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Original Article DERMATOLOGY

The relation between visceral fat markers and cardiometabolic disease risks in psoriasis patients

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ABSTRACT

OBJECTIVE: Psoriasis is a chronic, inflammatory disease that appears with variable trigger factors. We know that obesity and other metabolic syndrome criteria are high in psoriasis patients. The aim of this study is to evaluate the relationship between visceral fat markers, risk of cardiometabolic disease, and psoriasis area severity index (PASI) in individuals with and without psoriasis.

METHODS: A total of 203 subjects, 102 psoriasis patients and 101 healthy individuals, were included in the study. Lipid accumulation product (LAP) index, visceral adiposity index (VAI), plasma atherogenicity index (PAI), body mass index (BMI), PASI, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-c) values were measured.

RESULTS: LAP index, VAI, PAI, BMI, and TG levels were significantly high ($p<0.001$) and HDL-c levels were significantly low ($p=0.009$) in patients with psoriasis compared to healthy individuals.

CONCLUSION: LAP index, VAI, and PAI calculations can be recommended as a potential biomarker for early diagnosis of cardiometabolic diseases common in patients with psoriasis.

Keywords: Plasma atherogenicity index; psoriasis; visceral adiposity index.

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Psoriasis is a skin disease, seen with red papules and plaques which are localized or generalized, sharply circumscribed, usually symmetrical and covered with white or silver scales. It affects both genders equally. In 75% of the patients, the onset is earlier than 46 years. Its prevalence in the world ranges from 0.5% to 11.4% [1]. One of the most commonly used scales for determination is the psoriasis area severity index (PASI) [2].

Patients with psoriasis have an increased cardiovascular risk [3]. It is thought that both psoriatic inflammation and systemic therapies used, concomitant smoking and alcohol use, and the presence of metabolic syndrome increases cardiovascular risk [4]. When national and international literature was examined, increase in the prevalence of metabolic syndrome was observed in psoriasis patients [5–7] and independent of metabolic syndrome, hypertension [5–8], dyslipidemia [6, 7, 9], high fasting blood glucose/insulin resistance [6], and obesity [8, 10, 11] was found to related to psoriasis. It was determined that the higher the severity of the disease, the higher the risk. There are also studies in which the risk of myocardial infarction is higher in young patients with severe psoriasis [12] and the risk is similar to that of the community [13].

Waist circumference (WC) and body mass index (BMI) are used as obesity criteria. However, these cannot discriminate both visceral and subcutaneous fats.

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Visceral fat is more associated with metabolic disorders and cardiovascular diseases. Computed tomography (CT) and body fat analyzers have been used to measure the amount of visceral fat in psoriasis; however, it requires technological expertise and expensive equipment [14]. Studies showed that the lipid accumulation product (LAP) index and visceral adiposity index (VAI) have been successfully used to predict insulin resistance and cardiometabolic risk factors in various diseases and in general population as an indicator of visceral adipose tissue dysfunction [14–16]. Plasma atherogenic index (PAI) is a simple and easily calculated parameter that reflects the risk of coronary atherosclerosis. It was suggested that PAI <0.1 is related to low risk, 0.1–0.24 is related to moderate risk, and >0.24 is related to high risk [17, 18].

The aim of this study is to evaluate the relation between visceral fat markers (LAP, PAI, and VAI) and risk of cardiometabolic disease and PASI in individuals with and without psoriasis.

Highlight key points

- LAP index, VAI, PAI levels were significantly high in patients with psoriasis.
- No significant correlation between PASI and LAP, VAI, and PAI was detected.
- Simple, inexpensive visceral fat markers (LAP index, VAI, PAI) identify more people at higher risk of cardiometabolic morbidity than conventional anthropometric obesity measurements.
- Visceral fat markers can be recommended as a potential biomarker for early diagnosis of cardiometabolic diseases.

