the supernatant was added to 0.4 ml DTC and vortex mixed. Then, the mixture was incubated at 37°C for 3 hours. The test tubes containing the
mixture were placed into the ice bath for 10 minutes. Then, 2 ml of concentrated sulphuric acid was added and vortex-mixed. Spectrophotometer was used to read the absorption(520nm).

For analysis of GPx, 0.02 of sample was added to 0.88 ml of prepared substrate. Then, 0.1 ml hydrogen peroxide solution was added and the absorption was read using spectrophotometer (340nm).

**Statistical analysis**

Normality test was done. One way ANOVA was used to assess statistical significance between the two groups. The difference is considered to be significant at P< 0.05. All values were expressed as means ± SEM.

**Results:**

**Analysis of MDA level**

![Figure 1: MDA level (mean ± SEM) of each group following four weeks of study](image)

Figure 1 shows aortic MDA level of each group. Study showed NDMTx + (19.65 ± 1.61 nmol/l protein) was not significantly different compared to NDMTx o (37.60 ± 4.27 nmol/l protein). MDA level is increased significantly in DMTx o (147.49 ± 20.44 nmol/l protein) compared to NDMTx + (p<0.01) and NDMTx o (p<0.01). MDA level was decreased significantly in DMTx + (98.93 ± 13.57nmol/l protein) compared to DMTx o (p=0.04). However, DMTx + was increased significantly compared to NDMTx + (p<0.01) and NDMTx o (p=0.01).

**Analysis of Ascorbic Acid Level**
Figure 2: Ascorbic acid level (mean ± SEM) of each group following four weeks of study

a : significant compared to NDMTx°
b : significant compared to NDMTx+
c : significant compared to DMTx°

Figure 2 shows aortic ascorbic acid level of each group. Study showed ascorbic acid level in NDMTx+ (10.12 ± 1.06 mg/l) was not significantly different compared to NDMTx° (9.26 ± 1.20 mg/l). DMTx° (1.85 ± 0.53 mg/l) showed significant decrease in ascorbic acid level compared to NDMTx+ (p<0.01) and DMTx° (p<0.01). Ascorbic level in DMTx+ (9.88 ± 1.06 mg/l) was increased significantly compared to DMTx° (p<0.01). However, DMTx+ was not significantly different compared to NDMTx° and NDMTx+.

Analysis of GPx Level

Figure 3: GPx level (mean ± SEM) of each group following four weeks of study

a : significant compared to NDMTx°
b : significant compared to NDMTx+
Figure 3 shows aortic GPx level of each group. Study showed GPx level in NDMTx+ (0.029 ± 0.0036 µmol/min/mg protein) was not significantly different compared to NDMTx0 (0.027 ± 0.0028 µmol/min/mg protein). GPx level in DMTx0 (0.017 ± 0.0014 µmol/min/mg protein) decreased significantly compared to NDMTx+ (p=0.01) and NDMTx0 (p=0.04). Study also showed that GPx level in DMTx+ (0.017 ± 0.0018 µmol/min/mg protein) decreased significantly compared to NDMTx+ (p=0.03) and NDMTx0 (p=0.04). However, DMTx+ was not significantly different from DMTx0.

Analysis of Plasma VCAM

![Figure 4: Plasma VCAM level (mean ± SEM) of each group following four weeks of study]

Figure 4 shows plasma VCAM level in each group. Study showed that VCAM level in NDMTx+ (1.83 ± 0.40 ng/ml) was decreased significantly (p<0.01) compared to NDMTx0 (7.62 ± 0.89 ng/ml). VCAM level in DMTx0 (5.42 ± 1.02 ng/ml) increased significantly (p=0.01) compared to NDMTx+ and was not significantly different compared to NDMTx0. VCAM level in DMTx+ (2.13 ± 0.54 ng/ml) has decreased significantly (p<0.01) compared to NDMTx0 and also decreased significantly (p=0.04) compared to DMTx0. However, DMTx+ was not significantly different from NDMTx+.

Discussion

In the present study, oral administration of ALA has lowered MDA level significantly in DMTx+ compared to DMTx0. The finding shows that ALA successfully acts as antioxidant parallel to previous study which showed that ALA is a potent antioxidant in vivo and in vitro (Packer et al. 1996). DHLA is a potent sulphdryl reductant as redox potential of DHLA:ALA is as low as -0.32V (Roy & Packer 1998). The redox potential helps to neutralize free radical by donating electrons and thus reduces lipid oxidation which will decrease the MDA level.

Previous study also showed that ALA is able to reduce blood glucose level through glucose metabolism (Erik 2006), prostaglandin dehydrogenase and alpha ketoglutarate dehydrogenase. The hypoglycaemic effect will reduce collagen glycation in aorta. This will also reduce oxidative lipid dissociation and cause decrease in MDA level in diabetic subjects (Hicks et al. 1988).
Study also showed that ALA supplementation increases lipid and lipoprotein regulation (Heitzer et al. 2001), most probably through activity of lipoprotein lipase (Zulkhairi et al. 2008). Decrease in LDL and MDA will also reduce MDA-LDL which mediates proinflammation and proatherogenic processes. It may reduce the risk of atherosclerosis (Berliner & Heinecke 1996).

Ascorbic acid level was decreased significantly in DMTx<sup>o</sup> compared to NDMTx<sup>o</sup>. Thus, acid ascorbic plays an essential role in diabetic condition (Retsky et al. 1993). Meanwhile, the acid ascorbic level was increased in DMTx<sup>+</sup> significantly compare to DMTx<sup>o</sup>. This shows that ALA is able to regenerate acid ascorbic. This will prevent suffering of diabetic patient from acid ascorbic deficiency which may lead to impaired collagen synthesis and cause poor vessel support and impaired wound healing (Kumar et al. 2002).

ALA mediates dehydroascorbic acid reduction (Xu & Wells 1996). ALA becomes strong antioxidant when it is reduced to DHLA (<i>E_0</i> = -3.2 V). Although the reduction takes place in the cell, DHLA is able to seep through from cells (Handelman et al. 1994). This shows that ALA acts both in intracellular and extracellular regions (Kagan et al. 1992).

Ascorbic acid is used extensively and preferred compare to α-tocopherol. This is due to lower reduction potential of acid ascorbic compared to α-tocopherol (Nakagawa et al. 1991). Low reduction potential also allows regeneration of α-tocopherol but not the other way around (Buettner 1993). Ascorbic acid is also an antioxidant which prevents lipid peroxidation of ROS (Frei et al. 1989).

Thus, ALA regenerates ascorbic acid and indirectly regenerates vitamin E. Vitamin E and C act in concert. Because of these synergistic actions, both of these vitamins have attracted interest as agents that may retard atherosclerosis by reducing the oxidation of LDL (Kumar et al. 2002).

GPx level was decreased significantly in DMTx<sup>o</sup> compared to NDMTx<sup>o</sup>. GPx is used to reduce oxidative pressure in diabetic condition (Cameron et al. 1993). This may be due to tendency of atherosclerosis development in diabetic subject compared to healthy condition as proposed by Buczynski et al. (1993).

Treatment with ALA increases GSH levels in vivo and in vitro. Studies with human cells have provided insights into the mechanism through which ALA increases GSH levels. Cysteine availability is known as the rate-limiting factor in GSH synthesis. DHLA which is secreted into the medium reduces cystine to cysteine, resulting in enhancement of GSH biosynthesis (Han et al. 1997). It should be noted that the standard reduced-oxygen (redox) potential of the ALA/DHLA pair is -3.20 V compared to GSH/GSSG which is -0.24V. Hence, DHLA can reduce even oxidized glutathione (GSSG) chemically which is catalyzed by GPx normally (Jocelyn 1967).

In current study, GPx level of DMTx<sup>o</sup> was not significantly different compared to DMTx<sup>+</sup>. This may due to short treatment period to show any significant increase. In addition, GPx activity is the major intracellular detoxification mechanism of H<sub>2</sub>O<sub>2</sub> and lipid peroxide compare to catalase (Asahi et al. 1995). GPx level in this study might be in the compensatory mechanism. Multiple genes (Harris 1992) involve in enzymatic antioxidant activity. Organ variability, enzymatic cofactors availability (Lu et al. 1989), hormones and cytotoxic level (White et al. 1989) may affect the level of enzyme. This is due to presence of specific pathway for enzymatic antioxidant such as GPx (Sies 1995).

MDA, ascorbic acid and GPx levels in NDMTx<sup>o</sup> were not significantly different from NDMTx<sup>+</sup>. These findings may indicate that favourable vascular effects of ALA are more likely to occur in people with oxidative stress-associated pathologies (i.e. diabetes mellitus, hypertension and hypercholesterolaemia) rather than in healthy individuals as were examined in the previous study (Heitzer et al. 2001).
ALA decreased VCAM concentrations in DMTx\(^{+}\) significantly compare to DMTx\(^{0}\). Genetic deficiencies of adhesion molecules in mice are associated with decreased atherosclerosis. Therefore, modulation of monocyte–endothelial interactions may be an important target for the prevention and treatment of atherosclerosis (Knowles and Maedah 2000).

Activation of the transcription factor NF-kB, e.g., by inflammatory cytokines is required for the transcriptional activation of endothelial cell adhesion molecules such as VCAM. (Colin et al. 1995). NF-κB (nuclear factor κB) has been proposed to be a redox-sensitive transcription factor. Some studies have suggested that ROS play a role in the signalling events leading to NF-kB activation (Schreck et al. 1992). Therefore, NF-kB is believed to play a pivotal role in atherosclerosis (Colin et al. 1995).

In the previous study, it was found that ALA inhibits NF-kB activation and adhesion molecule expression in human aortic endothelial cells. ALA effectively inhibits TNF-a-stimulated mRNA and protein synthesis of cellular adhesion molecules (particularly E-selectin and VCAM-1) and consequent monocyte adhesion. ALA inhibited IKK activity and nuclear translocation of NF-kB. The data strongly suggest that ALA inhibits TNF-a-induced endothelial activation by affecting the NF kb/IKB signaling pathway at the level of IKK rather than by preventing DNA binding of NF-kB (Suzuki et al. 1995).

It would be expected that ALA also affects NF-kB-dependent expression of many other inflammatory genes, such as IL-1 and IL-6, tissue factor, and TNF-a, in numerous cell types, e.g., lymphoid cells, monocytes, and endothelial cells. Thus, the observed anti-inflammatory action of ALA in endothelial cells probably extends to many other important mediators of inflammation in a variety of cells and tissues (Wei-jian Zhang & Frei 2001).

It is possible that ALA may improve haemodynamics in diabetic patients by long-term protection against oxidative stress (Midaoui et al. 2002), vascular hypertrophy (Takaoka et al. 2001), the formation of advanced glycation end products (Midaoui et al. 2003) and the expression of atherogenic proteins (e.g. tissue factor and endothelin-1) via inhibition of the inflammatory cytokine nuclear factor kB (Packer et al. 1998). Chelation properties of ALA has been proposed to responsible for inhibition of NF-κB activation rather than its antioxidant properties (Bowie et al. 1997).

In addition, ALA decreased VCAM level in NDMTx\(^{+}\) significantly compare to NDMTx\(^{0}\). This proves that there is presence of direct effect of ALA on VCAM molecule and not only in pathological condition like diabetes. The finding was parallel to previous study whish stated that ALA may elicit cardio protective effect especially in reducing risk of atherosclerosis (Lodge et al. 1997).

**Conclusion**

ALA may have the potential in reducing cardiovascular complication such as atherosclerosis in diabetes mellitus.

**Competing interests:** The authors declare that they have no competing interests.

**Authors' contributions:** JM and SB conceived of the study, designed the experiment, carried out the main experiment and drafted the manuscript. KT carried out the biochemical analysis and performed the statistical analysis. All authors read and approved the final manuscript.
Acknowledgements: This study was supported by the Ministry of Health via grant, 05-02-01-SF0014 E-Science Project.

