Assessment of visfatin concentrations in the serum of male psoriatic patients in relation to metabolic abnormalities

Katarzyna Maria Chyl-SurdackaA–D, Joanna BartosińskaA,C,D, Małgorzata KowalB,C, Joanna Przepiórka-KosińskaB, Dorota KrasowskaE,F, Grażyna ChodorowskaA,C,E,F

Department of Dermatology, Venerology and Paediatric Dermatology, Medical University of Lublin, Poland

A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

Abstract

**Background.** Visfatin is one of the pro-inflammatory adipokines secreted by adipose tissue cells. Recent scientific research has drawn attention to the role of adipokines in the pathophysiology of metabolic disorders and their association with inflammatory diseases, including psoriasis. Visfatin may be one of the important links explaining the connection between psoriasis and diseases which are components of metabolic syndrome.

**Objectives.** The aim of this study was to assess the serum visfatin concentration in patients with psoriasis and to evaluate its possible correlations with parameters of metabolic syndrome and the clinical severity of psoriasis.

**Material and methods.** A group of 102 patients with psoriasis and a control group of 40 healthy subjects were examined. The clinical severity of psoriasis was assessed according to Psoriasis Area and Severity Index, BSA (Body Surface Area) and DLQI (Dermatology Life Quality Index) indicators, the presence and type of obesity, and hypertension. In both the study and control groups, laboratory tests (C-reactive protein (CRP), glucose concentration, total cholesterol, low-density-lipoprotein (LDL) cholesterol, high-density-lipoprotein (HDL) cholesterol, and triglycerides (TG)) were performed and serum visfatin concentrations were determined. The clinical data, results of laboratory tests and visfatin concentrations were then subjected to statistical analysis.

**Results.** There was a significantly higher concentration of visfatin in the psoriatic patients (p < 0.001) than in the control group. Significant positive correlations between visfatin concentration and PASI (\(p = 0.008\)) and BSA (\(p = 0.007\)) were observed. In the psoriatic group, there were positive correlations between the concentrations of visfatin and the concentrations of CRP (\(p = 0.008\)) and total cholesterol (\(p = 0.002\)). Visfatin concentration was elevated in the psoriatic patients who had elevated total cholesterol (\(p = 0.001\)), LDL cholesterol (\(p = 0.012\)) and TG levels (\(p = 0.001\)) compared to the psoriatic patients with normal levels of these lipid profile components.

**Conclusions.** The results indicate the possible participation of visfatin in pathophysiological and inflammatory processes in the course of psoriasis. Adipokines may be an important link connecting psoriasis with coexisting metabolic disorders.

**Key words:** psoriasis, visfatin, metabolic syndrome
Introduction

Psoriasis is a chronic, genetically determined inflammatory skin disease with autoimmune involvement and a pathogenesis which still has not been completely revealed. Recent literature data indicates that psoriasis can be included in the group of chronic inflammatory systemic diseases (CIDs). The presence of various mediators – including cytokines and adipokines – responsible for systemic inflammation and its metabolic consequences has been demonstrated not only in the affected skin but also in peripheral circulation. Inflammatory mediators, also secreted by adipose tissue cells, participate in inducing vascular endothelial dysfunction and insulin resistance, increasing the concentration of thrombogenic factors and promoting oxidative stress and lipid oxidation disorders. Adipokines may be an important link connecting psoriasis with coexisting metabolic disorders.

