

The Relation of Serum Visfatin Level and Non-Alcoholic Liver Disease with Metabolic Syndrome and its Components

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Research Article

Volume 2 Issue 3

Received Date: February 22, 2017

Published Date: March 24, 2017

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Abstract

Objective: Psoriasis is a chronic inflammatory skin disease, which is frequently associated with comorbidities including metabolic syndrome and nonalcoholic fatty liver disease. Visfatin is an adipokine secreted either from adipocytes or cells of the stromal vascular fraction of white adipose tissue and its high concentrations is known to be in a relationship with abdominal obesity and chronic inflammation. This study investigates serum levels of visfatin in patients with psoriasis to reveal that high levels of this novel adipokine is related to metabolic syndrome. Our patients are also undergo ultrasonographic liver screening, therefore we consider how psoriasis is linked to metabolic syndrome and non alcoholic fatty liver disease.

Method: In this study, we evaluated 80 severe and moderate psoriasis patients which are requested Canakkale Onsekiz Mart University, Faculty of Medicine, Dermatology Department outpatient clinic. They divided into 2 groups as patients with metabolic syndrome and without diagnosis of metabolic syndrome. A healthy control group, 40 people with no history and diagnosis of psoriasis and metabolic syndrome are also included. The body mass index (BMI), waist and hip circumference were calculated. The score of PASI, grade of non alcoholic fatty liver disease and levels of SGOP, SGPT were noted. For quantification of the visfatin, ELISA based assay was used in clinical biochemistry department.

Results: Visfatin levels have been analysed in 40 psoriasis and metabolic syndrome patients, 40 psoriasis patients without metabolic syndrome (healthy psoriasis patients) and 40 healthy volunteers. 64 patients have moderate psoriasis and 16 patients have severe psoriasis. The average age is 52 and the mean BMI score of psoriasis group is 28.74. The ultrasonographic examination revealed no steatosis in 4 patients (5%), grade 3 hepatosteatosis in 8 patients (10%). Non alcoholic fatty liver disease and the severity of hepatosteatosis were determined significantly higher in psoriasis patients with metabolic syndrome ($p < 0.001$). On the other hand the prevalence of the non alcoholic fatty liver disease has showed no difference between healthy controls and healthy psoriasis patients ($p = 0.469$). Visfatin levels were found statistically

higher in the healthy psoriasis group versus control group. Neither healthy psoriasis patients nor psoriasis patients with metabolic syndrome, a significant difference could be observed both group ($p=0.980$). Eventually we have evaluated the serum visfatin levels in psoriasis patients with metabolic syndrome components such as obesity, diabetes, hypertension, hyperlipidemia and/or NAFLD versus healthy controls but no correlation detected ($p=0.246$; $p=0.884$; $p=0.684$; $p=0.521$; $p=0.259$).

Conclusions: Prevalence of non alcoholic fatty liver disease was observed to be higher in psoriasis patients. However there were no difference between controls and healthy psoriasis patients for prevalence of non alcoholic fatty liver disease. Therefore we think that this result supports the metabolic syndrome and psoriasis relationship. Visfatin levels detected significantly higher in psoriasis patients independently from metabolic syndrome and its components. These findings suggest that high visfatin levels might play role in chronic inflammation seen in psoriasis.

Keywords: Psoriasis; Metabolic Syndrome; Non Alcoholic Fatty Liver Disease; Adipokine; Visfatin

Introduction

Psoriasis is a chronic, inflammatory skin disease with genetic and autoimmune factors in its etiopathogenesis and characterized by white squams in erythematous plaques. Psoriasis has many burden comorbidities such as obesity, hyperlipidemia, hypertension, coroner artery disease, metabolic syndrome (MS) and non-alcoholic fatty liver disease (NAFLD) [1]. MS and NAFLD are extensively studied comorbidities among psoriatic patients. MS is an umbrella terms that cluster of glucose intolerans, hypertension, obesity and dislipidemia [1-4]. In pathophysiology of the disease associated with proinflammatory cytokines (TNF-alpha, IL-6), insulin resistance plays a role mediated by adipokines such as leptin and adiponectin [2-4]. The cause of the syndrome is still unknown yet the main factors as advanced age, obesity, sedentary life style and genetic factors are accepted depends on literature data [5].

