



Correlation of visfatin level with non-alcoholic fatty liver in metabolic syndrome

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Abstract

Background: Metabolic syndrome (MS) and non-alcoholic fatty liver disease (NAFLD) is a common public health problem. Visfatin is secreted by visceral adipose tissue and is an adipocytokine.

It could be a pro-inflammatory adipocytokine and is related to the metabolic syndrome and non-alcoholic fatty liver disease. This study evaluated the association between visfatin levels in patients with the metabolic syndrome with and without non-alcoholic fatty liver disease (NAFLD).

Methods: In this cross-sectional study, 120 patients with metabolic syndrome were selected. They were categorized into two groups, patients with fatty liver (n=70) and without fatty liver disease (n=50). Laboratory and anthropometric options such as age, sex, systolic blood pressure, fasting blood sugar, lipid profile, liver enzymes, uric acid, visfatin, insulin, BMI, waist circumference, and TNF- α were measured. The chi-square test, Mann-Whitney, t test, Spearman and Pearson correlations were used for the data analysis.

Results: There was a significant difference between the fatty liver and non-fatty liver disease with visfatin, BMI, FBS and lipid profile ($p < 0.05$). The mean \pm SD level of visfatin was 37.1 ± 1.7 ng/dl in the non-fatty liver and was 44.4 ± 1.5 ng/dl in fatty liver participants ($p = 0.02$). 59% of patients with metabolic syndrome had fatty liver in ultrasonography.

Conclusion: According to this study, there was a correlation between visfatin levels and fatty liver disease.

Keywords: Metabolic Syndrome, Visfatin, Non-alcoholic fatty liver disease

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Introduction

Metabolic syndrome (MS) has become a common public health problem in the world and affects people across various ethnicities in various countries (1). It has been described as a cluster of multiple, partially or fully expressed, metabolic abnormalities within the single individual that increase the risk of developing cardiovascular disease and diabetes (2). It is well known that non-alcoholic fatty liver disease (NAFLD) mirrors insulin resistance, and patients with NAFLD tend to have the abnormal components of the MS. The adipose tissue or body fat, which is closely related to MS, is a type of loose connective tissue composed mostly of adipocytes that are derived from preadipocytes. Adipocytokines include adiponectin, leptin, resistin, and visfatin are secreted from adipose tissue (3).

Visfatin as an adipocytokine which is secreted by visceral adipose tissue, is upregulated in obesity (4, 5). Visfatin may act in the regulation of a variety of physiological functions including cell proliferation, and glucose homeostasis (6). Adipokines that derived from adipose tissue have positive effect in pathogenesis of fatty liver and even progression of that (7-12). The role of visfatin as one of adipokines in the pathogenesis of NAFLD is less clear (13,14).

The role of visfatin level in the pathogenesis of NAFLD and MS is controversial, whereas only very few studies have been conducted to clarify the relationships between visfatin, NAFLD and MS. The present study was designed to evaluate these relationships.

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↑What is “already known” in this topic:

There is no correlation between blood pressure and uric acid and triglyceride, and cholesterol with visfatin.

→What this article adds:

Visfatin has no correlation with metabolic syndrome, but has significant correlation with fatty liver disease and degree of fatty liver according to sonographic classification.

Table 1. Characteristics of study participants of metabolic syndrome with and without NAFLD

Variables	No-NAFLD (Mean±SD)	NAFLD (Mean±SD)	<i>p</i>
BMI (kg/m ²)	27.7±8.3	32.1±9.1	0.003
FBS (mg/dl)	126±10.2	132±14.1	0.007
Triglyceride (mg/dl)	190.5±25	220.1±36	0.001
Cholesterol (mg/dl)	189.9±20.2	242.5±24.4	0.001
LDL (mg/dl)	130±25	145±30	0.003
HDL (mg/dl)	43±3.2	39±5.4	0.001
ALT (U/L)	26.8±7.6	28.1±8.4	0.3
AST (U/L)	32.1±8.4	30.8±9.6	0.4
Uric acid (mg/dl)	5.3±2.6	6.1±3.4	0.2
Visfatin (ng/dl)	37.1±1.7	44.4±1.5	0.02
Insulin (μIU/mL)	27.9±3.9	17.1±9.8	0.2
HOMA-IR	2.9±3.2	3.3±2.1	0.4

Body mass index (BMI, kg/m), Homeostasis Model Assessment of Insulin Resistance (HOMA-IR)

Methods

In this cross-sectional study, 120 patients with metabolic syndrome (age range: 30-68 years) at Imam Reza Hospitals in Mashhad, were assessed for the enrollment in this study between 2012 and 2014. MS has been defined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III).

Patients with more than 3 kg change in weight during last 6 months, chronic inflammatory diseases, type 2 diabetes, hypertension, acute and gastrointestinal diseases, pregnancy, use medication, drug abuse, smoking and consumption of more than 2 alcoholic drinks per week were excluded.

