

## A Role of Leptin in Psoriasis?

Şebnem AKTAN<sup>1</sup>  
Simin ROTA<sup>2</sup>  
Berna ŞANLI ERDOĞAN<sup>3</sup>  
Şeniz ERGİN<sup>3</sup>  
Bünyamin KAPTANOĞLU<sup>2</sup>  
Mehmet BOSTANCI<sup>4</sup>

**Aim:** Although there is evidence of a positive association between psoriasis and body mass index (BMI) and leptin is known to play a part in the regulation of the immune system, the relationship between psoriasis and leptin is still not well known. The aim of this study was to evaluate the possible relation between leptin and psoriasis.

**Materials and Methods:** Serum leptin concentrations and BMI in 20 patients with psoriasis were compared to 20 age- and sex-matched healthy volunteers.

**Results:** There was no difference between serum leptin levels of psoriatic patients ( $32.3 \pm 24.9$  ng/ml) and controls ( $36.8 \pm 28.2$  ng/ml). Leptin levels of both psoriatic and healthy volunteers showed positive correlations with BMI. Serum leptin levels in the patient group did not correlate with psoriasis area severity index (PASI) score or duration of psoriasis.

**Conclusions:** In the setting of this study, our results did not support any possible relation between serum leptin levels and psoriasis.

**Key Words:** Psoriasis, leptin, BMI

<sup>1</sup> Department of Dermatology,  
Faculty of Medicine,  
Dokuz Eylül University,  
İzmir - TURKEY

<sup>2</sup> Department of Biochemistry,  
Faculty of Medicine,  
Pamukkale University,  
Denizli - TURKEY

<sup>3</sup> Department of Dermatology,  
Faculty of Medicine,  
Pamukkale University,  
Denizli - TURKEY

<sup>4</sup> Department of Public Health,  
Faculty of Medicine,  
Pamukkale University,  
Denizli - TURKEY

### Psoriasis'de Leptinin Rolü

**Amaç:** Psöriasis, ile vücut kitle indeksi (VKİ) arasındaki ilişki ve leptinin immun sistem düzenlenmesindeki rolü hakkında bildiğimiz olmasına rağmen, psöriasis ve leptin arasındaki ilişki hakkında kesin bir bildiğimiz yok. Çalışmamızın amacı, psöriasis ve leptin arasındaki olası ilişkiyi incelemektir.

**Yöntemler:** Yirmi psöriasisli hasta ile yaş ve cins bakımından uyumu 20 sağlıklı bireyde serum leptin ve VKİ değerleri karşılaştırıldı.

**Bulgular:** Serum leptin düzeyleri psöriasisli ( $32.3 \pm 24.9$  ng/ml) hasta grubu ve kontrol grubunda ( $36.8 \pm 28.2$  ng/ml) farklı bulunmadı. Her iki grupta da serum leptin düzeyleri ile VKİ arasında pozitif korelasyon saptandı. Hasta grubunda serum leptin düzeyleri psoriasis alan şiddet indeksi (PAŞİ) ve hastalık süresi ile ilişkili bulunmadı.

**Sonuç:** Çalışmamızdan elde ettiğimiz sonuçlar psöriasis ve leptin düzeyleri arasında herhangi bir ilişki olmadığını göstermektedir.

**Anahtar Sözcükler:** Psoriasis, leptin, VKİ

### Introduction

Psoriasis is a chronic inflammatory skin disease characterized by marked increases in keratinocyte proliferation, prominent alterations in dermal capillary vasculature and the presence of dermal and epidermal T cells, monocytes/macrophages and neutrophils (1). Although the influence of environmental factors on psoriasis is not defined precisely, body mass index (BMI) has been reported to be one of the important associated factors, and a positive association between BMI and psoriasis has been shown (2,3). Leptin, a protein secreted by the adipose tissue, has important roles in metabolism and immunity; it regulates body weight and exerts other biologic functions that modulate hematopoiesis, angiogenesis and immune responses (4). Additionally, leptin mediates proliferative and antiapoptotic activities in different cell types including T cells (5) and eosinophils (6). Leptin is also linked to energy storage, and it was also reported that serum leptin levels show a positive correlation with BMI and reflect the body fat mass (7). Leptin receptor is expressed primarily in the hypothalamus, but it is also expressed by peripheral blood mononuclear cells, vascular endothelial cells, smooth muscle cells,