NAFLD is known as accumulation of fat in the liver of people independence of alcohol usage and disease generally more common in patients with obesity and insulin resistance. NAFLD can progress to non-alcoholic steatohepatitis, cirrhosis or liver failure [6,7].

Abdominal obesity cause chronic inflammation due to elevated level of adipokine and triggers metabolic and cardiovascular disorders [8-10]. Psoriatic patients are generally over-weight and more prone to MS and cardiovascular disease. Adipokines may be the main regulator in pathogenesis of comorbidities in psoriasis due to shared inflammatory mechanisms behind psoriasis and obesity [11,12]. Visfatin is newly discovered adipocyte hormone that is secreted from visceral adipose

tissue [13,14]. Visfatin is also known as pre-B cell colony-enhancing factor and its related with many etiology and pathogenesis of many disease and also immunity, cell metabolism, prolong lifetime [11,13,15]. The studies indicate that serum visfatin levels increase in psoriasis [12,16,17] as well as MS [18-21] more than general population. In this study we aimed to evaluate the relation of serum visfatin level and NAFLD with MS in psoriatic patients.

Material and Methods

This study was constructed at Çanakkale Onsekiz Mart University, Faculty of Medicine, Dermatology Department. One hundred twenty individuals are divided three main groups as follow: psoriasis patients with MS (n:40); psoriasis patients without MS (n:39) and as a control group patients without psoriasis and MS (n:40). The control group is the same age and sex with psoriasis patients without MS. All psoriatic patients have moderate or severe psoriasis. The study was approved by the research ethics committee of Çanakkale Onsekiz Mart University, and all participants provided their written informed consent.

The exclusion criteria for participation were as follows; age under eighteen, Psoriasis Area Severity Indeks (PASI) below seven (PASI <7), regular alcohol consumption, presence of acute or chronic liver disease, celiac disease, Wilson disease. Aside patients were has medical problems such as total parenteral nutrition, quick weight loss, jejunioleal bypass, lipodystrophy, abetalipoproteinemia, quick weight gain after diets were not included in the study. The patients have long term drug usage that can

cause NAFLD such as amiodarone, stilbestrol, tamoxifen, high-dose corticosteroids, nifedipine, diltizem etc. and has genetic problems such as receptor mutations were also excluded from the study. PASI were use to evaluate severity of psoriasis. The demographic data included weight, height, body mass index, and waist circumference were recorded in dermatology department. The prevalence of various psoriasis related comorbidities and blood test results were evaluated for metabolic syndrome diagnosis. All patients were evaluated by ultrasound examination in radiology department by the same radiologist. Understanding hepatic steatosis Alanine Transaminase (ALT) and Aspartate Aminotransferase (AST) parameters were evaluated in all groups.

NCEP ATP III criteries of metabolic syndrome (≥ 3 of the following): waist circumference >88 cm for women or >102 cm for men, triglycerides ≥ 150 mg/dl, HDL < 50 mg/dl in women or < 40 mg/dl in men, blood pressure $\geq 130/85$ mm Hg, fasting glucose ≥ 110 mg/dl.

Laboratory Measurements

5 ml of venous blood samples were collected from all patients. Biochemical parameters including serum total cholesterol, triglyceride, low-density lipoprotein-cholesterol (LDL), high-density lipoprotein-cholesterol (HDL), fasting blood glucose (FBG), was determined using commercial kits. Blood samples were centrifuged (4000 rpm) at room temperature for 10 minutes and seperated plasma store -80°C until visfatin assay. Plasma visfatin levels were determined by enzyme-linked immunosorbent assay (ELISA) method.