References


Para Phenylene Diamine Poisoning—Clinical Manifestations & Short Term Prognosis

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Keywords: Para phenylene diamine, paronitroanaline, hair dye, E.D.T.A, Dyspnea, Upper respiratory tract edema, Seizures, Tracheotomy, Dialysis, acute kidney failure

Introduction

Para phenylene diamine, a derivative of paronitroanaline, has been used in the preparation of hair dye. It is commonly used for coloring the hair. It is not an uncommon suicidal agent in South India.

Aim & Objectives

The aim of the study is to:

1. Know the clinical manifestations of Para phenylene diamine poisoning.
2. Know the short term prognosis of the same.

Materials & Methods

40 Para phenylene diamine poisoning cases (22 females and 18 males) which came to the Emergency Department of Gandhi Hospital.

Inclusion Criteria

- Adults (18 – 50 Years) who showed the evidence of hair dye poisoning (PPD presence in urine on chromatographic study)
- Patients who reached the hospital within 12 hours of the intake of the poison and who have not received any treatment from outside hospital.

Exclusion Criteria (Limitations)

- Patients who have not shown any confirmation about the ingestion of hair dye poisoning.
Patient who are not willing for the study.

Suspected cases of hair dye poisoning.

Statistical tests used were Mean, Proportions’ and Chi square test with degree of freedom 1 (df=1).

Statistical analysis was done using Medcalc

Results

Out of 40 cases 18 were male & 22 were female. The mean age is 32.9 (+5.65). The quantity of dye consumed is 30-100 ml. The mean duration for the development of orofacial edema was 2.82 hours (+1.549). 32 people presented with dyspnea (80%) and emergency treacheostomy was needed in 18 (45%). The quantity of dye consumed by those people who required emergency treacheostomy was 72 (+16.5) ml. The clinical symptoms dominated were angioedema, asphyxia, oliguria & itching. 14 people (35%) presented with hypocalcemic tetany. Black colored urine was seen in 12 (30%). seizures were seen in 12 (30%). Dialysis was needed in 8 (20%). CPK values had been raised in these patients. The therapies used were stomach wash, fluid challenge (100%), Airway support; corticosteroids, local spray of adrenaline. Corticosteroids & local adrenaline spray had seemed to be no role in reducing angioedema. The amount of toxin, together level of azotemia, potassium, CPK values inducing rhabdomyolysis were significantly associated with higher mortality. 10 patients (25%) succumbed out of which 6 (15%) were died on the day of arrival.

Patient characteristics

Mean Age : 32.9 (+5.65) years
Male: Female : 18: 22
Mean volume ingested : 65.26 ml (+21.76)
Mean duration for development of : 2.82 hours (+1.549)
Orofacial oedema
Dyspnea : 32 (80%)
Upper respiratory tract oedema : 18 (45%)
Creatinine : 8.37 mg/dl (+1.725)
Potassium : 5.06 mEq/l (+0.79)]
CPK values (IU) : 20937.465 (+5869.12)
Tracheostomy was done at dose of : 72 ml + 16.5
<table>
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<tr>
<th>Recovered</th>
<th>Death</th>
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<tbody>
<tr>
<td><strong>Mean</strong></td>
<td><strong>Mean</strong></td>
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<tr>
<td>Dosage</td>
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<tr>
<td>Creatinine</td>
<td>8.76</td>
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<td>Potassium</td>
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<tr>
<td>CPK</td>
<td>34294.11</td>
</tr>
</tbody>
</table>

*This indicates the difference is due to chance*

**Discussion**

Hair dye poisoning is not an uncommon cause of suicidal death in south India. The clinical features are dominated by cervical and upper respiratory tract edema, black colored urine & oliguria, itching. 14 patients presented with hypocalcemic tetany with trismus & corporeal spasm & both chvostek’s & trousseau’s signs were positive. This can be attributed to E.D.T.A. present in the hair dye. The initial line of management for PPD poisoning patients was gastric lavage, fluid replacement (7+5 litres) & securing the air way. Emergency tracheostomy was needed in 18 (45%) These causes did not fully respond to antihistamines, steroids, adrenaline. Black coloured urine was seen in 12 (30%) CPK values were drastically increased in these patients. This can be attributed to massive rhabdomyolysis caused by the hair dye. 10 patients landed in acute renal failure indicated by raised creatinine, potassium levels and this is due to massive rhabdomyolysis & myoglobinuria. These patients require fluid replacement (7+5 Liters) to prevent acute tubular necrosis. Supportive therapy is essential for recovery.

**Conclusion**

Paraphenyline diamine is not a uncommon cause of suicidal death in South India. The commonest cause of death is due to acute respiratory distress caused by cervicofacial & upper respiratory tract edema & acute Kidney failure. Respiratory support & initial fluid replacement therapy is necessary to improve the prognosis. Prognosis also depends on amount of poison ingested.

**Aknowledgments:** We acknowledge our parents, teachers and friends and whoever helped us in completing this paper.
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Clinical profile of Kala-azar (Visceral Leishmaniasis) in North Bihar

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Introduction

Kala-azar or Visceral Leishmaniasis is a zoonotic infection caused by protozoa belonging to genus Leishmania. The term though still in use is now no longer applicable as the disease is not associated with black color of skin. This is due to early treatment of the disease.

The parasite is transmitted by the bite of sandfly (Phlebotomus & Lutzomyia). In visceral Leishmaniasis the parasite infects the immune system of the body, patients present with fever, wasting, anemia, splenomegaly or hepatosplenomegaly. If untreated the disease is fatal in one to four months in almost 100% patients.

The disease is endemic in 88 countries, infecting around two million people each year. Over 90% of VL cases occur in five countries – India, Bangladesh, Brazil, Nepal and Sudan. Kala-azar is hyper endemic in North Bihar region of India. The department of Medicine and pediatrics are flooded with the patients of VL. These days the combination of HIV and VL is also encountered and is a major threat to the already deteriorated health system of this region. (1)

The parasite has two stages – amastigote stage occurs in man & promastigote stage occurs in gut of sandfly. The reservoir for VL are human beings where as it is rodents in Africa and foxes in Brazil and canines for Mediterranean and Chinese VL.

History of Kala-azar in India

In 1852 William Twinning in Calcutta reported enlarged spleen along with acute anemia and intermittent fever. He advised Mercury as its treatment. In 1882 Dr. J J Clarke wrote an account of kala azar based on information gathered by Mr McNaught, the civil medical officer at Tura. In 1898 Ronald Ross thought that the peculiarities of Kala-azar were caused by a degree of immunity to malaria parasites.

It was in 1903 that William Leishman at Royal Victoria Hospital at Netly, as professor of pathology reported via BMJ that VL was a form of trypanosomiasis. In July, 1903 Charles Donovan, the professor of physiology also reported the same parasite and this was confirmed by Leveran. In 1930 Dr Brahmachri recommended pentavalent antimonials for the treatment. In 1942 it was seen that sandfly was the vector of this disease.

During 1945 to 1955 DDT spraying under National Malaria Eradication program wiped out VL, but this was not long lasting and VL had a comeback in 1970.(1)

About 80,000 cases were reported in northeast India in 1992. According to the WHO data in 1997 it is estimated that approximately 12 million people are currently infected and a further 367 million are at risk of acquiring Leishmaniasis in 88 countries.(2)
Aims and Objective

The study was done to study, analyze the current situation of Kala-azar in the area. I wished to study the data based on clinical, pathological and epidemiological findings and correlation of those findings to reflect the condition of VL. VL is quite prevalent here and I wished to study the patients throughout their stay in the college. VL is not a disease but a curse to this area, having the impact at various fronts of development in this poor socio-economic zone of globe. It’s a leading concern for various governmental and non-governmental health organization of the area.

My primary aim was to study the clinical profile of the disease. I did this project in 2nd year of my medical school. It was a great learning experience for me. I wished to experience and know research, its theme, methodology and writing of a report.

Material and Methods

Here I will present my findings that are based on observational study of the patients that are admitted in SKMCH.

To confirm the that they had VL we relied on following tests-

1) rk 39 strip test - This is easy to do and based on the concept of antigen antibody reaction and is quite sensitive. It may prove an important tool in epidemiological studies. The disadvantage being 5% cross reactivity with tuberculosis and malaria.

2) Spleen puncture - This test has a positivity rate of 90 to 95%. This is the best method to demonstrate LD body in a patient. Palpable spleen is a must for this test. Precautions must be taken as splenetic aspiration may cause hemorrhage which is very dangerous for the patient. We must be sure that there is no bleeding tendency in the patient.

3) Bone marrow aspiration test - Parasites can be demonstrated in the bone marrow of the patients. It has a positivity rate of 60 to 65%. Usually the iliac crest is used for aspiration. We use Xylocaine for local anesthesia as it’s a painful procedure.
Here is a flowchart of the procedure:

![Flowchart of the procedure]

Patients who test positive are admitted in the indoor ward of the department of medicine, RBC count, WBC count, Differential counts, ESR, Bleeding time, Clotting time and weight is recorded. X ray of chest is done sometimes when opportunistic infection of Tuberculosis is suspected.

General examination of patients is also done which includes- pulse, respiratory rate, pallor, icterus, decubitus, cyanosis, koilonychia, lymph gland enlargement, and edema. Inspection, palpation, percussion and auscultation of abdomen and chest are done. Palpable spleen and liver are recorded from the costal margin where the midclavicular line is supposed to pass.

Full history of all the aspects related to the condition is taken. Some of the parameters monitored daily were pulse, temperature and respiratory rate. The parameters that were recorded after an interval of 2-3 days are - spleen and liver palpation, weight and blood pressure.

**Management of VL in the hospital**

Pentavalent antimonials are of no use in this area as the resistance towards drugs has increased. The drug of choice is Amphotericin B, an antifungal drug that was the base of the treatment. Various other drugs were given as and when required. The mode of administration was intra-venous. Infusion fluids was prepared by dissolving 50 mg of Amphotericin in 10 ml of sterile water and making up to 500 ml with 5% glucose or dextrose to give a final concentration of 100 micrograms of Amphotericin B per ml. adverse effects noticed were- nausea, vomiting, rashes, hypotension, dyspnea, tachypnea and headache. 85% patients had fever with chills after some doses of Amphotericin B, which disappeared after 3 or 4 doses.

The dose of Amphotericin B was 1 mg per kg body weight as full dose and 1 mg as a test dose. The drug is administered by slow IV infusion in 4 to 5 hours. Liposomal form of Amphotericin B is
preferred in patients seriously ill. The patients having TB or HIV+ were referred to DOTS and ART centre respectively.

**Results**

Patients came from wide spread areas of North Bihar. The number of patients that were monitored was 21. Fever with chills was the major complain along with feeling of an abdominal lump on the left side near the costal margin. Most of the patients were poor and uneducated. Period of reporting was as long as six months from the start of fever. At a particular time nearly 60 patients are admitted in the hospital. There were about 35 patients in Department of Medicine and 25 patients in Department of Pediatrics usually when the study was done.

Temperature was normal during the treatment due to the use of antipyretics. The highest temperature recorded was 105 degree F and the average temperature was 100 degree F before the start of treatment. There is marked weakness seen in the patients. The average weight is 41 kgs with range from 22 to 60 kgs.

