

# Serum Visfatin, Adiponectin, and Tumor Necrosis Factor Alpha (TNF- $\alpha$ ) Levels in Patients with Psoriasis and their Correlation with Disease Severity

**Betul Sereflican<sup>1</sup>, Nadir Goksugur<sup>1</sup>, Guler Bugdayci<sup>2</sup>, Mualla Polat<sup>1</sup>, Ali Haydar Parlak<sup>1</sup>**

<sup>1</sup>Department of Dermatology, Medical Faculty, Abant Izzet Baysal University, Bolu, Turkey; <sup>2</sup>Department of Biochemistry, Medical Faculty, Abant Izzet Baysal University, Bolu, Turkey

**Corresponding author:**

Betul Sereflican, MD  
Abant Izzet Baysal University  
Medical Faculty  
Department of Dermatology  
12480 Golkoy-Bolu  
Turkey  
ozbetul@yahoo.com

Received: March 16, 2015

Accepted: January 15, 2016

**ABSTRACT** Psoriasis is a chronic, autoimmune, and inflammatory disease of unknown etiology, characterized by T lymphocyte mediated keratinocyte proliferation. In recent years the relationship between psoriasis and adipose tissue cytokines has been reported. Psoriasis as a triggering factor for the immune and metabolic disorders can be associated with diabetes mellitus, abnormal lipid metabolism, and metabolic syndrome. In this study we assessed the adipose tissue cytokines visfatin, adiponectin, and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) levels in psoriasis patients and evaluated the relationship between disease severity and cytokines. The study included 42 patients with psoriasis and 42 healthy individuals. Visfatin, adiponectin, and TNF- $\alpha$  levels were measured in both the psoriasis and the control group. The disease severity index was assessed in psoriatic patients by means of PASI. The relationship between visfatin, adiponectin, TNF- $\alpha$ , PASI score, and obesity was evaluated.

When serum TNF- $\alpha$ , adiponectin, and visfatin levels of the patient group were compared with those of the control group, the TNF- $\alpha$  levels were statistically higher ( $p = 0.00$ ) and the adiponectin levels were statistically lower ( $p = 0.024$ ). The visfatin levels were higher in the psoriatic patients compared to the control group, but this difference was not statistically significant ( $p = 0.73$ ). The relationship between PASI-TNF- $\alpha$  and between PASI-adiponectin was statistically significant ( $p = 0.009$  and  $p = 0.004$ ). A positive correlation was observed between body mass index (BMI) and visfatin ( $p = 0.031$ ).

These results indicate that TNF- $\alpha$  and adiponectin play a part in psoriasis etio-pathogenesis and can be used as parameters to evaluate the severity of the disease. However, the role of visfatin in psoriasis pathogenesis is unclear. Further clinical studies are needed to clarify the effect of visfatin in psoriatic patients.

**KEY WORDS:** psoriasis, adipokines, obesity, adiponectin, TNF-alpha, visfatin

## INTRODUCTION

Psoriasis is a chronic inflammatory disease caused by genetics and affected by other factors. It is characterized by hyperproliferation and altered differentiation of keratinocytes, T lymphocyte infiltration, and vascular changes (1,2). T lymphocytes, cytokines, and

chemokines are the main components required for the initiation and development of the disease (2).

In addition to storing energy, adipose tissue is known to be an active endocrine organ regulating body metabolism by secretion of metabolically im-

