Serum Visfatin Level in Egyptian Diabetics With and Without Microvascular Complications

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Abstract

**Background:** Recently an adipose-tissue-derived protein termed visfatin was described in 2005. It was previously identified as a growth factor for early B-lymphocytes termed pre-B cell colony enhancing factor (PBEF). Visfatin was reported to be expressed almost exclusively in visceral adipose tissue and has insulin-like metabolic effects. These findings are exiting news and could provide a novel mechanism by which visceral fat accumulation can promote the development of T2DM.

**Objectives:** The aim of our work is to study serum levels of visfatin and their relation to T2DM with and without microvascular complications.

**Subjects and Methods:** We studied 90 subjects divided into 3 groups as follows:
- Group A: 30 diabetic patients with microvascular complications.
- Group B: 30 diabetic patients without microvascular complications.
- Group C: 30 non-diabetic, age and sex-matched controls.

All individuals included in the study were subjected to detailed clinical examination, fundus examination, and measurement of BMI, fasting, 2 hours PP blood glucose level, glycosylated Hb, serum visfatin level, fasting plasma insulin level, plasma nitrite level, plasma nitrite level and Homeostasis Model Assessment (HOMA) for insulin resistance.

**Results:** Serum visfatin was higher in diabetics with microvascular complications (15.5±2.15) than in non-complicated diabetics (10.99±1.96) and control group (7.63±1.07) (p-value<0.001). A highly statistically significant positive correlation (p-value<0.001) was found between serum visfatin level and FBG (r=0.700), 2hr PP Blood Glucose, HbA1c fasting plasma insulin, HOMAIR, plasma nitrite level and BMI.

**Conclusion:** Our results suggest that visfatin may play a role in the pathogenesis of T2DM as well as its microvascular complications. Also visfatin may help in the identification of higher risk individuals for diabetes and cardiovascular disease with a better comprehension about the complex inter-correlation between adiposity, glucose metabolism and vascular disease.

**Key Words:** Visfatin — Type 2 Diabetes Mellitus — Adipose tissue.

Introduction

**DIABETES** mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism. III.

Excess adiposity is the most important risk in the development of insulin resistance and type 2 diabetes mellitus. Adipose tissue produces several proteins (adipocytokines) such as leptin, adiponectin, resistin, TNF, and IL-6, that modulate insulin sensitivity and appears to play an important role in the pathogenesis of insulin resistance, diabetes, dyslipidemia, inflammation, and atherosclerosis. However, the mechanisms by which fat tissue induces insulin resistance and the role of adipocytokines in the pathogenesis of T2DM has not been well established [2].

Visfatin, also known as pre-B-cell colony-enhancing factor and nicotinamide phosphoribosyl transferase, has been identified as a novel adipocytokine. In 2005, Fukuhara, et al., demonstrated that this protein is expressed in adipocytes and secreted from adipose tissue and named it "visfatin", as it is highly expressed in visceral fat [3].

The dual effects of visfatin, namely a global insulin-like one and a local adipogenic one, create a therapeutic challenge of visfatin or visfatin analogs are to be used in clinical practice to treat
T2DM. On one hand, they may facilitate glucose control; on the other hand, they may promote the development of obesity.

**Aim of the work:**
To study serum visfatin level in type 2 Egyptian diabetic patients with and without microvascular complications.

**Patients and Methods**

Cross sectional study were conducted on Sixty diabetic patients who consecutively visited the Diabetes & Endocrinology out-patient clinic at Kasr El Aini Hospital were studied during the period from January 2012 to November 2012. Thirty age and sex-matched non-diabetic subjects without clinical evidence of major diseases were recruited from an unselected population that underwent routine medical check-up and were used as the control group.

The 90 subjects were divided into 3 groups as follows:
- Group A: Consists of 30 diabetic patients with microvascular complications.
- Group B: Consists of 30 diabetic patients without microvascular complications.
- Group C: consists of 30 controls.

With the following exclusion criteria; (1) Patients with type 1 diabetes. (2) Patients who had renal disease, liver cirrhosis, congestive heart failure, macrovascular diseases, overt proteinuria, or other known major diseases were also excluded on the basis of interview, physical examination, and urine analysis.

All individuals included in the study were subjected to complete history taking, detailed physical examination, fundus examination, Body mass index (BMI = Weight in kilograms/height in m^2), albumin/creatinine ratio in a random urine sample, fasting, 2 hours PP blood glucose levels, Glycosylated Hb, fasting plasma insulin and Plasma visfatin levels were measured using an enzyme-linked immunosorbent assay (ELISA), Serum nitrite measurement using Nitrite Colorimetric Assay Kit and Homeostasis Model Assessment (HOMA) for insulin resistance.

\[ HOMA-IR = \frac{\text{Fasting plasma insulin} \ (\mu U/L) \times \text{Fasting blood glucose} \ (mmol/L)}{22.5} \]

**Statistical methods:**
Analysis of data was done by IBM computer using SPSS version 12 with Description of quantitative variables as mean±SD and range and description of qualitative variables as numbers and percentage. Chi-square test was used to compare qualitative variables between groups.

**Results**

Serum visfatin level was significantly higher in diabetes with microvascular complications (15.5±2.15) than in non-complicated diabetics (10.99±1.96) and control group (7.63±1.07) \( (p\text{-value D1001}) \).

Serum Nitrite level was significantly increased in group A compared to group B and group C \( (p\text{-value D1001}) \). It was higher in group B compared to group C \( (p\text{-value D1001}) \).

