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Original Article

Association of Leptin, Resistin, and High-Molecular-Weight Adiponectin Levels with Psoriasis Area and Severity Index Scores, Obesity, and Insulin Resistance in Psoriasis Patients

Emine Müge Acar[1]*, Nilsel İlter[2], Şehri Elbeg[3]

[1]Department of Dermatology, Kirsehir Ahi Evran University Training and Research Hospital, Kırşehir, Turkey,
[2]Department of Dermatology, Gazi University Faculty of Medicine, Ankara, Turkey,
[3]Department of Biochemistry, Gazi University Faculty of Medicine, Ankara, Turkey

Abstract

Background: Psoriasis is frequently associated with obesity and cardiovascular diseases. Adipocytokines have been implicated in the pathogenesis of psoriasis and its cardiometabolic comorbidities. **Objectives:** The aim of this study was to assess the roles of leptin, resistin, and high-molecular-weight (HMW) adiponectin in psoriasis as well as their relationship with Psoriasis Area and Severity Index (PASI), obesity, and insulin resistance. **Materials and Methods:** Forty-six psoriasis patients and equivalent age-, sex-, and body mass index (BMI)-matched controls were recruited in this study. PASI, waist and hip circumferences, and waist/hip ratio (WHR) were recorded, and total body fat mass (TBFM) values were measured using a bioimpedance body composition analyzer. Fasting serum leptin, resistin, and HMW adiponectin levels were measured, and homeostasis model assessment values for insulin resistance (HOMA-IR) were calculated. **Results:** After the adjustment for anthropometric variables, leptin levels did not differ significantly between the groups ($P = 0.736$). The patient group showed significantly elevated resistin and lower HMW adiponectin levels ($P = 0.007$, $P = 0.010$, respectively). The correlation of serum leptin, resistin, and HMW adiponectin with PASI was not significant ($r = -0.100$, $P = 0.506$; $r = -0.053$, $P = 0.726$; $r = -0.103$, $P = 0.494$, respectively). HOMA-IR positively correlated with leptin and negatively correlated with HMW adiponectin ($r = 0.426$, $P < 0.001$; $r = -0.393$, $P < 0.001$, respectively). The correlation of leptin and resistin with BMI was direct while that of HMW adiponectin with BMI was inverse ($r = 0.532$, $P < 0.001$; $r = 0.240$, $P = 0.021$; $r = -0.408$, $P < 0.001$, respectively). No significant differences were detected regarding TBFM, and waist and hip circumferences ($P = 0.187$, $P = 0.090$, $P = 0.543$, respectively). However, WHR was significantly higher in the patient group ($P = 0.015$). **Conclusion:** Altered adipocytokine levels in psoriasis patients suggest a possible role of adipocytokines in the relationship between psoriasis and its metabolic comorbidities. Fat distribution is also different from the healthy population with similar TBFM values, and abdominal obesity, which is an independent cardiovascular risk factor, is more prevalent in psoriasis patients.

Keywords: Adiponectin, body mass index, insulin resistance, leptin, molecular weight, psoriasis, resistin

Introduction

Psoriasis is a chronic inflammatory skin disease characterized by epidermal hyperproliferation and Th1 cell-mediated

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Address for correspondence: Dr. Emine Müge Acar, Kirsehir Ahi Evran University Training and Research Hospital, 2019 Street, No. 1, Kervansaray District, Kirsehir, Turkey.
E-mail: drmugeacar@gmail.com

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inflammation and affects approximately 1%–3% of the population.[1] Obesity has been closely associated with psoriasis, and more severe forms of psoriasis are encountered in obese patients.[2,3] The severity of obesity also affects treatment response and weight loss reportedly facilitates more favorable treatment outcomes.[4]

Recent studies have shown that the adipose tissue not only plays a role in energy storage but also in endocrinologic and metabolic functions, inflammation, and immunity by employing adipocytokines such as adiponectin, Pre-B cell colony-enhancing factor, visfatin, leptin, resistin, retinol-binding protein 4, tumor necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and monocyte chemotactic protein-1 (MCP-1 or CCL-2).[5,6] Obesity is characterized by low-grade, chronic inflammation; obese patients predominantly secrete proinflammatory cytokines from the adipose tissue, whereas lean individuals release anti-inflammatory cytokines.[4,6] Recently, it has been suggested that adipocytokines play a role in the pathogenesis of psoriasis and influence its metabolic comorbidities such as obesity and insulin resistance.[7]

Leptin is a 16 kDa adipokine mainly produced by adipocytes and primarily functions as a regulator of appetite, weight gain, and body fat.[7] Besides its metabolic functions, leptin directly or indirectly plays a role in modulating immune response.[8] Leptin promotes Th1 response and suppresses Th2-dependent inflammation and stimulates the release of TNF-α, IL-6, and interferon gamma (IFN-γ) from mononuclear cells.[8] Increasing evidence suggests that leptin is involved in autoimmune diseases including rheumatoid arthritis, diabetes, and psoriasis.[9]