portant proteins called adipokines, such as leptin, adiponectin, visfatin, and cytokines. It also secretes chemokines, such as tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin (IL)-6, and the monocyte chemoattractant protein-1 (3). TNF- $\alpha$  is a 25 kDa transmembrane protein. It is a multifunctional proinflammatory and immunoregulatory cytokine, produced in macrophages, lymphocytes, and to a lesser extent in adipocytes. Functions of TNF- $\alpha$  include inflammation, apoptosis, production of IL-1, IL-6 cytokines, and the induction of insulin resistance (3-5). Adiponectin exhibits structural homology with collagen VIII, X, and the complement factor C1q (6). Adiponectin is associated with increased insulin sensitivity, the regulation of NF $\kappa$ B, and the inhibition of TNF- $\alpha$ . Adiponectin levels are inversely related to obesity, insulin resistance, and cardiovascular disease. Hormone levels are known to be decreased in patients with type 2 diabetes mellitus, atherosclerosis, and obesity (4,7). Adiponectin reduces T-cell activation and proliferation, inhibits phagocytosis, and increases the anti-inflammatory mediator IL-10. It also restrains TNF- $\alpha$  secretion by inhibiting the NF $\kappa$ B pathway. Adiponectin decreases the TNF- $\alpha$  induced inflammatory response by directly suppressing TNF- $\alpha$  production. However, adiponectin secretion from adipocytes is inhibited by TNF- $\alpha$  and IL-6. In the general population, adiponectin and the CRP plasma levels are inversely related (3,6,8). Visfatin is a newly discovered 52 kDa protein that plays a role in glucose homeostasis. It is preferentially expressed by visceral adipose tissue compared with subcutaneous fat, so it is called visfatin (7,8). Plasma visfatin levels are associated with obesity, visceral fat mass, type 2 diabetes mellitus, and metabolic syndrome (9). With regard to the biologic functions of visfatin, a glucose reducing effect has been documented that activates the insulin signal via the insulin receptor, but in an alternative way to insulin (10). Visfatin is secreted by macrophages rather than adipocytes in adipose tissue. Previously, visfatin was known as pre-B cell colony enhancing factor (PBEF) because it plays a role in the development of early stage B cells. It exhibits an anti-apoptotic effect by inhibiting recombinant PBEF, caspase-3, and caspase-8. PBEF is an inflammatory cytokine that plays a basic role in delayed neutrophil apoptosis during sepsis. It can also be a useful biomarker in acute pulmonary injury. Visfatin induces matrix metalloproteinase activity in monocytes, and TNF- $\alpha$  and IL-8 activity in peripheral blood mononuclear cells. In light of these findings, visfatin is involved in many pathological processes and can be considered an inflammatory mediator (3).

We compared the levels of the adipose tissue cytokines involved in inflammatory processes and

associated with psoriasis in patients and healthy individuals, with the goal of exploring the relationship between these adipokines and psoriasis and disease severity.

## PATIENTS AND METHODS

We enrolled 42 patients who had attended our Dermatology outpatient clinic and had been diagnosed histopathologically with psoriasis and another 42 healthy subjects as the control group. The exclusion criteria for both groups were less than 18 years of age, a diagnosis of erythrodermic or pustular psoriasis with only palmoplantar involvement, and receiving any kind of systemic treatment for psoriasis including acitretin, cyclosporine, methotrexate, biological agents, and all kinds of phototherapies in the last three months. Subjects with hypertension, atherosclerotic cardiac disease, diabetes mellitus type 1 or 2, chronic renal or liver disease, chronic obstructive pulmonary disease, neurological disorders, nutritional disorders, autoimmune diseases, thyroid gland diseases, immunosuppressive diseases, receiving treatment, or having any infection at the time of diagnosis were also excluded from the study. The control group was selected from subjects with age, gender, and body mass index (BMI) similar to the patient group. BMI was calculated based on weight (kg) and height (cm). Type of psoriasis, duration of disease, previous and actual treatments, additional systemic diseases, and medications were all noted for each participant. The psoriasis area severity index (PASI) scoring was used to grade the severity of the disease.

Peripheral blood samples were obtained from the two groups after fasting for at least 8 hours. Blood samples were centrifuged at 4000 rpm and the serum was stored at -70°C until the end of the study. Raybio Human Visfatin Enzyme Immunoassay kits (RayBio- tech, Inc., Georgia, USA) were used to measure the serum levels of visfatin. Orgenium Human TNF- $\alpha$  enzyme-linked immunosorbent assay (ELISA) and Orgenium Human Adiponectin ELISA (Orgenium Laboratories, Vantaa, Finland) kits were used to measure serum TNF- $\alpha$  and adiponectin, respectively. All samples were studied using the Bio-Rad Benchmark Plus (Bio-Rad Laboratories Inc., California, USA) device using ELISA. Written informed consent was obtained from all participants.