Statistical Analyses

All statistical analysis of the data was evaluated using statistical processing software (SPSS-19). Kolmogorov-Smirnov test was used to estimate the variables' distribution characteristics. The mean, standard deviation, median, minimum and maximum values, frequency and percentages were used in the presentation of the descriptive data. Dependent and independent variables in the univariate analysis were examined using the chi-square test. Mann Whitney U test were used to compare visfatin values between patients and the controls. Comparisons of continuous variables among the groups were performed by analysis of Variance in normal distribution. Yet Kruskal Wallis Varyans Analyses were performed in abnormal distribution. It was considered statistically significant when the P-value below 0.05.

Results

The mean age of the patients with MS was 59.4 ± 11.9 (min/max: 18/78) and without MS was 44.6 ± 18.2 (min/max 33/87). The mean age was statistically different within two groups ($p < 0.001$). The distribution of gender difference within groups. The rate of men more in MS groups (62,5%) while the rate of women (60%) more in without MS groups ($p = 0.044$) as shown in the Table 1, BMI, waist circumference and hip circumference average was higher in MS group then non-MS group ($p < 0.001$, $p < 0.001$, $p < 0.001$ respectively). Although there was no differences in weight measurements between the two groups ($p = 0.124$), the average height of the non-metabolic syndrome group was statistically higher ($p = 0,001$). The obesity rate was higher in patients with metabolic syndrome then psoriatic patients without metabolic syndrome ($p < 0.001$).

	Psoriasis patients with MetS		Psoriasis patients without MetS		p
	Med \pm sd	Min-max	Med \pm sd	Min-max	
Waist circumference	89.48 \pm 12.01	64.00- 132.00	104.28 \pm 8.15	91.00- 133.00	<0.001
Hip circumference	98.67 \pm 10.85	86.00- 145.00	106.65 \pm 8.62	91.00- 129.00	<0.001
Height (cm)	169.60 \pm 8.58	150.00- 190.00	162.67 \pm 9.45	139.00- 180.00	0.001*
Weight (kg)	76.30 \pm 17.81	51.00- 150.00	82.00 \pm 14.86	58.00- 120.00	0.124*
BMI	26.45 \pm 5.85	20.00- 53.10	31.03 \pm 5.56	21.30- 53.30	<0.001

Table 1: The distribution of the body measurements of patients within groups.
med: median sd: standard deviation ; min-max: minimum-maximum; p: Mann-Whitney U test
*: Significance test of difference between the two average percent: Percentage line

The mean of serum levels of visfatin was 592.7 ± 133.5 in psoriasis groups and 404.3 ± 99.7 in control groups. The serum level of visfatin in patients with psoriasis were found to be higher than in healthy controls ($p < 0.001$). Beside the mean of serum levels of visfatin was 594.30 ± 137.61 in psoriatic patients with MS and 591.05 ± 131.06 in psoriatic patients without MS. There was no differences in serum levels of visfatin in psoriatic patients with or without MS ($p = 0.980$).

In our study, we did not find any significant difference in the serum visfatin level of psoriatic patients with diabetes (585.92 ± 139.84) or without diabetes (596.02 ± 131.62) ($p = 0.684$). Aside there were no significant difference in serum visfatin level in absence or presence of hypertension among psoriatic patients [HT (+) ($n = 31$) mean: 608.71 ± 147.48 HT (-) ($n = 48$) mean: 582.35 ± 124.28] ($p = 0.259$). There was no significant difference between the serum visfatin level of the hiperlipidemia and non-hiperlipidemia groups [(mean: 608.71 ± 147.48 and 582.35 ± 124.28) respectively, ($p = 0.259$)]. In addition, we did not find any significant difference in serum visfatin level of psoriatic patients with obesity (590.73 ± 118.04) or without obesity (593.90 ± 143.42) ($p = 0.884$).

The mean serum visfatin level were 609.73 ± 136.91 and 525.63 ± 96.2 (in the psoriasis moderate and severe psoriasis patients, respectively), and there was a statistically significant difference but this is not the result we expected because we were expecting higher in severe group ($p = 0.035$).