There was normochromic and normocytic anemia caused by various factors- replacement of bone marrow by parasites, splenic sequestration, hemorrhage, hemodilution and hemolysis. Leukopenia with relative lymphocytosis was also seen. The range of lymphocyte % was from 17 to 74% with mean of 42. The average WBC count was 4707 per micro liter. The lowest count of WBC was 1400 per dl. Thrombocytopenia contributes to the hemorrhagic tendency observed in some cases. Almost all the patients had anemia with hemoglobin ranging from 4.80 to 10.6 gm per dl. There was blood transfusion to increase the hemoglobin count.
Hepatosplenomegaly was also recorded. The ratio of palpable spleen to liver was 2.95: 1. The average size of spleen was 7.8 cms; range was 4 to 18 cms. Hepatomegaly was seen in 42 % patients. The average size of palpable liver was 1.2cms. In most cases there was regression of spleen and liver with a few doses of Amphotericin B.
Discussion

Children are mostly affected from the disease followed by males and females. Children have more chances of getting infection as – 1) they wear less clothes so they are more exposed to sandfly bite, 2) they have a less developed immune system. (3) Males are also more exposed to sandfly bite then females so they suffer more than females. Females are affected less but they show more morbidity and mortality. They are weak and malnourished as compared to males.(3,4,10) They are neglected as compared to males, so their clinical and pathological condition has deteriorated much when they first report to the hospital.
There is more likelihood of developing an infection when a person is malnourished. (3) The average weight of the patients was 44 kgs which is quite low. Females had an average of 34 kgs which is quite less as compared to the average. Usually there is some difference in the weight between male and females; this was exaggerated by the disease. The relative lymphocytosis and total WBC count is more severe in females as compared to males.

Reduced erythropoiesis due to bone marrow replacement by the parasite and due to reduced level of erythropoietin.(5) as there is damage to renal cells by Amphotericin B during treatment. There can be mild increase in bilirubin levels due to splenomegaly and also due to hepatotoxic nature of Amphotericin B. There is decrease in number of WBC is due to increased destruction of cells due to increase trapping by spleen, but a relative lymphocytosis is seen that shows that the infection is chronic. (6)

Size of liver and spleen- More increase occurs in spleen as compared to liver. There is a ratio of 2.9:1. Spleen is a soft structure without any capsule so it increases more than liver. The average splenomegaly of females was more then the average of males because disease is more severe in females due to prevalent under nutrition and other co morbid conditions. (7,9)

Leishmaniasis accompanied with TB and HIV+ cases - Both HIV+ and Leishmaniasis cause decrease in immunity. HIV may cause the infection of Leishmaniasis to flare up. It leads to more serious complications if there is a combination of HIV+ and Leishmaniasis. Cases are difficult to treat and there are frequent relapses. The efficacy of the anti retroviral drugs and anti Leishmaniasis drugs might be reduced due to drug interaction.

Cases of relapse were also seen. I grouped them into three-

1) Due to treatment by Sodium Stibogluconate or Sodium antimony gluconate. Most of the cases are resistant to these traditional drugs. Primary health centers are still providing these drugs. There is marked resistance seen and the disease relapses in a few weeks. So the goal must be clinical treatment along with parasitological treatment which is possible by the use of Amphotericin B. (8)

2) Relapse due to re-infection. This is also possible as there is no residual immunity left after the infection. People are still ignorant about the cause and the prevention of the disease. So re infection might be a major cause of relapse.

3) Relapse in HIV+ individuals. It is seen that HIV+ individuals are hard to treat. They have low immunity and are become easy prey to the infections. There are exaggerated symptoms in HIV+ patients. Some of the patients show continuous high fever.

Summary

VL is spreading by leaps and bounds and the situation is grim despite the efforts of government and many organizations. The cases of resistance and HIV combination will be the next trouble which will crop up soon. Bihar has lots of population which is migrant worker and they have more chances to get HIV+ due to the irresponsible behavior of the people. This disease is burden of the area and adds to the loss of life and valuable resources. We must find a way to resolve the crisis so that the area can develop and attain the health which is basic human right of every human being.
Acknowledgements: I wish to express my regards for:

1) Indian Council of Medical Research – The project was done as a short term studentship of ICMR.

2) My guide – Dr Kamlesh Tewary who guided me throughout and Dr Vijay Kumar Singh who guided me in indoor wards and in compilation.

References

1) Round table conference on Kala-azar.
Dengue Hemorrhagic Fever – Correlation of IgG & IgM Values & platelet count

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College grant number SMC G ICD-10S100

Keywords: Dengue fever, spleenomegalae, flavivirus, platelet count, PRP transfusion, DENGUE HEMORRHAHGIC FEVER, IgM, IgG.

Introduction

Dengue fever is an acute flavivirus infection that presents with fever & myalgia; it is commonly known as break bone fever. A hemorrhagic variant with a bleeding dyscrasia presents with petechial dermatitis. It is most commonly encountered in Southeast Asia & Africa. It is diagnosed positive IgM titers &/or four told raise in IgG titer.

Aims & Objective: The aims of the study are to

1. Know the clinical correlation between the raised IgM & IgG titers and decreased platelet count.
2. Know the short term prognosis of the patient who has both IgM & IgG raised titers.

Materials & Methods

90 (54 females & 36 males) Dengue serology positive cases by ELISA that have had admitted at Gandhi Hospital & Sir Ronald Ross institute of Communicable & Tropical Diseases.

Inclusion Criteria

- Patients who have positive Dengue serology by ELISA.

Exclusion Criteria

- Suspected Dengue cases
• Patients who are not willing for the study.

• Patients who are having co-infection with other organisms (Ex: positive for both Plasmodium & Dengue)

• Statistical tests used were Mean, Proportions’ and Chi square test with degree of freedom 1 (df=1).

Statistical analysis was done using Medcalc.

Results

All the patients, as selected, are having IgM positive titers.

• Patients with positive IgM & IgG have platelet count ranged between 20,000/mm³±15,000/mm³ (Least identified was 5,000/mm³)

• Positive IgM & IgG is seen in 42 (46.7%) (20,000/mm³±15,000/mm³)

• Positive IgM & splenomegalae in 30 (33.3%) & in these platelet count ranged between 80,000/mm³±15,000/mm³

• Positive IgM antibodies with No splenomegalae & IgG negative is seen in 8 & in theses platelet count longed between 1.2 lakh ± 25,000/mm³.

• 24 of the patients with platelet count 20,000/mm³±15,000/mm³ showed bleeding manifestations in the form of epistaxis & patechiae.

• 6 patients have had intracranial bleeding (evidenced on CT scan) & had seizures clinically.

• Patients with IgM & IgG positive needed 4±2 PRP transfusions.

• No of deaths with IgM & IgG positive – 3

Discussion

Dengue fever, an acute flavivirus infection presents with fever, myalgia and decreased platelet count. DHF is a severe form of dengue fever caused by infection with more than one dengue virus. Loss of appetite, vomiting, epigastric pain & tenderness in right coastal margin DHF is diagnosed by positive IgM titres & or four fold raise in IgG titre. Patients with both IgM & IgG positive titres have massive decrease in platelet count (20,000 ± 15,000 cells/mm³). This can be attributed to the exaggerated immune response to the second viral infection and damaging their own platelets. Patients with positive IgM titers with splenomegalae have moderate decrease in platelet counts (80,000± 20,000 cells/mm³). This is due to sequestration effect of spleen as spleen is the reservoir of platelets. Patients with only IgM positive have platelet count of 1.2 Lakh ± 25,000 cells/mm³.
Patient factors

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>IgM</th>
<th>IgG</th>
<th>Spleeno megale</th>
<th>Platelet count (cells /mm³)</th>
<th>Out come</th>
</tr>
</thead>
<tbody>
<tr>
<td>24</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
<td>1.2 lakh±25,000</td>
<td>Good prognosis</td>
</tr>
<tr>
<td>24</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
<td>80,000 ±20,000</td>
<td>Good prognosis</td>
</tr>
<tr>
<td>30</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
<td>20,000 ±15,000</td>
<td>Epistaxis</td>
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<td></td>
<td>IC bleed in 2</td>
</tr>
<tr>
<td>12</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>20,000 ±15,000</td>
<td>Epistaxis</td>
</tr>
<tr>
<td></td>
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<td>Petiechae</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IC bleed in 2</td>
</tr>
</tbody>
</table>

Reference range for diagnosis

**IgM Values (By ELISA)**
- Negative : < 0.9
- Equivocal : 0.90 – 1.10
- Positive : >01.10

**IgG values**
- Negative : < 0.9
- Equivocal : 0.90 – 1.10
- Positive : >01.10

The patients with both IgM & IgG positive required 4+2 platelet rich plasma transfusions an steroids can also be given in order to reduce the exaggerated immune response. Three patients succumbed due to intracranial bleed as evidence on C.T. Scan.

**Factors predicting the platelet value**

<table>
<thead>
<tr>
<th>Mean IgM Value</th>
<th>Mean IgG Value</th>
<th>Platelet count ranged</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.83 ± 1.28</td>
<td>4.93 ± 1.52</td>
<td>Between 20,000 + 15,000 cells/mm³</td>
</tr>
<tr>
<td>3.68 ± 1.32</td>
<td>1.12 ± 0.78</td>
<td>Between 80,000 + 20,000 cells/mm³</td>
</tr>
<tr>
<td>3.69 ± 1.34</td>
<td>0.98 ± 0.32</td>
<td>Between 1.2 lakh + 25,000 cells/mm³</td>
</tr>
</tbody>
</table>

*p VALUE= 0.05(estimated=3.84,observed=4.13)*
Conclusion

Cases with both IgG & IgM positive titers have massive decrease in platelet count & this may be due to exaggerated immune response. Cases with IgM positive & spleenomegalae have moderate decrease in platelet count. This can be attributed to sequestration effect of spleen. One patient succumbed due to intracranial bleed. Steroids can be tried in the management along with PRP transfusion aspirin and other NSAIDS are to be avoided in there patients as they exaggerate the bleeding manifestation.

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Role of Oxidative Stress and Antioxidants in Children with IDA

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Abstract

Background: Increased oxidative stress with free radical generation in iron deficiency anemia (IDA), its aggravation at therapeutic doses of iron and reduction of oxidative stress by antioxidant supplementation are well studied in adults. Studies in this regard are scanty in children.

Objective: The co-prescription of antioxidants with iron supplementation in IDA to counter the oxidative stress is a well studied and established fact in adults. Though iron supplementation is a common clinical practice in children it is not conventional to coprescribe anti-oxidants in children. Therefore a study was undertaken to evaluate the oxidative stress in IDA in children and the effect of antioxidants during iron supplementation and to evolve an optimal suitable therapeutic strategy to minimize oxidative stress and thereby adverse clinical effects.

Methods: All the children attending the pediatrics OPD in IRT PMCH during JULY/AUGUST 2008 were randomly screened for anemia by clinical and haemoglobin evaluation. 21 children whose parents gave consent for participation in the study were included for evaluation. They were in the age group of ten months to sixteen years. Nutritional status of the study population was recorded by a twenty four hour recall survey method. After deworming, children were started with oral iron supplementation in three different groups; group I – oral iron only, group II – oral iron with vitamin C, group III – oral iron with vitamin E. Lipid peroxides and Lipid hydroperoxides were measured as the indices of oxidative stress before initiation, tenth day (I follow up), thirtieth day (II follow up) after oral iron therapy. Serum iron profile was also studied for evaluation.
**Results:** There was no significant difference in serum iron profile response to oral iron therapy between the groups. Oxidative stress indices showed a decreasing trend in all the groups with no significant difference among the groups. There were no clinical adverse effects of oral iron supplementation in all the groups.

**Conclusion:** Unlike in adults, oxidative stress in iron deficiency anemia is not aggravated by oral iron supplementation in children. There was no significant difference between oral iron alone and oral iron with antioxidants in terms of clinical and biochemical response. Lipid hydroperoxides seems to be an early indicator of oxidative stress.