Visfatin is a 52 kDa protein composed of 473 amino acids secreted mainly by hepatocytes, macrophages and adipocytes of visceral adipose tissue.1-8 The intracellular form of the protein is crucial in cellular metabolism regulation, adaptation to extracellular stressors and cell survival. The extracellular form detected in the circulation and extracellular environment has an influence on the inflammatory and metabolic processes.3,5,9,10 Some studies have indicated the involvement of visfatin in the pathogenesis of abdominal obesity, atherosclerosis, type 2 diabetes mellitus, and vascular and inflammatory diseases,1,4-6,9,11 because the protein has enzymatic, metabolic, inflammatory, and immunomodulatory properties.5 Moreover, the protein affects vascular endothelial cells and vascular smooth muscle cells (VSMC) and it stimulates neangiogenesis.5,12 Visfatin contributes to increased expression of adhesion molecules, i.e., intercellular adhesion molecule 1 (ICAM-1), vascular cell adhesion molecule 1 (VCAM-1), selectin, and vascular endothelial growth factor (VEGF), which results in increased recruitment and adherence of the immune cells to the vascular endothelium, increased proliferation and migration of the endothelium, and the formation of new blood vessels. Visfatin affects the inflammatory reaction in the vessel, inducing increased secretion of the molecules interleukin 6 (IL-6), IL-8, monocyte chemoattractant protein 1 (MCP-1), tumor necrosis factor α (TNF-α), matrix metalloproteinase 2 (MMP-2), and MMP-9 by endothelial cells and monocytes,5,13-17 and activating nicotinamide adenine dinucleotide oxidase.3 Exogenous protein administration has been shown to increase the synthesis of the inducible nitric oxide synthase (iNOS) enzyme, impairing the production of nitric oxide (NO) and enhancing oxidative stress in atherosclerotic plaque.4,5,9,12,13,18,19 On the other hand, recently published scientific reports point to a beneficial effect of visfatin on the course of ischemic processes. It seems that due to its antiapoptotic properties, it promotes the prolonged survival of myocardial and neuronal cells; therefore, the protein may prove to be a useful therapeutic tool in reducing the area of myocardial or cerebral ischemia in the course of acute necrosis of these organs.3,5,20-22 The proangiogenic, antiapoptotic and pro-inflammatory properties of visfatin may indicate possible involvement in the development of cancer.5,9

Objectives

Due to the relationship between psoriasis and metabolic syndrome, as well as the important role of visfatin in the induction of vascular endothelial dysfunction, our research was undertaken to investigate the relationship between the serum visfatin concentrations, psoriasis and individual components of metabolic syndrome.

Material and methods

The study included 102 adult, male psoriatic patients and 40 healthy, age-matched men. The patients with psoriasis were interviewed about the duration of their disease, the coexistence of psoriatic arthritis, any medications taken, and the presence of systemic comorbidities – with special attention to disorders that are components of metabolic syndrome, such as hypertension, diabetes, lipid disorders, and coexisting ischemic heart disease. The clinical condition of the patients was assessed by measuring blood pressure; determining the extent and severity of psoriatic skin lesions with the use of the indicators PASI (Psoriasis Area and Severity Index), BSA (Body Surface Area) and DLQI (Dermatology Life Quality Index); and assessing the presence and extent of obesity with body mass index (BMI) and waist–hip ratio (WHR). Patients with BMI values above 30 were considered obese. The WHR values higher than 1 confirmed the presence of abdominal obesity. The PASI values exceeding 10 indicated a moderate course of the disease, whereas patients with values over 18 were classified as having severe psoriasis. Patients in both the psoriasis group and the control group were assessed for serum concentrations of visfatin and laboratory parameters: C-reactive protein (CRP) concentration and components of the lipid profile (total cholesterol, high-density-lipoprotein (HDL) cholesterol, low-density-lipoprotein (LDL) cholesterol, triglycerides (TG), and glucose). Serum visfatin concentrations were determined with the immunoenzymatic enzyme-linked immunosorbent assay (ELISA) method according to the manufacturer’s recommended procedure using an AdipoGen Nampt (Visfatin/PBEF) human ELISA Kit (test sensitivity: 3.0 pg/mL, absorbance reading: 450 nm) (AdipoGen Corp., San Diego, USA). For the analysis of the results obtained, using IBM SPSS software v. 19 (IBM Corp., Armonk, USA), statistical significance was assumed at a p-value <0.05.
Results