The mean serum visfatin level were not correlated with NAFLD in psoriasis [567.25 ± 64.40 ; 579.48 ± 139.47 ; 647.89 ± 132.06 ; 553.63 ± 99.84 ; $p = 0.246$] and control groups 401.76 ± 105.40 ; 457.67 ± 48.7 ; ($p = 0.334$) in Grade 0 to 3 respectively. In addition, we did not find any correlation in serum visfatin level and NAFLD among psoriatic patients with or without MS.

Psoriasis patients with MS and psoriasis patients without MS groups compared for liver steatosis and grade 1 steatosis seen more frequent in psoriasis patients without MS. But grade 2 and 3 steatosis seen more frequent psoriasis patients with MS and this difference was statistically significant ($p < 0.001$). Psoriasis patients without MS and control group compared for liver steatosis and no statistically significant differences between the two groups ($p = 0.469$).

USG	MS (-)		MS (+)		Total		p
	n	percent	n	percent	n	percent	
No steatosis	4	100.0	0	0.0	4	100.0	
Grade-1	30	61.2	19	38.8	49	100.0	<0.001
Grade-2	4	21.1	15	78.9	19	100.0	
Grade-3	2	25.0	6	75.0	8	100.0	

USG	MS (-)		Control		Total		p
	n	percent	n	percent	n	percent	
No steatosis	4	57.1	3	42.9	7	100.0	
Grade-1	30	46.9	34	53.1	64	100.0	0,469
Grade-2	4	57.1	3	42.9	7	100.0	
Grade-3	2	100.0	0	0.0	2	100.0	

Table 2: Comparison of hepatic steatosis on ultrasound findings in patients.
n: number; percent: Percentage line; p: Chi-square test

The average BMI of the patients with increasing adiposity was increasing in direct proportion to the intensity (No steatosis; 21.8 ± 1.4 grade 1; 27.3 ± 4.3 grade 2; 29.5 ± 4.0 grade 3; 38.4 ± 10.0) ($p < 0.001$).

Patients with DM have higher incidence of grade 2 and 3 from patients without DM and these findings are statistically significant ($p=0.004$). Patients with HT have higher incidence of grade 2 and 3 from patients without DM and these findings are statistically significant ($p=0.011$). Patients with hyperlipidemia compared with patients without hyperlipidemia, there is no statistically significant differences between the two groups ($p=0.421$).

Discussion

MS is the most important comorbidity in psoriasis, thus the association between psoriasis and MS has been studied extensively by several research groups. In several researches the prevalence of MS was found higher in psoriasis patients than the normal population [22,23]. There are conflicting results in studies that have studied the relationship between psoriasis severity and MS risk. Al-Mutairi et al. and Langan et al. has been indicated there was a positive correlation between psoriasis severity and MS yet Gisondi et al. could not shown statistically significant difference in metabolic syndrome prevalence in psoriasis group [22,23]. In our study, we could not find statistically significant association between metabolic syndrome and psoriasis ($p=0.161$). Al-Mutairi et al. has been shown that serum visfatin level increased significantly and there was a positive correlation between serum visfatin level and PASI score in Egyptian patients [22].

Similarly, Yan et al. has been shown positive correlation in serum visfatin level and psoriasis severity in Chinese population [24]. Okan et al. showed that the serum visfatin level can be increased in psoriasis patients and also it has positive correlation with PASI [25]. However, Gerdes et al. reported increased serum visfatin levels in psoriasis patients without correlation with psoriasis severity [12]. In our study, there was no difference in serum visfatin level between psoriatic patients without MS and age and sex related control group ($p<0.001$). In contrast to literature serum visfatin level decrease in severe psoriatic patients when compare to moderate psoriatic patients ($p=0.035$). There was a conflicting result about serum visfatin level with MS and its components. The serum visfatin level has been shown either increase [18-21] or decrease [26-28]. In MS patients depend on the study populations. In our study, the serum visfatin level did not differs in diabetes, hypertension, hyperlipidemia and MS subgroups [$p=0.684$; $p=0.521$; $p=0.259$, $p=0.98$ respectively].

