Serum Free IGF-1 and IGFBP-1 Levels are Linked to Insulin Sensitivity and Insulin Secretory Abnormalities in Bangladeshi Type 2 Diabetes Patients

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Abstract

Objectives: It is possible that insulin resistance and dysfunction in B-cell secretory function are associated with serum free insulin like growth factors-1 (IGF-1) and insulin like growth factor binding protein-1 (IGFBP-1). The purpose of this study is to determine whether type 2 diabetics in a Bangladeshi population have two distinct associations with IGF-1 and IGFBP-1.

Methods: Sixty-eight people with type 2 diabetes (DM) and 61 healthy controls without a family history of diabetes or prediabetes are studied alongside age, sex, and BMI-matched controls. The standard ELISA method is used to measure insulin, free IGF-1, and IGFBP-1. HOMA-CIGMA software uses fasting glucose and fasting insulin to calculate insulin secretory capacity (HOMA B) and sensitivity (HOMA S).

Results: The study groups did not significantly differ in their free IGF-1 and IGFBP-1 levels while fasting. However, when compared to controls in the low BMI group (BMI 23), the level of free IGF-1 in type 2 DM subjects is significantly higher (p = 0.03). There is a clear positive association between HOMA B and free IGF-1 in stepwise multiple regression analysis. In a similar manner, IGFBP-1 is positively correlated with HOMA B and HOMA S in various models. In different stepwise multiple regression analysis models, both free IGF-1 and IGFBP-1 have an inverse relationship with fasting insulin in the same study.

Conclusion: Fasting insulin levels are negatively correlated with both IGF-1 and IGFBP-1. IGF-1 is also positively associated with B-cell secretory dysfunction, and insulin sensitivity and IGFBP-1 are also positively associated with B-cell secretory dysfunction in type 2 diabetic patients.

Keywords: BMI; Free IGF-1; IGFBP-1; IGT; Type 2 DM

Introduction

Like insulin, insulin-like growth factor-1 (IGF-1) is a peptide hormone made up of an alpha and beta chain that are linked by disulfide bonds and share nearly 50% amino acid sequence homology with proinsulin. It is a multipotent growth factor that has a significant impact on metabolism and normal tissue growth. Insulin and IGF-1 share similar structures. It has been hypothesized that a decreased level of IGF-1 may play a role in diabetes. In healthy volunteers, this hormone simultaneously lowers the level of serum insulin. Although the role of IGF-1 in normal carbohydrate metabolism is still poorly understood, its mechanism of action appears to be independent of insulin receptor activation [1]. IGFs (insulin like growth factors), which in an unbound form induce glucose and amino acid uptake, circulate bound to insulin like growth factor binding proteins (IGFBPs), which modulate their bioavailability and activity. IGFBPs are a group of structurally related proteins. They also improve insulin resistance in subjects with more severe insulin resistance. Insulin is considered to be the primary regulator of IGFBP-1 level. IGFBP-1 level has been shown to be elevated in patients with insulin resistance syndromes and type 1 diabetes. These proteins are involved in a variety of metabolic functions that affect glucose and insulin metabolism in addition to their hormonal binding function. Insulin is considered to be the primary regulator of IGFBP-1 level. Serum IGFBP-1 levels tend to be low in type 2 diabetes. In a Biochemical Journal article, da Silva-Xavier et al. described a method for directly comparing the effects of knocking down expression of the insulin receptor and IGF-1 receptor genes in the MIN-6 -cell line [2]. Patients with insulin deficiency typically have elevated IGFBP-1 levels. Surprisingly, depolarizing agents' insulin secretion was not affected by either receptor loss, but glucose-mediated insulin secretion was. If hybrid IGF-insulin receptors were required for glucose-induced secretion, this could be explained by the fact that insulin and IGF-1 receptors play different roles in preserving -cells' ability to secrete insulin. In fact, these differences are found in the study. First, IGF-1 deficiency causes dysregulation of the mechanisms that regulate cellular ATP levels, which would clearly affect glucose's capacity to trigger insulin secretion [3]. On the other hand, the absence of insulin receptors does not have such a significant impact on the level of ATP in the cell. However, it does have a significant impact on the capacity of glucose to regulate the expression of key genes that regulate glucose, an effect that is absent in IGF-1 receptor knockdowns. According to Freund et al. insulin and IGF-1 regulate mitogenesis and glucose metabolism through functional insulin and IGF-1 receptors even in myeloma cell lines.

