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Original Article

Increased concentration of circulating visfatin associates with post-challenged hyperglycaemia and insulin resistance in IGT subjects

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الملخص

هدف البحث: إن "فيزفاتين" هو بروتين خلوي يزيد عند مرضى داء السكري من النوع الثاني والمصابين بالسمنة. ولكن دوره في نمو داء السكري لا يزال غير معروف. من هنا تهدف هذه الدراسة إلى بحث مستويات فيزفاتين بمصل الدم قبل الإصابة بداء السكري.

طرق البحث: تطوع ١٧ ممن لديهم اختلال السكر عند الصوم، و٤٤ لديهم ضعف تحمل الجلوكوز، و١٦ لديهم اختلال السكر عند الصوم وضعف تحمل الجلوكوز معا مع ٥١ شخصا صحيحا. تم قياس الأنسولين عند الصوم وفيزفاتين باستخدام تقنية "إليزا". تم تقدير نموذج تقييم حساسية الأنسولين المتوازن والقدرة الإفرازية للخلية ب باستخدام برمجيات هوما- سيجما.

النتائج: كانت قدرة الأنسولين الإفرازية أقل عند اختلال السكر عند الصوم، ولدى الذين لديهم اختلال السكر عند الصوم وضعف تحمل الجلوكوز معا، وحساسية الأنسولين عند اختلال السكر عند الصوم، وعند الذين لديهم اختلال السكر عند الصوم وضعف تحمل الجلوكوز معا أقل بكثير بالمقارنة بالمجموعة الضابطة. مستوى فيزفاتين بمصل الدم عند الصوم كان أعلى بكثير عند المصابين باختلال السكر عند الصوم (٢.٦١±٥.٠٨)، وعند ضعف تحمل الجلوكوز (٢.٨١±٤.٧٥)، وعند المصابين باختلال السكر عند الصوم وضعف تحمل الجلوكوز معا (٤.٣٣± ٢.٦٨) مقارنة بالمجموعة الضابطة (١.٢±٢.٦٠). وجد أثناء تحليل الإنحدار اللوجستي الثنائي أن فيزفاتين يرتبط بشكل كبير عند المصابين باختلال السكر عند الصوم، والمصابين بضعف تحمل الجلوكوز، والمصابين باختلال السكر عند الصوم وضعف تحمل الجلوكوز معا. وجد أن فيزفاتين يرتبط بشكل كبير بمستوى الجلوكوز بعد الأكل وضغط الدم عند المصابين بضعف تحمل الجلوكوز. تزيد نسبة المصابين باختلال السكر عند الصوم، وضعف تحمل الجلوكوز، والمصابين باختلال السكر عند الصوم مع ضعف تحمل الجلوكوز مع زيادة تركيز الفيزفاتين.

الاستنتاجات: يبدو أن مستوى الفيزفاتين يرتبط مع اختلال السكر عند الصوم، وضعف تحمل الجلوكوز، وبهما معا يرتبط مستوى الجلوكوز بعد الأكل وضغط الدم بشكل إيجابي مع الفيزفاتين عند المصابين بضعف تحمل الجلوكوز.

الكلمات المفتاحية: فيزفاتين؛ قبل السكري؛ ارتفاع السكر في الدم؛ مقاومة الأنسولين

Abstract

Objectives: The cytokine visfatin is increased in obesity and type 2 Diabetes; however, its role in the development of diabetes is still unsettled. The present study aimed to investigate the serum visfatin levels in prediabetic subjects.

Methods: Seventeen subjects with Impaired Fasting Glucose (IFG), 44 Impaired Glucose Tolerant (IGT), 16 IFG-IGT and 51 healthy subjects were recruited. Fasting insulin and visfatin were measured using enzyme-linked immunosorbent assay (ELISA) techniques. The Insulin sensitivity Homeostasis Model Assessment (HOMA%S) and B-cell secretory capacity (HOMA%B) were estimated using HOMA-CIGMA software.

