



Serum Leptin and Adiponectin Levels in Korean Patients with Psoriasis

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Psoriasis is a disorder caused by genetic and immunological factors. Leptin, a peptide hormone secreted predominantly from adipose tissue, regulates energy intake and expenditure, as well as the T-helper response. There have been conflicting reports regarding serum levels of leptin and adiponectin in patients with psoriasis. In the present study, we measured serum levels of leptin and adiponectin in Korean patients with psoriasis. Twenty-four patients with psoriasis and fifteen control subjects were included in the study. Serum leptin and adiponectin levels were determined by an immunometric sandwich enzyme-linked immunosorbent assay (ELISA). The mean serum leptin concentration in patients with psoriasis was higher than in controls, and the difference was statistically significant. In contrast, serum adiponectin levels in patients with psoriasis were significantly decreased compared with healthy controls. Leptin levels in vitamin D-deficient patients were statistically significantly higher than in vitamin D-sufficient patients. Serum adiponectin concentrations showed a negative correlation with body mass index (BMI) and psoriasis area and severity index (PASI) in patients with psoriasis. In conclusion, the present study demonstrated that leptin and adiponectin may play a role in the immunopathogenesis of psoriasis and may be useful biomarkers indicating severity of psoriasis in Korean patients.

Keywords: Adiponectin; Leptin; Metabolic Syndrome; Psoriasis

INTRODUCTION

Psoriasis is a chronic inflammatory skin disorder that is mediated by elements of the innate and adaptive immune systems (1). Although the influence of environmental factors on psoriasis is not precisely defined, body mass index (BMI) has been reported to be one of the important associated factors (2).

Leptin, a protein secreted by adipose tissue, plays important roles in metabolism and immunity. It regulates body weight and exerts other biologic functions that modulate hematopoiesis, angiogenesis, and immune responses (3). Leptin is also involved in inflammatory processes involving T cells and has been reported to modulate T-helper cell activity in the cellular immune response. Hence, leptin has three roles in inflammation: it activates monocytes and macrophages; potentiates the production of proinflammatory cytokines such as TNF- α , IL-6, and IL-9; and directs T-cell differentiation to the Th1 phenotype (4). Additionally, leptin has been shown to have stimulatory roles in keratinocyte proliferation, the expression of adhesion molecules, and angiogenesis (5, 6).

Adiponectin is another adipocyte-specific secretory protein that is abundant in circulation. Serum levels of adiponectin are decreased in obesity, insulin resistance, type 2 diabetes mellitus (DM), and hypoadiponectinemia, which are diseases thought to be closely associated with the metabolic syndrome (5).

In consideration of metabolic disorders seen in patients with psoriasis, it seems that there could be some abnormalities in serum leptin and adiponectin levels in psoriatic patients. However, the results regarding serum levels of leptin and adiponectin in patients with psoriasis have been conflicting (6-15). Here, we measured the serum levels of leptin and adiponectin in Korean patients with psoriasis to investigate their roles in inflammatory and metabolic aspects.

MATERIALS AND METHODS

Patients and controls

Twenty-four patients with a clinical diagnosis and histopathological confirmation of psoriasis vulgaris were selected from outpatients of the Department of Dermatology at Kyung Hee University Hospital from March to August 2012. These patients were recruited prospectively and consecutively. There were no exclusion criteria.

The clinical characteristics of patients (including age, gender, height, body weight, duration of disease, Psoriasis Area and Severity Index (PASI) at enrollment, presence of nail involvement, familial history of psoriasis, and psoriatic arthritis) were collected, along with comorbidities such as DM, hypertension, dyslipidemia (including hypercholesterolemia, hypertriglyceridemia, and reduced high density lipoprotein cholesterol concentra-

tion), and other cardiovascular diseases such as heart failure, ischemic heart disease, and cerebral ischemia incidents. Serum levels of 25-hydroxyvitamin D (25[OH]D), parathyroid hormone (PTH), and calcium were also measured. Fifteen healthy, age- and sex-matched controls without psoriasis were enrolled as controls.

Serum leptin and adiponectin analysis

Serum levels of leptin and adiponectin were determined by an immunometric sandwich enzyme-linked immunosorbent assay (ELISA) using commercially-available kits (Human Leptin Quantikine Elisa Kit, product code DLP00, and Human Total Adiponectin Quantikine ELISA Kit, product code DRP 300; R&D Systems, Minneapolis, MN, USA). The minimum detectable dose (MDD) of leptin is typically less than 7.8 pg/mL, and that of adiponectin is 0.891 ng/mL, allowing for sensitive and specific analyses of leptin and adiponectin in serum. Venous blood samples were drawn from the participants between 09:00 and 11:00 hr following a 12-hr fasting period. Following centrifugation of the blood samples at 1,500 g for 15 min, serum was collected and kept at -80°C until use. Serum samples were diluted, and the immunoassays were performed according to the manufacturer's instructions in duplicate.