Resistin is an adipokine that was first discovered in rodents in 2001. It was originally implicated in the pathogenesis of diabetes and diabetes–obesity relationship.[10] Recent studies have shown that resistin is involved in inflammation and immunity.[11] Resistin participates in the regulation of proinflammatory cytokine expression[11] and can induce IL-6, IL-8, and TNF-α expression *in vitro*.[12] Resistin is considered to be involved in TNF-α-related inflammation in psoriasis.[13]

Adiponectin is abundantly found in circulation and has antidiabetic, anti-inflammatory, and vasculoprotective properties.[14] High-molecular-weight (HMW) adiponectin is an adiponectin subtype with a molecular weight of 400–600 kDa and has a higher predictive value for insulin resistance than that of other adiponectin subtypes.[15] Adiponectin is suspected to act as an anti-inflammatory mediator in psoriasis etiopathogenesis, and decreased levels of HMW adiponectin has been reported in psoriasis patients.[16,17]

In our study, we aimed to determine the roles of leptin, resistin, and HMW adiponectin in psoriasis, obesity, and insulin resistance by measuring serum adipocytokine levels, homeostasis model assessment-insulin resistance (HOMA-IR) values, and body mass index (BMI), and total body fat mass (TBFM) values of psoriasis patients and comparing these values with those of the age-, sex-, and BMI-matched healthy population.

Materials and Methods

Recruitment of patients and controls

Forty-six patients who visited our dermatology department between January 2011 and December 2013 and whose diagnosis were confirmed both clinically and histopathologically were recruited. Inclusion criteria were an age of >18 years, disease duration of >1 year, and absence of systemic treatment for the past 1 month. Pregnancy, diabetes, hypertension, and inflammatory diseases other than psoriasis comprised the exclusion criteria. The study was approved by the Local Ethics Committee, and informed consent was obtained from all patients and participants in the control group.

Measurement of adipocytokines

Blood samples were collected from patients and controls after overnight fasting. Serum was extracted after clotting and centrifugation and preserved at − 80°C. Serum leptin (DRG GmbH, Marburg, Germany), resistin (eBioscience, San Diego, California, USA), and HMW adiponectin (RandD Systems Minneapolis, MN, USA) levels were measured using enzyme-linked immunosorbent assay. HOMA-IR was calculated by the following equation: fasting blood glucose × serum insulin level/405.

Measurement of anthropometric values

BMI, waist and hip circumferences, and waist/hip ratio circumference (WHR) values were recorded. Waist circumference was measured from the mid-point of the lowest rib and the iliac crest. Hip circumference was measured at the largest level of the symphysis pubis and gluteus maximus. The TANITA TBF 300 bioimpedance body composition analyzer was used for determining body weight and TBFM values.

Statistical analysis

The data were analyzed using SPSS for Windows 11.5 program (SPSS Inc., Chicago, IL, USA). Datasets were tested for normality using Shapiro–Wilk test. Descriptive statistics was demonstrated as mean ± standard deviation and median (minimum-maximum) for continuous and discrete variables; categoric variables were demonstrated as number and percentage. Categorical variables were analyzed by Fisher's exact test. The statistical difference between the groups was analyzed using Student's *t*-test for mean values and Mann–Whitney U-test for median values. Multiple linear regression analyses were performed to determine whether the effect of psoriasis on leptin, resistin, and adiponectin measurements was statistically significant after adjustment for confounding factors (i.e., body weight, BMI, and WHR). Coefficients of regression, 95% confidence intervals and t-statistic for each independent variable were also calculated. Due to the nonnormal distribution, log transformation was applied to leptin, resistin, and adiponectin levels in the multiple linear regression analysis. The correlations between the variables

were determined using Spearman's correlation coefficients and a $P < 0.05$ was considered to be statistically significant.

Results

The patient group comprised 46 psoriasis patients (29 males and 17 females) and equivalent age-, sex-, and BMI-matched volunteers with no history of skin disease. The Psoriasis Area and Severity Index (PASI) score was 11.2 (4.7–33.2) [Table 1]. Leptin levels did not differ significantly between patients and controls ($P = 0.290$), whereas serum resistin levels were significantly higher and HMW adiponectin levels were significantly lower in the patient group ($P = 0.002$ for both). After adjustments for BMI, body weight, and WHR with linear regression analysis, the results persisted; leptin levels were not significantly different between patients and controls, and the patient group showed elevated resistin and lower HMW adiponectin levels ($P = 0.736$, $P = 0.007$, $P = 0.010$, respectively). No significant difference was found in terms of HOMA-IR between the groups ($P = 0.430$) [Table 2 and Figure 1a and b].