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Results: HOMA%B was significantly lower in IFG ($p = 0.0001$) and IFG-IGT ($p = 0.001$) subjects. HOMA%S in IGT ($p = 0.0001$) and IFG-IGT ($p = 0.001$) subjects were significantly lower compared to controls. The fasting serum visfatin (ng/ml) level was significantly higher in IFG (5.08 ± 2.16, $p = 0.0001$), IGT (4.75 ± 2.81, $p = 0.0001$) and IFG-IGT subjects (4.33 ± 2.68, $p = 0.013$) compared to controls (2.60 ± 1.2). In binary logistic regression analysis, visfatin has found significantly associated with IFG ($B = 0.198$, $p = 0.040$), IGT ($B = 0.162$, $p = 0.043$) and IFG-IGT ($B = 0.188$, $p = 0.044$). Visfatin was also found significantly correlated with postprandial serum glucose and blood pressure in IGT subjects. Frequency of IFG, IGT and IFG-IGT subjects increased with increasing visfatin concentrations.

Conclusions: Serum visfatin appear to be associated with IFG, IGT and IFG-IGT. Postprandial serum glucose and blood pressure are positively associated with visfatin levels in IGT subjects.

Keywords: Hyperglycaemia; Insulin resistance; Prediabetes; Visfatin

Introduction

Visfatin is an adipocytokine that was identified in 2005.[1] This cytokine was named based on it being primarily produced by visceral fat. Visfatin has a molecular weight of 52 kda and is composed of 491 amino acid residues. Visfatin is identical to pre-Beta-cell colony-enhancing factor (PBEF), described in 1994 as a cytokine produced by lymphocytes, acting on lymphocyte maturation and inflammatory regulation.[2] In addition to being produced in human leukocytes and adipose tissue, visfatin is also expressed in human and animal hepatocytes and muscles[3,4] and in animal adipocytes, kidney and heart.[5–7] Visfatin is believed to exhibit endocrine, paracrine and autocrine activities. The autocrine effects of visfatin may play an important role in regulating insulin sensitivity in the liver.[6]

In mice, visfatin was found to play an important role in the reduction of the blood glucose concentration.[1] Visfatin displays insulin mimetic effects, which was thought to be mediated through the phosphorylation of signal transduction proteins in the insulin signalling pathway and through binding to the insulin receptor at a site distinct from that of insulin.[8] Recent studies also demonstrated that serum visfatin levels were significantly higher in the diabetic compared with the nondiabetic group and found a significant positive correlation of serum visfatin levels with the obesity indicator BMI and waist circumference, even after adjusting for age, sex, smoking status, blood pressure and lipid profile.[9,10]

Visfatin is an essential enzyme in NAD (nicotinamide adenine di-nucleotide) production, and it exists both in intra and extracellular environments.[7] Mice with heterozygous mutations in the visfatin gene display glucose intolerance mainly due to insulin secretion deficiency, and this insulin secretion defect can be corrected by the administration of nicotinamide mononucleotide (NMN), the product of visfatin in NAD biosynthesis.[7] Because the pancreas has very low levels of intracellular visfatin, some have suggested that the maintenance of high NMN circulating levels by extracellular visfatin are critical for normal beta-cell function.[7] A study that investigated glucose uptake in animal hepatocytes with reduced visfatin expression demonstrated reduced NAD biosynthesis and a significantly decreased incremental uptake of glucose after stimulation with insulin when compared with control hepatocytes with normal visfatin expression.[6] A negative correlation of visfatin levels with beta-cell function was demonstrated by studying acute insulin secretion assessed via an intravenous glucose tolerance test.[11] Furthermore, continuous glucose infusion in humans acutely increases visfatin levels. This effect is suppressed by insulin or somatostatin infusion.[12] The relationship between insulin resistance and blood or tissue visfatin concentrations remains unclear. Some studies indicate that blood visfatin concentrations significantly correlate with insulin resistance or type 2 diabetes but not with body fat percentage or body mass index (BMI).[13,14] Other studies demonstrated that the association between diabetes and blood visfatin concentrations was not significant after adjusting for body mass index (BMI) and waist circumference.[15] A recent study found that visfatin levels were inversely associated with insulin resistance in non-diabetic obese women with energy restricted diet intervention.[16]

The natural history of type 2 diabetes (T2D) has been demonstrated to pass through an intermediate stage of impaired fasting glucose (IFG) and/or impaired glucose tolerance (IGT), which is designated as impaired glucose regulation (IGR) by the World Health Organization (WHO) or pre-diabetes by the American Diabetic Association (ADA). The association of visfatin has not been extensively studied with the three groups of prediabetic (IFG, IGT and IFG-IGT) subjects, yet it is important to know whether visfatin levels increase before the onset of diabetes.