**Key Words:** IDA, Children, Oxidative Stress, Iron therapy

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n01-01.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n01-01.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRI MPH))
Perceived stress among tomorrow’s attorneys in Mansoura, Egypt

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Abstract

Background and Objectives: Few data are available on the level and sources of stress among law students in the Middle East generally and in Egypt specifically. We conducted this study to identify the prevalence and predictors of perceived stress among law students in Mansoura University, Egypt.

Subjects and Methods: A cross-sectional study covered 426 law students selected through a stratified cluster sampling method. The questionnaire covered four categories, including 15 items on sources of stress (stressors). Perceived stress scale and Hospital anxiety and depression scale were used to measure stress, anxiety and depression.

Results: A high level of perceived stress, anxiety and depression were reported by 42.2%, 59.2% and 18.2%, respectively. On the scale for sources of stress, 80% experienced personal troubles and two thirds of the sample had relationship, academic and environmental problems.

Conclusions: It appears that the law students have a high level of perceived stress and majority of it is generated from personal factors and less from the academic or environmental factors. Additional studies are needed to improve our understanding of the causes and consequences of law students' stress.

Key Words: Law students, Stress, Anxiety, Depression

Full Text: http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n01-01.htm (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
A hospital based cross sectional study of mucocutaneous manifestations in the HIV infected

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Abstract

Background: HIV infection produces a panorama of mucocutaneous manifestations ranging from macular, roseola like rash in the acute seroconversion illness to end-stage, extensive Kaposi sarcoma. Certain studies showed dermatological lesions are indicators of the immune status of the patient. So here is an attempt to find out the spectrum of dermatological lesions in HIV infected, their association with the CD4+ cell count, and to compare the pattern of dermatological lesions between patients on HAART and patients not on HAART.

Aims: To conduct a clinical study of mucocutaneous manifestations in HIV-positive patients visiting Skin and STD Dept. of Krishna Rajendra(K.R.) hospital, Mysore Medical College and Research Institute, with special reference to age, gender and risk factors.

Methodology: Cross-sectional study with simple random sampling technique was conducted at K.R.Hospital, Mysore Medical College and Research Institute, India between August 2007 and October 2008. The study involved 350 HIV positive patients aged between 16-60y of which 175 were on HAART presenting with some mucocutaneous manifestations and 175 were not on HAART consisting of patients who presented with a symptom of one of the mucocutaneous lesions. They did not know if they were HIV infected. After they were tested they were found to be positive and were included in the study. They were procured from the Anti Retroviral Centre of our hospital. Mean duration of HAART initiated life is 6months. Before involving the patients in the study ,written informed consent was obtained from the patient/legal guardian both in English and local language. Appropriate lab investigations were done i.e. HIV status, base line investigations like Hemoglobin, Peripheral Blood Smear, KOH test, VDRL test, CD4 cell count etc.

The data thus collected was tabulated with reference to some important parameters of the study. It was analysed using the software SPSS 11.4 version.

Results: Among the opportunistic infections and other infectious lesions (HAART and non-HAART put together), highest was viral(56%) followed by fungal (42%), bacterial(22%) and least being infestation. Viral infections were less on HAART initiated (32%) as compared to non HAART (80%). But the cases of bacterial and fungal infections were almost equal in both categories. There was significant increase in the cases of non infectious lesions on HAART population (88% against 40% in
non HAART; p<0.034) due to drug eruptions and pruritic papular eruption. One case of pityriasis rosea in non HAART, resistant to treatment was diagnosed. When opportunistic manifestations among non-HAART were considered, oral candidiasis was the leading manifestation seen among the 28% of the study group with mean CD4 count of 150 cells/cu.mm, followed by molluscum contagiosum- 24%, condyloma acumminatum-20% and herpes zoster-16%. Majority of the lesions were seen at the cell counts less than 200 cells/cu.mm. The study was comparable to many Indian and foreign studies.

**Conclusions:** In correlation with CD4 cell count, mucocutaneous manifestations increased with decreased CD4 cell count [Regression Coefficient (-0.31) with 0.64 standard error of estimate and p-value <0.05]. When dermatological lesions of patient who are on HAART was compared with that of non-HAART, there was significant reduction in the prevalence of dermatological viral infection in CAT 2 [under HAART-chi square=5.134; p<0.023]. But prevalence of bacterial and fungal infections showed no change [p=0.763(NS) and p=0.827(NS) respectively]. This may be due to poor socioeconomic status and poor hygiene.

**Key Words:** Highly active anti-retroviral therapy, Opportunistic infections, Human immunodeficiency virus, Mucocutaneous manifestations, Oral candidiasis, Herpes simplex

**Full Text:** [http://www.iomcworld.com/ijcirmsph/ijcirmsph-v02-n03-02.htm](http://www.iomcworld.com/ijcirmsph/ijcirmsph-v02-n03-02.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
A Study on Tuberculous Pleural Effusion

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Abstract

Background: Nearly one third of the global population i.e. two billion people are infected with mycobacteria tuberculosis and are at risk of developing the disease. Pleural effusion is one of the common complications of pulmonary tuberculosis. In this study, the clinical features, the positivity rate of microbiological procedures and blind pleural biopsies, radiological manifestations, biochemical and hematological profiles of serum and pleural fluid were analyzed.

Objectives: To report our experience of 108 patients with tuberculous pleural effusion and discuss the clinical features, radiological findings, biochemical, cytological and microbiological analysis of pleural fluid, hematological and biochemical profiles of serum and positivity rate of microbiological procedures and blind pleural biopsies in these patients.

Methods: This study was a hospital based descriptive cross sectional study performed at Chest Medical Ward, Yangon General Hospital, Myanmar, of study period from January 2004 through January 2005. A total of 108 patients were included. Thorough history taking and physical examinations, radiological findings, hematological and serum biochemical profiles were recorded. Pleural aspiration and biopsy were also performed. At least two pieces of pleural tissue were taken and one piece of each sample of pleural tissue was cultured for mycobacteria and the rest was sent for histological examination. Macroscopic findings, cytological, microbiological and biochemical analysis of pleural fluid were analyzed.

Results: A total of 108 patients, 74 males and 34 females were included. Their mean age was 42.60 ± 16.34 (range 12-81 years). Common presentations were breathlessness (82.4%), cough (81.5%), fever (80.6%), and night sweat (78.7%), loss of appetite (74.1%), significant weight loss (72.2%) and chest pain (67.6%). Only 39.3% of TB patients produced sputum in their history. Haemoptysis was present in only 7.4% of the patients. Regarding the physical signs, 53.7% of them had fever during admission, 15.7% were cachectic, cervical lymph nodes were palpable in 14.8% and had clubbing of fingers in 5.6%. They also had respiratory physical signs other than pleural effusion which include crepitation (31.5 %), collapse (15.7 %), pleural rub (13.0 %) and signs of consolidation (11.1 %). Only one patient (0.9%) had positive AFB smear in pleural fluid. Culture of pleural effusion and pleural biopsy reports for AFB were positive in 5.6% and 1.9% respectively. 91 patients (84.3 %) were diagnosed on first biopsy procedure and 15 (13.8%) and 2 (1.9 %) of patients needed second and third session of procedures respectively. Only 2 patients (1.9%) had bilateral pleural involvement.

Associated radiological pulmonary parenchymal lesions were noted in 28 patients (25.9 %). 7 patients revealed blood stained pleural fluid (6.48%). The rest had straw color aspirates.
Mean Pleural fluid and serum protein ratio was 0.69 ± 0.17. Pleural fluid LDH was high in most cases with a mean ± SD was 726.24 ± 383.64. Serum LDH also was high (507.39 ± 170.76). The mean ratio of pleural fluid and serum LDH was 1.56 ± 1.16. The main WBC subset was lymphocytes (mean 91.96% of total WBC population) and polymorph was detected only 6.86 ± 15.88 % (mean ± SD). Total and differential white cell counts of peripheral blood film were within normal limits. Mean ESR was high 77.4 mm/1st hour.

**Conclusion:** Analysis of pleural fluid can have an important contribution for investigation of patients with pleural effusion. Although highly specific, percentage positivity of microbiological examinations on pleural fluid does not reach the degree required for a single diagnostic investigation for tuberculosis. The Light’s criteria are fulfilled in all cases. Pleural biopsy will be useful as an ultimate procedure in cases with diagnostic problem as it is a procedure which can give a definitive tissue diagnosis.

**Key Words:** Tuberculosis, Pleural effusion, Pleural biopsy, Light’s criteria

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n03-01.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n03-01.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Risk factors for breast cancer among women attending a tertiary care hospital in southern India

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Abstract

Background: The incidence of Breast Cancer is increasing, particularly in previously low incidence areas such as Asia. In fact in India, it is considered the leading Cancer among women in certain metros such as Mumbai, Bangalore & Thiruvananthapuram. The risk factors responsible for the causation of breast cancer may be population specific. Moreover, there are inherent factors that aid in the late presentation of breast cancer patients to a hospital. Identifying these factors holds great promise in reducing the incidence, morbidity and mortality due to this disease.

Objectives: To study the socio-demographic and risk factors of breast cancer patients presenting to a tertiary care hospital and to determine the stage at presentation and factors contributing to delayed presentation.

Methods: This was a one is to four matched case control study with a sample of 315 individuals. The cases were enrolled in the order of their admission into the hospital during a four month study period. For each identified case an age matched control was recruited from the hospital. Cases and controls were personally interviewed by the investigator using a structured questionnaire and the data pertaining to treatment and diagnostic modalities were collected from the medical records.

Results: Most (46%) of the cases belonged to the 45 – 54 age group and only 8% were over the age of 60. Despite a high literacy status (80%), women in this study had poor awareness pertaining to breast cancer (63%). Considerable proportions of the cases were detected in stage III (46%) or stage IV (36.5%) of the disease when treatment options are limited and cure a distant probability. Nearly all the cases (98.4%) had accidently identified the breast lump and none of them had ever performed a breast self examination or undergone any screening procedure. First delivery at age > 30 years [OR = 2.27 (1.02 – 5.05) p < 0.05] showed a significant risk association. Menarche <11 years [OR = 0.321 (0.106 – 0.971) p < 0.05] showed a beneficial effect. Nearly 88% of the cases approached more than one...
primary care practitioner prior to being referred to a cancer detection center, thereby delaying the process of diagnosis.

**Conclusion:** The risk factor for breast cancer determined by our study was first delivery over the age of 30. Delay in referral of cases was another significant finding which is of concern and needs to be addressed pragmatically. Considering the low awareness levels of the participants and nonexistent screening practices a targeted intervention to tackle this problem seems to be the need of the hour.

**Study Limitations:** Since the controls were hospital based, generalisability of these findings could be limited. Besides, women in this study were more literate and employed as compared to many in other parts of India. Various factors that affect delayed presentation such as fear of diagnosis and affordability were not studied.

**Key Words:** Breast cancer, Risk factors, Stage at diagnosis, Breast self examination, Screening

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n04-04.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n04-04.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Liver Trauma: Operative and Non-operative Management

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Abstract

Background: The liver is the second most commonly injured organ in abdominal trauma, but liver damage is the most common cause of death after abdominal injury. Although urgent surgery continues to be the standard for hemodynamically compromised patients with hepatic trauma, there has been a paradigm shift in the management of patients who have stable hemodynamic. A marked change toward a more conservative approach in the treatment of abdominal trauma has been noted during the last decades. Modern treatment of liver trauma is increasingly non-operative.

Purpose: To find the epidemiology, etiologies and managements of liver trauma in a population based study in Iran.

Material and Method: A study including 16,287 trauma patients referred to the main hospitals of seven cities with different geographic patterns was done in Iran. Eighty-four patients with hepatic trauma during the 1-year period ending March 2000 included in this Cross-Sectional study. We determined the incidence, etiology and management of the patients suffering liver injury. Analysis was done using SPSS 18. Statistical significance was set at $P<0.05$.