PASI levels showed no significant correlations with serum leptin, resistin, and HMW adiponectin levels ($r = -0.100$, $P = 0.506$; $r = -0.053$, $P = 0.726$; $r = -0.103$, $P = 0.494$, respectively). Serum leptin levels and HMW adiponectin levels positively and negatively correlated with HOMA-IR ($r = 0.426$, $P < 0.001$; $r = -0.393$, $P < 0.001$), respectively. Serum resistin levels did not correlate with HOMA-IR ($r = -0.020$, $P = 0.85$). Serum leptin and resistin levels correlated with BMI ($r = 0.532$, $P < 0.001$; $r = 0.240$, $P = 0.021$, respectively). Serum HMW adiponectin levels inversely correlated with BMI ($r = -0.408$, $P \leq 0.001$) [Table 3 and Figure 2].

The body weight and TBFM values of the patient group did not differ from those of the control group ($P = 0.270$). Waist and hip circumference values of patient and control groups were not significantly different ($P = 0.090$). However, WHR values of the patient group (0.93 ± 0.07) were significantly higher than those of the control group (0.89 ± 0.07) ($P = 0.015$) [Table 4].

Discussion

Psoriasis is strongly associated with obesity, diabetes, hypertension, metabolic syndrome, and cardiovascular comorbidities; growing evidence has shown that psoriasis is "more than skin deep."[18,19] Chronic inflammation is associated with obesity, which is characterized by abnormal cytokine production, increased synthesis of acute phase reactants, and activation of inflammatory signaling pathways,[5] and has been suggested to increase the risk of psoriasis development.[4] In this study, we noted that serum resistin levels were higher and HMW adiponectin levels of the patients were lower than those of the healthy controls, whereas leptin levels were not significantly different. No correlation between these adipocytokine levels and psoriasis severity was found.

Leptin reportedly stimulates keratinocyte proliferation, adhesion molecule expression, and angiogenesis as well as is

Table 1: Comparison of the characteristics of patients and controls

Variables	Patient group ($n=46$)	Control group ($n=46$)	*P*
Age	37.4±11.5	38.5±14.0	0.992
Gender (%)			-
Female	17 (37.0)	17 (37.0)	-
Male	29 (63.0)	29 (63.0)	-
Disease duration (year)	12 (1-40)	-	-
PASI	11.2 (4.7-33.2)	-	-

PASI: Psoriasis area and severity index

Table 2: Comparison of serum leptin, resistin and high-molecular-weight adiponectin levels and homeostasis model assessment insulin resistance with control group

Variables	Patient group ($n=46$)	Control group ($n=46$)	*P*
Leptin (ng/mL)	10.7 (0.1-48.8)	6.8 (0.0-77.7)	0.290
Resistin (pg/mL)	4334 (1913-9858)	3340 (1034-6373)	0.002*
HMW adiponectin (ng/mL)	25.7 (8.9-101.8)	37.5 (8.7-222.9)	0.002*
HOMA-IR	1.5 (0.4-6.4)	1.5 (0.7-3.5)	0.430

*$P<0.05$. HMW: High-molecular-weight, HOMA-IR: Homeostasis model assessment insulin resistance

Table 3: Correlation coefficients and significance values of serum leptin, resistin and high-molecular-weight adiponectin levels and psoriasis area and severity index, homeostasis model assessment insulin resistance and body mass index

Variables	Leptin	Resistin	HMW adiponectin
PASI			
Correlation coefficent (*r*)	−0.100	−0.053	−0.103
P†	0.506	0.726	0.494
HOMA-IR			
Correlation coefficent (*r*)	0.426	−0.020	−0.393
P†	<0.001*	0.850	<0.001*
BMI			
Correlation coefficent (*r*)	0.532	0.240	−0.408
P†	<0.001*	0.021*	<0.001*

*$P<0.05$. †: Spearman correlation test, HMW: High-molecular-weight, HOMA-IR: Homeostasis model assessment insulin resistance, PASI: Psoriasis area and severity index, BMI: Body mass index

Table 4: Comparison of the anthropometric values of patient group with control group

Variables	Patient group ($n=46$)	Control group ($n=46$)	*P*
BMI (kg/m^2)	26.8±5.0	25.1±4.6	0.093
Body weight (kg)	75.3±14.8	72.0±13.3	0.270
TBFM (kg)	18.5 (2.5-58.4)	16.0 (2.0-39.0)	0.187
Waist circumference (cm)	94.1±12.8	89.5±13.3	0.090
Hip circumference (cm)	100.6±9.3	99.4±10.1	0.543
WHR	0.93±0.07	0.89±0.07	0.015*