Materials and Methods

Seventy-five prediabetic subjects (IFG 17; IGT 44 and IFG-IGT 14) were recruited in this study from the Out-Patient Department (OPD) of BIRDEM (Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders) Hospital, Dhaka. The subjects were considered as IFG, IGT or IFG-IGT based on the WHO guidelines.[17] Fifty-one healthy subjects without a family history of diabetes were also recruited in this study to serve as the controls.

On a prescheduled morning, the subjects were requested to arrive after overnight fast (8–10 h to provide a fasting blood sample. The theme of the study was explained to the subjects and a written consent was taken. After taking 10 ml of fasting blood samples, the subjects were given 75 g of glucose dissolved in 250 ml of water. The blood was taken via

venepuncture during the 2 h after the glucose load. After 10–15 min of collection, the blood samples were centrifuged for 10–15 min at 3000 rpm to obtain the serum, which was then kept frozen at −30 °C until further biochemical analysis.

The anthropometric indices and total body fat mass were determined following standard procedures. Glucose was measured using the glucose-oxidase method, and the lipid profiles were measured using the enzymatic endpoint method (Randox Laboratories, Northern Ireland, UK). Insulin (Linco Research, Missouri 63304, USA) and plasma visfatin (ALPCO Diagnostics, USA, cs@alpco.com) were measured using an enzyme linked immunosorbent assay (ELISA). Visfatin intra assay variation was measured using 6 replicates of a pooled serum sample, and the coefficient of variation was 8%. Insulin secretory capacity (HOMA%B) and insulin sensitivity (HOMA%S) were determined using fasting glucose and fasting insulin using HOMA-Sigma software.[18]

Statistical analysis

The data were analysed using Statistical Package for Social Science (SPSS, Chicago, Illinois, USA) for Windows version 12. The quantitative variables were expressed as the mean ± standard deviation (SD). The baseline characteristics between the prediabetic groups (IFG, IGT and IFG-IGT) and non-diabetic controls were assessed using student's t-test. The data that were not normally distributed were log transformed before the analysis. The distribution of prediabetes in the different quartiles of visfatin were analysed by χ^2-test. The associations of the serum visfatin with prediabetes were analysed using binary logistic regression. The correlations between the two continuous variables were analysed using Spearman's correlation. A p-value of <0.05 was considered statistically significant.

Results

The fasting insulin levels were significantly higher in the IGT ($p = 0.002$) and IFG-IGT ($p = 0.017$) subjects compared with the controls (Table 1). The mean TG levels were significantly higher in the IFG ($p = 0.002$), IGT ($p = 0.0001$) and IFG-IGT ($p = 0.013$) subjects compared with the controls. The insulin secretory capacity (HOMA% B) was significantly lower in the IFG ($p = 0.0001$) and IFG-IGT ($p = 0.001$) subjects and significantly higher in the IGT subjects compared with the controls. Insulin sensitivity (HOMA%S) was significantly lower in the IGT ($p = 0.0001$) and IFG-IGT ($p = 0.001$) subjects compared with the controls (Table 2). Insulin resistance (HOMA IR) was also significantly higher in the IFG ($p = 0.031$), IGT ($p = 0.0001$) and IFG-IGT ($p = 0.002$) subjects compared with the controls (Table 1).

The fasting serum visfatin (ng/ml) level was significantly higher in the IFG (5.08 ± 2.16, $p = 0.0001$), IGT (4.75 ± 2.81, $p = 0.0001$) and IFG-IGT (4.33 ± 2.68, $p = 0.013$) subjects compared with the controls (2.60 ± 1.20) (Table 1). In the binary logistic regression analysis, when the control group was set as the reference and the effects of age, gender and BMI were justified, the serum visfatin levels significantly associated with the IFG ($B = 0.198$, $p = 0.040$), IGT ($B = 0.162$, $p = 0.043$) and IFG-IGT ($B = 0.188$, $p = 0.044$) groups (Table 2).