US display a relatively large inter- and intra-observer variability. A way of reducing this variability is real-time ultrasonography by an expert radiologist in fatty liver disease. Because of availability and low cost of abdominal US, we selected ultrasonography for diagnosis of fatty liver. Transabdominal ultrasonography of liver was performed for each participant by an experienced radiologist using a scanner (Acuson X300, Siemens, Germany). Anthropometric measurements (weight, height, waist circumference) and blood pressure were measured in all subjects.

Serum total cholesterol and triglycerides, low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein cholesterol was measured in serum. Serum alanine transaminase (ALT) and aspartate transaminase (AST) were measured too.

Visfatin levels were assayed by ELISA kit (BioVendor Laboratory Medicine Inc., Canada and Mexico, USA).

The serum levels of glucose and insulin were determined using commercially available assays. HOMA-insulin resistance (HOMA-IR) was calculated as (fasting insulin (μIU/mL) * fasting glucose (mmol/L)/22.5).

Statistical analysis

Statistical analysis was performed using the SPSS 16.0 statistical software package (SPSS Inc, Chicago, IL, USA) using Student's t-test, chi-square test, and, Pearson's correlation. The *p*<0.05 was considered as statistical significant.

Results

From 120 recruited participants who fulfilled the inclusion criteria, seventy cases had NAFLD and the reminders were in the normal group. Based on the sonographic classification of fatty liver as grade 1, grade 2 and grade 3, in 40 (33.3%), 28 (23.3%) and 2 (1.7%) of participants grade 1 to 3 of fatty liver was seen. The mean ± SD age of the patients was 46.1±12.1 years in normal group and 47.6±12.7 years in NAFLD group (*p*=0.4). In the normal population, 38% of the patients were male, whereas in the NAFLD group, male patients accounted for 35.7% (*p*=0.8). Mean BMI were 27.7±8.3 and 32.1±9.1 kg/m² in normal and NAFLD groups respectively (*p*=0.003).

Laboratory parameters characteristic of both groups are shown in Table 1. The mean±SD level of visfatin was 37.1±1.7 ng/dl in the non-fatty liver and was 44.4±1.5 ng/dl in fatty liver participants (*p*=0.02).

There was a significant positive correlation between

Table 2. Correlation between Visfatin and other factors between two groups

Variables	No-NAFLD		NAFLD	
	Pearson Correlation	<i>P</i>	Pearson Correlation	<i>P</i>
Age	0.7	<0.001	0.86	<0.001
Gender	0.25	0.07	0.01	0.9
Waist circumference	-0.1	0.4	0.3	0.01
BMI (kg/m ²)	-0.1	0.4	-0.1	0.3
FBS (mg/dl)	-0.02	0.9	-0.02	0.057
Triglyceride (mg/dl)	-0.16	0.2	-0.13	0.2
Cholesterol (mg/dl)	0.0009	0.9	0.03	0.7
LDL (mg/dl)	-0.1	0.5	0.2	0.08
HDL (mg/dl)	0.04	0.7	0.2	0.07
LDL/HDL	0.07	0.6	0.25	0.04
ALT (U/L)	-0.06	0.6	0.1	0.3
AST (U/L)	0.13	0.3	0.14	0.2
Uric acid (mg/dl)	0.27	0.053	0.001	0.9
Insulin (μIU/mL)	0.07	0.5	0.15	0.2

visfatin level and participant's age in both non-fatty liver and fatty liver groups ($r= 0.7$, $p= 0.0001$; $r= 0.86$, $p= 0.0001$, correspondingly) (Table 2). However, in the non-fatty liver group no static correlation was observed between visfatin level and other parameters of the study. On the other hand, visfatin level in NAFLD was related with waist circumference and LDL/HDL ($r= 0.3$, $p= 0.01$; $r= 0.25$, $p= 0.04$ respectively). Also, a significant correlation was found between visfatin level and degree of fatty liver according to sonographic classification ($r= 0.2$, $p= 0.02$).

Discussion

Visfatin secreted from visceral adipose tissue and might have an important role in the rapid accumulation of visceral fat via an autocrine or paracrine route.

The findings of the current study provide evidence-based information about the impacts of visfatin levels and degree of fatty liver in MS patients.

59% of patients with MS had NAFLD and others had a normal liver. The mean level of visfatin was 44.39 ± 1 and 37.13 ± 1.7 in patients with NAFLD and normal liver, respectively. Mann-Whitney test showed a significant difference between two groups ($p=0.027$).

Aler and his colleagues in 2008 showed, there was a significant correlation between visfatin level and having non-alcoholic fatty liver disease (15). We saw a significant correlation between age and level of visfatin in the NAFLD group. Kaminska also showed this correlation, but in their study by increasing the age, the level of visfatin was decreased (16).

There was no correlation between BMI and level of visfatin in our study that is verified by another study too (16). Similar to Reimann et al. there was no significant correlation between the level of visfatin and systolic blood pressure (17). In a study by Gilgor and his team, there was lack of correlation between triglyceride, uric acid and cholesterol with the level of visfatin (16,18).

In our study, there was a correlation between visfatin and fatty liver disease but not with MS, and there was no correlation between the ratio of LDL/HDL and visfatin, but against us, Gilgor saw a correlation between them (18).