## Statistical Analysis

An independent sample test was used for data with normal distribution to investigate differences between the two groups. For abnormally distributed data, the Mann-Whitney U test was used to establish

differences between the two groups. Correlation between the data was evaluated by the Pearson correlation test. In all of the statistical tests, a *P* value less than 0.05 was considered to be statistically significant.

## RESULTS

The psoriatic group included 23 male (54.8%) and 19 female (45.2%) patients, and the control group included 19 male (45.2%) and 23 female (54.8%) subjects. The average age in the patient group was 35.74±12.42 and 33.90±11.19 years in the control group. No significant differences were observed between the groups in terms of age or gender (*P*>0.05). BMI values were 25.81±4.92 in the patient group and 24.12±3.91 in the control group; this difference was not statistically significant (*P*=0.084).

In the psoriatic group, 21 patients had plaque, 10 patients had guttate, nine patients had plaque with guttate, one patient had the inverse, and one patient had palmoplantar with plaque type psoriasis.

The mean PASI score was 6.12±4.31, and the mean duration of disease was 106.29±113.11 months in the patient group.

The mean visfatin levels in the patient and control group were 6.94±2.29 ng/mL and 6.01±2.35 ng/mL, respectively. Although visfatin levels were higher in the patient group than in the control group, this difference was not statistically significant (*P*=0.73) (Table 1). No statistically significant correlation was observed between PASI and visfatin levels (*P*>0.05) (Table 2).

The mean serum adiponectin levels in the patient and control group were 6573.31±3393.72 ng/mL

and 8320.21±3547.91 ng/mL, respectively. Adiponectin levels in the patient group were significantly lower than in the control group (*P*=0.024) (Table 1). Comparison of PASI score and adiponectin levels revealed a statistically significant linear correlation between these two parameters (*P*=0.004) (Table 2). The patient group had significantly higher TNF-α levels than the control group (101.97±31.95 pg/mL versus 12.75±7.71 pg/mL, *P*=0.00) (Table 1).

A statistically significant linear correlation was found between PASI scores and the TNF-α levels (*P*=0.009) (Table 2). The clinical type of psoriasis was not significantly correlated with PASI score or TNF-α, adiponectin, or visfatin levels (Kruskal Wallis test, *P*>0.05). Within the psoriatic group, a small but statistically significant correlation was observed between the levels of TNF-α and adiponectin (*r*=0.311, *p*=0.045), while no significant correlation was observed between the levels of adiponectin and visfatin (*p*=0.536). Additionally, no statistically significant correlation was observed between the levels of TNF-α and visfatin (*p*=0.376) (Table 3).

Within the patient group, no significant correlation was observed between BMI and adiponectin or TNF-α levels, while a statistically significant positive correlation was observed between BMI and visfatin levels in this group (*r*=0.333, *p*=0.031).

## DISCUSSION

Psoriasis is one common immune-dependent inflammatory disease developing from immune-mediated mechanisms characterized by disruptions in key cytokines. Psoriasis is considered a multisystem disease, and is accompanied by many comorbidities.