MATERIALS AND METHODS

Type of Research, Place, and Universe

This case–control study group involved patients those aged over 18, diagnosed with psoriasis, new and with follow-up and without comorbidity. Ethics committee was approved on May 22, 2019, with the number 14567952-05/859. Control group was constituted by scanning retrospectively dossiers of healthy individuals applied to family physician for any reason, who are aged over 18, without any systemic disease and not using any drug.

Sample Selection of Research

As a result of studies conducted in our country, the incidence of psoriasis was found to be between 0.5% and 4.7% [19, 20]. In our study, since the number of individuals in the universe is unknown, the number of subjects required to be included in the study was calculated using the formula $n=t^2.p.q/d^2$.

n=Number of subjects to be included in the study

t=Since the number of individuals in the universe is unknown, degree of freedom was defined as ∞. At 0.05, degree of freedom ∞, the theoretical t value was found as 1.96 according to table.

p=Prevalence of psoriasis was accepted as 2% in our country. P=0.02 was taken. q=Non-psoriasis frequency (1-p) is 1–0.02=0.98. d=The amount of standard deviation desired to be made according to the frequency of occurrence of the event (d=0.03, since ±3% deviation is desired).

$n=(1.96)^2\times(0.02\times0.98)/(0.03)^2=84$

In accordance with this calculation, it is planned to recruit at least 200 individuals aged 18 and over to our study. Of these, 100 were considered as control and 100 as case group. However, based on planned date range and excluding the patients with incomplete analysis and sociodemographic characteristics and psoriasis patients with comorbid disease, the data collection process was completed with a total of 203 people including 102 cases and 101 control groups.

Ethics Permission of the Study

The ethical permission of the study was obtained before starting the study, from Necmettin Erbakan University Meram Faculty of Medicine, Department of Drug and Medical Device Research Ethics Committee with the number 2019/1860 dated May 22, 2019. The participants were informed about the study and their written and verbal consent was obtained according to the principles of Helsinki Declaration.

Data Collection

Age, gender, marital status, education and working status, smoking status (pack/year), height, weight, WC, triglyceride (TG), and high-density lipoprotein cholesterol (HDL-c) values of all participants were scanned retrospectively and recorded. In addition, for psoriasis patients, the age of onset of psoriasis (initial diagnosis), duration of disease, PASI score, and family history of psoriasis (1-2-3 degree relatives) were scanned retrospectively and recorded.

Table 1. Sociodemographic characteristics of case and control groups

	With psoriasis %	Without psoriasis %	Total n	χ^2	p
Gender				1.782	0.182
Female	45.6	54.4	103		
Male	55.0	45.0	100		
Marital status				8.617	**0.003**
Married	56.3	43.7	151		
Unmarried	32.7	67.3	52		
Profession status				9.972	**0.002**
Employee	61.0	39.0	105		
Unemployed	38.8	61.2	98		
Education level				24.204	**<0.001**
Middle school or lower	70.6	29.4	85		
High school and higher	35.6	64.4	118		
Smoker/non-smoker				0.686	0.408
Non-smoker	48.1	51.9	131		
Smoker	54.2	45.8	72		
Body mass index				13.653	**0.001**
Normal weight	33.3	66.7	66		
Overweight	52.6	47.4	78		
Obese	66.1	33.9	59		

BMI

It is calculated by the formula weight (kg)/height square (m^2). BMI between 18 and 24.9 kg/m^2 was classified as normal weight, 25–29.9 kg/m^2 as overweight, and 30 kg/m^2 and above as obese.

LAP Index

Visceral adipose is an indicator of tissue dysfunction and reflects the risk of cardiometabolic disease. It is calculated using the formula ([WC (cm)−65]×TG [mmol/L]) and ([WC (cm)−58]×TG [mmol/L]) for men and women, respectively.

