Araştırma Makalesi *Research Article*

Pamukkale Tıp Dergisi
Pamukkale Medical Journal

doi:https://dx.doi.org/10.31362/patd.540973

Visfatin concentration in patients with newly-diagnosed glucose metabolism disorders

Yeni tanı konulmuş glukoz metabolizma bozukluğu olan hastalarda serum visfatin konsatrasyonunun değerlendirilmesi

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Gönderilme tarihi:16.03.2019 Kabul tarihi:30.07.2019

Abstract

Purpose: Visfatin, protein secreted by visceral adipose tissue, visfatin is an intracellular enzyme that has insulinmimetic effects and lowers plasma glucose levels. Data about the role of visfatin in newly diagnosed glucose metabolism abnormalities are limited. The aim of the work was to assess serum concentration of visfatin in impaired fasting glucose and impaired glucose tolerance.

Materials and Methods: With diagnosis of abnormal glucose metabolism 57 patients were divided into the subgroups according to the oral glucose tolerance test results as impaired fasting glucose (n=39) and impaired fasting glucose+impaired glucose tolerance (n=18). The control group consisted of 44 healthy controls with normal glucose tolerance and without any metabolic disorders. Serum lipids, high sensitive C-reactive protein(hsCRP), uric acid, glycated haemoglobin (HbA1c) and serum visfatin levels were measured in all participants.

Results: The mean visfatin level of impaired fasting glucose group was 93.92±12.95 ng/mL, impaired fasting glucose+impaired glucose tolerance group was 37.79±29.36 ng/mL and control group was 43.96±38.57 ng/mL. There was statistically significant difference between serum visfatin levels of the groups (p<0.001). Mean visfatin level of impaired fasting glucose group was statistically higher than impaired fasting glucose+impaired glucose tolerance and control groups (p<0.001 and p<0.001 respectively). Mean visfatin level of impaired fasting glucose+impaired glucose tolerance group was lower than the control group however, the difference was not statistically significant (p=0.785). Visfatin levels were negatively correlated with total cholesterol, HDL, LDL, hsCRP and HbA1c levels, positively correlated with triglycerides, HOMA-IR and body mass index values, however these relationships were not statistically significant.

Conclusion: The results of this study revealed that prediabetes status was associated with an elevated level of circulating plasma visfatin, and these results were supported by a significant association between visfatin and insulin resistance.

Key Words: Visfatin, impaired fasting glucose, impaired glucose tolerance.

Gonderen K, Bılgetekın I, Gonderen A, Yıldız M. Visfatin concentration in patients with newly-diagnosed glucose metabolism disorders. Pam Med J 2019;12:401-406.

Özet

Amaç: Visfatin, visseral adipoz doku tarafından salgılanan, insülinmimetik etkileri olan ve plazma glukoz seviyelerini düşüren hücre içi bir enzimdir. Yeni tanı konulan glukoz metabolizma bozukluklarında visfatinin rolü ile ilgili yapılan çalışmalar sınırlıdır. Bu çalışmanın amacı bozulmuş açlık glukozu ve bozulmuş glukoz toleransı olan hastalarda visfatin serum konsantrasyonunu değerlendirmektir.

Gereç ve Yöntem: Anormal glukoz metabolizması tanısı alan 57 hasta, oral glukoz tolerans testi sonuçlarına göre bozulmuş açlık glukozu (BAG) (n=39) ve BAG+ bozulmuş glukoz toleransı (BGT) (n=18) olarak alt gruplara ayrıldı. Kontrol grubu, normal glukoz toleransı olan ve herhangi bir metabolik bozukluğu olmayan 44 sağlıklı bireyden oluşuyordu. Tüm katılımcıların serum lipid, yüksek duyarlı C-reaktif protein(hsCRP), ürik asit, glikozile hemoglobin (HbA1c) ve serum visfatin düzeyleri ölçüldü.