Statistical analysis

The demographic characteristics of cases and controls were compared using the Mann-Whitney and χ^2 tests. Differences in serum leptin/adiponectin levels were compared using the non-parametric Mann-Whitney test. Correlations between serum leptin/adiponectin levels and age, BMI, and PASI were compared using Spearman's correlation analysis. Nonparametric Mann-Whitney tests were performed to evaluate the association of serum leptin/adiponectin levels and clinical features of patients with psoriasis (presence of familial history of psoriasis, nail involvement, psoriatic arthritis, or vitamin D deficiency). Data were analyzed using commercially-available statistical software (SPSS for Windows, version 17.0; SPSS Inc, Chicago, IL, USA).

Table 1. Demographic characteristics of patients (n = 24) and controls (n = 15)

Characteristics	Patients*	Controls*	P value
Age (yr)	46.83 ± 13.47 (24-70)	45.47 ± 12.29 (26-62)	0.752
Gender			
Male	16	9	NA
Female	8	6	NA
BMI (kg/m ²)	24.43 ± 3.30 (18.13-31.38)	22.88 ± 2.47 (18.37-27.23)	0.127
PASI	14.65 ± 8.67 (4.0-33.8)	NA	NA

*Patients and controls are in mean ± SD (range). BMI, body mass index; PASI, psoriasis area and severity index.

Ethics statement

The study protocol conformed to the guidelines of the 1975 Declaration of Helsinki and was approved by the Kyung Hee Medical Hospital institutional review board (KMC IRB 1212-02). A full verbal explanation of the study was given to all participants, and the patients who consented to participate in this study on a voluntary basis were subjected. Missing clinical information from patients with psoriasis and control subjects was recorded as censored data.

RESULTS

Demographic differences between patients and controls

Twenty-four psoriatic patients took part in our study. The patients included 8 female patients (33.3%) and 16 male patients (66.7%). A group of 15 healthy individuals (9 males [60%] and 6 females [40%]) participated in our study as controls. Descriptive data of the patients and controls are shown in Table 1 and 2. No statistically significant difference was noted in age between psoriatic patients and controls. The mean ± SD BMI in psoriatic patients was higher than that of the controls but the difference was not statistically significant.

The mean ± SD PASI in patients with psoriasis was 14.65 ± 8.67. The presence of nail involvement, familial history of psoriasis, psoriatic arthritis, and vitamin D deficiency were observed in 29.2% (7 patients), 20.8% (5 patients), 50% (12 patients), and 45.8% (11 patients), respectively.

Serum leptin levels in relation to occurrence of psoriasis, patient characteristics, age, BMI, and PASI

The mean ± SD serum leptin concentration in patients was statistically significantly higher than that in controls (Fig. 1 and Table 3). Leptin levels of male patients with psoriasis were significantly higher than control males. Also, leptin levels of female patients with psoriasis were significantly higher than control females.

There was no significant difference in leptin levels of patients with a presence of nail involvement, familial history of psoriasis, or psoriatic arthritis. However, leptin levels in vitamin D-deficient patients were statistically significantly higher than those of patients with sufficient vitamin D (Table 4). Serum leptin concentrations showed no correlations with age, BMI, or PASI

Table 2. Additional demographic characteristics of patients (n = 24)

Characteristics	No. of patients	
	Yes	No
Nail involvement	7	17
Familial history	5	19
Psoriatic arthritis	12	12
Vitamin D deficiency*	11	13

*Vitamin D deficiency; 25-hydroxy vitamin D < 20 ng/mL.