VAI

Visceral adipose is an indicator of tissue dysfunction and reflects the risk of cardiometabolic disease. For calculation, the formula (WC/[36.58+(1.89×BMI)])×[(TG (mmol/L)/0.81)×(1.52/HDL-c (mmol/L))]] and (WC/[39.68+) (1.88×BMI)])×[(TG (mmol/L)/1.03)×(1.31/HDL-c (mmol /L))] was used for women and men, respectively.

PAI

It is a parameter reflecting the risk of coronary atherosclerosis. [log (TG/HDL-c)] was calculated by taking the logarithm of the ratio of TG to HDL-c. PAI risk classification; according to the calculated values, it is classified as low risk below 0.1, medium risk between 0.1–0.24, and high risk above 0.24.

Statistical Analysis

Statistical Package for the Social Sciences for Windows 20.0 program was used for statistical analysis while evaluating results of the study. Descriptive statistics of continuous variables were expressed as mean and standard deviation, and descriptive statistics of categorical data were expressed as frequency and percentage. Independent samples t-test and one-way ANOVA were used in the comparison of quantitative data. Mann–Whitney U and Kruskal–Wallis analysis were used for the data not meeting the normal distribution assumption and showing skewed distribution. Chi-square test was used to compare categorical data. The results were evaluated at 95% confidence interval and $p<0.05$ significance lev-

Table 2. Comparison of distribution of some parameters in case and control groups

	With psoriasis Mean (Min–Max)	Without psoriasis Mean (Min–Max)	Z*/t**	p
LAP	55.9 (4.8–310.5)	30.5 (–10.2–229.5)	–4.982*	<0.001
VAI	2.3 (0.4–18.1)	1.4 (0.4–8.8)	–4.552*	<0.001
TG (mg/dl)	140.2 (34.0–653.0)	96.1 (33.0–407.3)	–4.669*	<0.001
	Mean±SD	Mean±SD		
PAI	0.5±0.3	0.3±0.3	4.777**	<0.001
HDL-c	43.8±13.0	48.4±12.1	–2.622**	0.009
BMI (kg/m^2)	29.1±4.8	26.3±5.3	3.970**	<0.001

Min.: Minimum; Max.: Maximum; SD: Standard deviation; *: Mann–Whitney U-test; **: Student's t-test was applied; LAP: Lipid accumulation product; VAI: Visceral adiposity index; TG: Triglyceride; PAI: Plasma atherogenicity index; HDL-c: High-density lipoprotein cholesterol; BMI: Body mass index.

el. The relation between the parameters was searched by Pearson correlation analysis. Correlation coefficient (r) was accepted as a weak between 0.00 and 0.24, moderate between 0.25 and 0.49, strong between 0.50 and 0.74, and very strong between 0.75 and 1.00.

RESULTS

A total of 203 subjects, 102 psoriasis patients and 101 healthy individuals, were included in the study. The mean age of psoriasis patients was 43.5±16.8 years; the mean age of healthy individuals was 32.6±8.9 years. The mean age at first diagnosis was 28.9±14.5 years for males, 34.2±14.3 years for females and mean duration of disease was 12.5±9.0 years. Family history was present in 27.5% of the cases. Calculated mean PASI values were found to be 3.0±3.7. The demographic data of the cases and the control group are summarized in Table 1. The rate of being married was higher (p=0.003), education level was lower (p<0.001), and working status was higher (p=0.002) in psoriasis patients. About 78.4% (n=80) of the case group were overweight and obese (p=0.001).

LAP index, VAI, PAI, BMI, and TG levels were significantly high (p<0.001) and HDL-c levels were significantly low (p=0.009) in patients with psoriasis (Table 2). When the effect of smoking was examined in the case and control groups, it was seen that PAI was significantly lower in non-smokers in both groups (p=0.020 and p=0.008, respectively); HDL-c was higher (p=0.006 and p=0.001, respectively). There was no difference in terms of other parameters (Table 3).