Table 1: Clinical characteristics and glycaemic, insulinaemic, lipidaemic and serum visfatin status among the control, IFG, IGT and IFG-IGT subjects.

	Controls, n = 51	IFG, n = 17	IGT, n = 44	IFG-IGT, n = 14	*p-values*		
					Control vs. IFG	Control vs. IGT	Control vs. IFG-IGT
M/*F* ratio	27/24	7/10	24/20	6/8	–	–	–
Age, yrs	42 ± 6	45 ± 7	42 ± 7	43 ± 6	0.103	0.958	0.435
BMI, kg/m^2	24.5 ± 4.1	24.3 ± 3.3	25.3 ± 4.6	26.3 ± 5.5	0.881	0.366	0.167
WHR	0.91 ± 0.06	0.94 ± 0.06	0.93 ± 0.07	0.91 ± 0.09	0.062	0.212	0.851
BF (%)	28 ± 6	31 ± 7	30 ± 7	29 ± 9	0.085	0.278	0.666
SBP, mm-hg	110 ± 13	113 ± 9	116 ± 16	113 ± 10	0.519	0.068	0.525
DBP, mm-hg	74 ± 8	78 ± 6	76 ± 10	71 ± 8	0.080	0.159	0.326
FSG, mmol/l	5.1 ± 0.4	6.4 ± 0.3	5.3 ± 0.5	6.4 ± 0.3	***0.0001***	0.617	***0.0001***
PPSG, mmol/l	6.1 ± 1.1	6.4 ± 1.2	9.3 ± 0.8	9.9 ± 0.7	0.221	***0.0001***	***0.0001***
Insulin, μIU/ml	9.6 ± 2.5	9.2 ± 1.3	12.4 ± 4.7	11.8 ± 3.0	0.538	***0.002***	***0.017***
HOMA %B	107 ± 25	68 ± 14	121 ± 45	79 ± 18	***0.0001***	***0.019***	***0.001***
HOMA %S	85 ± 18	76 ± 14	65 ± 18	61 ± 16	0.662	***0.0001***	***0.001***
HOMA IR	1.17 ± 0.21	1.38 ± 0.24	1.69 ± 0.54	1.71 ± 0.43	***0.031***	***0.0001***	***0.002***
TG, mg/dl	119 ± 37	191 ± 82	186 ± 89	197 ± 101	***0.002***	***0.0001***	***0.013***
Chol, mg/dl	193 ± 31	214 ± 78	203 ± 50	202 ± 36	0.370	0.423	0.508
LDL, mg/dl	135 ± 31	142 ± 80	132 ± 43	125 ± 31	0.649	0.686	0.285
HDL, mg/dl	34 ± 11	35 ± 6	29 ± 8	35 ± 12	0.896	***0.009***	0.750
Visfatin (ng/ml)	2.6 ± 1.2	5.08 ± 2.16	4.75 ± 2.81	4.33 ± 2.68	***0.0001***	***0.0001***	***0.013***

Data are expressed as the mean ± SD. IFG, impaired fasting glucose; IGT, impaired glucose tolerance; BMI, body mass index; WHR, waist:hip ratio; WHtR, waist:height ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; FSG, fasting serum glucose; PPSG, postprandial (2 h after 75 g glucose challenge) serum glucose; TG, triglyceride; Chol, cholesterol; HOMA%S, insulin sensitivity; HOMA% B, insulin secretory capacity; HOMA-IR, Insulin resistance using the HOMA method; RBP4, retinol-binding protein-4.

Table 2: Binary logistic regression analysis of serum visfatin levels prediabetes with the control as the reference group adjusted for the effects of covariate age, gender and BMI.