Cross-sectional correlations between altered circulating levels of IGF-1 and its binding proteins (IGFBPs) and prediabetic states, such as impaired fasting glucose and impaired glucose tolerance, are found in both type 2 diabetes and prediabetes. Recombinant human IGF-1 has been shown to increase insulin sensitivity in both healthy people and those with insulin resistance and type 2 diabetes when administered [4]. Further, IGF-1 might gainfully affect fundamental irritation, a gamble factor for type 2 diabetes and on pancreatic β-cell mass and capability. A recent study of Bangladeshi prediabetic subjects demonstrated that IGF1 and IGFBP-1 appear to be negatively associated with fasting glucose in impaired glucose tolerance (IGT) subjects, and insulin sensitivity (HOMA S) may also be negatively associated with IGFBP-1 in IGT subjects.15 However, the association was not investigated in Bangladeshi type 2 diabetic subjects [5]. There is a significant amount of inter-individual heterogeneity in the endogenous level of IGF-I and its binding proteins. As a result, the purpose of the current study is to determine whether or not the levels of insulin-like growth factor-I (IGF-I) and insulin-like growth factor binding protein-1 (IGFBP-1) in the blood are related to the primary defects of type 2 diabetes, which are insulin resistance and the capacity of beta cells to secrete insulin [6].

Materials and Methods

The Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine, and Metabolic Disorders (BIRDEM), Dhaka, hosted this cross-sectional observational study. Purposely selected from the Out-Patient Department (OPD) of BIRDEM were 68 people with type 2 diabetes and 61 healthy people with the same age, sex, and BMI who had no family history of diabetes to serve as controls with the same socioeconomic status. All of the volunteers provided written consent; using a pre-designed questionnaire, a

registered physician conducted clinical examinations. Patients with serious illness, pregnant women, and people with mental disorders were excluded from the study, as were those with Type 2 DM who had been diagnosed just one year prior [7].

Standard techniques were used to take anthropometric measurements. After a night of fasting, subjects were asked to come in the morning for the blood sample; then, 250 milliliters of water and 75 grams of anhydrous glucose were given to the subjects [8]. Two hours after loading glucose, blood was taken during fasting conditions. The commercial kits from Randox Laboratories Ltd., UK, were used to determine serum glucose, cholesterol, triglyceride, and high density lipoprotein (HDL). The following formula was used to determine the serum low density lipoprotein (LDL) cholesterol: Total cholesterol is comprised of TG/5 and HDL cholesterol [9]. The enzyme-linked immunosorbent assay (ELISA) method (Linco Research Inc., USA) was used to measure the level of insulin in the blood. The enzyme-linked immunosorbent assay (ELISA) method (Ray Biotech, USA) was used to measure serum free IGF-1 and IGFBP-1 concentrations. Using the HOMA-CIGMA software, insulin secretory capacity (HOMA B) and insulin sensitivity (HOMA S) were calculated from fasting glucose and fasting insulin.

Statistical analysis

SPSS (Statistical Package for Social Science) software for Windows version 10 was utilized for the statistical analysis. The mean, standard deviation, median, and/or percentage (%) were all used to represent the data. ANOVA or the Mann-Whitney U test were used to determine whether or not the differences in values were statistically significant. The data were analyzed using logistic and multiple regression models. It was thought to be statistically significant if the two-tailed p value was less than 0.05.