Results: Out of 16287 trauma patients 84 (0.5%) had hepatic trauma with male predominance 68(81%). The most type of trauma was blunt and the main cause was motor vehicle crashes. Thirty patients (35.7%) managed non-operatively. There was no significant difference in hospital stay between patients operated and managed non-operatively. There was no mortality in the patients managed non-surgically.

Conclusion: In this study hepatic trauma was in 3.7% of abdominal trauma patients. This study concluded non-operative management of hepatic injuries is associated with a low overall morbidity and does not result in increases in length of stay. Non-operative management is a safe approach for the patients of liver trauma with stable hemodynamic.

Key Words: Liver trauma, Management, Non-operative

Full Text: [http://www.iomcw.com/ijcrimph/ijcrimph-v02-n04-03.htm](http://www.iomcw.com/ijcrimph/ijcrimph-v02-n04-03.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Evaluation of Falcivax against Quantitative Buffy Coat (QBC) for the Diagnosis of Malaria

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Abstract

Introduction: Microscopic detection of appropriately stained blood smear for the diagnosis of Malaria has been the standard diagnostic technique for identifying malaria infections for more than a century. The technique is capable of accurate and reliable identification when performed by skilled microscopists using defined protocols. The problems associated with implementing and sustaining a level of skilled microscopy appropriate for clinical diagnosis have particularly prompted the development of malaria rapid diagnostic devices (MRDDs).

The current MRDDs are based on antigen capture immunoassay methodologies using immunochromatographic strip (ICS) technology. The newer generations of MRDDs are using more antigens like Merozoite protein 2 and circumsporozoite proteins. Further these antigens are obtained using recombinant techniques. This study was done for the evaluation of two commercially available immunossays against QBC for the diagnosis of Malaria.

Aim of the study: The aim of the study is to evaluate Falcivax (Immunochromatographic Strip) test for the diagnosis of Malaria and to compare with Quantitative Buffy Coat (QBC).

Materials & methods: A total of 100 patients attending outpatient department of Kasturba Hospital, Manipal, India, with their own initiative and meeting the inclusion criteria are included in the study. 2ml of blood was collected by venipuncture into tubes (Vacutainer blood collection system) containing EDTA as anticoagulant from all patients. Tests were run in batches of 8 samples at a time for Falcivax, Smear status by QBC, clinical features and relevant laboratory data of each sample was noted down.

Results: Out of 100 patients 70 tested positive for malaria by QBC with P. falciparum accounting for 32(45.7%) and P. vivax 37(52.9%). In comparison with the study control – QBC in the detection of malaria, Falcivax test showed sensitivity, specificity, positive predictive value and negative predictive value of 90.0%, 100.0%, 100.0% and 81.0% respectively.
Conclusion: Falcivax showed a reduced sensitivity compared to the QBC. Hence QBC still continues to be better option than MRDDs for detection of plasmodium infection in health care facilities with all expertise.

Key Words: Malaria, Immunochromatographic method, Falcivax, Quantitative Buffy Coat

Severity of Menopausal symptoms and the quality of life at different status of Menopause: a community based survey from rural Sindh, Pakistan

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Abstract

Background: Menopause is the time in women’s life when her ovaries stops producing Estrogen and Progesterone, the deficiency of these hormones elicit various somatic, psychological, vasomotor and sexual symptoms that affect the overall quality of life of women. Assessment of quality of life during menopause deserves special attention as with increase in the life expectancy women lives about one third of their lives with hormone deficient state. Studies on menopause and quality of life of menopausal women are scarce and none is conducted before among rural women of Sindh Province, Pakistan.

Objective: To investigate the severity of menopausal symptoms associated with menopausal status and to determine the quality of life of menopausal women from rural Sindh.

Material and Methods: This cross-sectional survey was conducted in 19 Union Councils of Matiary district, Hyderabad Division from November 2007 to October 2008. Among 5, 25,082 population dwelling in 1509 villages and 56,053 households of these Union Councils, 3062 women were selected by multistage random sampling method within the age range of 40-70 years. Along with collection of socio-demographic data the Menopause rating Scale (MRS) and WHO Quality of life Brief (WHO QOL Brief) Questionnaire translated in Sindhi Language were filled for each individual subject. Data was entered and analyzed by SPSS version 15.

Results: The mean age at Menopause was 49.38±14.29 years; the mean scores of menopause rating Scale were high in all domains, the significant difference was found in the mean somatic scores of women in Premenopause, perimenopause and post menopause status (P=<0.001).

The psychological symptoms were more severe for women in perimenopause and post menopause status while the scores for urogenital symptoms were found to be higher in perimenopause women (P=<0.001). The mean scores for the physical, psychological, social and environmental domains of WHO QOL questionnaire were found significantly impaired for all women at different status of menopause.

Conclusion: To best of our knowledge this is the first attempt to provide data on menopause and quality of life of women from rural Sindh. The mean scores of all the domains of Menopause rating
scale were significantly high in Peri and postmenopausal women from rural Sindh. The severity of menopausal symptoms decreases the quality of life in everyday life of these rural women.

**Key Words:** Menopause, Severity of symptoms, Menopause Rating Scale (MRS), Quality of life, WHOQOL

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n05-01.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n05-01.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCIMPH))
Percutaneous Valve Replacement: Where do we stand? Where are we going?

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Abstract

**Background:** Percutaneous valve replacement is a relatively new treatment modality that is rapidly growing in application.

**Aim & Objectives:** Percutaneous treatment of valve diseases has been an alternative to open surgery since the early 1980's. In patients with mitral and aortic stenosis, use of percutaneous catheter-based techniques as balloon valvuloplasty has been a good therapeutic option. Later on, percutaneous aortic valve replacement was demonstrated in the 1990s in vitro, followed by successful in vivo applications. Although these techniques have difficulties such as paravalvular leakage difficulty in deployment; migration of valved stent; percutaneous valve replacement is currently one of the most researched and actively debated subjects in interventional cardiology. In this study we are aiming to review the current state and evaluate the pros and cons of this new treatment modality.

**Methods/Study Design:** We enumerated the pros and cons from different perspectives, referenced and discussed them from articles that were obtained through Pubmed.

**Results and Findings:** Percutaneous valve replacement procedures offer substantial advantages to patients. The reducing of surgical risks, the fact that the procedures are less invasive in comparison to open heart surgery, and that rehabilitation times are shorter are positive aspects [2]. However, there are complications such as paravalvular leakage difficulty in deployment; migration of valved stent, that needed to be taken into consideration and the selection of patients for the procedure needs improvement.

**Study Limitations:** Percutaneous valve replacement is a relatively new treatment modality, few publications exist for consideration.

**Conclusion:** With 12 different kinds of valves available for use, and improvement in patient selection, we expect to see an increase in percutaneous valve replacements worldwide.

**Keywords:** Percutaneous Valve Replacement Mitral Aortic

**Full Text:** http://www.healthmedjournal.com (HealthMED Journal)
Evaluation of serum levels of interleukin-6 and interleukin-8 in patients with recurrent aphthous ulcerations

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Abstract

Introduction: Recurrent aphthous ulcers (RAU) are one of the most common ulcers in oral cavity. Several studies have shown conflicting variations for inflammatory cytokines and other biologic markers in RAU.

Aim: The aim of the present study was to determine the level of IL-8 and IL-6 in the serum of patients with RAU.

Materials and method: In this case – control study, serum levels of IL-8 and IL-6 levels were measured in patients with RAU (n=40) and in healthy control subjects (n=40). The cytokines levels were measured in serum by ELISA. The SPSS software was used to analyze the results.

Results: The mean value of IL-8 and IL-6 in patients (52.24 pg/ml and 9.39) was 10 and 4 fold higher than control group (5.01 pg/ml and 2.09 pg/ml), respectively. The difference was statistically significant (t-test  p=0.01).

Conclusion: The results of our study showed that serum levels of IL-8 and IL-6 were significantly higher in patients compared to controls.

Keywords: Interleukin-8, Interleukin-6, Recurrent aphthous ulcers

Full Text: http://www.healthmedjournal.com (HealthMED Journal)
Serum Interleukin-6 as a Serologic Marker of Chronic Periapical Lesions; A Case-control Study

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Abstract

Background and aims: Chronic periapical disease with pulp origin is an inflammatory disorder caused by bacterial infection. Cytokines such as interleukin-6 have important role in pathogenesis of inflammatory diseases. Chronic infection could affect general health by increasing production of cytokines such as interleukin-6 that probably play some roles in pathogenesis of pulpal and periapical diseases. The aim of present study was a comparative evaluation of serum interleukin-6 in patients with periapical lesions and healthy controls.

Materials and Methods: This analytical case-control study included 40 patients suffering from chronic periapical lesions and 40 healthy persons without any oral diseases. After informed consent was obtained, clinical and radiographical examination was carried out and blood samples were collected. Serum interleukin-6 was measured by ELISA method. Data were subjected to SPSS software and t-test was used for statistical analysis.

Results: Serum interleukin-6 concentration was significantly higher in patients group in comparison with healthy controls (P<0.001).

Conclusion: The results of present study indicate that interleukin-6 produced in periapical lesions may serve as a marker of pathologic inflammatory activities in chronic periapical lesions.

Keywords: Cytokine, Interleukin-6, Periapical lesions

Full Text: http://www.healthmedjournal.com (HealthMED Journal)
Novel in Situ Gel System for Effective Treatment of Bacterial Conjunctivitis

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Abstract

Background: Hyperacute bacterial conjunctivitis is a severe, sight threatening ocular infection that warrants immediate ophthalmic work-up and management. Treatment to bacterial conjunctivitis is provided to shorten the course of disease, reduce person-to-person spread, lower the risk of sight-threatening complications such as corneal ulceration, and eliminate the risk of more widespread extraocular disease. Bacterial conjunctivitis requires treatment with antibiotics for 5 to 7 days that may result in poor patient compliance with conventional dosage forms due to greater frequency of drug administration (2 drops every 2-3 hrs). Poor ocular bioavailability of drugs (< 1%) from conventional eye drops (i.e. solution, suspension and ointments) is due mainly to the precorneal loss factor that include rapid tear turnover, non productive absorption, transient residence time in cul-de-sac and the relative impermeability of the drugs to corneal epithelial membrane. In general, ocular efficacy is closely related to ocular drug bioavailability, which may be enhanced by increasing corneal drug penetration and prolonging precorneal drug residence time. A variety of ocular drug delivery system, such as hydrogels, microparticles, nanoparticles, microemulsions, liposomes and collagen shields have been designed and investigated for improved ocular bioavailability. In situ hydrogel system can be formulated as a liquid dosage form suitable to be administered by instillation into the eye which, upon exposure to physiological conditions (pH, temperature, ionic activation), changes to the gel phase, thus increasing the pre-corneal residence time of the delivery system and enhancing ocular bioavailability. Flouroquinolones are one of the promising groups of antibiotics, currently being used topically to treat...
conjunctivitis and corneal ulcers. It has a wider antibacterial spectrum, better bioavailability, better ocular penetration, and has the least chance of developing resistance compared with antibiotics of other groups.

**Aims & Objectives:** The purpose of our work was to develop and evaluate an ocular drug delivery system of a fluoroquinolone antibacterial agent, sparfloxacin, based on the concept of pH (Chitosan), temperature (pluronic F-127) and ion-activated (gellan gum) in situ gelation. The formulation so developed should be in liquid form at formulation condition, but when it will drop in to the eyes, the viscosity of the formulation should be increased due to physiological condition of eye i.e. pH (~7.2), temperature (~32°C) and ion (calcium ion etc present in tear buffer). Thus this will increase precorneal residence time of the drug with no compromise with vision and therapeutic efficacy of formulation.