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#### Correspondence

Simin ROTA  
Department of Biochemistry,  
Faculty of Medicine,  
Pamukkale University,  
Kınıklı Kampusu,  
Morfoloji Binası,  
Denizli - TURKEY

siminrota@yahoo.co.uk

osteoblasts and fibroblasts. Leptin produced by fibroblasts may thus exert important local autocrine and paracrine actions (8). Since psoriasis is an immune-mediated inflammatory disease, characterized by hyperproliferation of keratinocytes and infiltration of mostly T lymphocytes, leptin may provide a link between T cell function and inflammation in psoriasis.

In our preliminary study, we assessed serum leptin levels in patients with psoriasis and healthy controls. The aim of this study was to evaluate a possible relation between leptin and psoriasis.

## Materials and Methods

Twenty consecutive patients with psoriasis who admitted to the dermatology outpatient clinic in Pamukkale University School of Medicine and 20 healthy controls were enrolled in this study. Psoriasis was diagnosed clinically and/or histopathologically. Patients with a history of topical or systemic antipsoriatic therapy within four weeks were not included in the study. Subjects with a history of acute or chronic infection, chronic renal or liver disease, diabetes mellitus, coronary heart disease, hypertension, peripheral or cerebral vascular disease, hypothyroidism, bronchial asthma or chronic obstructive lung disease were also not included. All of the subjects were non-smokers and none was taking any systemic medication. No individual in the psoriasis or control group was following a special dietary regimen.

Anthropometric measurements were done by the same physician on the day blood specimen was taken. Height and weight of the subjects were obtained in light clothing without shoes. Height was measured as the distance from the top of the head to the bottom of the feet (no shoes) using a fixed stadiometer. BMI was calculated as the weight (kg) divided by square of the height (m). Psoriasis area and severity index (PASI) score was determined in each patient.

Venous blood samples were drawn from the participants after a 12-h fast between 08:00 and 10:00 a.m. Samples were collected in serum separator tubes, allowed to clot for 30 min, and centrifuged for 15 min at 2000x g at room temperature; serum was collected and stored at -70 °C until analyzed. Serum leptin level was determined by ELISA method using a commercial kit (Diagnostic System Lab, USA). Informed consent was obtained from each subject.

All statistical analyses were performed by means of SPSS statistical software package for Windows (version 11.0; SPSS Inc., Chicago, Illinois). The gender, age and BMI of the groups were compared by chi-square test and leptin levels by Mann-Whitney U test.

## Results

Demographic features and serum leptin levels in psoriatic patients and controls are given in Table 1.

Table 1. Demographic features and serum leptin levels in psoriatic patients and controls.

	Patients (n=20)	Controls (n=20)
Female/Male	8/12	10/10
Age	48.0 ± 8.8	50.9 ± 11.4
PASI score (years)	6.2 ± 6.0	-
Duration of psoriasis (years)	18.1 ± 14.9	
BMI (kg/m <sup>2</sup> )	28.1 ± 5.0	25.6 ± 3.6
Leptin (ng/ml)	32.3 ± 24.9	36.8 ± 28.2

PASI: Psoriasis area severity index.

Plaque psoriasis was the most common clinical form (75%) and in the remaining cases, clinical form was consistent with guttata psoriasis (25%). The mean PASI score and age of onset of disease in the psoriasis group were 6.2 ± 6.0 years and 29.9 ± 14.2 years, respectively. Duration of psoriasis ranged from 0.5 to 45 years (18.1 ± 14.9 years).

There was no difference between serum leptin levels of psoriatic patients and controls. Leptin levels of psoriatic patients and healthy volunteers showed positive correlations with BMI ( $r=0.551$ ,  $p=0.012$  and  $r=0.559$ ,  $p=0.010$ , respectively), but serum leptin levels in the patient group correlated with neither PASI scores nor the duration of psoriasis.