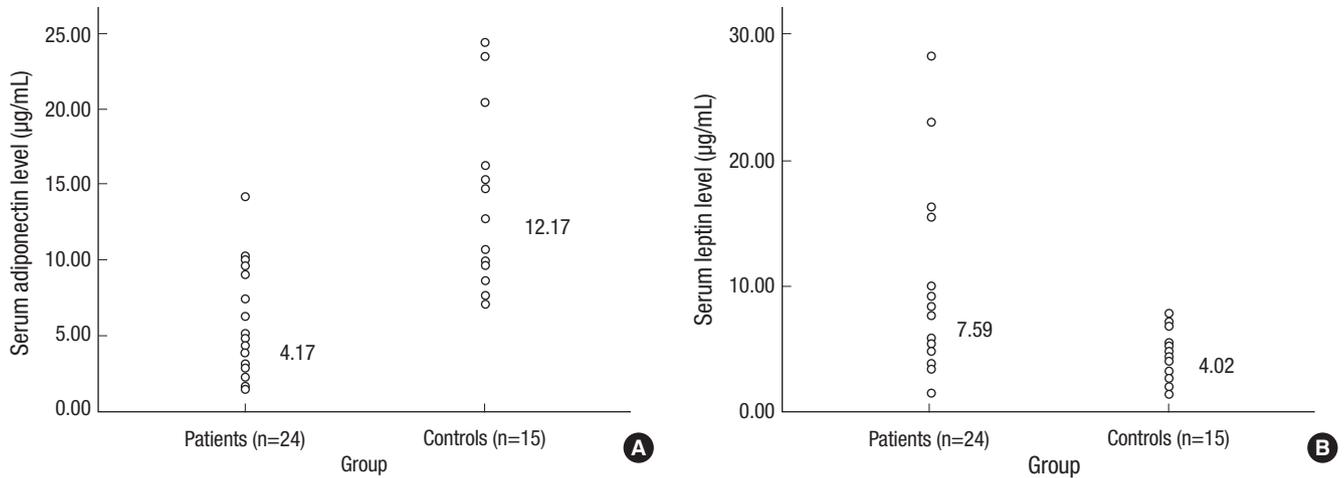


Fig. 1. Serum adiponectin (A) and leptin (B) levels in patients and controls. Values noted are medians.

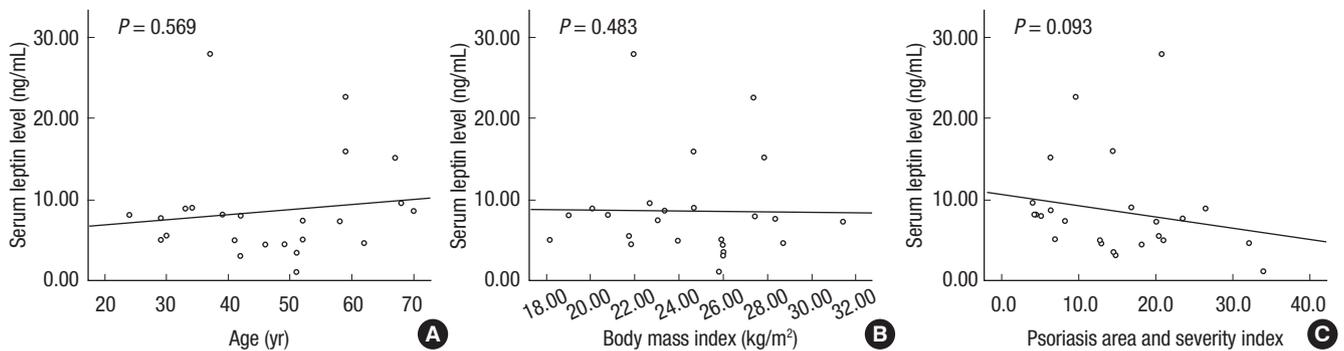


Fig. 2. Correlation between serum leptin levels and age (A), BMI (B), and PASI (C).

Table 3. Serum leptin levels in patients (n = 24) and controls (n = 15) according to gender

Characteristics	Patients* (ng/mL)	Controls* (ng/mL)	P value
Total	8.65 ± 6.19 (1.16-27.94)	4.17 ± 2.12 (1.38-7.94)	0.001
Male	5.77 ± 2.30 (1.16-9.05)	2.75 ± 1.12 (1.38-4.53)	0.001
Female	14.41 ± 7.58 (7.49-27.94)	6.29 ± 1.26 (4.78-7.94)	0.001

*Patients and Controls are in Mean ± SD (range).

in patients with psoriasis (Fig. 2).

Serum adiponectin levels in relation to occurrence of psoriasis, patient characteristics, age, BMI, and PASI

The mean ± SD serum adiponectin concentration in patients was statistically significantly lower than that in controls (Fig. 1 and Table 5). Adiponectin levels of male patients with psoriasis were significantly lower than control males. Also, adiponectin levels of female patients with psoriasis were significantly lower than control females.