**Methods/Study Design:** Different placebo formulation were prepared and tested for best combination. Formulation which gave the best result was considered the optimized formulation and subjected to rheological studies and in vitro release studies. The optimized formulations were subjected to Microbiological assay which was carried out against *Pseudomonas aeruginosa* using cup-plate method. Precorneal residence time was studied on albino rabbits by gamma scintigraphy after radiolabelling of sparfloxacin by Tc-99m. Ocular tolerance of developed formulation was also studied by HET-CAM method. Stability studies were carried out as per ICH (International Conference on Harmonization) guidelines to determine the shelf life of the developed formulation.

**Results/Findings:** A combination of 0.5% w/v Chitosan, 9% w/v pluronic F-127 and 0.25% of gellan gum was found appropriate for in situ gel formulation. Gelation pH and gelation temperature of the formulation was found to be ~ 7.2 and 32°C respectively (Table 1). In vitro release from developed formulation in simulated tear fluid, pH 7.4 showed an extended release profile of sparfloxacin. Curve fitting of in-vitro release data of optimized formulation was compared with different release model to select best fitting model using PCP Disso V 3.0 software. The best fit kinetic model was matrix model, suggesting non-fickian diffusion process. Microbial assay shows clear zone of inhibition. And reveals prolong microbial efficacy of developed in situ gel as compared to marketed eye drops. The observation of acquired gamma camera images showed good retention over the entire precorneal area for developed formulation as compared to marketed formulation (Fig.1). Marketed drug formulation cleared very rapidly from the corneal region and reached to systemic circulation through nasolachrymal drainage system, as significant radioactivity was recorded in kidney and bladder after 2h of ocular administration, whereas developed formulation cleared at a very slow rate (p<0.05) and remained at corneal surface for longer duration as no radioactivity was observed in systemic circulation. HET-CAM assay further proves the non irritant property of developed in situ gel. Formulation was non-irritant up to 8 h (mean score 0) while the mean score was found to be 0.33 up to 24 h The developed in situ gel was found to be stable for longer duration of time imparting a shelf life of 2 years to the product.

**Limitations:** Clinical trial was not done yet. Application is under consideration of Human ethical committee for approval.

**Conclusion:** The developed in situ gel formulation gives extended release with better tolerability and prolonged retention at corneal site as compare to marketed formulation. It is suitable for sustained ocular drug delivery and can go up to the clinical evaluation and application.

**Key words:** Ophthalmics, conjuctivitis, in situ gel, gamma scintigraphy

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**Table 1:** Physicochemical properties of the developed in situ gel formulation

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clarity</td>
<td>Clear solution</td>
</tr>
<tr>
<td>pH</td>
<td>6.0-6.1</td>
</tr>
<tr>
<td>Osmolarity</td>
<td>296-301 mOsmol</td>
</tr>
<tr>
<td>Gelation pH</td>
<td>7.0-7.2</td>
</tr>
<tr>
<td>Refractive Index</td>
<td>1.332-1.337</td>
</tr>
<tr>
<td>Viscosity (at pH 6.0)</td>
<td>40±5 cps</td>
</tr>
<tr>
<td>Viscosity (at pH 7.2)</td>
<td>450±10 cps</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± S.D. (n=5)

**Fig. 1.** Static whole body image after 2 h of drug administration in albino rabbits (a) marketed formulation (b) developed in situ gel system
Computer tomography angiography and digital subtraction angiography as two valuable methods in the early diagnosis and treatment of intracranial aneurysms - a comparative study

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Abstract

Background: CT angiography (CTA) has been used for the early diagnosis of ruptured intracranial aneurysms whereas digital subtraction angiography (DSA) is the accepted diagnostic procedure for the assessment of intracranial aneurysms and for the preoperative treatment planning of patients suffering from subarachnoid hemorrhage (SAH). However, DSA is not the most valuable diagnostic method in all cases of aneurysms. The reported rate of negative angiography in SAH ranges from 10 to 20%. CTA can be used not only as the first diagnostic tool, but also as a control for diagnostic procedure when DSA was used firstly but the localization of aneurysm was not found or the location of SAH is unsure.

Aims: The aim of our study was to evaluate the diagnostic value of CTA in comparison with DSA and with surgical findings for the detection of intracranial aneurysms (IA) in patients with symptoms or signs indicating the presence of an aneurysm.

Material and Methods: A retrospective analysis was performed of 328 patients with the diagnosis of subarachnoid haemorrhage, who underwent open aneurysm repair or preservative treatment between January 2006 and December 2008. Eighteen cases were selected, as diagnosed with the use of both CTA and DSA for the detection of aneurysms. From the group, 9 patients (2 men, median age 46±8 years) were treated using neurosurgical intervention and 9 patients (6 men, median age 53±16,9 years) were qualified to preservative therapy. The data were evaluated with the use of statistical analysis.

Results: Comparison of demographic data, preoperative aneurysm anatomic features revealed no significant differences. Overall rate of diagnostic use of CTA and DSA in time after starting the verification of aneurysm diagnosis showed, that more frequently firstly used is CTA (mean time 0,27±0,59 day, p>0,15), whereas DSA is also used, but as the second tool, for the diagnostic confirmation (mean time 0,44±0,63 day, p>0,15). It is correlated with the accuracy of CTA and DSA in detection of IA, which were appropriately 91% in all aneurysms in CTA (ACoA-67%, MCA-100%, PCoA-100%) and 63,6% in all aneurysms in DSA (ACoA-100%, MCA-60%, PCoA-100%), p=0,118.

Conclusions: We conclude that cerebral CTA is equally sensitive to DSA in the detection of intracranial aneurysms. CTA is nowadays the best choice of diagnostic tool for detection rate in AcoA and MCA bifurcation aneurysms, besides microaneurysms, smaller than 2mm. But sensitivity in smaller aneurysms can be improved with optimization of the technique. However some locations of IA still may remain problematic.

Keywords: cerebral aneurysms, CT angiography, digital subtraction angiography
Comparison of clipping vs coiling as methods of treatment in poor-grade subarachnoid hemorrhage

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Abstract

Background: Both endovascular coil embolization and surgical clipping are now firmly established as treatment options for the management of cerebral aneurysms; however both regimens have inherent risks. The standard treatment for several decades has been surgical clipping of the neck of the aneurysm. In recent years, endovascular embolization has evolved worldwide. Moreover, controversy still surrounds especially the management of poor-grade subarachnoid hemorrhage (SAH) that historically fared poorly and often were excluded from aggressive treatment.

Aims: The aim of our study was to evaluate both treatment techniques in poor-grade patients.

Methods: We retrospectively reviewed the charts, operative and embolization reports and imaging of 328 patients with the diagnosis of SAH, who underwent aneurysm treatment at single center between January 2006 and December 2008. Clinical status of the patients was assessed using World Federation of Neurological Surgeons (WFNS) grade and Glasgow Coma Scale (GCS). 27 patients were selected as cases with IV and V grade WFNS SAH. These group consisted of 18 female between the ages 30 and 71 years (mean 52,7) and 9 male between ages 24 and 70 years (mean 52,5). Patients were divided into 2 groups: group A, patients who underwent clipping; group B, patients who underwent coil embolization. The following data were evaluated: age, sex, localization of aneurysm, morphological parameters of aneurysms found in CTA and DSA. Short-term outcome was measured with Glasgow Outcome Scale (GOS).

Results: 33 aneurysms were treated. The aneurysm location were middle cerebral artery (45,5%), anterior communicating artery (24,2%), internal carotid artery (12,1%), pericallosal artery (6,1%), basilar artery (6,1%), vertebral artery (3%) and posterior communicating artery (3%). The diameter of the aneurysms ranged from 2 to 47 mm with mean 8,8 mm. The mortality rate after 14 days in group A was 47,8% and 25% in group B. In group A 30,4% were GOS 2, 43,5% were GOS 3 and 26,1% were GOS 4 after the operation. In this group in 52,2% patients conditions had worsen during one to fourteen days. In group B 50% were GOS 3 and 50% were GOS 4. In this group in 25% patients conditions had worsened. The periprocedural technical complication rate was 17,4% in group A and 25% in group B. Coil embolizations were unsuccessful due to vasospasms and atherosclerosis.

Conclusion: The results of this study demonstrate that endovascular treatment is associated with better outcome in patients with ruptured intracranial aneurysms with WFNS grades IV and V. This is especially important in patients within these grades due to their potential for obtaining higher functional and physical recoveries.

Keywords: cerebral aneurysms, subarachnoid hemorrhage, coil embolization, surgical clipping
Comparing Different Antiemetic Regimens for Chemotherapy Induced Nausea and Vomiting

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Saugat Dey
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Abstract

Background: Chemotherapy Induced Nausea and Vomiting (CINV) is a major problem for all cancer patients. 5-hydroxytryptamine 3 (5-HT3)-receptor antagonists or serotonin antagonists used along with dexamethasone is the most widely used antiemetic regimen in chemotherapy. But the best drug of the different serotonin antagonists, which is both efficacious and economic, remains a matter of debate.

Aims & Objectives: To compare the relative efficacies and safeties of ondansetron, granisetron and palonosetron, when used along with equal dose of dexamethasone, in moderately to highly emetogenic chemotherapy by a double blind, randomized controlled trial in order to obtain the most potent and cost effective drug.

Methods: 1213 adult patients, 487 on highly and 726 on moderately emetogenic chemotherapy, admitted in various departments of a teaching hospital in India from November 05, 2007 to September 30, 2009 were included in the study. Patients were randomly assigned to receive ondansetron 8 mg or granisetron 3mg or palonosetron 0.75 mg (single dose), 30 min before receiving chemotherapy, along with 16 mg of intravenous dexamethasone on Day 1 and 4mg on Day 2 and 3. The observation period started with the initiation of chemotherapy (0 h) and continued for 24 h after completion of the chemotherapy for acute emesis and up to Day 5 for delayed nausea and vomiting.

Results: For highly emetogenic regimens, 52 of 64 patients (81.2%) had complete response during the acute phase in palonosetron group compared with 181 of 237 patients (76.4%) in the ondansetron group and 130 of 186 patients (69.9%) in granisetron group. During the delayed phase, 41 patients (64%) had complete response in the palonosetron group compared with 133 patients (56.1%) in the ondansetron group and 114 patients (61.2%) in granisetron group.

For moderately emetogenic regimens, 86 of 93 patients (92.5%) had complete response during the acute phase in palonosetron group compared with 291 of 379 patients (76.8%) in the ondansetron group and 210 of 254 patients (82.6%) in granisetron group. During the delayed phase, 63 patients (67.7%) had complete response in the palonosetron group compared with 216 patients (57%) in the ondansetron group and 162 patients (63.8%) in granisetron group. Main treatment related side effects were constipation and elevation of liver enzymes which was comparable for all the 3 drugs.

Conclusion: When administered with dexamethasone before chemotherapy, although palonosetron is found to be more efficacious, cost wise ondansetron may be preferred in highly emetogenic regimens, although palonosetron requires only a single dosing. However in moderately emetogenic regimens, granisetron outshines ondansetron and is further outshined by palonosetron in both acute and delayed emesis and thus the decision should be taken as per patient profile.

Study Limitations: The study has fewer numbers of patients taking palonosetron due to financial limitations of the patients, which is present in any developing country. Although we have compared
the cost and availability of the 3 drugs, a detailed cost analysis could not be done due to paucity of resources.

**Keywords:** Chemotherapy induced nausea and vomiting, 5-HT3 receptor antagonist, dexamethasone, ondansetron, granisetron, palonosetron.

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n05-03.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n05-03.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Influence of Alpha-Lipoic Acid on Streptozotocin Induced Diabetic Cardiomyopathy in Adult Male Albino Rats: A Biochemical and Microscopical Study

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Abstract

Background: Cardiovascular disease is responsible for 80% of deaths among diabetic patients. These patients may suffer from diabetic cardiomyopathy.