Results

Insulinemic status of the study subjects

When compared to the control group, the fasting serum insulin level was significantly higher in type 2 diabetes (p = 0.01). Insulin responsiveness (HOMA S) and B cell capability (HOMA B) was altogether lower in type 2 DM (p = 0.001) contrasted with that in Controls. Type 2 DM subjects' fasting serum free IGF-1 level and IGFBP-1 level were not significantly different from controls. However, the level of free IGF-1 in type 2 DM subjects was significantly higher (p = 0.03) than in controls in the low BMI group (BMI 23). Additionally, controls with a BMI greater than or equal to 23 had significantly higher levels of free IGF-1 than lean controls with a BMI less than or equal to 23 (p = 0.05). However, there was no significant difference in IGFBP-1 levels between the low BMI group and the high BMI group.

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Discussion

The primary cause of type 2 diabetes is insulin resistance or impaired B cell function. In comparison to healthy control subjects, the diabetic subjects in this study also demonstrated significantly lower insulin sensitivity (HOMA S) and insulin secretory capacity (HOMA B). Studies on obese type 2 diabetic subjects have shown an increasing tendency of free IGF-1 and a decreasing tendency of IGFBP-1 [10]. Studies on obese IGT subjects have also claimed similar results.19 In the present study, Bangladeshi type 2 diabetic subjects appear to have an increasing tendency of free IGF-1 and IGFBP-1 but it was not statistically significant when compared to control subjects. It has been documented that free IGF-1 and IGFBP-1 are associated with type 1 diabetes as well as obesity. Studies on Frystyck and co. 1999) have shown that the level of free IGF-1 was higher in obese controls (BMI, 31.6 0.7) than in lean controls (BMI, 22.8 0.2), but that the level of free IGF-1 in obese type 2 diabetes (BMI, 32.3 0.8) was not significantly different from that of either lean or obese controls21. 1997) have demonstrated that compared to age- and sex-matched healthy controls, the free IGF-1 level was significantly lower [11]. Another study suggested that type 2 diabetes leads to a decrease in the IGF-I while elevating the IGFBP-1 level. In a representative sample of US adults without clinical cardiovascular disease, they found that a low level of serum IGF-1 was positively associated with diabetes. The author also found that subjects with diabetic retinopathy had an age-adjusted free IGF-1 level that was higher than those of subjects without diabetic retinopathy. Contradictory results also exist in other studies where they looked at the relationship between serum IGF-1 and diabetes by age, Sandhu et al. found that only subjects under the age of 65 and not those over 65 had a positive association with diabetes. reported a positive association between a low IGF-1 level and diabetes or glucose intolerance in a sample of 615 people between the ages of 45 and 65 [12]. However, Rajpatak et al. IGF-1 levels were significantly (p = 0.03) higher in type 2 DM subjects in the low BMI group (BMI 23) compared to their counterpart controls in the Cardiovascular Health Study, which included 922 subjects over the age of 65. On this basis, we classified our subjects and found that in the low BMI group (BMI 23), the level of free IGF-1 was significantly (p = 0.03) higher in type 2 DM subjects compared to their counterpart controls. There was no independent Free IGF-1 concentrations were significantly elevated in obese subjects (free IGF-1, 1.46 1.1 g/l; another European population study supports this finding). A Korean population study reported similar findings, namely that free IGF-1 concentrations were significantly elevated in obese subjects (free IGF-1, 1.46 1.1 g/l; when compared to controls (free IGF-1, 0.91 0.9 g/l; BMI, 30 2.5) BMI, 21.3 1.4). In this study, neither type 2 diabetic subjects nor controls had significantly different IGFBP-1 levels in the low (BMI 23) or high (BMI > 23) BMI groups. In stepwise multiple regression analysis, free IGF-1 was inversely associated with fasting insulin and positively associated with insulin secretory capacity (model 7, model 8) in type 2 DM subjects [13]. However, studies have shown that obese people have significantly lower values of IGFBP-1 than lean controls and obese type 2 DM subjects. Another study conducted in the United States has shown that IGFBP-1 in type 1 diabetes was significantly higher than in healthy controls and type 2 DM subjects In type 2 DM subjects, Pearson's correlation analysis revealed a significant association between free IGF-1 and fasting serum triglyceride (r = 0.361, p = 0.03). Stepwise multiple regression analysis also revealed an inverse association between free IGF-1 and fasting triglyceride (models 6, 8, and 9) in type 2 DM subjects. Therefore, dyslipidemia may influence the blood level of free IGF-1 or the other way around [14].