Variables	Control *vs*, IFG			Control *vs*. IGT			Control *vs*. IFG-IGT		
	B	S.E.	*p-value*	B	S.E.	*p-value*	B	S.E.	*p-value*
Age	0.037	0.048	0.433	−0.004	0.039	0.910	0.046	0.055	0.404
Gender	1.045	0.681	0.125	0.540	0.482	0.263	−0.150	0.757	0.843
BMI	−0.029	0.092	0.755	−0.002	0.066	0.970	0.073	0.089	0.409
Visfatin	0.198	0.096	***0.040***	0.162	0.080	***0.043***	0.188	0.093	***0.044***
Constant	−4.303	3.218	0.181	−1.228	2.359	0.603	−5.595	3.438	0.104

IFG, impaired fasting glucose; IGT, impaired glucose tolerance BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure.

In the Spearman correlation analysis, visfatin was found to be positively associated with both systolic ($r = 0.33$, $p = 0.05$) and diastolic ($r = 0.41$, $p = 0.017$) blood pressure in the IGT subjects. Postprandial (2 h after 75 g glucose ingestion) serum glucose was also found to be positively correlated ($r = 0.36$, $p = 0.041$) with the fasting serum visfatin levels in these subjects. The insulin secretory capacity and insulin sensitivity did not show a significant correlation with the fasting serum visfatin levels (Table 3). The insulin secretory capacity (HOMA B) was found to be significantly correlated with the serum visfatin levels in the control subjects but not with the other groups. Upon regression curve fitting, the fasting serum visfatin level was significantly correlated with BMI in the IFG ($R^2 = 0.716$, $p = 0.001$) and IGT ($R^2 = 0.180$, $p = 0.014$) subjects and marginally significant in the IFG-IGT ($R^2 = 0.382$, $p = 0.057$) subjects, but it was not significant in the controls (Figure 1).

To examine the association between the plasma visfatin concentrations and other parameters related to insulin resistance, we divided our study subjects into plasma visfatin concentration quartiles (Table 4). The proportion of the IFG, IGT and IFG-IGT subjects increased with increasing visfatin concentrations, which is significantly associated in the χ^2-test. Additionally, the female sex, body fat percentage, diastolic blood pressure, post-challenge plasma glucose levels, TG levels and HOMA-IR values positively correlated with increasing visfatin concentrations. Body fat percentage, diastolic blood pressure and postprandial plasma glucose in the subjects of the fourth quartile were significantly higher compared with the first quartile using unpaired student's t test. Similarly, the HOMA IR and TG values were also shown significantly higher in the third quartile compared with the first quartile.

Discussion

This study, which examined the inflammatory mediator visfatin in prediabetic subjects, has three major findings. First, the fasting serum visfatin level was significantly higher in the IFG, IGT and IFG-IGT subjects compared with the controls, and binary logistic regression analysis showed a significant association of visfatin with IFG, IGT and IFG-IGT after adjusting for the effects of age, BMI and gender. Second, the serum visfatin levels in the IGT subjects significantly correlated with blood pressure and postprandial blood glucose levels. Third, in the regression curve fitting, the serum visfatin concentration was significantly and positively associated with BMI in the IFG and IGT subjects.

Type 2 diabetes mellitus has been suggested to be a disease of the innate immune system responsible for an ongoing cytokine-mediated acute phase response and low-grade chronic inflammation, which may be involved in the atherosclerosis exhibited in diabetes mellitus patients.[19] Therefore, it is important to determine whether signs of an activated innate immune system are present before the onset of type 2 diabetes mellitus. Recent studies documented that the adipose tissue derived cytokine, visfatin, has a role in the activation of insulin receptors in different cells. Additionally, visfatin enhanced glucose and lipogenic transfer in 3T3-L1 adipocytes and L6 myocytes and decreased glucose secretion by hepatocytes *in vitro*.[1] Visfatin may be secreted from 3T3-L1 adipocytes and may be associated with endoplasmic reticulum and Golgi or micro-vesicles.[20] Another study reported that hyperglycaemia might increase the synthesis of visfatin in cultured adipocytes.[12]

This study attempted to measure the circulating visfatin levels in healthy subjects of the Bangladeshi population. The

Table 3: Correlation of visfatin with blood pressure, glycaemic and insulinaemic status among the study subjects.