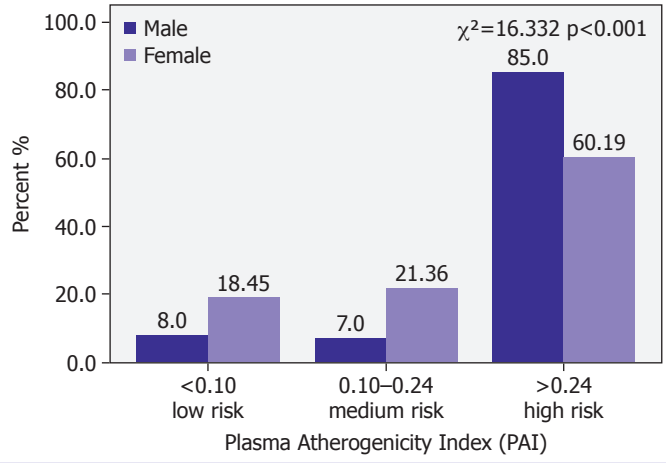

Figure 1. Comparison of PAI risk groups by gender.

When compared according to gender, TG was significantly higher in men with psoriasis (p=0.016). In both psoriasis cases and healthy individuals, in males, PAI was found to be higher (case control, p<0.001 and p=0.013, respectively) and HDL-c was lower (case control, p<0.001 and p<0.001, respectively) (Table 4). While the percentage of women with low and moderate risk of PAI was higher, the percentage of men was higher in those with high risk (Fig. 1), PAI value of 84.3% of patients with psoriasis was 0.24 and above which had risk (Fig. 2).

Correlation between PASI, LAP, VAI, PAI, age at first diagnosis, and disease duration is demonstrated in Table 5. Strong positive correlation was observed between LAP and VAI (r=0.873, p<0.001). When linear regression analysis was performed, 76.2% of eleva-

Table 3. Effect of smoking on some parameters in case and control groups

	With psoriasis		Without psoriasis	
	With psoriasis Mean (Min–Max)	Without psoriasis Mean (Min–Max)	Smoker Mean (Min–Max)	Non-smoker Mean (Min–Max)
LAP	56.1 (15.2–302.3)	55.3 (4.8–310.5)	34.7 (–10.2–142.0)	30.4 (2.5–229.5)
	–1.016*	p=0.310	–1.868*	p=0.062
VAI	2.7 (0.6–18.1)	2.1 (0.4–9.1)	1.7 (0.5–8.8)	1.4 (0.4–8.12)
	–1.236*	p=0.216	–1.817*	p=0.069
TG (mg/dl)	146.7 (56.0–653.0)	137.1 (34.0–443.5)	123.5 (42.0–407.3)	89.9 (33.0–327.8)
	–1.229*	p=0.219	–1.651*	p=0.099
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
PAI	0.6±0.4	0.5±0.3	0.4±0.3	0.3±0.3
	2.367**	p=0.020	2.690**	p=0.008
HDL-c (mg/dl)	39.3±12.1	46.5±12.9	42.6±8.7	51.2±12.5
	–2.788**	p=0.006	–3.566**	p=0.001
BMI (kg/m^2)	28.2±3.2	29.6±5.5	25.7±4.0	26.5±5.8
	–1.545**	p=0.126	–0.722**	p=0.472

Min.: Minimum; Max.: Maximum; SD: Standard deviation; *: Mann–Whitney U-test; **: Student's t-test was applied; LAP: Lipid accumulation product; VAI: Visceral adiposity index; TG: Triglyceride; PAI: Plasma atherogenicity index; HDL-c: High-density lipoprotein cholesterol; BMI: Body mass index.