Bulgular: BAG grubunun visfatin düzeyi 93,92±12,95 ng/mL, BAG+BGT grubunun 37,79±29,36 ng/mL kontrol grubunun 43,96±38,57 ng/mL idi. Grupların serum visfatin düzeyleri arasında istatistiksel olarak anlamlı fark vardı (p<0,001). BAG grubunun ortalama visfatin düzeyi, BAG+BGT ve kontrol gruplarından istatistiksel olarak daha yüksekti (sırasıyla p<0,001, p<0,001). BAG+BGT grubunun visfatin düzeyi kontrol grubununkinden düşüktü, ancak aradaki fark istatistiksel olarak anlamlı değildi (p=0,785). Visfatin düzeyleri toplam kolesterol, HDL, LDL, hsCRP ve HbA1c düzeyleri ile negatif korelasyon gösterdi, trigliserit, HOMA-IR ve vücut kütle indeksi ile pozitif korelasyon gösterdi, ancak bu ilişkiler istatistiksel olarak anlamlı değildi.

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Sonuç: Bu çalışmanın sonucu, prediyabetin yüksek plazma visfatin seviyesi ile ilişkili olduğunu ve bu sonuçların visfatin ve insülin direnci arasındaki anlamlı ilişki tarafından desteklendiğini ortaya koymuştur.

Anahtar Kelimeler: Visfatin, bozulmuş açlık glukozu, bozulmuş glukoz toleransı.

Gönderen K, Bilgetekin İ, Gönderen A, Yıldız M. Yeni tanı konulmuş glukoz metabolizma bozukluğu olan hastalarda serum visfatin konsatrasyonunun değerlendirilmesi. Pam Tıp Derg 2019;12:401-406.

Introduction

Prediabetes is defined as the stage with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) [1] . The oral glucose tolerance test (OGTT)is used to determine a person's ability to handle a glucose load. Prediabetes is defined by the American Diabetes Association as fasting plasma glucose between 100 and 125 mg/dL and/or by a two-hour plasma glucose during OGTT of 140-199 mg/dL [2]. Prediabetes is of importance as subjects with prediabetes have an increased risk of developing overt type 2 diabetes mellitus (DM). Recent studies suggest that visfatin may also act as a proinflammatory cytokine and in this way may indirectly participate in the development of insulin resistance and type 2 diabetes [3]. Inflammation markers were studied to exclude inflammation and the other chronic diseases such as anemia and hyperlipidemia.

Visfatin is a protein secreted by visceral adipose tissue, Visfatin is an intracellular enzyme, known as nicotinamide phosphoribo syltransferase (Nampt) and pre-B-cell colony-enhancing factor (PBEF-1) [4]. It has insulin-mimetic effects and lowers plasma glucose levels. Visfatin concentration increases in patients with longer-standing type 2 DM with progressive β-cell dysfunction [5]. However, there are limited data about the role of visfatin in newly diagnosed glucose metabolism abnormalities.

The aim of this study was to assess the serum concentration of visfatin in patients with prediabetic disorders as impaired fasting glucose and impaired glucose tolerance.

Material and methods

Patients and recruitment

We have excluded the patients, if there is a possibility that might change oral glucose tolerance test (OGTT), serum ferritin, high sensitive C-reactive protein and other laboratory test results: hemoglobin levels below 12 mg/dL, acute and chronic infections, chronic diseases, acute coronary syndromes, autoimmune diseases, endocrine diseases, inflammatory diseases, cancer and also regular drug usage: oral contraceptive, glucocorticoids, diuretics, thyroxine, beta-blockers. All clinical investigations were conducted in accordance with the Guidelines in the Declaration of Helsinki and approved by the Institutional Review Committee. All subjects were carefully instructed about the aims of the study and written informed consent was obtained from each participant. Ethics committee approval was taken from Ankara Dıskapı Yildirim Beyazit Training and Research Hospital.