Visfatin *Vs*	Controls, n = 51	IFG, n = 17	IGT, n = 44	IFG-IGT, n = 14
SBP	r = 0.026, p = 0.873	r = −0.044, p = 0.866	***r = 0.33, p = 0.05***	r = −0.013, p = 0.97
DBP	r = 0.108, p = 0.508	r = 0.159, p = 0.543	***r = 0.41, p = 0.017***	r = 0.053, p = 0.88
PPSG	r = 0.15, p = 0.46	r = 0.35, p = 0.26	***r = 0.36, p = 0.04***	r = −0.23, p = 0.54
Insulin	***r = 0.32, p = 0.12***	r = −0.57, p = 0.14	r = 0.18, p = 0.28	r = −0.20, p = 0.61
HOMA%B	***r = 0.45, p = 0.024***	r = −0.47, p = 0.23	r = 0.07, p = 0.71	r = 0.28, p = 0.46
HOMA%S	***r = −0.29, p = 0.15***	r = 0.34, p = 0.40	r = −0.16, p = 0.37	r = −0.20, p = 0.61
HOMA IR	r = 0.22, p = 0.39	r = −0.377, p = 0.358	r = 0.12, p = 0.51	r = 0.21, p = 0.59

IFG, impaired fasting glucose; IGT, impaired glucose tolerance; SBP, systolic blood pressure; DBP, diastolic blood pressure; PPSG, postprandial (2 h after a 75 g glucose challenge) serum glucose; HOMA%B, insulin secretory capacity; HOMA%S, insulin sensitivity; HOMA-IR, Insulin resistance using HOMA method.