**Table 1.** Psoriasis area severity index (PASI), body mass index, tumor necrosis factor alpha (TNF-α), visfatin, and adiponectin levels in the patient and control group

		n	Mean±Standard deviation	P
PASI	case	42	6.12±4.31	-
	control			
Body mass index	case	42	25.81±4.92	0.084
	control	42	24.12±3.90	
TNF-α (pg/mL)	case	42	101.97±31.95	0.00
	control	42	12.75±7.71	
Visfatin (ng/mL)	case	42	6,4±2.29	0.73
	control	42	6.01±2.35	
Adiponectin (ng/mL)	case	42	6573.31±3393.72	0.024
	control	42	8320.21±3547.91	

**Table 2.** Correlations between psoriasis area severity index (PASI) score and tumor necrosis factor alpha (TNF- $\alpha$ ), visfatin, adiponectin, disease duration, and body mass index

	<b>TNF-<math>\alpha</math>,</b>	<b>Visfatin,</b>	<b>Adiponectin,</b>	<b>Disease duration,</b>	<b>BMI,</b>
	r (P-value)	r (P-value)	r (P-value)	r (P-value)	r (P-value)
<b>PASI</b>	0.400 (0.009*)	-0.021 (0.895)	0.438 (0.004*)	0.125 (0.428)	0.046 (0.772)

PASI: psoriasis area and severity index; BMI: body mass index; \* $P < 0.05$  was considered statistically significant  
 \*\* can be added before  $p < 0.05$

Chronic inflammation is considered to play a role in the development of metabolic and vascular disorders (11,12). Metabolic syndrome, dyslipidemia, obesity, diabetes and insulin resistance, nonalcoholic fatty liver disease, and Crohn's disease are potential comorbidities associated with psoriasis (13).

TNF- $\alpha$  increases the expression of many mediators such as IL-1, IL-6, IL-8, TGF- $\alpha$ , and GM-CSF. It also increases LTB<sub>4</sub>, PGE<sub>2</sub>, and adhesion molecules such as E-selectin, ICAM-1, and VCAM-1. Due to its multiple effects, TNF- $\alpha$  has a key role in the etiology of psoriasis. Studies have demonstrated reduction of this cytokine in serum and skin lesions after effective treatment, highlighting its importance in the pathogenesis of psoriasis (14,15). Mussi *et al.* found that TNF- $\alpha$  levels were significantly higher compared to the control group, and found a significant relationship between PASI scores and TNF- $\alpha$  levels. They also found that after effective treatment, both PASI scores and cytokine levels were significantly decreased (16). Ragab *et al.* reported that TNF- $\alpha$  levels were higher in patients with psoriasis, and that this elevation was more significant in severe compared to mild psoriasis (17). Arican *et al.* found that serum TNF- $\alpha$ , IFN- $\gamma$ , IL-6, IL-8, IL-12, and IL-18 levels were significantly higher in patients with psoriasis than in the control group, but found no statistically significant relationship between TNF- $\alpha$  levels and disease severity (18). Borska *et al.* did not detect a significant difference in TNF- $\alpha$  levels between psoriatic patients and the control group (19). In our study, TNF- $\alpha$  values were significantly higher in the patient group than in the control group. Additionally, we observed a statistically significant linear

relationship between PASI and TNF- $\alpha$  levels in the patient group. These results suggest that TNF- $\alpha$  plays a role in the pathogenesis of psoriasis and may be used as a marker to assess disease severity.

Adiponectin is an anti-inflammatory adipokine and reduces the secretion of TNF- $\alpha$  and its inflammatory response. However, adiponectin secretion is suppressed by TNF- $\alpha$  and IL-6. Adiponectin and TNF- $\alpha$  antagonize each other's action in their target tissues. In vitro and in vivo experimental studies have revealed that adiponectin alleviates the unfavorable consequences of proinflammatory cytokines, inhibits the release of adhesion molecules and the activation of the inflammatory signaling cascade, and prevents oxidative damage (3,4,20). Takahashi *et al.* reported that plasma adiponectin levels were statistically decreased in psoriasis patients and also reported a negative correlation between plasma adiponectin levels and PASI scores (21). Kaur *et al.* found that plasma adiponectin levels were increased in normal-weight patients with psoriasis compared to levels in healthy controls or obese patients with psoriasis. They found no relationship between adiponectin levels and PASI scores (22). Shibata *et al.* found that adiponectin levels were significantly lower in patients than in the control group. However, they did not find a significant relationship between PASI scores and adiponectin levels (23). Coimbra *et al.* found that adiponectin levels were lower in patients with psoriasis, and also observed lower values in cases of moderate and severe psoriasis compared with mild cases (24). Oon *et al.* reported a positive correlation between adiponectin levels and PASI scores (25). In our study, as with previous studies,

