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Visfatin and Gestational, Type 1 and Type 2 Diabetes Mellitus: A Review of Literature

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Abstract

Background: Adipose tissues produce adipocytokines and other various substances that have useful actions in the body. One of such adipocytokines is visfatin which has been linked to diabetes mellitus. Aim: This study aimed at investigating the existence of a probable correlation between plasma levels of visfatin and the various types of diabetes mellitus: type 1, type 2 and gestational diabetes mellitus. Methods: A comprehensive literature search was performed using the Internet search engines linked to academic databases including Pubmed, Google Scholar, Ebsco, Hinari, etc. Studies involving visfatin were thoroughly searched and the references of such articles were also searched for any probable relevant information. Results/Findings: There is no agreed finding regarding the correlation between visfatin and diabetes mellitus. While some authors believed that plasma visfatin levels are elevated in diabetes mellitus, others believed that the contrary might be true. Conclusion: Various studies conducted so far have contrasting opinions about the correlation between plasma visfatin levels and diabetes mellitus.

Keywords: Visfatin; Diabetes mellitus; Gestational; Adipocytokines; Adipose tissue

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Introduction

Recently, adipose tissue has been widely studied and it is currently recognized as an endocrine organ that produces adipocytokines that have different effects on body metabolic processes (1,2). Visfatin is one of such adipocytokines (adipokines) or adiponectins. Other adipokines are leptin, resistin, and adiponectin1. Visfatin is a newly discovered adipocyte hormone (2,3). These adipokines have various biological and pharmacological functions (4,5). Adipocytokines are important because of their metabolic functions, roles in immunity of the body (e.g. complement factor), and endocrine functions (e.g. leptin, adiponectin, apelin, resistin, and omentin) (6,7).

VISFATIN

Historical overview/structural pattern

Visfatin, also called pre-B colony enhancing factor (PBEF), is a 52Kda molecule discovered in 2005 by Fukuhara et al. (8). In humans, visfatin is an enzyme that is encoded by the PBEF 1 gene8,9. In humans, the gene for visfatin is located on the long arm of chromosome 7 from 7q22.1 to 7q31.33, encoding a polypeptide of 491 amino acid types found in adipocytes, lymphocytes, bone narrow, liver, muscle cells, trophoblasts and fetal membranes (2,8,10, 11).

Morphology/function/structure

Nicotinamide phosphoribosyl transferase (NAM- PRTASE) is an enzyme involved in nicotinamide adenine nucleotide (NAD) biosynthesis from nicotinamide. Hence, visfatin is also called NAMPTR. Researchers have found the crystal structure of NAMPT/PBEF/visfatin to be a dimeric type (11). Phosphoribosyl transferase enzyme is involved in the formation of NAD10. Visfatin is considered to be an endocrine, autocrine as well as paracrine peptide with many functions including cell proliferation, biosynthesis of nicotinamide, and hypoglycemic effects. It is made up of a highly conserved protein (2,10).

Role of Visfatin in Different Disease Entities

Visfatin has been linked with various diseases entities. Revello et al. and Dahl et al. established the fact that visfatin is implicated in atherosclerotic-related diseases (12,13). Several studies have highlighted that visfatin levels correlate with obesity, visceral fat mass, type 2 diabetes and metabolic syndrome (14,15,16). Vistafin has also been correlated with many other diseases entities such as atherosclerosis, endothelial dysfunction (17), metabolic syndrome18, hepatic fat diseases (19,20), tumor replication (21), renal impairment17, beta cell function impairment and obesity (12,15,22,23). Plasma visfatin concentration correlates strongly with the amount of visceral fat (24). Visfatin is also known to be involved in glucose homeostasis by exerting hypoglycemic effect through enhancing glucose utilization in peripheral tissues and reducing glucose release from liver cells. The administration of recombinant visfatin lowers plasma glucose levels in both insulin-resistant and insulin deficient mice (24).

Visfatin in Diabetes Mellitus

Visfatin has been described as an adipocyte hormone with highly important effects on glucose metabolism1. Various studies have been carried out to establish a correlation between the levels of plasma visfatin and diabetes mellitus (25,26). This is based on many reports and findings by many researchers that visfatin has insulin-mimetic properties (27,28). This insulinomimetic property enables visfatin to bind to insulin receptors, thereby enhancing glucose intake into 3T3-L1 adipocytes, L6 myocytes and cultured mesangial cells in a dose dependent manner. However, it does not compete with insulin to bind the insulin receptors. This suggests that it may bind to

another portion of the extracellular domain. These insulin-like properties of vistafin are linked to its ability to catalyze the biosynthesis of nicotianmide adenine dinucleotide (NAD), a classic enzyme involved in cellular redox reaction (29,30). In 2007, Fukahara et al. identified vistafin as an adipokine that lowers plasma glucose due to its ability to stimulate receptors of insulin (8).

Visfatin in Gestational Diabetes Mellitus (GDM)

Liang et al. described visfatin as an adipocytokine which exerts an insulin-like effect by binding to insulin receptor-1. They concluded that visfatin appears to be involved in lipid and glucose metabolism. In their study groups, the levels of visfatin in gestational diabetes mellitus (n=38) patients was higher than in the control group (n=38) (P<0.001) (31). They concluded that visfatin is associated with glucose and lipid metabolic disorders of gestational diseases mellitus (GDM) (31).

Krzyanowaski et al. suggested that the level of visfatin in gestational diabetes mellitus increased (P=0.00) and it even rose further after delivery (P=0.014). They concluded that visfatin is elevated in women with gestational diabetes mellitus and increases during the course of pregnancy as well as after delivery (32).