This study was performed on a group of 57 patients diagnosed with abnormal glucose metabolism, comprising 35 females and 22 males, aged 42.3±7.5 years. OGTT was performed in all patients with a diagnosis of abnormal glucose metabolism. Before three days the preciding test, patients were given a diet containing at least 200 grams of carbohydrates. The test was applied after the patient had completed a minimum 8-hour fasting period. A fasting blood sample was taken to establish a baseline glucose level, then the patient drank 75 grams of glucose. Samples were taken at 120 minutes post consumption of the glucose. The patients with abnormal glucose metabolism were divided into subgroups according to the OGTT results as IFG (n=39) and IFG+IGT (n=18). Clinical evaluation of the 75-g OGTT was performed according to the current TEMD guidelines: fasting plasma glucose 100-125 mg/dL for impaired fasting glucose and 2-hour plasma glucose 140-199 mg/dL during the OGTT for impaired glucose tolerance [2]. A control group was formed of 44 healthy, lean individuals, comprising 32 females and 12 males, aged 41.3±8.1years, with normal glucose tolerance and with no metabolic syndrome. Serum lipids, highly sensitive C-reactive protein (CRP),

glycated haemoglobin (HbA1c) and serum visfatin levels were measured in all participants. In the examined and control subjects, body weight, height, and waist circumference were measured, then body mass index (BMI) were calculated. BMI is a person's weight in kilograms divided by his or her height in meters squared.

Statistical Analysis

Data obtained in the study were analysed statistically using the Statistical Package for Social Science (IBM SPSS) version 16software. Conformity of the data with normal distribution was assessed with the Kolmogorov Smirnov test. Continuous variables were compared using the Mann Whitney U test for data with normal distribution and the Kruskal Wallis test for data not showing normal distribution. The Mann Whitney U test was applied to test the significance of pairwise differences using the Tukey test to adjust for multiple comparisons. The relationship between two variables was assessed with the Spearman linear correlation coefficient (r). A value of $p<0.05$ was considered statistically significant.

Laboratory analysis

Approximately 5 mL venous blood was withdrawn from each patient after overnight fasting (8-12 hrs.). Plasma glucose (Olympus AU-2700, Mishima, Japan) and insulin (Roche E-170, Hitachi Corp, Osaka, Japan) levels were measured. HbA1c was measured using HPLC (high performance liquid chromatography) methods. Then the serum was divided into aliquots and stored at -80°C until assay for serum visfatin. Visfatin C-terminal was measured using enzyme immunometric assay (Phoenix Pharmaceuticals Inc, Belmont, CA, USA)" and "The minimum detectable concentration (sensitivity) was 1 ng/mL with a detection range of 0.1-1000 ng/mL. and its intra- and inter-assay coefficients of variation (CVs) were 3.59% and 9.25%, respectively. Lipid parameters and hsCRP were studied by Roche E-170 Modular Analyzer Clinical Chemistry instrument or Olympus AU-2700, Mishima, Japan Analyzer. The fasting glucose and insulin measurements were used to derive estimates of β-cell function and insulin sensitivity using the Homeostatic model assessment of insulin resistance (HOMA-IR) algorithm [6]. The HOMA-IR was used instead of the hyperinsulinaemic-euglycaemic clamp test in the measurement of IR because of ease-of-use and low cost. HOMAIR index was estimated by the following formula: HOMA-IR=(fasting glucose[mmol/L]×baseline insulin[μU/ml])/22.5 [7]. In the present study, a HOMA-IR value greater than 2.5, which was the median value of the study population, was accepted as the cut-off point for insulin resistance.

Results

There was a statistically significant difference between the groups in respect of BMI scores. There was no significant difference between the groups according to the waist circumference measurements (Table 1).

The mean visfatin level was 93.92±12.95 in the IFG group, 37.79±29.36 ng/mL in the IFG+IGT group and 43.96±38.57 ng/mL in the control group. The difference between the groups was statistically significant ($p<0.001$). The mean visfatin level of the IFG group was statistically significantly higher than that of the IFG+IGT and control groups ($p<0.001$ and $p<0.001$ respectively). The mean visfatin level of the IFG+IGT group was lower than that of the control but not at a statistically significant level ($p=0.785$). The levels of insulin and HOMA-IR of the prediabetic patients were higher than those of the control group, but there was no statistically significant difference between the groups (Table 2). There was a statistically significant difference between the groups in respect of the levels of HbA1c, cholesterol and triglycerides. The comparisons between the groups of the mean levels of the examined parameters are shown in Table 2.