**Table 3.** Correlations between tumor necrosis factor alpha (TNF- $\alpha$ ), adiponectin, and visfatin levels with each other in patients with psoriasis

	<b>TNF-<math>\alpha</math>,</b>	<b>Adiponectin,</b>	<b>Visfatin,</b>
	r (P-value)	r (P-value)	r (P-value)
<b>TNF-<math>\alpha</math></b>		0.311 (0.045*)	0.140 (0.376)
<b>Adiponectin</b>	0.311 (0.045*)		-0.098 (0.536)
<b>Visfatin</b>	0.140 (0.376)	-0.098 (0.536)	

\* $p < 0.05$  was considered statistically significant

adiponectin levels were statistically lower in patients with psoriasis compared with the control group. Our results indicate that the anti-inflammatory effects of adiponectin decreases in patients with psoriasis, potentially speeding up the inflammatory process. We also observed a statistically significant linear relationship between adiponectin levels and PASI scores. Studies investigating the relationship between adiponectin and PASI scores in different centers have yielded contradictory results: no correlation, negative correlations, and positive correlations (21,22,25). Therefore, multifactorial reasons may affect the severity of psoriasis, and adiponectin levels may be a contributing factor. We observed a statistically significant positive correlation between TNF- $\alpha$  and adiponectin levels in patients. Our results demonstrate that more case-controlled studies are needed to compare the relationship between adiponectin and TNF- $\alpha$  levels to arrive at a meaningful conclusion.

Visfatin can induce cellular expression of inflammatory cytokines such as TNF- $\alpha$ , IL-1, and IL-6. It also increases cell surface expression of co-stimulatory molecules such as CD54, CD40, and CD80. Visfatin expression is up-regulated in a variety of acute and chronic inflammatory diseases, including sepsis and rheumatoid arthritis, and plays a key role in the persistence of inflammation through its capacity to inhibit neutrophil apoptosis (26). Koczan *et al.* focused on the gene expression profiles of peripheral blood mononuclear cells from patients with psoriasis suffering from severe generalized disease, comparing the diseased stage and the cured stage. They tested expression of mRNA in peripheral blood mononuclear cells from 11 patients with psoriasis before and after treatment with dithranol. They found that IL-8, annexin A3, cyclooxygenase-2, cell cycle regulator G0S2, and visfatin expression were all increased during illness. However, they included no data about the relationship between visfatin and other cytokines, the severity of the psoriasis, BMI, or the duration of disease (27). Zhou *et al.* found that psoriatic skin had increased tissue expression of visfatin (28). Bozkurt *et al.* found no statistically significant difference in the serum visfatin levels between patients with psoriasis and the control group, but found a slightly positive correlation between visfatin and PASI in patients (29). Ismail *et al.* found that serum visfatin levels were significantly higher in patients with psoriasis compared with the control group and found a statistically significant positive correlation between PASI and visfatin levels (30). Gerdes *et al.* also reported that visfatin levels were significantly higher in patients with psoriasis than in the control group (31). In our study, although visfatin levels were higher in patients with psoriasis

than in the control group, the difference was not statistically significant. However, we observed a statistically significant correlation between PASI and visfatin levels, as well as a statistically significant positive correlation between BMI and visfatin levels in patients. The relationship between BMI and visfatin is not yet clear. Some authors have reported increased visfatin levels in obese subjects and others have reported a negative correlation between visfatin and BMI (26,32). Our results suggest that visfatin is associated with visceral fat mass. In our study, patients did not have any systemic disease and the two groups did not differ significantly in terms of age, gender, and BMI, increasing the reliability of our results. Although no significant differences were observed in terms of gender or BMI between patients and the control group, the psoriasis group contained more men than the control group, and the average BMI was higher in the psoriasis group. These small differences may have affected our results. However, the disease severity of our patients with psoriasis was moderate and PASI scores were relatively low, so visfatin levels may be lower than expected due to this situation.