There was a significantly higher concentration of visfatin in psoriatic patients than in the control group (p < 0.001) (Fig. 1, Table 1). In the study population, a significant correlation between serum visfatin concentration and CRP value (p = 0.008) was found; a positive correlation was also observed between the serum concentration of visfatin and PASI (p = 0.008) (Fig. 2) and BSA (p = 0.007) (Fig. 3). The protein concentrations were also significantly higher in the patients with severe psoriasis, as measured with PASI, compared to patients with mild disease severity (p = 0.013). However, no significant correlations were observed between the serum concentration of visfatin and DLQI (p = 0.544) or duration of the disease (p = 0.576). There were no correlations between the serum concentration of visfatin and BMI or fat distribution (WHR) (p = 0.380 and p = 0.095, respectively). In the psoriatic group, there was a significant positive correlation between serum visfatin concentration and total cholesterol level (p = 0.002). Serum visfatin concentration was significantly higher in the psoriatic patients who also had elevated total cholesterol, LDL cholesterol and TG levels compared to the patients with normal values of these parameters (p = 0.001, p = 0.012 and p = 0.001, respectively). The concentration of visfatin was not different in the psoriatic patients with and without concomitant arterial hypertension (p = 0.749).

Discussion

Visfatin belongs to the group of adipokines produced by adipose tissue cells. The literature indicates visfatin involvement in the pathogenesis of many inflammatory diseases, e.g., ulcerative colitis, Crohn's disease or hepatitis C. It is possible that the protein also participates in pathophysiological processes in psoriasis. In our own study, significantly higher concentrations of visfatin were observed in the group of psoriatic patients than in the control group. Moreover, in the experimental group, positive correlations between serum visfatin concentration and PASI and BSA values were also found.

Similar results have been presented by Ismail et al. in investigating the serum concentrations of visfatin and

<p>| Table 1. The concentration of visfatin in patients with psoriasis and in the control group |
|---------------------------------|--------|--------|--------|--------|--------|--------|--------|</p>
<table>
<thead>
<tr>
<th>Visfatin</th>
<th>Number of patients</th>
<th>Average</th>
<th>Median</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Lower quartile</th>
<th>Upper quartile</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental group</td>
<td>102</td>
<td>5.19</td>
<td>4.07</td>
<td>0.67</td>
<td>16.48</td>
<td>2.66</td>
<td>7.11</td>
<td>3.31</td>
</tr>
<tr>
<td>Control group</td>
<td>40</td>
<td>0.93</td>
<td>0.78</td>
<td>0.15</td>
<td>2.67</td>
<td>0.40</td>
<td>1.38</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Z = 8.694; p < 0.001; SD – standard deviation.
OMENTINE IN A GROUP OF 46 PATIENTS WITH PLAQUE PSORIASIS. THE AUTHORS FOUND A SIGNIFICANTLY ELEVATED CONCENTRATION OF VISFATIN IN THE PSORIATIC PATIENTS COMPARED TO A GROUP OF 42 HEALTHY PEOPLE. IN ADDITION, THEY OBSERVED POSITIVE CORRELATIONS BETWEEN VISFATIN CONCENTRATION AND PASI VALUE AND DISEASE DURATION. HOWEVER, VISFATIN CONCENTRATION WAS SIGNIFICANTLY HIGHER IN THE PATIENTS WITH SEVERE PSORIASIS.

THE RESULTS OF OUR OWN STUDY ARE ALSO IN AGREEMENT WITH THE ONES PRESENTED BY OKAN ET AL.24 WHO OBSERVED A POSITIVE CORRELATION BETWEEN VISFATIN CONCENTRATION AND DISEASE SEVERITY IN A GROUP OF 45 PATIENTS WITH PLAQUE PSORIASIS, AS ASSESSED WITH PASI.


IN OUR STUDY, HIGHER CONCENTRATIONS OF CRP WERE RECORDED IN THE STUDY GROUP THAN IN THE CONTROL GROUP (P = 0.008), AND A POSITIVE CORRELATION BETWEEN SERUM CRP AND VISFATIN CONCENTRATION (P = 0.008) WAS FOUND. SIMILARLY, CATALÁN ET AL.27 STUDYING A GROUP OF 30 OBSESE MEN AND A 14 CONTROL GROUPS, FOUND A POSITIVE CORRELATION BETWEEN VISFATIN CONCENTRATION AND NOT ONLY CRP CONCENTRATION BUT OTHER INFLAMMATORY PARAMETERS AS WELL, I.E., THE LEVELS OF FIBRINOGEN AND VON WILLEBRAND FACTOR. LU ET AL.28 INVESTIGATED A GROUP OF 173 PATIENTS WITH CHRONIC KIDNEY DISEASE AND ALSO SHOWED POSITIVE CORRELATIONS BETWEEN SERUM VISFATIN CONCENTRATION AND CRP VALUE AND THE TOTAL NUMBER OF LEUKOCYTES AND NEUTROCYTES.