Gok et al. investigated 45 pregnant women at 24-28 weeks of gestation who were diagnosed with gestational diabetes mellitus. Levels of plasma visfatin and lipids were checked. Plasma visfatin levels were significantly higher in the pregnant diabetic than the control groups. It was concluded that visfatin levels were highly elevated in women with GDM during the course of pregnancy and increased visfatin concentration were reduced 6-10 weeks after delivery (33).

Nevertheless, there is no agreed consensus regarding data of visfatin levels in GDM patients. Rezvan et al. found that plasma visfatin levels were much lower in pregnant women with GDM compared to healthy pregnant individuals in their study (34).

Park et al. studied 215 GDM and 531 non-GDM women. They found that gestational diabetes is associated with reduced plasma visfatin and adiponectin levels in circulation than in non-GDM (35).

Study of Kiran et al. on 65 pregnant revealed that levels of visfatin in pregnant women with GDM were more than women with normal glucose tolerance (36).

Chan et al. studied the pattern of visfatin levels in pregnant women with gestational diabetes (n=20). They found that visfatin levels in GDM women were significantly in lower levels (9.4±3.8 ng/ml) than the control group (12.6 ±4.5 ng/ml) (P=0.023). They concluded that visfatin may have a role in the pathogenesis of gestational diabetes (37).

Yet another study by Lewandoski et al. showed there was elevated fasting plasma visfatin levels which correlated with both fasting and post-glucose load insulin secretion in women with GDM (38).

Telejko et al. suggested that, between 26-33 weeks of pregnancy, plasma visfatin levels did not differ in women with gestational diabetes mellitus and normal glucose tolerance. However, at term, circulating visfatin was significantly lower in GDM patients than in the women with normal glucose tolerance (39).

Haider et al. also reported that visfatin levels in GDM women is reduced when compared to the control group (40).

Conclusively, many authors have made different conclusions regarding the pattern of visfatin levels in women with gestational diabetes mellitus.

Visfatin in Type 1 Diabetes Mellitus

Hontzch et al. studied 124 patients with type 1 diabetes, and found that visfatin levels were higher in the adolescent and children with type 1 diabetes than the control group. They even suggested an influence on glucose metabolism in insulin-deficient patients, independent from body mass index (41).

Haider et al. studied the effects of exercise training on plasma visfatin concentration and discovered that elevated visfatin concentrations were found to be lower in type 1 DM patients on regular physical exercises (42).

Alexiadou et al. found that plasma visfatin in type 1DM patients which they measured and compared with healthy individual. They found that fasting visfatin levels were lower in patient with type 1 DM in comparison with healthy subjects. This implies an enhanced effect of insulin deficiency on visfatin secretion (43).

Brown et al. found that adding visfatin at lower glucose levels (2 .2 mmol/L or 45mg/dL) could cause a 46% increase in insulin secretion when compared to the control group (P<0.001) (44).

Similarly, Torunner et al. studied the relationship between type 1DM and visfatin levels. They found that visfatin levels are lower in Type 1DM patients (23).

Visfatin in Type 2 Diabetes Mellitus

Revollo et al. suggested that visfatin does not exert insulin-mimetic effects either in vitro or in vivo. They also examined whether visfatin reduced glucose and were not able to deduce any decreases in blood glucose even when very high doses of recombinant visfatin were injected (12).

Tofighi et al. studied plasma visfatin levels in 45 women with type 2 DM who also took aerobic training courses. It was found that the levels of plasma visfatin was significantly reduced when compared to control subjects (45).

Rabo et al. also studied 40 (20 obese and 20 non-obese) subjects and found that plasma levels of visfatin were increased in patients with type 2DM compared to the control group, regardless of the degree of obesity (P<0.01) (46).

Likewise, Shelbaya et al. studied visfatin pattern in 80 type 2 DM patients. Their findings suggested that serum visfatin levels were higher in type 2 DM than the control group patients. These results postulated a link between visfatin and diabetes mellitus, regardless of obesity (47).

Ahmed et al. also studied 116 subjects with type 2 diabetes mellitus and found that plasma visfatin levels were significantly higher in diabetic patients than in the healthy control group (P<0.005). They suggested that visfatin may be implicated in the pathogenesis of diabetes mellitus (48).

Similarly, Osama et al. studied 80 people with type 2 diabetes mellitus and a control group. They aimed at finding a link between plasma levels of visfatin and type 2diabetes patients. Accordingly, visfatin, glycated haemoglobin (HbA1C), fasting insulin level and HOMA-IR were significantly higher than those in the control group. A positive correlation existed between levels of visfatin and HbA1C. They concluded that visfatin may play a role in the pathogenesis of type 2 diabetes through deterioration of beta cells in diabetic patients (49).

In another study, Chen et al. studied 61 patients with type 2 diabetes mellitus and 59 non-diabetic controls of similar sex and age. They found that plasma visfatin was elevated in the patients with type 2 diabetes when compared to the controls (P=0.002). Multiple logistic regression analysis emphasized that visfatin was independently associated with type

2 diabetes mellitus. This was even after adjusting for other parameters like age, body mass index, sex, waist/hip ratio, smoking, and blood pressure (14).

Drogue et al. studied plasma visfatin in recently diagnosed patients who were yet to receive treatment for type 2 diabetes mellitus50. El-Shafey et al. studied 74 subjects who were diabetic and compared them with controls. Their results showed elevated circulating serum visfatin in type 2 diabetes and obese subjects. This was further supported by a significant association between visfatin and insulin resistance (3).

Conclusion

From various studies, it appears that no standard conclusion has been reached regarding the correlation between diabetes and plasma levels of visfatin. While some authors are of the opinion that plasma visfatin levels are higher in diabetes mellitus, others gave a contrary opinion. More studies with larger sample sizes are required to verify any probable correlation between diabetes mellitus and plasma visfatin levels.

Conflict Of Interest: None

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