The visfatin level was not significantly correlated with HOMA-IR, BMI, TG, HDL, LDL, hsCRP, HbA1c or total cholesterol levels (Table 3).

Discussion

The results of this study showed that visfatin levels were higher in the IFG group than in the control group. In isolated IFG, hepatic IR and insufficiently suppressed endogenous glucose production have been reported to be the main pathophysiological phenomena. Using an intravenous glucose tolerance test, Lopez et al. [8] showed that visfatin is increased in normal subjects with deteriorated insulin secretion to

Table 1. Daemographic features.

	IFG(n)	IFG+IGT(n)	Control group(n)	*p**
Age(years)	42.7±8.2 (24-58)	41.5±5.9 (26-54)	41.3±8.1 (28-60)	0.712
Gender(female/male)	27(69.2%)/12(30.8%)	8(44.4%) 10(55.6%)	32(72.7%)/ 12(27.3%)	0.689
Body mass index(kg/m²)	26.9±2.5	27.2±2.1	24.5±3.3	0.955
Waist circumference measurements(cm)	91.3±11.4	95.1±8.4	81.2±13.4	0.438

IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance

* Mann Whitney U Test

Table 2. The relation ship of variables between groups.

	IFG (mean with ± SD)	IFG+IGT(mean with ± SD)	Control group(mean with ± SD)	*p**
HDL (mg/dL)	44.8±12.3	47.8±20.7	46.5±11.5	0.830
LDL (mg/dL)	116.1±32.5	121.1±19.4	104.3±27.7	0.071
hsCRP (mg/L)	2.5±2.6	4.2±19.4	2.3±3.0	0.067
HbA1c (%)	5.7±0.9	6.2±0.5	5.3±0.4	**<0.001**
HOMA-IR	3.3±3.1	3.8±3.2	2.4±1.5	0.157
Visfatin(ng/mL)	93.9±13.0	37.8±29.4	44.0±38.6	**<0.001**

IFG: Impaired fasting glucose, IGT: Impaired glucose tolerance, HDL: High density lipoprotein, LDL: Light density lipoprotein, hsCRP: High sensitive C reactive protein, HbA1c: Glycated haemoglobin, HOMA-IR: Homeostatic Model of Assessment-Insulin Resistance

* Kruskal Wallis Test

Table 3. Correlation coefficient r values for visfatin with other variables.

	r	*p**
HOMA-IR	0.076	0.252
hsCRP(mg/L)	-0.115	0.126
HbA1c(%)	-0.054	0.297
Total cholesterol(mg/dL)	-0.013	0.450
LDL cholesterol(mg/dL)	-0.022	0.413
HDL cholesterol (mg/dL)	-0.018	0.428
TG cholesterol (mg/dL)	0.079	0.216
Body mass index(kg/m²)	0.074	0.232

HOMA-IR: Homeostatic Model of Assessment-Insulin Resistance, hsCRP:High sensitive C reactive protein, HbA1c: glycated haemoglobin LDL:Light density lipoprotein, HDL: High density lipoprotein, TG:Triglycerides

* Spearman correlation analysis

glucose. This evidence suggests that visfatin can be stimulated under a hyperglycaemic environment. The current study results may support the idea that elevated plasma visfatin in patients with IFG is a consequence of the hyperglycaemia condition. Brown et al. [9] demonstrated that incubation with visfatin in clonal mouse pancreatic β cells increased insulin upregulation 9-fold, and they also showed that visfatin caused a significant 46% increase in insulin secretion compared with a low glucose environment. This evidence suggests that the

elevated visfatin concentration in type 2 DM may be a physiological protective response to a hyperglycaemic environment. Showing an increased visfatin concentration in type 2 DM may also support the hypothesis that visfatin is associated with IFG.