Table 4. Effect of gender on some parameters in case and control groups

	With psoriasis		Without psoriasis	
	Women Mean (Min–Max)	Men Mean (Min–Max)	Women Mean (Min–Max)	Men Mean (Min–Max)
LAP	52.8 (4.8–222.6)	57.1 (6.8–310.5)	28.7 (2.5–229.5)	34.7 (–10.2–142.1)
	–0.836*	p=0.403	–1.237*	p=0.216
VAI	2.3 (0.4–7.2)	2.2 (0.6–18.1)	1.4 (0.4–8.1)	1.4 (0.4–8.8)
	–0.903*	p=0.367	–0.143*	p=0.886
TG (mg/dl)	123.0 (34.0–318.0)	150.0 (46.2–653.0)	89.9 (33.0–327.8)	104.1 (42.0–407.3)
	-2.420*	p=0.016	–1.428*	p=0.153
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
PAI	0.4±0.2	0.6±0.3	0.3±0.3	0.4±0.3
	4.301**	p<0.001	2.530**	p=0.013
HDL-c (mg/dl)	50.1±11.2	38.3±12.0	52.4±12.6	43.5±9.5
	–5.065**	p<0.001	–3.924**	p<0.001
BMI (kg/m^2)	29.8±5.6	28.5±3.9	26.7±6.1	25.7±4.0
	–1.380**	p=0.171	–0.959**	p=0.340

Min.: Minimum; Max.: Maximum; SD: Standard deviation; *: Mann–Whitney U-test; **: Student's t-test was applied; LAP: Lipid accumulation product; VAI: Visceral adiposity index; TG: Triglyceride; PAI: Plasma atherogenicity index; HDL-c: High-density lipoprotein cholesterol; BMI: Body mass index.

Table 5. Correlation between PASI, LAP, VAI, PAI, first diagnosis age, and disease duration

	1	2	3	4	5	6
1. Disease duration						
r						
p						
2. First diagnosis age						
r	–0.425**					
p	<**0.001**					
3. PASI						
r	–0.022	0.001				
p	0.826	0.989				
4. LAP						
r	0.188	0.062	–0.009			
p	0.059	0.533	0.928			
5. VAI						
r	0.217*	–0.063	–0.019	0.873**		
p	**0.029**	0.527	0.851	<**0.001**		
6. PAI						
r	0.247*	–0.077	–0.019	0.755**	0.863**	
p	**0.012**	0.443	0.849	<**0.001**	<**0.001**	

r: Correlation coefficient; *: Weak relationship; **: Medium-strong relationship; PASI: Psoriasis area severity index; LAP: Lipid accumulation product; VAI: Visceral adiposity index; PAI: Plasma atherogenicity index.

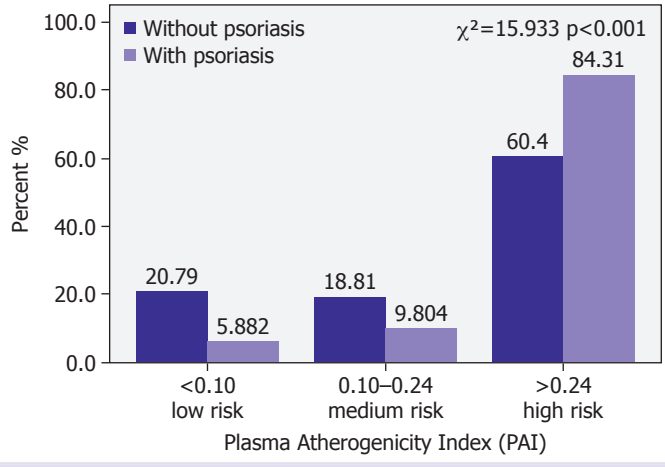

Figure 2. Comparison of PAI risk groups in case–control group.