VISFATIN IS KNOWN TO BE A PROTEIN PRODUCED BY MACRAPHAGES OF THE VISCERAL ADIPOSE TISSUE, AMONG OTHER TISSUES. HOWEVER, PREVIOUS STUDIES HAVE YIELDED CONFLICTING DATA ON CONCENTRATIONS OF THE PROTEIN IN CORRELATION WITH BMI AND ADIPOSE TISSUE DISTRIBUTION. IN OUR OWN STUDY, THERE WAS NO STATISTICALLY SIGNIFICANT CORRELATION BETWEEN SERUM VISFATIN CONCENTRATION AND BMI (P = 0.380) OR WHR (P = 0.095) IN THE GROUP OF PSORIATIC PATIENTS. THIS RELATIONSHIP WAS STILL NOT OBSERVED AFTER DIVIDING THE STUDY POPULATION INTO SUBGROUPS OF NORMAL BODY MASS, OVERWEIGHT AND OBESITY, AS WELL AS SUBGROUPS WITH GLUTEAL-FEMORAL AND ABDOMINAL FAT DISTRIBUTION.

OTHER AUTHORS23,25,29 INVESTIGATING THE CONCENTRATION OF VISFATIN IN PATIENTS WITH PSORIASIS AND LIPID DISORDERS, INSULIN RESISTANCE AND HYPERTENSION OBTAINED SIMILAR RESULTS. IN THE PSORIATIC PATIENTS, THE AUTHORS DID NOT FIND ANY CORRELATION BETWEEN SERUM VISFATIN CONCENTRATION AND OBESITY RATE. SIMILARLY, OZAL ET AL.30 DID NOT OBSERVE A SIGNIFICANT CORRELATION WITH BMI VALUES IN PATIENTS WITH HYPERTENSION WITH AND WITHOUT EXISTING OBESITY.


DISLIPIDEMIA IS AN ESSENTIAL ELEMENT OF METABOLIC SYNDROME, OCCURRING MORE OFTEN IN PEOPLE SUFFERING FROM PSORIASIS. DATA ON THE RELATIONSHIP BETWEEN SERUM VISFATIN LEVEL AND PROFILE COMPONENTS IS DIVERGENT AND DOES NOT GIVE A DEFINITE ANSWER AS TO WHETHER THE PROTEIN CAN SERVE AS A PREDICTOR OF THESE DISORDERS.

WHILE STUDYING LIPID DISORDERS, WE FOUND SIGNIFICANTLY HIGHER TOTAL CHOLESTEROL LEVELS IN OUR GROUP OF PSORIATIC PATIENTS IN COMPARISON TO THE CONTROL GROUP (P < 0.001). THERE WAS ALSO A SIGNIFICANT POSITIVE CORRELATION BETWEEN SERUM VISFATIN AND TOTAL CHOLESTEROL CONCENTRATIONS (P = 0.002). HOWEVER, NO SIGNIFICANT CORRELATION WAS OBSERVED BETWEEN SERUM VISFATIN CONCENTRATION AND THE LEVEL OF LDL CHOLESTEROL (P = 0.059), HDL CHOLESTEROL (P = 0.249) AND TG (P = 0.224). HOWEVER, AFTER DIVIDING THE SUBJECTS INTO GROUPS WITH NORMAL AND ABNORMAL LIPID PROFILES, A SIGNIFICANTLY HIGHER CONCENTRATION OF VISFATIN IN PATIENTS WITH BOTH PSORIASIS AND ELEVATED TOTAL CHOLESTEROL (P = 0.001), LDL CHOLESTEROL (P = 0.012) AND TG (P = 0.001) WAS FOUND IN COMPARISON WITH THE PATIENTS WITHOUT DYSLIPIDEMIA.