There are conflicting results in studies that have studied the relationship between serum visfatin level and obesity [16,29-31]. In our study, we could not find any difference within the obese and non-obese groups among psoriatic patients ($p=0.884$). Dalamaga et al. has been shown that serum visfatin level has a strong association with NAFLD [32]. Alexander et al. has been shown that serum visfatin level was decreased after weight loss in NAFLD patients in Australian population [33]. In contrast, Genç et al. could not find any association between serum visfatin level and NAFLD [34]. In our study, we could not find any association between serum visfatin level and NAFLD among control, psoriasis, psoriasis with MS, psoriasis without MS groups ($p=0.334$; $p=0.246$; $p=0.296$; $p=0.656$; respectively).

Marchesini et al., has been shown that MS increase in NAFLD patients more than general populations [35]. Chen et al. has been reported that prevalence of MS components [obesity, diabetes, hypercholesterolemia, hypertriglyceridemia] has been increase in NAFLD patients [36]. Socha et al. has been reported that MS and NAFLD shares similar mechanisms [37]. Gisondi et al. has been shown that psoriasis patients were more prone to developed NAFLD in Italian population. Aside, there was a positive correlation was found between psoriasis severity and NAFLD [38]. In this current study, NAFLD prevalence was found higher in psoriatic patients than control group. Aside we have found that grade-1 hepatosteatosis was more common in psoriasis patients without MS yet grade 2-3 hepatosteatosis was more common in psoriasis patients with MS ($p<0.001$). Also we could not found any significant relation between psoriasis severity and NAFLD ($p=0.762$).

Results

In our study, we could not find any statistically difference in obesity, MS, NAFLD and its severity between subgroups of moderate and severe psoriasis. In contrast the current knowledge there was a negative correlation between serum visfatin and psoriasis severity. The reason for this unexpected results occurs due to there is no strick difference in PASI values in moderate and severe subgroups. Aside proportion of the subgroups are different and number of severe psoriatic patients were four times less than moderate psoriatic groups. Those with more patients to be done in the study may give more significant results.

In our study, the serum visfatin level was statistically significantly higher in psoriatic patients without MS when compared to age and sex matched control groups ($p < 0.001$). But there was no differences in serum levels of visfatin in psoriatic patients with or without MS ($p = 0.980$). In addition, we evaluated serum visfatin level in psoriatic patients with MS components in terms of obesity, diabetes, hypertension, hyperlipidemia and NAFLD and there were no statistically significant differences found in psoriatic subgroups then age and sex matched controls ($p: 0.246$ and $p: 0.884$, $p: 0.684$, $p: 0.521$; $p: 0.259$ respectively). As a result, serum visfatin levels were significantly higher in patients with psoriasis, but this elevation was independent from MS and components and the correlation occurs due to chronic inflammation plays a crucial role in the pathogenesis of psoriasis. In this current study, we found positive correlation probability of occurrence as well as severity of NAFLD with weight, waist circumference, hip circumference ($p < 0.001$; $p < 0.001$; $p < 0.001$; $p < 0.001$; respectively). These correlations are consistent with the literature.

In this study, we found that the prevalence of NAFLD was higher than the control group in patients with psoriasis. The distribution of the steatosis level is different in patients with or without MS. As a result grade 1 steatosis higher in psoriasis patients without MS while grade 2 and 3 steatosis higher in psoriasis patients with MS and this difference was statistically significant ($p < 0.001$). We also found the occurrence and severity of NAFLD was significantly higher in patients with MS, yet there was no statistically difference found between healthy individuals and psoriatic patients without MS ($p: 0.469$).

In conclusion, we found increased NAFLD prevalence among psoriasis patients, in contrast there was no difference between control groups and patients without MS in terms of NAFLD presence. Thus we concluded that increased NAFLD prevalence in patients with psoriasis in concordance with MS. NAFLD prevalence of increased among psoriasis patients directly with presence of MS and that supports the view that increased NAFLD might be related with MS.

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