There was no significant difference in adiponectin levels of patients with a presence of nail involvement, familial history of psoriasis, psoriatic arthritis, and vitamin D deficiency (Table 6). Serum adiponectin concentrations showed no correlation with

Table 4. Serum leptin levels according to patient characteristics

Characteristics	Concentrations* (ng/mL)		P value
	Yes	No	
Nail involvement	6.28 ± 3.55 (1.16-15.19)	11.02 ± 7.43 (3.14-27.9)	0.078
Familial history	10.83 ± 8.04 (3.55-22.66)	8.08 ± 5.73 (1.16-27.94)	0.783
Psoriatic arthritis	10.04 ± 6.66 (3.55-22.66)	8.08 ± 6.10 (1.16-27.94)	0.576
Vitamin D deficiency	11.01 ± 7.94 (1.16-27.94)	6.65 ± 3.37 (3.14-15.98)	0.041

*Concentrations are in Mean ± SD (range).

age in patients with psoriasis. However, serum adiponectin concentrations showed negative correlations with BMI and PASI in patients with psoriasis (Fig. 3).

DISCUSSION

Recent studies have demonstrated that the risk of psoriasis is directly related to BMI, and that patients with obesity are likely to have more severe psoriasis (2, 7, 16). Psoriasis and obesity share similar mediators of inflammation, mainly TNF-α and IL-6, and the effectors of adipocytic and psoriatic inflammation, largely adipocytes and macrophages, which are derived from a com-

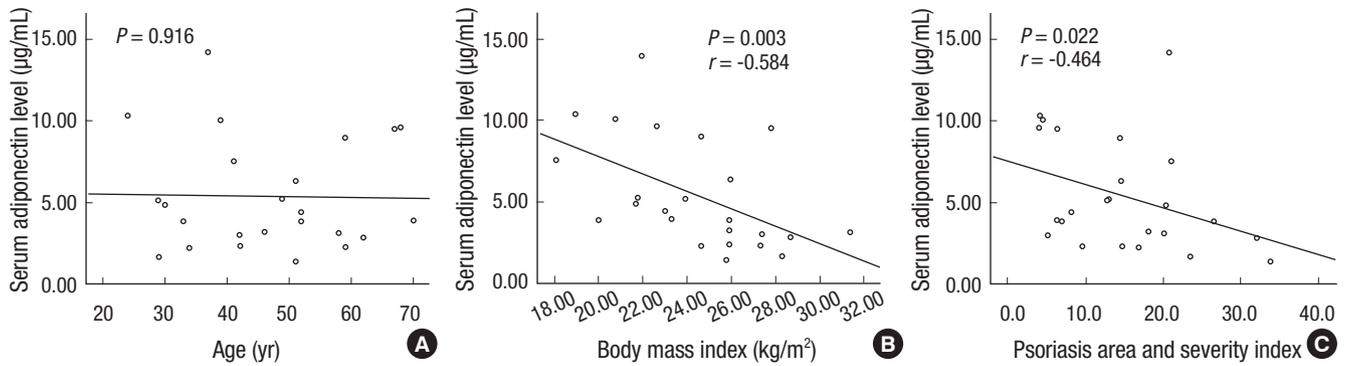


Fig. 3. Correlation between serum adiponectin levels and age (A), BMI (B), PASI (C).

Table 5. Serum adiponectin levels in patients (n = 24) and controls (n = 15) according to gender

Characteristics	Patients* ($\mu\text{g/mL}$)	Controls* ($\mu\text{g/mL}$)	P value
Total	5.42 \pm 3.40 (1.43-14.23)	13.58 \pm 5.66 (7.07-24.44)	0.000
Male	3.79 \pm 1.68 (1.43-7.52)	10.12 \pm 2.90 (7.07-14.88)	0.000
Female	8.68 \pm 3.70 (2.30-14.23)	18.78 \pm 4.71 (12.77-24.44)	0.000

*Patients and Controls are in Mean \pm SD (range).

mon mesothelial origin (17, 18). It has been documented that circulatory levels of TNF- α are significantly increased in obese as compared with non-obese subjects (19, 20). In 2005, Naldi and colleagues reported in a case-controlled study (2) that BMI is one of the risk factors associated with psoriasis. Although the underlying mechanisms may be complex, the "obesity of psoriasis" is thought to be a key link to cardiovascular diseases, including DM, stroke, heart disease, hypertension, and myocardial infarction (6, 21-23).

Adipose tissue is considered to be an important endocrine organ that contributes to the regulation of body metabolism and other vital functions related to inflammation and immune responses (22). It secretes multiple metabolically-active proteins termed adipokines. Some well-known adipokines include leptin, resistin, adiponectin, apelin, and visfatin (24).