*$P<0.05$. TBFM: Total body fat mass, BMI: Body mass index, WHR: Waist/hip ratio

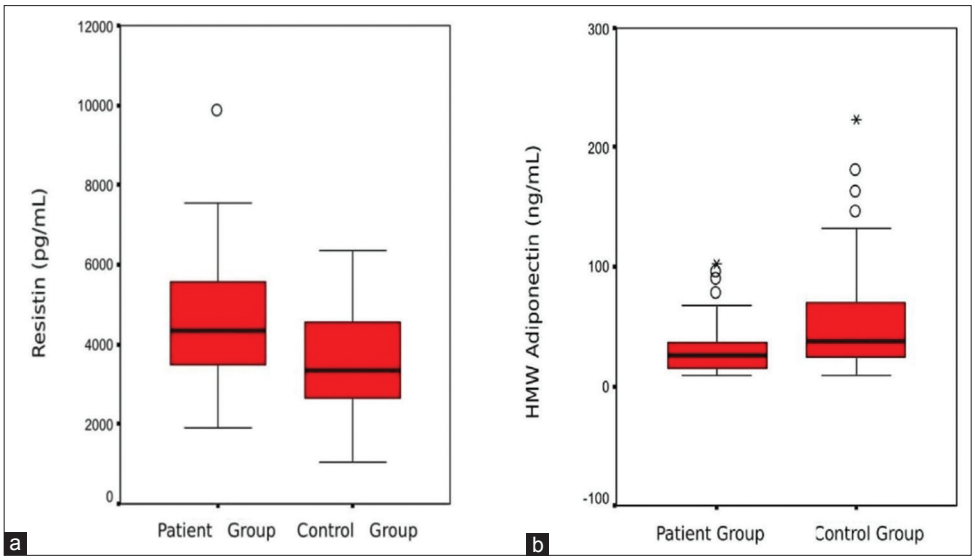

Figure 1: (a and b) Serum resistin and high-molecular-weight adiponectin levels in patients and controls

likely involved in obesity–psoriasis relationship by inducing or augmenting inflammation.[9] Previous studies concerning leptin levels in psoriasis patients have produced inconsistent results. Elevated and unchanged leptin levels in psoriasis patients have been reported.[20-24] In this study, although serum leptin levels were higher in the patient group, the difference was not statistically significant (P = 0.290) and had no correlation with PASI. Consistent with the findings in our study, Johnston *et al*. and Ozdemir *et al*. found that leptin levels did not differ between the patient and control groups and did not correlate with disease severity.[23,24] Serum leptin levels can be affected by many factors such as diet, exercise, anxiety, and depressive mood.[25-27] It is also possible that effects of such factors on leptin levels together with the limited number of patients included in the study and low-PASI levels led to the nonsignificant difference in the leptin levels between the patient and control groups noted in our study.

Resistin was first defined as an adipocyte-secreted peptide that was proposed to be related to obesity and diabetes. Recently, *in vivo* and *in vitro* studies have revealed that resistin plays a role in the process of inflammation.[28] Resistin has been shown to stimulate the secretion of TNF-α and IL-12 from macrophages, and TNF-α and IL-1 β, IL-6, or lipopolysaccharides strongly induce resistin expression.[28,29] Previous studies have reported elevated levels of resistin in psoriasis patients.[30-33] Consistently, serum resistin levels were significantly higher in the patient group in our study. In the studies conducted by Takahashi *et al*. and Rajappa *et al*., a correlation between serum resistin levels and psoriasis severity was reported.[22,33] As this correlation was not found in our study, we believe that resistin plays a role in psoriasis etiopathogenesis, but serum resistin levels are not associated with disease severity. However, since our study population included a limited number of patients, further studies with larger series investigating the relationship between serum resistin and psoriasis severity are necessary.

Adiponectin circulates in plasma in the form of oligomeric complexes including trimeric, hexameric, and HMW structures.[16] Biological functions of adiponectin have been suggested to be related to its molecular weight.[16,17] HMW adiponectin is the most active form of adiponectin, and it has been shown to be a more sensitive marker for inflammation and metabolism.[17] Adiponectin has anti-inflammatory functions and inhibits T-cell activation and proliferation as well as decreases TNF-α, IL-6, IFN-γ, and phagocytic activity of macrophages.[14] It has been suggested that adiponectin acts as a protective anti-inflammatory factor in psoriasis. In a study by Nakajima *et al*., no significant difference was observed between total adiponectin levels of patients and controls, whereas low levels of HMW adiponectin have been reported in psoriasis patients.[17] Shibata *et al*. also reported decreased levels of HMW adiponectin in psoriasis patients.[16] Consistent with the results of the studies conducted by Shibata *et al*., and Nakajima *et al*., we found that HMW adiponectin levels were significantly lower in the patient group. TNF-α and IL-6 inhibit adiponectin synthesis, and thus, elevated IL-6 and TNF-α levels may be responsible for the decrease in adiponectin levels in psoriasis.[7] Nakajima *et al*. reported that HMW adiponectin levels inversely correlated with psoriasis severity (P = 0.002).[17] In our study, we did not detect a correlation between HMW adiponectin levels and disease severity (P = 0.14). Our results indicate that HMW adiponectin may play a role in psoriasis pathogenesis. The absence of a correlation between HMW adiponectin levels and psoriasis severity may be related to the small size of the patient group and low PASI scores. Therefore, larger studies are required to confirm this relationship.