Visfatin has insulin mimicking effects through activation of an insulin receptor [10]. To date, the pathophysiological roles of visfatin in glucose homeostasis and chronic inflammatory disease have been studied. No associations were observed between visfatin and BMI, other metabolic data (HDL, total cholesterol, TG, and LDL). hsCRP, a parameter of inflammation, were found higher in IFG+IGT group than controls and IFG group but that was not statistically significant (p=0.067). In Ridker et al. study they suggest that the measurement of CRP adds clinically important prognostic information to the metabolic syndrome.

Elevated plasma visfatin levels have been reported in insulin-resistant states, such as overweight/obesity, type 2 DM, gestational diabetes mellitus (GDM), IR and metabolic syndrome [10, 11]. Prediabetes is a state indicating an increased relatively high risk for future development of DM and IR in prediabetic patients. Yet there are still controversies regarding the role of visfatin in the pathogenesis of these diseases. Many of the studies on the effects of visfatin have produced conflicting results [5, 12]. Several articles have confirmed that circulating plasma visfatin levels are increased in patients with type 2 DM, while other studies do not support this result [5]. Toruner et al. [13] reported low visfatin levels which correlated negatively with both glycemic control and disease duration in type 1 diabetics. This result might have been due to freze-thaw cycles and different sample additives, which have a considerable influence on the measurement of visfatin concentrations [14]. In Oki et al. study the insulin resistance and HOMA-IR was found not correlated with visfatin levels [15]. Körner et al. [16] also demonstrated that there was a difference between some commercially available immunoassays in terms of specificity and sensitivity of visfatin detection in human serum and plasma.

In the current study, BMI, insulin level and IR were determined to be higher in the IFG+IGT group than in the control group and the IFG group, whereas the visfatin level of the IFG+IGT patients was lower than that of the control group. This result could be attributed to the small study cohort.

As expected, the IR of the prediabetic patients was higher than that of the control group. Therefore, the circulating visfatin level was found to be positively associated with insulin resistance but in this study the HOMA-IR results were not corelated with serum visfatin levels.

Although the prediabetic group had significantly higher TG, total cholesterol and HbA1c levels, there were no statistical differences between the groups in respect of HDL, LDL and hsCRP levels between the groups.

Chen et al. [10] reported that plasma visfatin did not correlate with BMI and other biochemical markers. Most previous studies have suggested that elevated visfatin levels were not related with adiposity parameters such as BMI, waist-hip ratio and percentage of body fat [17, 18]. In the current study, the serum visfatin levels were positively correlated with TG, BMI and IR in both the prediabetic and control groups but not to a statistically significant level. These findings suggest that adiposity is related with circulating visfatin, but only if there are remarkable differences for adiposity among the study subjects. Studies on the relationship of circulating visfatin to adiposity have yielded variable results. Davutoglu et al. [19] found elevated plasma visfatin levels in obese children and reported that these levels were positively correlated with BMI. In another study by Berndt et al. [20], plasma visfatin concentrations were also determined to be positively correlated with BMI. Pagano et al. [21] reported reduced plasma visfatin levels in obese adults.

Limitation of this study was significant heterogeneity resulting from a combination of factors, such as age, gender, medication history, etc which may have reduced the reliability of the results. Owing to the lack of prospective studies, all the visfatin concentrations were compared cross-sectionally. Therefore, it was difficult to clarify the cause–effect relationship between visfatin and HbA1c, IR, BMI. In conclusion, the results of this study revealed that prediabetes status was associated with an elevated level

of circulating plasma visfatin, and these results were supported by a significant association between visfatin and IR.

Conflict of Interest: The authors declare that there is no conflict of interest.