Leptin hormone, the product of the obese gene, is an adipocyte-derived hormone which is a key factor in regulating a wide range of biological responses, including energy homeostasis, immune responses, and inflammatory processes (8). Leptin receptor is expressed primarily in the hypothalamus, but is also expressed in various other tissues, including peripheral blood mononuclear cells, endothelial cells, and fibroblasts (25). Mice with either a leptin (*ob/ob*) or leptin receptor (*db/db*) deficiency develop severe obesity, diabetes, and impaired cell-mediated immune responses (26, 27). Serum leptin levels are known to show a positive correlation with BMI and marked sexual dimorphism, with levels presenting two to three times higher in women than in men (28). The immunological and proliferative effects of leptin and immunopathogenesis of psoriasis have

Table 6. Serum adiponectin levels according to patient characteristics

Characteristics	Concentrations* ($\mu\text{g/mL}$)		P value
	Yes	No	
Nail involvement	4.55 \pm 2.42 (1.43-9.52)	6.29 \pm 4.07 (2.30-14.23)	0.41
Familial history	6.35 \pm 3.61 (2.30-10.34)	5.18 \pm 3.40 (1.43-14.23)	0.489
Psoriatic arthritis	6.88 \pm 3.14 (2.30-10.34)	4.82 \pm 3.40 (1.43-14.23)	0.099
Vitamin D deficiency	6.12 \pm 4.30 (1.43-14.23)	2.43 \pm 4.84 (2.36-10.34)	0.955

*Concentrations are in Mean \pm SD (range).

many overlapping features.

Adiponectin is a collagen-like protein of 247 amino acids that circulates at relatively high serum concentrations (2–20 $\mu\text{g/mL}$) and regulates the metabolism of lipids and glucose (29). The mechanism of adiponectin action involves activation of multiple signaling pathways, which mediate its anti-inflammatory and anti-atherogenic functions (30). Low levels of adiponectin are associated with adverse metabolic states such as diabetes (22), metabolic syndrome, atherosclerotic cardiovascular disease (31), and psoriasis (9, 10, 32, 33).

The purpose of this current study was to investigate the possible roles of leptin and adiponectin in psoriasis pathogenesis. We investigated serum leptin and adiponectin levels in patients with psoriasis and controls. The mean serum leptin concentrations in patients with psoriasis were statistically significantly higher than those in controls. Circulating leptin levels showed marked sexual dimorphism, which was two to three times higher in females than in males (11, 34). As sex appeared to be an important factor in relation to levels of serum adipokines, all comparisons were made among sex-stratified populations. Serum leptin levels in male and female psoriatic patients were significantly higher than those in gender-matched controls. In contrast, serum adiponectin levels in patients with psoriasis were significantly decreased compared with healthy controls. Serum adiponectin levels in male and female psoriatic patients were significantly lower than those in gender-matched controls.

There were no significant differences in leptin levels with respect to the presence of nail involvement, familial history, or psoriatic arthritis. However, leptin levels in vitamin D-deficient patients were statistically significantly higher than those in vitamin D-sufficient patients. Several studies have been performed concerning the association between hypovitaminosis D and metabolic syndrome (35). Our results help to explain the link between leptin and the association of hypovitaminosis D with metabolic syndrome.

Serum leptin concentrations showed no correlation with age, BMI, or PASI in patients with psoriasis. Serum adiponectin concentrations showed no correlation with age in patients with psoriasis. However, serum adiponectin concentrations showed a negative correlation with BMI and PASI in patients with psoriasis. This may be due to the fact that there are multiple factors involved in regulating serum leptin levels.

Several studies concerning the association between leptin and psoriasis showed results similar to ours (6, 8-14). These data support the view that leptin may be involved in the pathogenesis of psoriasis. Çerman et al. showed that serum leptin levels were significantly higher in patients with severe psoriasis than those of patients with BMI-matched mild to moderate psoriasis and controls (8). Serum leptin levels showed a positive correlation with PASI score, suggesting that they might serve as a marker of severity in psoriasis patients (8).

The results of studies by Johnston et al. (7) and Aktan et al. (15) did not support any possible relationship between serum leptin levels and psoriasis. However, Aktan et al. suggested that further studies investigating severe inflammatory forms of psoriasis (15) were necessary due to the relatively small number of subjects (20) and relatively low mean PASI (6.2) scores in their patient group.

In conclusion, it was demonstrated that serum leptin concentrations of patients with psoriasis were significantly higher than those of controls. In contrast, serum adiponectin levels of patients with psoriasis were significantly decreased compared with those of healthy controls. Therefore, leptin and adiponectin may play some role in the immunopathogenesis of psoriasis and might be used as biomarkers to assess the severity of psoriasis in Korean patients.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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