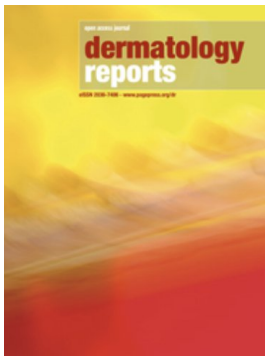

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The association between serum leptin level and the atherogenic index of plasma in psoriatic patients

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Conflict of interest: the authors declare that they have no competing interests.

Ethics approval and consent to participate: the study protocol was approved by the Scientific Committee of the College of Medicine, University of Basrah, Basrah, Iraq (Approval No. 030409-04-2024). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment.

Availability of data and materials: the datasets generated and analyzed during the current study are available from the corresponding author on reasonable request. Individual-level data are not publicly available due to patient confidentiality.

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Abstract

Psoriatic patients have increased cardiometabolic risk and elevated serum leptin levels; however, the association between these factors remains unknown. In this report, serum leptin and the atherogenic index of plasma (AIP) were measured in a cross-sectional study of 100 patients with psoriasis. The results showed that the mean ± standard deviation (SD) serum leptin was 19.9±9.7 ng/mL. AIP was 0.3±0.06; 46% of patients were classified as low risk, 15% as intermediate risk, and 39% as high risk. Leptin levels increased with age, body mass index (BMI), and AIP and were associated with a twofold increase in the likelihood of elevated AIP (odds ratio [OR]=2.0; p=0.025). AIP was an independent predictor for higher leptin levels. These data suggest that serum leptin and AIP are linked in psoriasis and may reflect a shared inflammatory mechanism that contributes to increased cardiovascular risk.

Introduction

Psoriasis is a chronic systemic inflammatory condition associated with considerable cardiometabolic comorbidities. The ongoing inflammatory environment causes endothelial damage, plaque formation, and increased oxidative stress, all of which accelerate atherogenesis.[1] As a result, people with psoriasis are more likely to have common risk factors for heart disease, such as being overweight, having high blood pressure, insulin resistance, and dyslipidemia.[2] Leptin is a hormone produced by adipose tissue and regulates food intake, energy expenditure, and body weight, and leptin levels are closely linked to body fat.[3] Leptin also has cytokine-like effects. It promotes the proliferation and activation of Th1 lymphocytes, enhances the synthesis of pro-inflammatory cytokines, and suppresses regulatory T cells, thereby amplifying the inflammatory response.[4] Leptin levels are significantly elevated in psoriasis compared with healthy controls and frequently correlate with disease activity.[5] Moreover, hyperleptinemia may increase cardiovascular risk in patients with psoriasis by promoting endothelial dysfunction, enhancing oxidative stress, and altering atherogenic lipid profiles.[6]

The atherogenic index of plasma (AIP) is a logarithmic ratio of plasma triglycerides to high-density lipoprotein cholesterol (HDL-C), which reflects the balance between atherogenic and anti-atherogenic lipoproteins. AIP is a cost-effective biomarker that has gained clinical significance in predicting the prevalence and severity of both overt and subclinical atherosclerosis.[7]

Understanding the correlation between leptin and AIP in psoriatic populations may provide critical insights into the mechanisms underlying the increased cardiovascular risk. However, there appears to be a gap in the literature directly examining the association between serum leptin and AIP in patients with

psoriasis. The current study aimed to evaluate this association and assess its relationship with disease severity and metabolic risk factors in a cohort of Iraqi patients with psoriasis.

Materials and Methods

A cross-sectional study was conducted at the Basrah Dermatology Teaching Center in Basrah, Iraq, from October 1, 2024, to October 1, 2025. A total of 100 adult patients with plaque psoriasis aged ≥18 years were included; patients with other types of psoriasis (*e.g.*, guttate, pustular, or erythrodermic), those receiving medications known to affect lipid profiles or leptin levels (*e.g.*, corticosteroids, statins), and pregnant or lactating women were excluded. Informed consent was obtained from all patients after a detailed explanation of the study's purpose and procedures. The study protocol received ethical approval from the Scientific Committee of the College of Medicine, University of Basrah.

A structured questionnaire was administered *via* direct interviews to collect data on patient sociodemographic characteristics, psoriasis-related variables (age at onset and disease duration), comorbidities, and current medication history. Each participant underwent a comprehensive dermatological examination and a disease severity assessment using the Psoriasis Area and Severity Index. Anthropometric measurements were obtained at enrollment, and body mass index (BMI) was calculated. Participants were instructed to fast overnight for analysis of the fasting lipid profile, including total cholesterol, triglycerides, HDL-C, and low-density lipoprotein cholesterol.