References

1. Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26:3160-3167. https://doi.org/10.2337/diacare.26.11.3160
2. Diabetes mellitus çalışma ve eğitim grubu, Türkiye Endokrinoloji ve Metabolizma Derneği, Diabetes mellitus ve komplikasyonlarının tanı, tedavi ve izlem kılavuzu- Güncellenmiş 12. baskı 2019;15-22.
3. McGee KC, Harte AL, daSilva NF, et al. Visfatin is regulated by rosiglitazone in type 2 diabetes mellitus and influenced by NFkb and JNK in Human Abdominal Subcutaneous Adipocytes. PLoS one 2011;6:20287.
4. Ognjanovic S, Bao S, Yamamoto SY, Garibay-Tupas J, Samal B, Bryant-Greenwood GD. Genomic organization of the gene coding for human pre-B-cell colony enhancing factor and expression in human fetal membranes. J Mol Endocrinol 2001;26:107-117.
5. Chang YH, Chang DM, Lin KC, Shin SJ, Lee YJ. Visfatin in overweight/obesity, type 2diabetes mellitus, insulin resistance, metabolic syndrome and cardiovascular diseases: A meta-analysis and systemic review. Diabetes Metab Res Rev 2011;27:515-527. https://doi.org/10.1002/dmrr.1201
6. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: Insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 1985;28:412-419.
7. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27:1487-1495.
8. Lopez-Bermejo A, Chico-Julia B, Fernandez-Balsells M, et al. Serum visfatin increases with progressive beta-cell deterioration. Diabetes 2006;55:2871-2875 https://doi.org/10.2337/db06-0259
9. Brown JE, Onyango DJ, Ramanjaneya M, et al. Visfatin regulates insulin secretion, insulin receptor signalling and mRNA expression of diabetes-related genes in mouse pancreatic beta-cells. J Mol Endocrinol 2010;44:171-178. https://doi.org/10.1677/JME-09-0071
10. Chen MP, Chung FM, Chang DM, et al. Elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 2006;91:295-299. https://doi.org/10.1210/jc.2005-1475
11. Krzyzanowska K, Krugluger W, Mittermayer F, et al. Increased visfatin concentrations in women with gestational diabetes mellitus. Clin Sci (Lond) 2006;110:605-609. https://doi.org/10.1042/CS20050363
12. Stephens JM, Vidal-Puig AJ. An update on visfatin/pre-B cell colonyenhancing factor, a ubiquitously expressed, illusive cytokine that is regulated in obesity. Curr Opin Lipidol 2006;17:128-131. https://doi.org/10.1097/01.mol.0000217893.77746.4b
13. Toruner F, Altinova AE, Bukan N, et al. Plasma visfatin concentrations in subjects with type 1 diabetes mellitus. Horm Res 2009;72:33-37. https://doi.org/10.1159/000224338
14. Nüsken KD, Nüsken E, Petrasch M, et al. Preanalytical influences on the measurement of visfatin by enzyme immuno assay. Clin Chim Acta 2007;382:154-156. https://doi.org/10.1016/j.cca.2007.04.004
15. Oki K, Yamane K, Kamei N, et al. Circulating visfatin level is correlated with inflammation, but not with insulin resistance. Clin Endocrinol 2007;67:796-800.
16. Körner A, Garten A, Blüher M, et al. Molecular characteristics of serum visfatin and differential detection by immunoassays. J Clin Endocrinol Metab 2007;92:4783-4791. https://doi.org/10.1210/jc.2007-1304
17. Zahorska-Markiewicz B, Olszanecka-Glinianowicz M,Janowska J, et al. Serum concentration of visfatin in obese women. Metabolism 2007;56:1131-1134. https://doi.org 10.1016/j.metabol.2007.04.007
18. Kamińska A, Kopczyńska E, Bronisz A, et al. An evaluation of visfatin levels in obese subjects. Endokrynol Pol 2010;61:169-173.
19. Davutoglu M, Ozkaya M, Guler E, et al. Plasma visfatin concentrations in childhood obesity: relationships to insulin resistance and anthropometric indices. Swiss Med Wkly 2009;139:22-27. https://doi.org smw-12400
20. Berndt J, Klöting N, Kralisch S, et al. Plasma visfatin concentrations and fat depot-specific mRNA expression in humans. Diabetes 2005;54:2911-2916.
21. Pagano C, Pilon C, Olivieri M, et al. Reduced plasma visfatin/pre B-cell colony enhancing factor in obesity is not related to insulin resistance in humans. J Clin Endocrinol Metab 2006;91:3165-3170. https://doi.org 10.1210/jc.2006-0361

Ethics committee approval was taken from Ankara Diskapi Yildirim Beyazit Training and Research Hospital. 27.02.2012, 01/13.