In another study which was published recently, there is no correlation between visfatin and MS too. (19)

Base on all of these studies there was no correlation between visfatin and metabolic syndrome by definition of APT III, although there was a correlation with some risk factors of MS like triglyceride, and cholesterol. Although NAFLD was seen in 59% of our patients with MS, but a high level of visfatin was seen just in patients who had fatty liver disease.

Since storage of lipid in the liver can cause inflammation and fibrosis, we suggest adipocytokines like visfatin can have a special effect in pathogenesis and progression of fibrosis in NAFLD and in one study adipocytokine levels in the liver were correlated with the histologic findings. (20)

Our limitation in this study was, not having fibroscan for more accurate diagnosis of fatty liver and fibrosis, and not doing a liver biopsy because of being invasive. We use

TUS as a sensitive way for fatty liver detection.

Conclusion

There was a significant correlation between visfatin levels and sonographic classification of NAFLD. Visfatin exclusively secreted from visceral adipose tissue and might have an important role in the rapid accumulation of visceral fat via an autocrine or paracrine route.

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Conflict of Interests: None declared.

References

- Procopiou M, Philipe J. The metabolic syndrome and type2 diabetes: epidemiological figures and country specificities. *Cerebrovasc Dis* 2005;20(1S): 2-8.
- Uchiyama S. Impact of metabolic syndrome as a risk factor for atherothrombotic stroke. *Intern Med*. 2003; 44(10): 1011-1012.
- Gitrome L. Metabolic syndrome and cardiovascular disease. *J Psychopharmacol* 2005;19(6S):84-93.
- Fukuhara A, Matsuda M, Nishizawa M, et al. Visfatin: a protein secreted by visceral fat that mimics the effect of insulin. *Science*. 2005; 307: 426-30.
- Bernt J, Klötting N, Kralisch S, et al. Plasma visfatin concentrations and fat depot – specific mRNA expression in humans. *Diabetes*. 2005; 54: 2911-6.
- Aeghate E. Visfatin: structure, function and relation to diabetes mellitus and other dysfunctions. *Curr Med Chem*. 2008; 15: 1851-62.
- McCullough AJ. Pathogenesis of non-alcoholic steatohepatitis: human data. *Clin Liver Dis*. 2007; 11: 75–104.
- Mulhall BP, Ong JP, Younossi ZM. Non-alcoholic fatty liver disease: an overview. *J Gastroenterol Hepatol*. 2002; 17:1136–43.
- Baranova A, Gowder SJ, Schlauch K, et al. Gene expression of leptin, resistin, and adiponectin in the white adipose tissue of obese patients with non-alcoholic fatty liver disease and insulin resistance. *Obes Surg*. 2006; 16: 1118–25.
- Lutchman G, Promrat K, Kleiner DE, et al. Changes in serum adipokine levels during pioglitazone treatment for nonalcoholic steatohepatitis: relationship to histological improvement. *Clin Gastroenterol Hepatol*. 2006; 4: 1048–52.
- Musso G, Gambino R, Biroli G, et al. Hypoadiponectinemia predicts the severity of hepatic fibrosis and pancreatic beta-cell dysfunction in nondiabetic nonobese patients with nonalcoholic steatohepatitis. *Am J Gastroenterol*. 2005; 100:2438–46.
- Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. Williams textbook of endocrinology. Elsevier Health Sciences; 2015; Nov 30. Chapter 36.
- Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metabol*. 2004; Jun 1;89(6):2548-56.
- Polyzos SA, Kountouras J, Zavos C. Nonalcoholic fatty liver disease: the pathogenetic roles of insulin resistance and adipocytokines. *Cur Molecul Med*. 2009 Apr 1;9(3):299-314.
- Chin HK. Nonalcoholic fatty liver disease: A manifestation of the metabolic syndrome. *Cleveland Clinic J Med*. October 2008; 75(10): 721-728.
- Kamińska A, Kopczyńska E, Bronisz A, Żmudzińska M, Bieliński M, Borkowska A. An evaluation of visfatin levels in obese subjects. *Pol J Endocrinol* 2010; 61 (2): 169–173.
- Reimann M, Ziemssen T, Huisman HW, Schutte R, Malan L, Van Rooyen JM, et al. Ethnic-specific correlations of visfatin with circulating markers of endothelial inflammation and function. *Obesity (Silver Spring)*. 2009;17(12):2210-2215.
- Gligor R, Zdremtan D, Luminita P, Matei I. Correlations of visfatin with the lipidic metabolism in diabetic and obese patients. *Proc Rom Acad. Series B*, 2012; 1: 37–43.
- Hosseinzadeh-Attar MJ, Golpaie A, Foroughi M, Hosseinpanah F,

- Zahediasl S, Azizi F. The relationship between visfatin and serum concentrations of C-reactive protein, interleukin 6 in patients with metabolic syndrome. *J Endocrinol Invest*. 2016 Aug;39(8):917-22.
20. Jamali R, Hatami H, Kosari F. The Correlation Between Serum Adipokines and Liver Cell Damage in Non-Alcoholic Fatty Liver Disease. *Hepat Mon*. 2016 May; 16(5):e37412.