## CONCLUSION

Our results suggest that by triggering effects of inflammation of the adipose tissue cytokine, TNF- $\alpha$  plays a role in the inflammatory processes and the anti-inflammatory effects of adiponectin. However, the role of another adipokine, visfatin, is still unclear in psoriasis. Further studies including more patients with psoriasis with higher PASI scores are needed to investigate the role of visfatin in psoriasis pathogenesis. In addition, the relationship between adiponectin and TNF- $\alpha$  and the relationship between adiponectin and psoriasis severity need to be clarified. However, because of the cross-sectional character of the study it is difficult to determine if psoriasis is a cause or consequence of the differences found in adipokine levels.

The effects of TNF- $\alpha$ , which has been shown to affect the pathogenesis of psoriasis, has led the possibility of anti-TNF therapy, so a new epoch has been started together with biological agents in the treatment of psoriasis, particularly in resistant cases. This situation has attracted attention to adipokines and has increased interest in new adipokines.

## Acknowledgements:

This study was supported by the Research Fund of the University of Abant Izzet Baysal. (Project no: 2009.08.03.311)





## References:

1. Nestle FO. Psoriasis. *Curr Dir Autoimmun* 2008;10:65-75.
2. Krueger G, Ellis CN. Ellis, Psoriasis--recent advances in understanding its pathogenesis and treatment. *J Am Acad Dermatol* 2005;53:94-100.
3. Antuna-Puente B, Feve B, Fellahi S, Bastard JP. Adipokines: the missing link between insulin resistance and obesity. *Diabetes Metab* 2008;34:2-11.
4. Fonseca-Alaniz MH, Takada J, Alonso-Vale MIC, Lima FB. Adipose tissue as an endocrine organ: from theory to practice. *Pediatr (Rio J)* 2007;83:192-203.
5. Ahima RS, Flier JS. Adipose tissue as an endocrine organ. *Trends Endocrinol Metab* 2000;11:327-32.
6. Chudek J, Wiecek A. Adipose tissue, inflammation and endothelial dysfunction. *Pharmacol Rep* 2006;58 Suppl:81-8.
7. Vazquez-Vela ME, Torres N, Tovar AR. White adipose tissue as endocrine organ and its role in obesity. *Arch Med Res* 2008;39:715-28.
8. Guzik TJ, Mangalat D, Korbut R. Adipocytokines - novel link between inflammation and vascular function? *J Physiol Pharmacol* 2006;57:505-28.
9. Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. *Mol Med* 2008;14:741-51.
10. Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, *et al.* Visfatin: a protein secreted by visceral fat that mimics the effects of insulin. *Science* 2005;307:426-30.
11. Christophers E. Comorbidities in psoriasis. *Clin Dermatol* 2007;25:529-34.
12. Kalkan G, Karadağ S. The association between psoriasis and cardiovascular diseases. *Eur J Gen Med* 2013;10:10-16.
13. Gisondi P, Ferrazi A, Girolomoni G. Metabolic comorbidities and psoriasis. *Acta Dermatovenereol Croat* 2010;18:297-304.
14. Bonifati C, Ameglio F. Cytokines in psoriasis. *Int J Dermatol* 1999;38:241-251.
15. Victor FC, Gottlieb AB, Menter A. Changing paradigms in dermatology: tumor necrosis factor alpha (TNF-alpha) blockade in psoriasis and psoriatic arthritis. *Clin Dermatol* 2003;21:392-97.
16. Mussi A, Bonifati C, Carducci M, D'Agosto G, Pimpinelli F, D'Urso D, *et al.* Serum TNF-alpha levels correlate with disease severity and are reduced by effective therapy in plaque-type psoriasis. *J Biol Regul Homeost Agents* 1997;11:115-18.
17. Ragab HM, El Maksoud NA, Farid Roaiah MM. Biochemical significance of proinflammatory cytokines in psoriasis vulgaris among Egyptian patients. *J Am Sci* 2010;6:423-9.
18. Arican O, Aral M, Sasmaz S, Ciragil P. Serum levels of TNF-alpha, IFN-gamma, IL-6, IL-8, IL-12, IL-17, and IL-18 in patients with active psoriasis and correlation with disease severity. *Mediators Inflamm* 2005;2005:273-79.
19. Borská L, Fiala Z, Krejsek J, Andrýs C, Vokurková D, Hamáková K, *et al.* Selected immunological changes in patients with Goeckerman's therapy TNF-alpha, sE-selectin, sP-selectin, sICAM-1 and IL-8. *Physiol Res* 2006;55:699-706.
20. Shetty S, Kusminski CM, Scherer PE. Adiponectin in health and disease: evaluation of adiponectin-targeted drug development strategies. *Trends Pharmacol Sci* 2009;30:234-9.
21. Takahashi H, Tsuji H, Takahashi I, Hashimoto Y, Ishida-Yamamoto A, *et al.* Plasma adiponektin and leptin levels in Japanese patients with psoriasis. *Br J Dermatol* 2008;159:1207-8.
22. Kaur S, Zilmer K, Kairane C, Kals M, Zilmer M. Clear differences in adiponectin level and glutathione redox status revealed in obese and normal-weight patients with psoriasis. *Br J Dermatol* 2008;159:1364-67.
23. Shibata S, Saeki H, Tada Y, Karakawa M, Komine M, Tamaki K. Serum high molecular weight adiponectin levels are decreased in psoriasis patients. *J Dermatol Sci* 2009;55:62-3.
24. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, *et al.* Circulating levels of adiponectin, oxidized LDL and C-reactive protein in Portuguese patients with psoriasis vulgaris, according to body mass index, severity and duration of the disease. *J Dermatol Sci* 2009;55:202-4.
25. Oon HH, Liew CF, Theng CCT, Ho MSL. Adiponectin is associated with disease activity of psoriasis (abstract). *J Am Acad Dermatol* 2009;60:AB 163. Abstract P 3307.
26. Luk T, Malam Z, Marshall JC. Pre-B cell colony-enhancing factor (PBEF)/visfatin: a novel mediator of innate immunity. *J Leukoc Biol* 2008;83:804-16.
27. Koczan D, Guthke R, Thiesen HJ, Ibrahim SM, Kundt G, Krentz H, *et al.* Gene expression profiling of peripheral blood mononuclear leukocytes from psoriasis patients.