Serum leptin concentrations were measured using a standardized enzyme-linked immunosorbent assay kit, according to the manufacturer's instructions. Reference serum leptin concentrations were interpreted according to BMI category as follows: normal weight, <0.7-8.3 ng/mL; overweight, 1.5-19.3 ng/mL; and obesity, 4.0-32.0 ng/mL. The AIP was calculated using the following formula: AIP = log (triglycerides/HDL). According to established guidelines, AIP values are interpreted as follows: low cardiovascular risk, AIP<0.11; intermediate risk, 0.11-0.21; and high cardiovascular risk, >0.21.[8]

Data were analyzed using IBM SPSS Statistics, version 26. Descriptive statistics were used to summarize the data: means and standard deviations (SDs) for continuous variables and frequencies and percentages for categorical variables. To assess statistical associations, the Chi-square (χ^2) test or the independent *t*-test was used to compare variables between two groups. Correlation analysis was performed to assess the strength and direction of associations between continuous variables using Pearson's correlation coefficient. Logistic regression analysis was used to identify independent predictors of key outcomes after adjusting for potential confounding variables. Adjusted odds ratios

(ORs) with corresponding 95% confidence intervals were calculated to estimate the strength of associations. Serum leptin levels among psoriatic patients were compared with those of a control group reported in previous studies conducted in Iraq. Differences in methodology between the studies were acknowledged and considered during interpretation.[9-11] A p-value less than 0.05 was considered statistically significant throughout the analysis.

Results

The sociodemographic and clinical characteristics of participants are summarized in Table 1.

Laboratory investigations showed elevated levels of total cholesterol (27%), triglycerides (41%), very-low-density lipoprotein (39%), and low-density lipoprotein (31%), and a low HDL level (56%). The mean ± SD of serum leptin level was 19.8±9.7; serum leptin levels were elevated in 26% of patients (6% with normal weight, 11% overweight, and 9% obese) and were significantly higher in females than in males (25.9±15.7 *vs.* 16.2±12.7 ng/mL, p=0.001). The mean AIP was 0.3±0.06 mg/dL; 46% of patients were classified as low risk, 15% as intermediate risk, and 39% as high risk (*Supplementary Table 1*).

Correlation analysis showed that mean serum leptin levels were significantly positively correlated with age, BMI, waist circumference, and AIP, and weakly correlated with lipid profile parameters. In contrast, serum leptin showed a statistically significant negative correlation with HDL-C, indicating that higher leptin levels were associated with lower HDL concentrations. No significant correlation with disease duration was observed (Table 2).

Serum leptin did not differ significantly between psoriatic and healthy subjects with normal BMI, irrespective of sex (males: 3.79±0.81 *vs.* 3.90±2.80 ng/mL, p=0.865; females: 9.22±5.00 *vs.* 7.40±3.20 ng/mL, p=0.334). In contrast, overweight and obese psoriatic subjects had significantly higher circulating leptin concentrations than sex-matched controls. This increase was observed in both males (19.12±15.12 *vs.* 13.90±1.60 ng/mL, p=0.019) and females (31.20±15.4 *vs.* 2.00±0.48 ng/mL, p=0.001 (*Supplementary Table 2*).

After adjustment for confounders, female sex, increased BMI, larger waist circumference, and higher AIP were independent predictors of elevated serum leptin. Females had more than a threefold higher likelihood of elevated leptin, and each unit increase in BMI was associated with an 18% increase in the OR. Moreover, higher serum leptin levels were associated with a twofold increase in the odds of elevated AIP (Table 3).

Discussion

The current study implies that serum leptin levels were elevated in a clinically meaningful subgroup of psoriatic patients with different metabolic profiles. Significantly, elevated leptin levels were found not only in obese patients but also in normal-weight patients. This supports the hypothesis that leptin dysregulation in psoriasis is not solely driven by adiposity but may also reflect disease-related inflammatory mechanisms.[12]

A sex-specific study found that female patients have significantly higher leptin levels than male patients. In line with established physiological differences associated with greater body fat and estrogen-mediated leptin expression. This pattern has been consistently reported in both psoriatic and non-psoriatic populations.[9,12,13]

The research revealed that nearly 40% of those with psoriasis were labeled as having high cardiovascular risk based on AIP measurements. This finding is consistent with the report of Tuo *et al.*[14] and Gonzalez-Gonzalez *et al.*,[15] underscoring the substantial cardiometabolic burden in this relatively young study population and also highlighting the utility of AIP as a sensitive, cost-effective marker for stratifying cardiovascular risk in this population.