Consistent with previous studies, leptin and resistin levels directly correlated with BMI values (P < 0,001; P = 0.021,

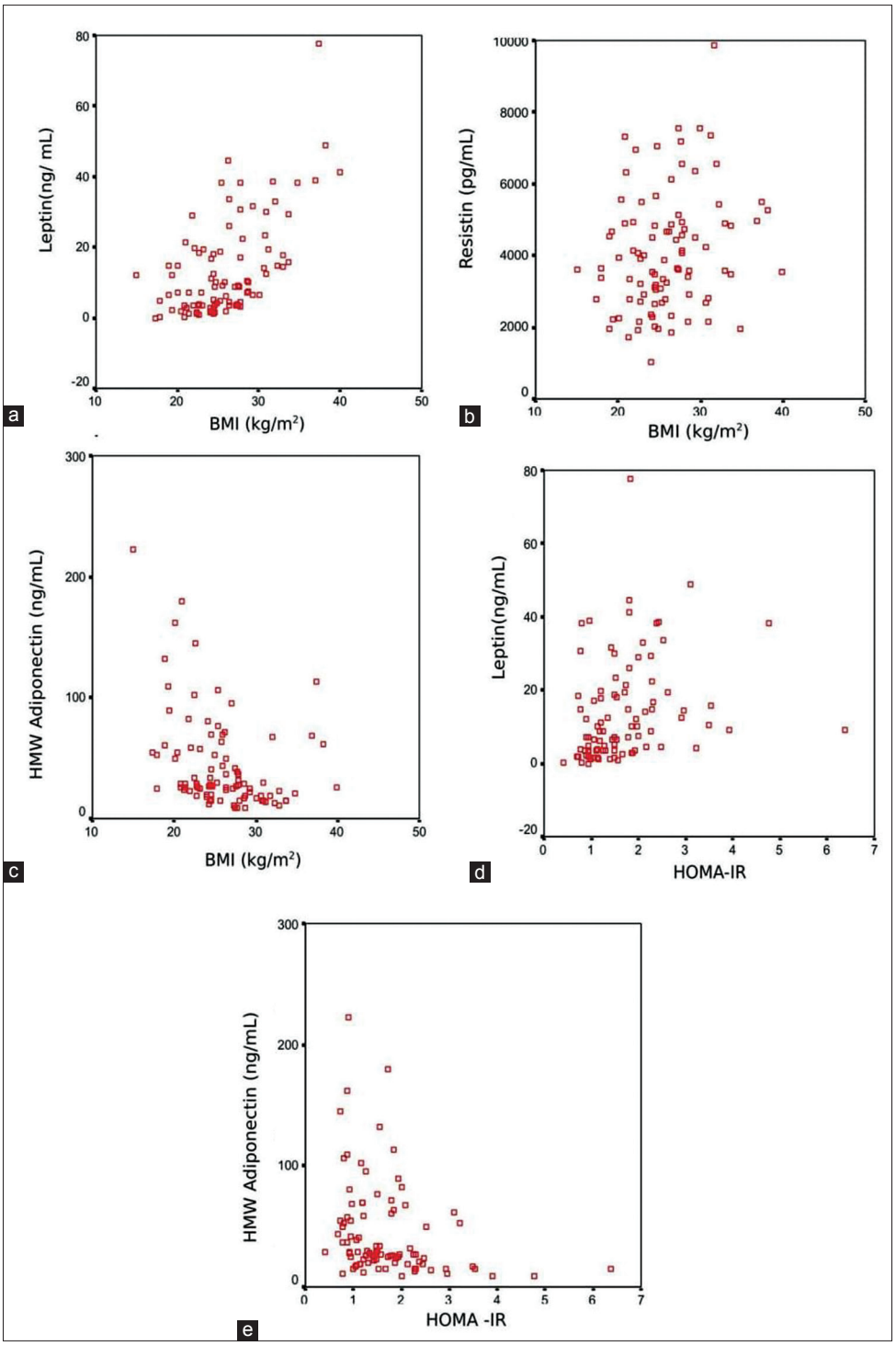

Figure 2: Correlation between leptin, resistin and high-molecular-weight adiponectin with body mass index and homeostasis model assessment insulin resistance. (a-c) Leptin and resistin levels show a positive correlation with body mass index, high-molecular-weight adiponectin levels inversely correlated with body mass index (d and e). Leptin levels show positive correlation with homeostasis model assessment insulin resistance, high-molecular-weight adiponectin levels negatively correlate with homeostasis model assessment insulin resistance