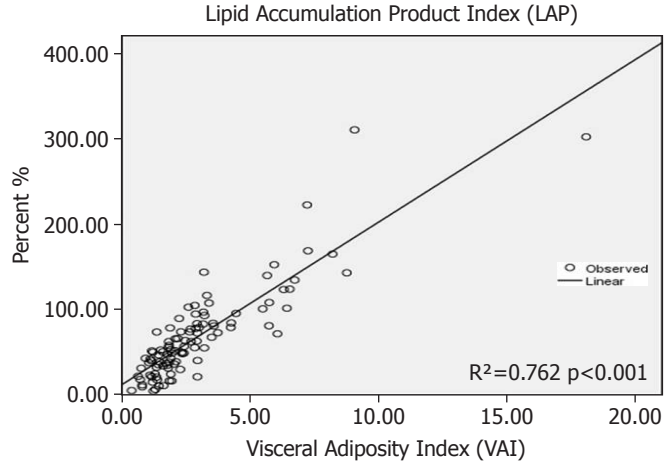

Figure 3. Linear regression analysis between LAP index and VAI in psoriasis patients.

tion in LAP level was attributed to the increase in VAI level (R^2=0.762, p<0.001) (Fig. 3). Positive significant correlation between LAP and PAI (r=0.755, p<0.001), VAI and PAI (r=0.863, p<0.001) was established. No significant correlation between PASI and LAP, VAI, and PAI was detected (Table 5).

DISCUSSION

Psoriasis disease is an immune-mediated chronic inflammatory disease accompanied with many comorbidities, seen with a frequency of 0.5%–4.7% in our country [19, 20]. Risks of cardiometabolic disease are high in the pso-

riasis patients, because of psoriatic inflammation, systemic therapies used, concomitant smoking, and alcohol use [4]. The incidence of metabolic syndrome and the risk of cardiovascular disease were associated with PASI, and it was found that the risk is increased in patients with more involved body surface area and longer disease duration [21].

In the present study, HDL-c levels were significantly lower in men and smokers in the case and control groups. As to TG only in psoriasis patients, significant increase in male gender was observed. In the patient group with psoriasis, TG level increased and HDL-c level decreased compared to the control group. In some studies, the difference was found to be statistically significant for TG [6, 9, 22] and for HDL-c [7, 9, 22]. In the study, which was presented in accordance with the literature, it was found that serum TG levels were significantly higher and serum HDL-c levels were lower in psoriasis patients. However, no relation between disease duration, first diagnosis age, and PASI was established.

In the study of Naldi et al. [23], it was shown that psoriasis was 1.6 and 1.9 times higher in patients with BMI between 26 and 29 kg/m^2 and in those with BMI above 30, respectively. It was found that the risk of obesity increases more in patients with severe psoriasis than in those with mild psoriasis [8, 10, 11]. In this study, 78.4% (n=80) of 102 psoriasis patients were overweight and obese. However, there was no correlation between BMI and disease duration, first diagnosis age, and PASI.

In international and national studies, LAP index and VAI, as an indicator of visceral adipose tissue dysfunction, were found to be associated with metabolic disorders and cardiovascular diseases in various populations and general population and were stated that they may be used as cardiometabolic risk markers [14–16]. In the study conducted with 40 psoriasis patients and 42 controls in South India, the mean LAP index was found as 46.4±27.2 in psoriasis patients; 23.7±13.0 in the control group, and a statistically significant difference was observed. In addition, it was found to be significantly higher in moderate-severe psoriasis group than that of mild psoriasis group [14]. In the present study, the median LAP index was 55.9 in psoriasis patients and 30.5 in healthy subjects. Significant difference was determined between them. Nevertheless, relation with duration of disease, first diagnosis age, and PASI was not found.

In a study conducted in Japan in 2009, visceral lipidosis and body fat ratio were measured by bioelectrical impedance analysis using body fat counter, and it was found to be significantly higher in psoriasis patients and more correlation was found compared to PASI and BMI [24]. In a cohort study conducted in 2018, cardiovascular risk was calculated by demonstrating vascular inflammation by positron emission tomography/CT in psoriasis patients, visceral lipidosis was found to be more associated with cardiovascular disease compared to subcutaneous fat deposition, BMI, and waist–hip ratio. As the severity of the disease increased, visceral fat deposition increased as well [25]. In another study conducted in our country, body composition values were measured using Tanita SC-330 analyzer, and statistically significant differences were found in patients in terms of weight, body fat percentage, fat mass, visceral fat ratio, and BMI compared to the control group and a weak correlation was found with PASI score [26]. In the literature search, no study using VAI as a marker of visceral fat deposition in psoriasis patients was encountered. This present study possess the feature of being first in this sense. The median VAI value in psoriasis patients was 2.3; found to be 1.4 in healthy individuals. The difference was statistically significant. Yet, relation between the duration of the disease, first diagnosis age, and PASI was not established.