WHILE CATALÁN ET AL.27 SHOWED A POSITIVE CORRELATION BETWEEN THE CONCENTRATION OF VISFATIN AND LIPID PROFILE COMPONENTS – I.E., TOTAL CHOLESTEROL, HDL CHOLESTEROL AND TG – IN THEIR STUDY OF 30 INDIVIDUALS WITH MORBID OBESITY, INDEPENDENT OF OTHER FACTORS, COBAN ET AL. OBSERVED A NEGATIVE CORRELATION BETWEEN VISFATIN CONCENTRATION AND TOTAL CHOLESTEROL AND LDL CHOLESTEROL LEVELS IN A GROUP OF PSORIATIC PATIENTS.36

SOME DATA INDICATE A SIGNIFICANT EFFECT OF VISFATIN ON THE CARDIOVASCULAR SYSTEM.5 IN ADDITION TO INVOLVEMENT IN THE INDUCTION OF VASCULAR ENDOTHELIAL DYSFUNCTION, VASCULAR DAMAGE AND ATHEROSCLEROSIS, THERE IS MORE AND MORE EVIDENCE ON THE ASSOCIATION OF THIS ADIPOKINE WITH THE REGULATION OF ARTERIAL BLOOD PRESSURE, THOUGH IT REMAINS THE SUBJECT OF NUMEROUS CONTROVERSYES.

IN OUR OWN ANALYSIS, AFTER DIVIDING THE PATIENTS INTO THOSE SUFFERING FROM ARTERIAL HYPERTENSION AND THOSE WITHOUT THE DISEASE, THERE WAS NO STATISTICALLY SIGNIFICANT DIFFERENCE IN VISFATIN CONCENTRATION BETWEEN THESE SUBGROUPS (P = 0.749). SIMILAR RESULTS WERE PRESENTED BY KOCELAK ET AL.37 FROM A STUDY ON A LARGE GROUP OF 2,789 OLDER POLISH.
patients. The authors divided the patients into groups composed of people without hypertension, patients with pharmacologically regulated hypertension and those untreated for the disease. The authors did not observe significantly higher visfatin values in patients with hypertension compared to patients not suffering from the disease, nor did they find any influence of treatment or disease severity on the hormone levels. In contrast, significantly higher visfatin values were observed in patients with elevated CRP levels (hs-CRP) and homeostatic model assessment of insulin resistance (HOMA-IR).

Likewise, other authors have reported that there was no significant correlation between serum visfatin concentrations and systolic and diastolic blood pressure values in groups of patients with ischemic heart disease and metabolic disorders.\(^{28,38,39}\)

Different results were presented by Ozal et al.\(^{30}\) when they compared the serum visfatin concentrations of a group of 71 patients with refractory hypertension with a group of 94 pharmacologically controlled patients. The results showed significantly higher adipokine concentrations in the first group and a positive correlation with systolic and diastolic blood pressure. Moreover, in this study, visfatin turned out to be an independent predictor of the severity of hypertension.

Liakos et al.,\(^{30}\) whose results were consistent with the previous authors’ reports, compared serum visfatin and apelin concentrations in patients with upper-limit values with the concentrations in healthy subjects. Significantly higher concentrations of visfatin and lower apelin concentrations were found in the study group, suggesting a possible contribution of both adipokines in the prognosis of hypertension.

**Conclusions**

Visfatin is a pro-inflammatory adipokine and some literature data indicate its involvement in metabolic disorders, autoimmune diseases and cancer. In our study, the significantly higher concentrations of visfatin found in the patients with psoriasis compared to the control group indicate a possible involvement of this adipokine in the pathophysiological processes present in the course of psoriasis. Since positive correlations between serum visfatin concentration and CRP level and PASI and BSA values have been demonstrated, visfatin may prove to be a useful biomarker of systemic inflammation and psoriasis severity.

**References**