Aim of the work: Investigation of biochemical and ultrastructural changes of the diabetic hearts and effect of supplementation with alpha-lipoic acid (ALA).

Materials and Methods: Thirty adult male albino rats were divided into: group I control, group II diabetic and group III diabetic rats receiving ALA. Diabetes was induced in groups II and III by streptozotocin drug. The animals were sacrificed after 16 weeks. The hearts and sera were prepared for biochemical and microscopical studies.

Results: Diabetic (group-II) animals showed significant increase in sera of glucose, malondialdehyde (MDA), cholesterol and hepatic tissue glucose-6-phosphatase enzyme (G-6-Pase) activity in addition to a significant decrease in heart tissue glutathione (GSH). Structurally, cardiac muscle fibers appeared swollen with areas devoid of fibers, with collagen deposition. Ultrastructurally, diabetic hearts showed poorly organized myofibrils and sarcomeres, disrupted Z lines, dilated sarcoplasmic reticulum, abnormal mitochondria with heterogenous electron dense matrix and disrupted mitochondrial membranes. In diabetic (group-III) animals, ALA ameliorated biochemical, structural and ultrastructural changes.

Conclusion: The supplementation of ALA in diabetic rats had a possible protective effect against the risk of the progression of cardiovascular diseases during diabetes.

Keywords: Diabetic cardiomyopathy, Alpha-lipoic acid, ALA, ultrastructural, biochemicals
A Novel Psychophysiological Model of the Effect of Alcohol Use on Academic Performance

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Abstract

Background: The blood glucose concentration might determine the degree of academic performance. Decrease in the glucose concentration leads to a lowering of cognitive functions.

Aims & Objectives: To produce a model of students’ alcohol use based on glucose homeostasis control and cognitive functions.

Methods / Study Design: The study involved 13 male volunteers (8 moderate alcohol users and 5 non-alcohol users) – medical students and took 6.5 hours on fasting. Selection criteria were based on a screening survey conducted among students in Minsk, Belarus. Out of 1499 students, 185 were abstainers, 1052 – moderate drinkers, 262 – problem drinkers. The experiment was divided into three phases: first phase – the students were administered AUDIT, MAST, CAGE, STAI, Academic Performance questionnaires; second phase - the students worked with text № 1 (physiology of bone tissue and subsequently answered on the questions that followed it); third phase – with text № 2 (physiology of autonomic nervous system and also answered subsequently on the questions that followed it). Blood glucose level was measured at 2 hours intervals, including the initial level. Tests on short-term, long-term memory and attention were used in every phase of the experiment. The t-test was employed for statistical analysis of results. The probability value for significance was set at p<0.05.

Results / Findings: The moderate drinkers had significantly lower glucose concentration after 4-6 hours, compared to their initial concentration, as well as to the values of the abstainers. Disturbances in cognitive functions, precisely a decrease in the effectiveness of active attention and a faster development of fatigue after 4-6 hours of mental work in alcohol users, compared to abstainers was statistically proven. The Intellectual Capacity on various tests/tasks positively correlated with the blood glucose level and in the 2-3 phases of the experiment and according to the results of the academic performances (r= +0.75; p<0.01). Alcohol users had 12.5–40.0 times higher number of errors on various tests/tasks than the non-alcohol users (p<0.001). The errors made on various tests/tasks increased with decrease in the blood glucose concentration (r= – 0.83; p<0.01). Significant increase in VPC among abstainers was also observed (p<0.05).

Conclusion: This is the first study to show that alcohol use, even in episodic moderate doses (28ml/person with 1-2 times frequency per month) is accompanied by long-term glucose homeostasis
disorders, leading to cognitive function disturbances and a decrease in the effectiveness of mental activities. These disorders in glucose homeostasis, cognitive functions were retained after 7-10 days of moderate alcohol use and might be the reason for the low academic performances among students who use alcoholic beverages.

**Keywords:** Psychophysiological model, alcohol use, academic performance, glucose homeostasis, cognitive functions, students

**Full Text:** [http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n06-01.htm](http://www.iomcworld.com/ijcrimph/ijcrimph-v02-n06-01.htm) (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Developing a transgenic marker to research Huntington’s disease in Drosophila melanogaster

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Abstract

Background: Huntington’s disease is an autosomal dominant disease where the huntingtin protein is expanded by polyglutamines, increasing its capacity to aggregate. This results in a toxic gain of function of the protein. One of the major ways soluble monomer, oligomers and aggregations can be degraded is by macroautophagy (from here after referred to as autophagy). Furthermore, defective autophagy is involved in the pathology of neurodegenerative diseases. LC3 is a protein incorporated uniquely into the membrane of an autophagosome, which is the apparatus of autophagy, and is widely accepted as a marker of autophagy. A relatively new assay has been developed by Kimura where the different stages and activity of autophagy can be more closely studied. This system is based on the production of a fusion protein of LC3 tagged with two fluorescent markers, monomeric red fluorescent protein (mRFP) and a green fluorescent protein (EGFP), and has already been used in mammalian cells.

Aims & Objectives: The aim of this project is to use this system in vivo targeting the mRFP-EGFP-rLC3 construct into the Drosophila genome by site specific integration.

Methods/Study Design: We attempted this by placing the LC3 marker into a Drosophila vector pUAST attB. After inserting the marker into the vector the construct was then tested using Drosophila embryonic cell cultures and analysis by fluorescence microscopy.

Results/Findings: When the construct was tested in Drosophila embryonic cells, expression of the two colours red and green were seen, showing that the construct was being expressed correctly. These were the phenotypes of the mRFP and EGFP. The intensity of these colours changed when the levels of autophagy were varied using bafilomycin and rapamycin; however, only a small qualitative difference was seen.

Conclusion: For this construct to be used as a useful marker for autophagy, a robust quantitative analysis still needs to be undertaken. Dose response curves would also produce important data in trying to ascertain what level of calibration is needed to effectively use this transgenic marker.

Keywords: Huntington’s, autophagy, transgenesis

Full Text: http://www.ijcrimph.org/ijcrimph-v02-n06-02.htm (International Journal of Collaborative Research on Internal Medicine & Public Health (IJCRIMPH))
Implications of Weight Gain during Pregnancy in Pakistan

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Abstract

Background

Maternal weight and weight gain during pregnancy are related to fetal weight and outcome as they are surrogates for maternal nutrition and health. Prepregnant body mass index and total weight gain during pregnancy are important determinants of birth weight. Obesity is associated with major risks of adverse pregnancy outcome in deprived population. This communication describes the modern changes in obesity during pregnancy especially in deprived society.

Objectives: To determine the influence of maternal Prepregnancy body mass index (BMI) and total weight gain during pregnancy on perinatal outcome in a low resource Pakistani community.

Study design: Population based prospective cohort study

Setting: Periurban area of three union councils (UCs) in Gadap Town, Karachi, Pakistan

Duration: from June 2007 to June 2008

Methodology: A total of 1039 women were assessed for nutritional status (BMI Kg/m^2 and waist measurements in centimeters) before conception and/or in early first trimester pregnancy before 10th weeks of pregnancy. Prepregnancy BMI categorized into four major groups recommended by Institute of medicine and WHO guidelines for Asian and Pacific populations. All pregnancies were followed for weight gain for Perinatal outcome. Data were analyzed using SPSS windows version 15. Mean ±SD for numerical and proportions for categorical data was obtained. Statistical tests chi square test was used to compare means and calculation of P values.
**Results:** Total numbers of deliveries were 1039 observed during the study period. Mean estimated weight gain from conception was 6.5 Kg±4.2. The average weight gain during pregnancy in the first trimester was 1.50 ±.06 Kg. Total weight gain during second and third trimester ranged between 0.40-0.90 Kg per week. The Prepregnancy Waist measurement at categories (≤80≥Cms) on Perinatal outcome revealed live 488 (69.6%) and Perinatal mortality 213(30.4%). Most of the mothers delivered alive babies 701 (67.5%) and reproductive failure was abortion 209(20%) and Perinatal mortality 129(12.4%). Low birth weight <2500 gms were 145(17.6%) and above 2500 gms 680(82.4%).

**Study Limitations:** The study had logistic limitations of collecting data for whole length of pregnancy therefore three to five observations were collected from each index pregnancy included in the study.

**Conclusion:** The implication of these findings are that BMI can no longer be used as a measure of over nutrition leading to increased fetal size in deprived populations and that the mechanisms of fetal death are different in deprived situations where fetal precedence does not apply.

**Keywords:** Prepregnancy Body Mass Index, weight gain during pregnancy, Perinatal outcome, Waist measurement, Obesity and pregnancy, Low birth weight
Narakas Classification of Obstetric Brachial Plexus Palsy Revisited

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Abstract

Background

Narakas classified babies with obstetric palsy into 4 groups: upper Erb's, extended Erb's, total palsy, and total palsy with a Horner. Over the last 15 years, it was noted at our obstetric palsy clinic that good spontaneous recovery in newborns with extended Erb's palsy (C5, C6, C7 injury) was more likely if they recovered active wrist extension against gravity before two months of age. A hypothesis was made that newborns with extended Erb's palsy (Narakas Group II) may be subclassified into two groups according to this "early recovery of wrist extension." In a retrospective study of 581 cases with strict inclusion criteria, the hypothesis was found to be true: patients with extended Erb's and "early recovery of wrist extension" have a highly significant higher percentages of good spontaneous recovery of limb function than those with extended Erb's and "no early recovery of wrist extension" (P<0.0001 by Chi-square test).

Narakas (1987) classified babies with obstetric brachial plexus palsy (OBBP) into four groups (Table 1). Birch (2002) considered the classification an important contribution to the clinical analysis of OBBP and stated that it deserves to be better known and more widely used. Birch recommended that the classification should be applied after about two weeks (post-delivery), by which time lesions due to simple conduction block have begun to recover. He also recommended that the classification should not be used as indication for primary exploration of the brachial plexus. However, as one goes down from Group 1 to 4, the overall prognosis for spontaneous recovery gets worse and hence the likelihood for primary surgery gets higher and this was confirmed by Bisinella and Birch (2003).

Over the past 15 years, the senior author (MMA) has noted that good spontaneous recovery in newborns with extended Erb's (Group 2) was more likely if they recovered active wrist extension against gravity before two months of age. A hypothesis was put that patients with extended Erb's may be subclassified into two groups according to this "early recovery of wrist extension". The following study was designed to test this hypothesis.

Patients and Methods

A retrospective review of the data from our OBBP clinic over the last 15 years was done. Inclusion criteria were as follows: vaginal delivery, cephalic presentation, the first visit to our clinic before three weeks of age, regular attendance at clinic visits, and a minimum follow-up period of 36 months. Newborns were classified into five groups as shown in Table 2. The percentage of "good spontaneous recovery" of the motor function of the limb was documented and compared between the groups. Five functions were tested: shoulder abduction, shoulder external rotation, elbow flexion, wrist extension and the overall hand function. For the former four functions, "good spontaneous recovery" was defined as full spontaneous recovery or spontaneous recovery of greater than half range of motion compared to the contralateral normal limb. Good spontaneous recovery of hand function was defined
as the recovery of a good grip and the absence of intrinsic minus posture. In our center, we perform primary brachial plexus exploration for Erb's and total palsies if there is no active elbow flexion against gravity by 4 and 3 months of age, respectively. All patients who underwent primary brachial plexus surgery in our series were found intra-operatively to have root rupture or avulsion which also confirmed that recovery would have been poor without surgery. In all patients, spontaneous recovery was documented prior to any surgical procedure to improve function. The percentages of good spontaneous recovery were compared using the Chi-square test.