respectively).[23,34,35] Our results show that serum leptin and resistin levels are related to obesity, and an increase in the number of adipocytes causes an increase in leptin and resistin levels; therefore, they can be used as biomarkers for obesity. In line with the study by Eglit *et al*., HMW adiponectin levels negatively correlated with BMI in our study.[36] It has been hypothesized that increased synthesis of MCP by hypertrophic adipocytes leads to elevated TNF-α and increased free fatty acid concentrations and results in the suppression of adiponectin secretion.[37] It has been suggested that HMW

adiponectin levels are more useful in the prediction of insulin resistance and metabolic syndrome than total adiponectin levels.[15] Our results also confirm that HMW adiponectin is a sensitive biomarker for the assessment of metabolic risk.

Leptin has been implicated in glucose homeostasis and insulin sensitivity regulation.[38] A significant correlation between HOMA-IR and serum leptin levels has been reported in previous studies.[39,40] Our study also demonstrated that serum leptin levels directly correlated with HOMA-IR values, indicating a relationship between leptin and insulin resistance. On the contrary, the role of resistin in insulin resistance remains controversial.[41-43] Our results show that serum resistin is not directly involved in insulin resistance because no correlation between serum resistin levels and HOMA-IR values was detected. In line with the study by Eglit *et al*., our results suggested that HMW adiponectin levels inversely correlated with HOMA-IR value.[36] Adiponectin is a beneficial cytokine owing to its anti-inflammatory, antiatherogenic, antidiabetic, and cardioprotective effects.[44] Our results support the hypothesis that low levels of adiponectin are associated with increased metabolic risk and that HMW adiponectin may play a protective role against insulin resistance.

In this study, no statistically significant difference in TBFM values between the groups was detected. Mashayekhi-Goyonlo *et al*. reported that total fat mass percentages did not differ between the groups, whereas abdominal fat mass percentages were significantly higher in the patient group.[45] Central obesity, characterized by an increase in abdominal fat mass values, is a marker representing high risks of insulin resistance and metabolic syndrome development.[46] Because we did not measure abdominal fat mass values, we believe that the sole measurement of TBFM may be insufficient for estimating metabolic risk. However, WHR, which is also a marker for abdominal obesity was found to be significantly higher in the patient group than that in the control group. Waist circumference and WHR have been reported to be independently associated with type 2 diabetes mellitus, arterial disease, and mortality risk.[47,48] WHR has been suggested to be a more reliable risk factor for myocardial infarction (MI) comparing to waist circumference.[49] Psoriasis has been demonstrated to be associated with cardiovascular morbidities and independently associated with increased MI risk.[50] Our results reveal that psoriasis patients have increased the risk of cardiovascular morbidities.

Conclusion

Our results indicate that resistin and HMW adiponectin levels are altered in comparison with the BMI-matched healthy population that has similar TBFM values. Leptin and HMW adiponectin are associated with insulin resistance. Leptin, resistin, and HMW adiponectin levels facilitate the assessment of obesity-related inflammation. This study supports the view that adipocytokines may play a role in the relationship between psoriasis and its metabolic comorbidities. Our study also indicates that fat distribution in psoriasis patients is different from the healthy population with similar TBFM values and that abdominal obesity, which is an independent cardiovascular risk factor, is more prevalent in psoriasis patients. Further large-scale studies are necessary to examine and determine the role of adipocytokines in psoriasis pathogenesis and its comorbidities.

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Conflicts of interest

There are no conflicts of interest.