- riasis patients identifies new immune regulatory molecules. *Eur J Dermatol* 2005;15:251-57.
28. Zhou X, Krueger JG, Kao MCJ, Lee E, Du F, Menter A, *et al.* Novel mechanisms of T-cell and dendritic cell activation revealed by profiling of psoriasis on the 63,100-element oligonucleotide array. *Physiol Genomics* 2003;13:69-78.
29. Bozkurt NM, Yıldırım M, Ceyhan AM, Kara Y, Vural H. Psoriasisli hastalarda serum visfatin düzeylerinin araştırılması. *Turkderm* 2010;44:15-8.
30. Ismail SA, Mohamed SA. Serum levels of visfatin and omentin-1 in patients with psoriasis and their relation to disease severity. *Br J Dermatol* 2012;167:436-9.
31. Gerdes S, Osadtschy S, Rostami-Yazdi M, Buhles N, Weichenthal M, Mrowietz U. Leptin, adiponectin, visfatin and retinol-binding protein-4 mediators of comorbidities in patients with psoriasis? *Exp Dermatol* 2012;21:43-7.
32. Chen CC, Li TC, Li CI, Liu CS, Lin WY, Wu MT, *et al.* The relationship between visfatin levels and anthropometric and metabolic parameters: association with cholesterol levels in women. *Metabolism* 2007;56:1216-20.