**Results**

A total of 581 cases of OBBP were included in the study and were classified as follows: Group I, n = 279 (48%); Group II, n = 59 (10%); Group III, n = 44 (8%); Group IV, n = 138 (24%); and Group V, n = 61 (10%).

The percentages of good spontaneous recovery in each group at each function tested are shown in Table 3. Using the Chi-square test, the difference between Groups II and III was highly significant (P<0.0001) in all functions tested indicating that Group II have a better chance for good spontaneous recovery of all affected functions. An unexpected finding was the comparison between Groups I and II which showed better percentages of good spontaneous recovery in Group II; and the differences reached statistical significance in shoulder abduction and shoulder external rotation (P=0.034 and 0.048, respectively by Chi-square test). Furthermore, a comparison between Groups III and IV showed worse percentages of Group III in all functions except shoulder external rotation; and statistical significance was reached for elbow flexion (P=0.002 by Chi-square test). Finally, the worst spontaneous recovery was in shoulder external rotation in all five groups.

**Discussion**

Narakas classification of OBBP is useful in clinical practice because it provides an overall view of the expected prognosis soon after birth of the affected newborn. The senior author is frequently asked about the expected prognosis by the anxious parents as well as by the referring obstetrician fearing medico-legal litigation. Neurophysiological studies are difficult to interpret in the newborn because of the well known “collateral sprouting” and hence, these studies may only reach a high level of accuracy with an experienced operator (Smith, 1996). Similarly, the presence of pseudomeningocele on CT myelogram or MRI may give an idea regarding root avulsion despite the false positive/negative occurrences (Clarke and Curtis, 1995). We do not do these tests in our center because they require general anaesthesia or heavy sedation in the newborn and the radiological findings will have no impact on the decision for primary exploration of the brachial plexus.

The results of our study proved that the hypothesis is true: patients with extended Erb’s palsy may be subclassified into two groups according to “early recovery of wrist extension.” In fact, those with “early recovery” have a better outcome at the shoulder and elbow when compared to the upper Erb’s group and those with "late or no recovery" have a worse outcome in most upper limb functions when compared with total palsy and no Horner. The explanation of these findings may be withdrawn from forces applied to the brachial plexus during delivery. It is important to realize that breech babies were not included in the current study because they present a unique group with unusually high percentage of upper root avulsion (Al-Qattan, 2003; Geutjens et al., 1996; Ubachs et al.; 1995). This is explained by the fact that during difficult delivery of the “after-coming head” of breech babies, the following events occur concurrently: hyperextension of the neck of the foetus, elongation of the spinal cord and direct downtraction on the shoulders. This puts the transmitted force directly on the upper nerve roots at their fixed entry in the intervertebral foramina leading to upper root avulsion (Sunderland’s central
avulsion mechanism, Sunderland, 1991). All cases included in the current study had cephalic presentation and upper root avulsion is known to be extremely rare in these newborns (Gilbert et al, 1988). In cephalic babies with traumatic delivery, the anterior shoulder of the baby is ‘stuck’ at the symphysis pubis of the mother and lateral forces on the head lead to widening of the head-shoulder angle. As described by Sever (1916) in his experimental studies on infant cadavers, forcible separation of the head and shoulder puts the upper two cords under tension and they "stand out like violin strings." Further force will then cause a stretch injury and finally extraforaminal rupture of the upper three roots. These experimental findings could provide an explanation to our results. Group II (with early recovery of wrist extension) may have been mostly a "stretch" injury with better prognosis while Group III (with late or no recovery of wrist extension) were probably a "rupture" injury with worse prognosis. If we combine both groups, the percentage of good spontaneous recovery for elbow flexion would be 72% (74 out of 103 cases with C5/C6/C7 injury). This percentage will then be intermediate between the percentages of the "upper Erb's" group and the group with "total Erb's and no Horner".

Finally, several authors (Al-Qattan, 2003; Birch, 2000; Gilbert et al, 1988; Kay, 1998) have noted that internal rotation contracture of the shoulder is the most common secondary deformity in older children with OBBP. Our results not only confirm this observation, but also establish the fact that spontaneous recovery of external rotation of the shoulder is the worst among all affected limb functions in all types of OBBP (Table 3).

References
**Table 1: Narakas classification of obstetric palsy**

<table>
<thead>
<tr>
<th>Group</th>
<th>Name</th>
<th>Roots Injured</th>
<th>Site of Weakness/Paralysis</th>
<th>Likely Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Upper Erb's</td>
<td>C5, C6</td>
<td>Shoulder abduction/external rotation, elbow flexion</td>
<td>Good spontaneous recovery in over 80% of cases.</td>
</tr>
<tr>
<td>2</td>
<td>Extended Erb's</td>
<td>C5, C6, C7</td>
<td>As above with drop wrist</td>
<td>Good spontaneous recovery in about 60% of cases.</td>
</tr>
<tr>
<td>3</td>
<td>Total palsy with no Horner syndrome</td>
<td>C5, C6, C7, C8, T1</td>
<td>Complete flaccid paralysis</td>
<td>Good spontaneous recovery of the shoulder and elbow in 30-50% of cases. A functional hand may be seen in many patients.</td>
</tr>
<tr>
<td>4</td>
<td>Total palsy with Horner syndrome</td>
<td>C5, C6, C7, C8, T1</td>
<td>Complete flaccid paralysis with Horner syndrome</td>
<td>The worst outcome. Without surgery, severe defects throughout the limb are expected.</td>
</tr>
</tbody>
</table>

**Table 2: Classification of newborns with OBBP in the current study**

<table>
<thead>
<tr>
<th>Group</th>
<th>Name</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Upper Erb's</td>
<td>C5/C6 injury as per the first examination 2-3 weeks after birth.</td>
</tr>
<tr>
<td>II</td>
<td>Extended Erb's with early recovery of wrist extension</td>
<td>C5/C6/C7 injury as per the first examination 2-3 weeks after birth. Active wrist extension against gravity recovers on follow-up within the first two months after birth.</td>
</tr>
<tr>
<td>III</td>
<td>Extended Erb's with no early recovery of wrist extension</td>
<td>C5/C6/C7 injury as per the first examination 2-3 weeks after birth. Active wrist extension against gravity does not recover on follow-up within the first two months after birth.</td>
</tr>
<tr>
<td>IV</td>
<td>Total palsy with no Horner</td>
<td>C5/C6/C7/C8/T1 injury as per the first examination 2-3 weeks after birth. There is no Horner syndrome.</td>
</tr>
<tr>
<td>V</td>
<td>Total palsy with Horner</td>
<td>Same as group IV but with a Horner syndrome present at the initial examination.</td>
</tr>
</tbody>
</table>
Table 3: The percentages of good spontaneous recovery in the five groups of OBBP in the current study

<table>
<thead>
<tr>
<th>Function tested</th>
<th>Group I (n = 279)</th>
<th>Group II (n = 59)</th>
<th>Group III (n = 44)</th>
<th>Group IV (n = 138)</th>
<th>Group V (n = 61)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good spontaneous recovery of shoulder abduction (n, %)</td>
<td>169 (60.6%)</td>
<td>45 (76.3%)</td>
<td>8 (18.2%)</td>
<td>28 (20.3%)</td>
<td>8 (13.1%)</td>
</tr>
<tr>
<td>Good spontaneous recovery of shoulder external rotation (n, %)</td>
<td>105 (37.6%)</td>
<td>31 (52.5%)</td>
<td>5 (11.4%)</td>
<td>9 (6.5%)</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Good spontaneous recovery of elbow flexion (n, %)</td>
<td>246 (88.2%)</td>
<td>54 (91.5%)</td>
<td>20 (45.5%)</td>
<td>100 (72.5%)</td>
<td>22 (36.1%)</td>
</tr>
<tr>
<td>Good spontaneous recovery of wrist extension (n, %)</td>
<td>Not applicable</td>
<td>56 (94.9%)</td>
<td>16 (36.4%)</td>
<td>56 (40.6%)</td>
<td>17 (27.9%)</td>
</tr>
<tr>
<td>Good spontaneous recovery of hand function (n, %)</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>63 (45.7%)</td>
<td>18 (29.5%)</td>
</tr>
</tbody>
</table>

Definitions of the groups are shown in Table 2.
Outcome of Macrosomic Infants in a Low Socioeconomic Groups

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Introduction
There has been no test to predict fetal macrosomia with certainty. Fetal macrosomia is missed during pregnancy and labour. Perinatal mortality associated with fetal macrosomia is documented in some studies of few countries. The route of delivery with suspected macrosomia is still controversial. There have been maternal and fetal complications contributing in high maternal and fetal mortality and morbidity.

Rationale
The incidence and risk of macrosomia in our population is unknown. This study will provide information about: incidence of macrosomia in a rural community. There is a need for macrocosmic infants screening, National planning & implementation for macrosomia in developing countries.

Objective
To estimate the incidence and obstetric outcome of fetal macrosomia in both diabetic and non diabetic mothers

Patients and Methods
Baseline information was collected in the form of a questionnaire. Counseling and awareness regarding the presence of macrosomia was given. Prepregnancy weight was taken in the initial visit at home or hospital and total weight gain at delivery. Obstetrics outcome in terms of birth weight, mode of delivery, morbidity were collected and analyzed.

Study Design: Community-based prospective cohort study

Study Setting: The study was conducted at 3 union councils of Gadap Town Karachi, Pakistan.

Study duration: From May 2008-April 2008

Study population: All prospective mothers including diabetes and non diabetics with estimated weight greater than 3.5 Kg in last trimesters

Exclusion criteria: Women not consenting Twin pregnancy
Results

The incidence rate of macrosomia in my study was 7% per year.

9.7 Kg is the mean difference between Prepregnancy weight and total weight gain in both groups. The obstetric outcome of fetal macrosomia in both diabetic and non diabetic mothers have been shown in graph I and Tables I & II.

Fig. 1: Proportion of Macrosomiac Infants in Diabetics and Non Diabetics Patients
Table I: Weight of Baby * Mode of Delivery

<table>
<thead>
<tr>
<th>Weight of Baby</th>
<th>Mode of Delivery</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SVD</td>
<td>Instrumental Delivery</td>
</tr>
<tr>
<td>Less than 3.5</td>
<td>249(70.3%)</td>
<td>91(25.7%)</td>
</tr>
<tr>
<td>More than 3.5</td>
<td>155(67.98%)</td>
<td>53(23.24%)</td>
</tr>
<tr>
<td>Total</td>
<td>404(69.41%)</td>
<td>144(24.74%)</td>
</tr>
</tbody>
</table>

Table II: Demographic Characteristics of Study Population

<table>
<thead>
<tr>
<th>Demographic Characteristics of Study Population</th>
<th>Non Diabetics Patients</th>
<th>Diabetics Patients</th>
<th>95% C.I. for difference of Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Standard Deviation</td>
<td>Mean</td>
</tr>
<tr>
<td>Maternal Age</td>
<td>26.95</td>
<td>5.08</td>
<td>26.69</td>
</tr>
<tr>
<td>Parity</td>
<td>2.16</td>
<td>2.01</td>
<td>2.09</td>
</tr>
<tr>
<td>BMI</td>
<td>28.76</td>
<td>5.76</td>
<td>28.12</td>
</tr>
<tr>
<td>Pre-Pregnancy Weight</td>
<td>63.69</td>
<td>7.40</td>
<td>64.24</td>
</tr>
<tr>
<td>Total Weight Gain</td>
<td>73.41</td>
<td>7.09</td>
<td>73.88</td>
</tr>
<tr>
<td>Gestational Age</td>
<td>37.87</td>
<td>1.53</td>
<td>37.29</td>
</tr>
</tbody>
</table>

**Conclusion**

Incidence of fetal macrosomia in our study population was 7%.

Based on these results it is recommended that fetal macrosomia screening should be an integral part of antenatal care.