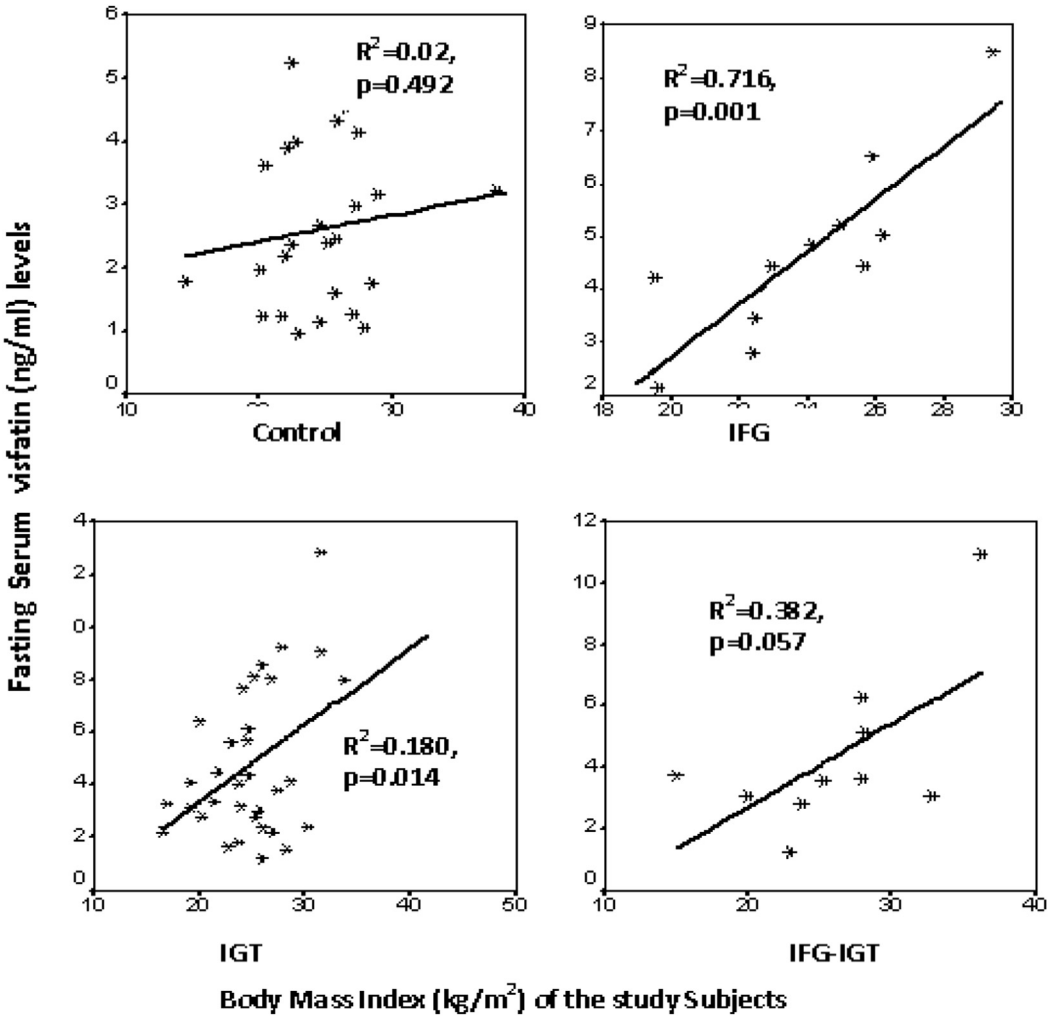

Figure 1: Relationship of serum visfatin levels with BMI of Control, IFG, IGT and IFG-IGT subjects.

level was found to be 2.6 ± 1.2 ng/ml, which is similar with the healthy Iranian population[21] but less than a Spanish population.[11] A study on Chinese women[22] also showed much higher values of serum visfatin compared with the Bangladeshi population. A number of articles have reported increased levels of serum visfatin in type 2 diabetic and obese patients,[21,23] but IFG and IGT subjects have not been studied extensively regarding the serum visfatin levels; however, it is essential to know whether the increase in the circulating visfatin levels begin before the onset of diabetes. Similar to type 2 diabetes mellitus, this study showed increased levels of serum visfatin in the IFG and IGT subjects compared with healthy Bangladeshi control subjects, which suggests that increase in hyperglycaemia and development of type 2 diabetes is delayed through the hypersecretion of adipose tissue derived visfatin. A recent experiment using streptozotocin-induced diabetic rats also showed that visfatin has a significant blood glucose lowering effect.[24] Therefore, increased serum visfatin levels may be a compensatory mechanism or part of the pathophysiology of diabetes mellitus.

Contradictory results have also been outlined in a review article.[25] These discrepancies can be explained by the different subject characteristics, the duration of T2DM and the medication taken by the patients. Furthermore, there is evidence that the release of visfatin by adipocytes is dependent on the duration and magnitude of glucose elevation.[12] Visfatin is also associated with other diseases including obesity, hypertension, dyslipidaemia, renal failure and cardiovascular disease (CVD). The discrepancies in clinical studies may be explained by the multifactorial regulation of visfatin.

The blood pressure and BMI of the IFG, IGT and IFG-IGT subjects were not different from the control subjects, but both the systolic and diastolic pressure were found to be significantly correlated with the serum visfatin levels in the IGT subjects. Therefore, this finding suggests that inflammation may have a role in the development of hypertension in type 2 diabetic patients, which is supported by a previous study.[26] In the present study, the BMI was found to be significantly correlated with the visfatin levels in the IFG and IGT subjects and marginally significant in the IFG-IGT subjects, but it was not significant in the healthy controls (Figure 1). These results are supported by a study carried in Egypt,[27] where patients with type 2 diabetes mellitus and the BMI between the groups were not significantly different, but the BMI in type 2 diabetic patients were shown to be significantly associated with visfatin.

Table 4: Frequency distribution of NGT, IFG, IGT and IFG-IGT along with other clinical and biochemical parameters according to the quartiles of the plasma visfatin concentrations among the study subjects.