In the stepwise multiple regression analysis, IGFBP-1 was found to be positively associated with HOMA S and HOMA B in type 2 diabetic subjects, while IGFBP-1 was found to be significantly associated with fasting insulin in the simple Pearson's correlation. The positive relationship of IGFBP-1 and HOMA S was additionally seen in the various relapse bend examination (r = 0.42, p = 0.001) in type 2 DM subjects.

Conclusion

Fasting insulin is negatively correlated with both IGF-1 and IGFBP-1. In Bangladeshi type 2 diabetics, IGF-1 is positively correlated with insulin secretory capacity, and IGFBP-1 is positively correlated with both insulin secretory capacity and insulin sensitivity.

Acknowledgement

None

Conflict of Interest

None

References

1. Clemmons DR. Role of insulin like growth factor in maintaining normal glucose homeostasis. Horm Res. 2004; 62: 77-82.
2. Rajpathak SN, Gunter MJ, Wylie-Rosett J, Ho GY, Kaplan RC. The role of insulin like growth factor-I and its binding proteins in glucose homeostasis and type 2 diabetes. Diabetes Metab Res Rev. 2009; 25(1): 3-12.

3. Kaushal K, Heald AH, Siddals KW, Sandhu MS, Dunger DB. The impact of abnormalities in IGF and inflammatory systems on the metabolic syndrome. Diabetes Care. 2004; 27(11): 2682-2688.

4. Cianfarani S, Clemmons DR. IGF-I and IGF binding proteins. Basic research and clinical management. Endocr Dev.2005; 9: 121-134.

5. Lehtihet M, Efendic S, Brismar K. Postprandial paradoxical IGFBP-1 response in obese patients with Type 2 diabetes. Clin Sci (Lond). 2008; 115(5): 167-174.

6. Jones JI, Clemmons DR. Insulin like growth factors and their binding proteins: biological actions. Endocrine Rev. 1995; 16: 3-34.

7. Hwa V, Oh Y, Rosenfeld RG. Insulin like growth factor binding proteins superfamily. Endocr Rev. 1999; 20(6): 761-787.

8. Lee PD, Conover CA, Powell DA. Regulation and function of insulin like growth factor binding protein-1. Proc Soc Exp Biol Med. 1993; 204: 4-29.

9. Hills FA, Gunn LK, Hardiman P. IGFBP-1 in the placenta, membranes and fetal circulation: level at term and preterm delivery. Early Hum Dev. 1996; 44(1): 71-76.

10. da Silva-Xavier G, Qian Q, Cullen PJ, Rutter GA. Distinct roles for insulin and insulin like growth factor-1 receptors in pancreatic β-cell glucose sensing revealed by RNA silencing. Biochem J. 2004; 377: 149-158.

11. Freund GG, Kulas DT, Mooney RA. Insulin and IGF-1 increase mitogenesis and glucose metabolism in the multiple myeloma cell line, RPM1 8226. J Immunol. 1993; 15: 1811-1820.

12. Swapnil N Rajpathak, Marc J Gunter, Judith Wylie-Rosett, Gloria YF Ho, Robert C Kaplan. The role of insulin like growth factor-I and its binding proteins in glucose homeostasis and type 2 diabetes. Diabetes Metab Res Rev. 2009; 25: 3-12.

13. Rajpathak SN, McGinn AP, Strickler HD, Rohan TE, Pollak M. Insulin like growth factor-(IGF)-axis, inflammation, and glucose intolerance among older adults. Growth Horm IGF Res. 2008; 18(2): 166-173.

14. Sandhu MS, Heald AH, Gibson JM, Cruickshank JK, Dunger DB. Circulating concentrations of insulin like growth factor-I and development of glucose intolerance: a prospective observational study. Lancet. 2002; 359(9319): 1740-1745.

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