References

1. Azfar RS, Gelfand JM. Psoriasis and metabolic disease: Epidemiology and pathophysiology. Curr Opin Rheumatol 2008;20:416-22.
2. Marino MG, Carboni I, De Felice C, Maurici M, Maccari F, Franco E. Risk factors for psoriasis: A retrospective study on 501 outpatients clinical records. Ann Ig 2004;16:753-8.
3. Herron MD, Hinckley M, Hoffman MS, Papenfuss J, Hansen CB, Callis KP, *et al.* Impact of obesity and smoking on psoriasis presentation and management. Arch Dermatol 2005;141:1527-34.
4. Hamminga EA, van der Lely AJ, Neumann HA, Thio HB. Chronic inflammation in psoriasis and obesity: Implications for therapy. Med Hypotheses 2006;67:768-73.
5. Tilg H, Moschen AR. Role of adiponectin and PBEF/visfatin as regulators of inflammation: Involvement in obesity-associated diseases. Clin Sci (Lond) 2008;114:275-88.
6. Piya MK, McTernan PG, Kumar S. Adipokine inflammation and insulin resistance: The role of glucose, lipids and endotoxin. J Endocrinol 2013;216:T1-15.
7. Gerdes S, Rostami-Yazdi M, Mrowietz U. Adipokines and psoriasis. Exp Dermatol 2011;20:81-7.
8. Juge-Aubry CE, Meier CA. Immunomodulatory actions of leptin. Mol Cell Endocrinol 2002;194:1-7.
9. Davidovici BB, Sattar N, Prinz J, Puig L, Emery P, Barker JN. Psoriasis and systemic inflammatory diseases: Potential mechanistic links between skin disease and co-morbid conditions. J Invest Dermatol 2010;130:1785-96.
10. Steppan CM, Bailey ST, Bhat S, Brown EJ, Banerjee RR, Wright CM, *et al.* The hormone resistin links obesity to diabetes. Nature 2001;409:307-12.
11. Pang SS, Le YY. Role of resistin in inflammation and inflammation-related diseases. Cell Mol Immunol 2006;3:29-34.
12. Bokarewa M, Nagaev I, Dahlberg L, Smith U, Tarkowski A. Resistin, an adipokine with potent proinflammatory properties. J Immunol 2005;174:5789-95.
13. Nakajima H, Nakajima K, Tarutani M, Sano S. Clear association between serum levels of adipokines and T-helper 17-related cytokines in patients with psoriasis. Clin Exp Dermatol 2013;38:66-70.
14. Guzik TJ, Mangalat D, Korbut R. Adipocytokines-novel link between inflammation and vascular function? J Physiol Pharmacol 2006;57:505-28.
15. Hara K, Horikoshi M, Yamauchi T, Yago H, Miyazaki O, Ebinuma H, *et al.* Measurement of the high-molecular weight form of adiponectin in plasma is useful for the prediction of insulin resistance and metabolic syndrome. Diabetes Care 2006;29:1357-62.
16. 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.
17. Nakajima H, Nakajima K, Tarutani M, Morishige R, Sano S. Kinetics of circulating th17 cytokines and adipokines in psoriasis patients. Arch Dermatol Res 2011;303:451-5.
18. Gisondi P, Cazzaniga S, Chimenti S, Giannetti A, Maccarone M, Picardo M, *et al.* Metabolic abnormalities associated with initiation