	1st Quartile	2nd Quartile	3rd Quartile	4th Quartile
N (%)	27 (100)	27 (100)	27 (100)	27 (100)
M/F	18/9	11/16	11/16	10/17
[a]Visfatin, ng/ml	1.02 (0.4–1.79)	2.77 (1.79–3.37)	4.33 (3.44–6.10)	10.38 (6.25–18.20)
Glycaemic status				
NGT, n (%)	18 (66.7)	9 (33.3)	7 (25.9)	6 (22.2)
IFG, n (%)	1 (3.7)	3 (11.1)	7 (25.9)	6 (22.2)
IGT, n (%)	7 (25.9)	12 (44.4)	9 (33.3)	11 (40.7)
IFG-IGT, n, (%)	1 (3.7)	3 (11.1)	4 (14.8)	4 (14.8)
$\chi^2 = 17.86, p = 0.037$				
Age, yrs	43 ± 6	41 ± 6	42 ± 7	42 ± 7
BMI, kg/m^2	24.0 ± 3.1	24.4 ± 4.7	24.0 ± 3.1	26.2 ± 4.1*
BF, %	27.3 ± 5.9	28.6 ± 7.5	28.3 ± 6.3	31.8 ± 6.5**
SBP, mm-hg	114 ± 16	111 ± 13	109 ± 12	117 ± 12
DBP, mm-hg	74 ± 10	73 ± 8	74 ± 9	79 ± 8*
FG, mmol/l	5.3 ± 0.5	5.5 ± 0.7	5.6 ± 0.7	5.6 ± 0.7
PPG, mmol/l	6.8 ± 1.6	7.8 ± 2.1	7.7 ± 2.2	8.2 ± 1.9**
HOMA-IR	1.37 ± 0.43	1.44 ± 0.32	1.89 ± 1.28*	1.57 ± 0.65
TG, mg/dl	143 ± 65	155 ± 76	198 ± 102*	157 ± 71

M/F, male/female ratio.
NGT, normal glucose tolerance; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; BMI, body mass index; BF%, body fat percent; SBP, systolic blood pressure; DBP, diastolic blood pressure; FG, fasting glucose; PPSG, postprandial (2 h after a 75 g glucose challenge) serum glucose; HOMA-IR, Insulin resistance using the HOMA method; TG, triglyceride in serum. *$p < 0.05$ compared with 1st quartile and **$p < 0.01$ compared with 1st quartile in unpaired student's t test.
[a] Visfatin expressed as median (range).

Although serum visfatin was raised in the hyperglycaemic states, no significant correlation of fasting blood glucose with visfatin was observed in this study, which contradicts the findings of a previous study.[28] The reason for this discrepancy is unclear, but it may result from the study different population because ethnic heterogeneity can affect visfatin levels. The postprandial (2 h after a 75 g glucose ingestion) serum glucose in the IGT subjects showed a positive correlation with the fasting visfatin levels in this study. The serum visfatin levels in the studied IFG, IGT and IFG-IGT subjects did not exhibit any significant correlation with insulin sensitivity, which is consistent with other studies.[9,29] Although animal experiments have shown visfatin to display insulin-mimetic actions and increased serum visfatin concentrations can respond to a compensatory mechanism aimed at ameliorating the functional consequences of insulin deficiency and promote insulin sensitivity by its stimulatory effects on peroxisome proliferator–activated receptor-γ and adiponectin gene expression, both unresponsiveness to visfatin actions (as seen for insulin and leptin) and a contribution of visfatin to β-cell deterioration has been shown that circulating visfatin levels are increased with progressive β-cell deterioration.[11] Supporting these experimental findings, our study showed that increasing concentrations of plasma visfatin levels increased the frequency of IFG, IGT and IFG-IGT and increased the trends of the 2 h post-challenge plasma glucose and insulin resistance (HOMA-IR).

The major limitation of this study is the small number of subjects recruited because of infrastructural constraints. Additionally, measurements of mRNA expression levels in the studied IFG, IGT and IFG-IGT subjects would enhance this work.

Conclusion

Our findings suggest that a) the serum visfatin levels appear to be associated with IFG, IGT and IFG-IGT and b) postprandial serum glucose and blood pressure are positively associated with fasting serum visfatin levels in IGT subjects.

Conflict of interest

The authors have no conflict of interest to declare.

Author contribution

Fahmida Kabir: Sample collection and drafting the article; Farzana Akter Jahan: Collection of the samples and literature survey; Imran Khan: Analysis of the data; M Omar Faruque: Conception and design of the study; Zahid Hassan: Revising the manuscript critically for important intellectual context; Liaquat Ali: Approval of the final version.

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