Correlation study among all diabetics found a highly statistically significant positive correlation \( (p\text{-value 0.001}) \) between serum visfatin level and FBG \( (r=0.700) \), 2hr PP Bl. Glu. \( (r=0.715) \), HbAlc \( (r=0.682) \) fasting plasma insulin \( (r=0.822) \), HOMA-IR \( (r=0.807) \), and BMI \( (r=0.485) \).

Also a highly significant positive correlation was found between serum visfatin and serum nitrite \( (p\text{-value 0.001}) \), \( (r=0.668) \) in studying correlations among all diabetics.
Fig. (3): Correlation between visfatin & HOMA-IR in diabetic patients.

Fig. (4): Correlation between visfatin and HBA1C in diabetic patients.

Fig. (5): Correlation between visfatin and blood glucose 2hrs PP in diabetic patients.

Fig. (6): Correlation between visfatin and fasting plasma insulin in diabetic patients.

Fig. (7): Correlation between visfatin and BMI in diabetic patients.

Fig. (8): Correlation between visfatin and Nitrite in diabetic patients.
**Discussion**

Visfatin as an adipokine, has recently been identified and named as such because of its much greater expression in visceral fat than in SC adipose tissue [3].

In the present study, we found a statistically high serum visfatin level in diabetic groups compared to control group (pD1001). This result is consistent with the findings of Dogru, et al. [4]. Also Retnakaran, et al., found that visfatin levels were higher in patients with T2DM compared to controls even after adjustment for age, sex and traditional metabolic risk factors [5].

In line with our study, Haider, et al., found that plasma visfatin is increased with elevated blood glucose by the glucose clamp test [6]. In cultured adipocytes, Haider, et al., found that the expression of visfatin is up regulated in a glucose-dependent manner [7]. Similarly, Lopez, et al., showed that visfatin is increased in normal subjects with deteriorated insulin secretion to glucose by an intravenous glucose tolerance test [8].

Nevertheless, Takebayashi found no correlation between diabetes and visfatin [9] while another study, demonstrated decreased visfatin in diabetic patients and inverse relationship between A1C and visfatin levels [10].

A highly significant statistical correlation (pD1001) between serum visfatin and fasting blood glucose as well as HbA1c, was found in the present study. However, serum visfatin level was not found to be correlated with fasting blood glucose in another study [11].

Serum visfatin level was also found to be significantly correlated with fasting plasma insulin and HOMAIR (pD1001). This result could be explained by the relationship between visfatin level and a chronic sub-clinical inflammatory state in T2DM [12].

On the other hand Jin, et al., found no correlation between serum visfatin levels and HOMAIR in diabetics [13].

Correlation study among all diabetics involved in this study found a highly statistically significant positive correlation (p<0.001) between serum visfatin level and BMI. This is in correspondence with Berndt J., et al., who found a significant positive association between plasma visfatin and BMI [14]. Haider, et al., also found that plasma visfatin level significantly correlated to body mass index (BMI) and waist-hip ratio (WHR) in male but not in female diabetic patients [7].

In our study we found that visfatin serum level was significantly increased in diabetics with microvascular complications compared to diabetics without microvascular complications (p-value 0.001). This result is consistent with Yilmaz, et al., who found that visfatin levels were positively associated not only with insulin resistance but also with the degree of albuminuria in type 2 diabetic patients. They suggested that the endothelial dysfunction in early diabetic nephropathy is associated with altered circulating levels of visfatin [15]. Also Kang, et al., found that plasma visfatin levels were elevated in patients and animals with type 2 diabetic nephropathy [16]. In this study, serum nitrite levels were significantly increased in diabetics with microvascular complications compared to diabetics without microvascular complications and controls (p-value 0.001). Nitrite level was higher in diabetics without microvascular complications compared to controls (p-value 0.001). These findings came in agreement with the study done by Konukoglu, et al., which reported that plasma NO (NO; nitrite plus nitrate) levels were significantly higher in subjects with diabetic glucose tolerance (DGT) than in subjects with normal glucose tolerance (p<0.001) and impaired glucose tolerance (IGT) (p<0.05) at baseline. This might be related with the enhanced oxidative stress [16].

A positive correlation between serum visfatin and plasma nitrite was found suggesting a possible role of visfatin expression in development of endothelial dysfunction and microvascular complications of T2DM. A study of Takebayashi, et al., found a negative correlation between visfatin and endothelial function evaluated through flow-mediated or nitroglycerin-mediated dilation [9]. Visfatin can promote vascular smooth muscle inflammation, being associated with a potential role in vascular dysfunction and inflammation associated with some metabolic disorder [17].

It is becoming clear that adipose tissue is not simply a reservoir for excess nutrients but an active and dynamic organ capable of expressing several cytokines and fat-derived peptides [18].

Elevated visfatin levels in patients with T2DM may point to a potential relevant role of this novel adipocytokine in either the pathogenesis or the clinical phenotype of type 2 diabetes [8].

**Conclusion:**

Our study suggests that the use of visfatin may help in the identification of higher risk individuals for diabetes and cardiovascular disease with a
better comprehension about the complex intercorrelation between adiposity, glucose metabolism and vascular disease.

**Recommendations:**

Further studies involving a larger population need to be done to clarify both the mechanisms of production and action of visfatin and to study the possible role of visfatin in each type of diabetic microvascular complications.

It would be interesting to measure serial changes of plasma visfatin levels in obese, insulin-resistant, and prediabetic subjects to further clarify the role of visfatin in the pathogenesis of T2DM.

The effects of oral hypoglycemic drugs especially insulin sensitizers as well as effects of insulin therapy on plasma visfatin levels also need to be clarified.

**References**