## Discussion

Body mass index is a complex variable that seems to affect immunity. It has been documented that circulatory levels of tumor necrosis factor-alpha (TNF- $\alpha$ ) and soluble TNF- $\alpha$  receptors and in vitro TNF- $\alpha$  production are significantly increased in obese as compared with non-obese subjects (9,10). In addition, Tanaka et al. (10) detected a reduction in the population and function of

two major subsets of T cells (CD4+Th, CD8+Tsc) in obesity followed by a recovery after adequate weight loss. BMI was reported to be independently correlated with psoriasis in a case-controlled study that assessed the risk factors associated with psoriasis (2). BMI  $\geq 25$  has also been reported to have significant effects on long-term prognosis of plaque psoriasis after diagnosis (11).

Leptin (OB protein) is a 16 kDa adipokine, which was initially described as an adipocyte-derived hormone. The adipose tissue is a major source of leptin and its circulating concentrations indirectly reflect body fat stores. Leptin is an important signal in the regulation of food intake and energy balance and its levels usually correlate with BMI (7). It links nutritional status with neuroendocrine and immune functions, and its role in the modulation of immune response and inflammation has recently become increasingly evident. The increase in leptin production that occurs during infection and inflammation strongly suggests that leptin is a part of the cytokine network that governs the inflammatory-immune response and the host defense mechanisms. Leptin plays an important role in inflammatory processes involving T cells and has been reported to modulate T-helper cell activity in the cellular immune response (4). Hence, leptin has a dual role in inflammation: it activates monocyte/macrophage cells and potentiates production of the proinflammatory cytokines, TNF- $\alpha$ , interleukin (IL)-6 and 9, and directs T cell differentiation to Th1 phenotype, expressing interferon (INF)- $\gamma$  and IL-2. On the other hand, it expresses certain anti-inflammatory properties by releasing IL-1 receptor antagonist (12,13). Several studies have implicated leptin in the pathogenesis of autoimmune inflammatory conditions, such as rheumatoid arthritis (RA). In patients with RA, it is reported that fasting leads to an improvement in disease activity, which was associated with a marked decrease in serum leptin and a shift towards Th2 cytokine production (14). Other studies showed that serum levels of leptin were not increased in patients with RA as compared with controls. In addition, no correlation was detected between leptin levels and disease activity, whereas a positive correlation was seen between leptin and BMI or

the percentage of body fat (15,16). Thus, it was concluded that although leptin levels cannot be used to assess disease activity in rheumatic diseases, existing data warrants longitudinal studies to assess the potential influence of leptin on disease outcome (17). Recently, a significant inverse correlation between inflammation and leptin concentrations was reported in patients with active RA. Plasma leptin concentration was not found to be significantly different from that in healthy controls, so the authors suggested that active chronic inflammation may lower plasma leptin concentrations (18).

In psoriasis, an effector-immune response develops to unknown skin antigens and T cell activation is mainly of type 1 cytokine pattern. INF- $\gamma$  production induces activation of keratinocytes and endothelial cells and it also induces production of inflammatory cytokines (IL-1, TNF- $\alpha$ ) and chemokines (IL-8) (19). TNF- $\alpha$ , other cytokines such as IL-6 and growth factors are involved in the pathogenesis of psoriasis and in the mechanism of hyperproliferation. Serum levels of these compounds can be related to disease activity (20). Since leptin promotes Th1 cell differentiation and cytokine production with levels showing a positive correlation with BMI, we aimed to investigate serum leptin levels in psoriasis. In our study, serum leptin levels were found to be similar in patients with psoriasis and healthy controls. Correlation analysis in our patient group also did not reveal any statistically significant correlations between serum leptin levels and PASI scores. Leptin levels of both psoriatic and healthy volunteers showed positive correlations with BMI, as expected. A MEDLINE search failed to reveal any studies investigating serum leptin levels in psoriasis. Insulin secretion and sensitivity were investigated in psoriasis and the values were found to be similar between patients and controls (21).

In conclusion, in the setting of this study, our results did not support any possible relation between serum leptin levels and psoriasis. Considering the relatively small number of subjects with relatively low mean PASI scores in our patient group, further studies investigating severe inflammatory forms of psoriasis (including erythroderma) seem to be essential.

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