A significant positive correlation was observed between serum leptin and AIP. Such correlation links a worse lipid profile (triglyceride elevation and HDL reduction) with serum leptin elevation, thus strengthening the role of leptin as a mediator linking adiposity to cardiovascular risk. The lack of a significant correlation with disease duration suggests that leptin level is more indicative of current metabolic status than total disease exposure.[16]

The present study provides novel insight into the metabolic-atherogenic axis in psoriasis by linking leptin to AIP-defined cardiovascular risk. Previous studies examining AIP in psoriasis have not evaluated leptin in conjunction with this index, and the combined evaluation and independent association of these factors in the same cohort have not been well characterized. Furthermore, these results suggest that leptin may serve as a mediator linking psoriatic inflammation, dyslipidemia, and cardiovascular risk, supported by evidence that leptin promotes endothelial dysfunction, oxidative stress, and lipid abnormalities.[17] Thus, AIP and leptin together may offer a more reliable assessment of cardiometabolic burden in psoriasis, independent of traditional lipid parameters. AIP is easily derived from routine lipid testing, making this association readily applicable to clinical practice.

This study has several limitations that should be acknowledged. First, the cross-sectional design limits the ability to establish causal relationships among serum leptin levels, psoriasis severity, and metabolic

abnormalities. Second, the relatively modest sample size and single-center setting may limit the generalizability of the findings; third, potential confounders, such as dietary habits, physical activity, and socioeconomic status, which may influence serum leptin and AIP, were not fully assessed.

Conclusions

High levels of serum leptin are linked to increased cardiovascular risk, as indicated by the AIP in psoriatic patients. Combining serum leptin and AIP will identify a high-risk group, indicating that cardiometabolic monitoring should play a significant role in overall psoriasis management. Prospective research studies in the future should help to understand the prognostic utility of leptin in cardiovascular events and determine whether early metabolic treatment can alter cardiovascular risk in these patients.

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Table 1. Sociodemographic and clinical characteristics of the studied psoriatic patients (n=100).

Variable		**n**
Age	Mean±SD (range)	37.7±14.9 (18-70)
Sex	Male	62
	Female	38
Marital status	Single	33
	Married	67
Smoking status	Non smoker	72
	Smoker	28
Alcohol consumption	Yes	3
	No	97
BMI (kg/m^2)	Mean±SD (range)	28.7±6.04 (18.6-49.2)
	Normal**	21
	Overweight**	40
	Obese**	39
Waist circumference	Mean±SD (range)	104.2±12.9 (73-140)
Systolic BP	Mean±SD (range)	132.9±20.3 (90.0-200.0)
Diastolic BP	Mean±SD (range)	81.7±11.3 (60.0-110.0)
Family history	Present	42
	Absent	58
Duration of disease (years)	Mean±SD (range)	9.4±2.41 (0.3-40)
Current treatment	Topical	77
	Systemic	25
	Phototherapy	10
	Biological	15
PASI	Mean±SD (range)	16.33±10.61 (00.0-65.0)
Metabolic syndrome	Present	46
	Absent	54

SD, standard deviation; BMI, body mass index; BP, blood pressure; PASI, Psoriasis Area and Severity Index.

Table 2. The correlation between serum leptin level and demographic, clinical characteristics, AIP, and lipid profile.

Variable	Correlation coefficient	p-value
Age	0.217	0.03
BMI	0.234	0.021
Waist circumference	0.201	0.045
Disease duration	0.117	0.247
AIP	0.268	0.009
Total cholesterol (mg/dL)	0.14	0.17
Triglycerides (mg/dL)	0.15	0.14
HDL (mg/dL)	−0.25	0.01
VLDL (mg/dL)	0.16	0.104
LDL (mg/dL)	0.19	0.05

BMI, body mass index; AIP, atherogenic index of plasma; HDL, high-density lipoprotein; VLDL, very low-density lipoprotein; LDL, low-density lipoprotein.

Table 3. The multivariable regression analysis of elevated serum leptin with different demographic and laboratory parameters in psoriatic patients.

Variable	OR	95% CI	p-value
Sex (female)	3.42	1.55-7.56	0.003
Age (years)	1.02	0.98-1.05	0.242
BMI (kg/m^2)	1.18	1.11-1.31	0.001
Waist circumference (cm)	1.04	1.02-1.92	0.014
HDL (mg/dL)	0.97	0.93-1.01	0.128
LDL (mg/dL)	1.01	0.99-1.02	0.331
ALT (U/L)	1.08	0.98-1.06	0.281
AIP	2	1.08-3.29	0.025

OR, odds ratio; CI, confidence interval; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ALT, Alanine Aminotransferase; AIP, atherogenic index of plasma.

Online supplementary material:

Supplementary Table 1. Laboratory investigations (n=100).

Supplementary Table 2. The comparison of serum leptin among cases and healthy controls.