of systemic treatment for psoriasis: Evidence from the İtalian psocare registry. J Eur Acad Dermatol Venereol 2013;27:e30-41.
19. Tarkin JM, Rudd JH. Psoriasis: More than just skin deep. Arterioscler Thromb Vasc Biol 2015;35:2487-8.
20. Takahashi H, Tsuji H, Takahashi I, Hashimoto Y, Ishida-Yamamoto A, Iizuka H. Plasma adiponectin and leptin levels in Japanese patients with psoriasis. Br J Dermatol 2008;159:1207-8.
21. Aly DG, Abdallah IY, Hanafy NS, Elsaie ML, Hafiz NA. Elevated serum leptin levels in nonobese patients with psoriasis. J Drugs Dermatol 2013;12:e25-9.
22. Rajappa M, Rathika S, Munisamy M, Chandrashekar L, Thappa DM. Effect of treatment with methotrexate and coal tar on adipokine levels and indices of insulin resistance and sensitivity in patients with psoriasis vulgaris. J Eur Acad Dermatol Venereol 2015;29:69-76.
23. Johnston A, Arnadottir S, Gudjonsson JE, Aphale A, Sigmarsdottir AA, Gunnarsson SI, *et al.* Obesity in psoriasis: Leptin and resistin as mediators of cutaneous inflammation. Br J Dermatol 2008;159:342-50.
24. Ozdemir M, Yüksel M, Gökbel H, Okudan N, Mevlitoğlu I. Serum leptin, adiponectin, resistin and ghrelin levels in psoriatic patients treated with cyclosporin. J Dermatol 2012;39:443-8.
25. Talaei M, Nazem F, Ranjbar K. The impact of rapid weight loss (4%) on leptin, adiponectin, and insulin resistance in elite adult free style wrestlers. J Sports Med Phys Fitness 2017;57:434-40.
26. Greco M, Chiefari E, Montalcini T, Accattato F, Costanzo FS, Pujia A. Early effects of a hypocaloric, mediterranean diet on laboratory parameters in obese individuals. Mediators Inflamm 2014;2014:750860.
27. Akter S, Pham NM, Nanri A, Kurotani K, Kuwahara K, Jacka FN, *et al.* Association of serum leptin and ghrelin with depressive symptoms in a Japanese working population: A cross-sectional study. BMC Psychiatry 2014;14:203.
28. Filková M, Haluzík M, Gay S, Senolt L. The role of resistin as a regulator of inflammation: Implications for various human pathologies. Clin Immunol 2009;133:157-70.
29. Silswal N, Singh AK, Aruna B, Mukhopadhyay S, Ghosh S, Ehtesham NZ. Human resistin stimulates the pro-inflammatory cytokines TNF-alpha and IL-12 in macrophages by NF-kappaB-dependent pathway. Biochem Biophys Res Commun 2005;334:1092-101.
30. Coimbra S, Oliveira H, Reis F, Belo L, Rocha S, Quintanilha A, *et al.* Circulating adipokine levels in Portuguese patients with psoriasis vulgaris according to body mass index, severity and therapy. J Eur Acad Dermatol Venereol 2010;24:1386-94.
31. Corbetta S, Angioni R, Cattaneo A, Beck-Peccoz P, Spada A. Effects of retinoid therapy on insulin sensitivity, lipid profile and circulating adipocytokines. Eur J Endocrinol 2006;154:83-6.
32. Kawashima K, Torii K, Furuhashi T, Saito C, Nishio E, Nishida E, *et al.* Phototherapy reduces serum resistin levels in psoriasis patients. Photodermatol Photoimmunol Photomed 2011;27:152-5.
33. Takahashi H, Tsuji H, Honma M, Ishida-Yamamoto A, Iizuka H. Increased plasma resistin and decreased omentin levels in Japanese patients with psoriasis. Arch Dermatol Res 2013;305:113-6.
34. Wang Y, Chen J, Zhao Y, Geng L, Song F, Chen HD, *et al.* Psoriasis is associated with increased levels of serum leptin. Br J Dermatol 2008;158:1134-5.
35. Owecki M, Miczke A, Nikisch E, Pupek-Musialik D, Sowiński J. Serum resistin concentrations are higher in human obesity but independent from insulin resistance. Exp Clin Endocrinol Diabetes 2011;119:117-21.
36. Eglit T, Ringmets I, Lember M. Obesity, high-molecular-weight (HMW) adiponectin, and metabolic risk factors: Prevalence and gender-specific associations in estonia. PLoS One 2013;8:e73273.
37. Kaser S, Tatarczyk T, Stadlmayr A, Ciardi C, Ress C, Tschoner A, *et al.* Effect of obesity and insulin sensitivity on adiponectin isoform distribution. Eur J Clin Invest 2008;38:827-34.
38. Ceddia RB, William WN Jr., Carpinelli AR, Curi R. Modulation of insulin secretion by leptin. Gen Pharmacol 1999;32:233-7.
39. Leon-Cabrera S, Solís-Lozano L, Suárez-Álvarez K, González-Chávez A, Béjar YL, Robles-Díaz G, *et al.* Hyperleptinemia is associated with parameters of low-grade systemic inflammation and metabolic dysfunction in obese human beings. Front Integr Neurosci 2013;7:62.
40. Zuo H, Shi Z, Yuan B, Dai Y, Wu G, Hussain A, *et al.* Association between serum leptin concentrations and insulin resistance: A population-based study from China. PLoS One 2013;8:e54615.
41. Singh AK, Tiwari S, Gupta A, Shukla KK, Chhabra KG, Pandey A, *et al.* Association of resistin with insulin resistance and factors of metabolic syndrome in North İndians. Indian J Clin Biochem 2015;30:255-62.
42. Sadashiv, Tiwari S, Paul BN, Kumar S, Chandra A, Dhananjai S, *et al.* Over expression of resistin in adipose tissue of the obese induces insulin resistance. World J Diabetes 2012;3:135-41.
43. Bu J, Feng Q, Ran J, Li Q, Mei G, Zhang Y. Visceral fat mass is always, but adipokines (adiponectin and resistin) are diversely associated with insulin resistance in chinese type 2 diabetic and normoglycemic subjects. Diabetes Res Clin Pract 2012;96:163-9.
44. Ouchi N, Parker JL, Lugus JJ, Walsh K. Adipokines in inflammation and metabolic disease. Nat Rev Immunol 2011;11:85-97.
45. Mashayekhi-Goyonlo V, Zilaee M, Daghighi N, Nematy M, Salehi M. Assessment of obesity in chronic plaque psoriasis patients in comparison with the control group. World J Med Sci 2014;10:379-83.
46. Mathew B, Francis L, Kayalar A, Cone J. Obesity: Effects on cardiovascular disease and its diagnosis. J Am Board Fam Med 2008;21:562-8.
47. Heid IM, Jackson AU, Randall JC, Winkler TW, Qi L, Steinthorsdottir V. Meta-analysis identifies 13 new loci associated with waist-hip ratio and reveals sexual dimorphism in the genetic basis of fat distribution. Nat Genet 2010;42:949-60.
48. Singh R, Prakash M, Dubey R, Roy K, Kotwal A, Mahen A. Body composition parameters as correlates of coronary artery disease. Indian J Med Res 2013;138:1016-9.
49. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, *et al.* Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: A case-control study. Lancet 2005;366:1640-9.
50. Gelfand JM, Neimann AL, Shin DB, Wang X, Margolis DJ, Troxel AB. Risk of myocardial infarction in patients with psoriasis. JAMA 2006;296:1735-41.