PAI can be recommended as a potential biomarker for early detection of cardiovascular diseases in both genders [27]. In the study of Fernandez-Macias et al. [28], serum asymmetric dimethylarginine, that is, a molecular biomarker, and Framingham risk score, that is, adipocyte fat binding protein and atherogenic indices, showed a strong positive correlation with the Castelli risk index. The atherogenicity index calculated by lipoprotein-a and HDL-c in psoriasis patients was found to be significantly higher than the controls and was found to be associated with PASI [29]. In this study, PAI was calculated using TG and HDL-c. The mean PAI value in psoriasis patients and in the control group was 0.5±0.3 and 0.3±0.3, respectively. It was significantly higher in the case group. Duration of disease, first diagnosis age, and PASI were not found to be associated with PAI. In the studies performed, PAI was found to be significantly higher in male individuals, smokers, and patients with metabolic syndrome [17, 18]. In the present study, in both case and control groups, PAI was found to be significantly higher in men and smokers.

Smoking increases the risk of developing cardiovascular diseases, cancer, and metabolic syndrome. According to the data of Global Adult Tobacco Survey Turkey 2016, the rate of smoking is average 31.6% in our country [30]. Cigarette consumption is more common in patients with psoriasis associated with psychological problems. Smoking is thought to play a role both in the development of

psoriasis and exacerbation of the existing disease and in increase in the disease-related comorbidities [31]. In studies carried out in our country, smoking rate in psoriasis patients varies between 28.2% and 54.5% [20, 32, 33]. In a study conducted in Germany, habit of smoking was found to be 45.4% on average in patients with psoriasis whereas 21% in the control group [5]. In this study, the rate of smoking in the case group was 38.2%; 32.7% in the control group, which is in accordance with literature.

Conclusion

In this study, LAP index, VAI, TG, PAI, and BMI were higher and HDL-c was lower in psoriasis patients compared to healthy individuals. HDL-c levels were lower and PAI levels were higher in the case and control groups, males and smokers. There was a relationship between VAI, PAI, and LAP index, whereas no correlation was established between PASI and these parameters.

In patients with psoriasis, simple, inexpensive LAP index, VAI, and PAI calculation identify more people at higher risk of cardiometabolic morbidity than conventional anthropometric obesity measurements. It can be recommended as a potential biomarker for early diagnosis of cardiometabolic diseases.

Particularly in smoking male patients, morbidity screen with these indices at diagnosis and occasionally afterward should be part of treatment and follow-up.

The important limitations of the study are the fact that it was a case–control study with a small sample size and that the majority of the psoriasis patients were followed up and received regular treatment and therefore the average PASI values were low. We consider that this is the reason why LAP index, VAI, PAI, TG, and HDL-c levels, BMI and PASI are not related. Therefore, larger scale epidemiological studies are required for correlation of these parameters with PASI.

Ethics Committee Approval: The Necmettin Erbakan University Clinical Research Ethics Committee granted approval for this study (date: 22.05.2019, number: 14567952-05/859).

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Authorship Contributions: Concept – LU, RK, AA; Design – LU, RK; Supervision – AA, RK; Fundings – AA, RK; Materials – LU, AA; Data collection and/or processing – LU, AA; Analysis and/or interpretation – RK; Literature review – AA; Writing – RK, LU, AA; Critical review – AA, RK.

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