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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

Psoriatic arthritis and psoriasis severity as metabolic syndrome and insulin resistance predictors

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SUMMARY

Introduction/Objective The aim of this study was to evaluate psoriasis severity and psoriatic arthritis (PsA) as metabolic syndrome (MetS) and insulin resistance (IR) predictors in patients with chronic plaque psoriasis as well as to evaluate if psoriasis severity and PsA are independent predictors for IR regardless of the MetS presence.

Methods This prospective, observational descriptive cross-sectional study was conducted at Dermatovenereological Clinic of the University Clinical Centre of Vojvodina, and included a total of 105 psoriasis patients divided into three groups: group with mild psoriasis (Psoriasis Area Severity Index – PASI score < 10), group with moderate to severe psoriasis (PASI ≥10), and group with PsA diagnosed on the basis of the CASPAR criteria.

Results Percentage of patients who had MetS was higher in the group with the severe form of psoriasis ($p < 0.05$) as well as IR ($p = 0.05$). PsA was also more frequently associated with MetS ($p = 0.05$) and IR ($p < 0.01$). In patients without MetS, no association between psoriasis severity and IR was found ($p = 1.0$), although there was a positive correlation between PASI and index of β-cells secretory capacity % (HOMA B), which shows tendency for IR development. The association between PsA and presence of IR in patients without MetS was statistically significant ($p < 0.05$).

Conclusion MetS and IR prevalence increases in patients with PsA and in patients with the moderate and severe form of chronic plaque psoriasis. Both psoriasis severity and PsA are independent predictors for IR regardless of the MetS presence.

Keywords: psoriasis; psoriasis severity; psoriatic arthritis; insulin resistance; metabolic syndrome

INTRODUCTION

Psoriasis disease spectrum comprises numerous cutaneous, mucosal, and articular manifestations. Psoriasis and psoriatic arthritis (PsA) are frequently associated with obesity, dyslipidemia, insulin resistance (IR), and diabetes, causing psoriasis patients to be susceptible to metabolic syndrome (MetS) and cardiovascular morbidities' development [1].

PsA is an inflammatory type of arthritis characterized by chronic inflammation of the peripheral joints and the axial skeleton and extra-articular manifestations including enthesitis, dactylitis, and skin/nail disease [2, 3]. Several studies have demonstrated the high prevalence of MetS, cardiovascular diseases, and IR in PsA [4–7].

METHODS

This prospective, observational descriptive cross-sectional study was conducted at the Dermatovenereological Clinic of the University Clinical Centre of Vojvodina, and included a total of 105 psoriasis patients organized into three groups, 35 patients in each one. Mild psoriasis patients were with Psoriasis Area Severity Index (PASI) score below 10, the group of moderate to severe psoriasis were with PASI score of 10 and above (in further text 'severe psoriasis'), and the third group were patients with PsA diagnosed on the basis of the Classification Criteria for Psoriatic Arthritis (CASPAR). The study was approved by the Ethical Committee of the University Clinical Centre of Vojvodina.

The inclusion criteria were clinically confirmed diagnosis of psoriasis that lasted for more than six months before the study. The exclusion criteria were patients with secondary hyperlipidemia including hypothyroidism, diabetes, nephrotic syndrome, chronic renal insufficiency, cholestatic liver disease; patients taking beta blockers, thiazides, corticosteroids, antilipemic drugs; patients suffering from malignancies, other autoimmune diseases, systemic connective tissue diseases, pregnant and lactating women.

Measurements of waist circumference, blood pressure, fasting serum glucose, serum insulin, serum triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), cholesterol, systolic and diastolic blood pressure, rheumatoid factor (RF), radiographic imaging of joints were performed for each patient, in addition to taking demographic data (age, sex, family history of psoriasis). The enzymatic GOD-pap method was used to determine glucose values. Insulin was determined by an

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automated immunometric system (ADVIA Centaur system XP, Siemens Healthcare GmbH, Erlangen, Germany), which is based on direct chemiluminescent immunoassay (CLIA). Cholesterol levels in plasma were determined by enzymatic method, HDL by direct accelerator selective detergent method, triglycerides by glycerol 3-phosphate oxidase method, and LDL was calculated by Friedewald equation. RF testing was performed using a latex-enhanced immunoturbidimetric assay.

The measurement of systolic and diastolic blood pressure was performed using an aneroid sphygmomanometer in the left arm. Blood pressure was measured two times and recorded as the average of two measurements after the patient was sitting for five minutes. To determine the waist circumference, the tape was placed at the level of the uppermost part of the hipbone around the abdomen without causing compression on the skin.

Severity of the disease was determined using PASI. It is a validated psoriasis severity assessment tool [8]. It consists of evaluation and grading of the severity of erythema, thickness and scaling of psoriatic plaques in four regions of the body (head, trunk, arms, and legs). The total score ranges 0–72 [9]. In the present study, mild psoriasis PASI index values are up to 10, while moderate to severe psoriasis has the PASI index score of 10 and above [10].

The diagnosis of PsA was established according to the CASPAR [11].

HOMA2 calculator was downloaded from the official website of the University of Oxford, Oxford Centre for Diabetes, Endocrinology and Metabolism and Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), and HOMA-S (index of insulin sensitivity %) and HOMA-B (index of β-cells secretory capacity %) were calculated [12].

MetS was diagnosed in the presence of three or more criteria of the National Cholesterol Education Program, Adult Treatment Panel III (NCEP/ATP III): waist circumference ≥ 102 cm in men or ≥ 88 in women; hypertriglyceridemia ≥ 1.7 mmol/l; HDL < 1.03 mmol/l in men or < 1.29 mmol/l in women; blood pressure ≥130/85 mmHg or use of antihypertensive drugs; fasting plasma glucose ≥ 5.6 or diagnosis of diabetes type II [13].

Statistical analyses were performed using IBM SPSS Statistics, Version 23.0 (IBM Corp., Armonk, NY, USA). Data was tested for normality using a Kolmogorov–Smirnov test and the Shapiro–Wilk test of normality. The χ^2 test and Fisher's exact test were utilized for the study of the association of categorical variables. Difference in quantitative variables between subject groups were calculated with Mann–Whitney test, Student's t-test or Kruskal–Wallis H test, and for correlation analysis Spearman's correlation was used.

RESULTS

A total of 105 patients were included in this study, 57 (54.3%) of whom were male and 48 (45.7%) were female. The mean age was 50 (± 15.21) years, and the mean time since the diagnosis was 16.2 ± 15 years. There was no significant difference between the groups for age and sex distribution. Waist circumference above European standards was measured in 57.1% patients, 38.1% had hypertriglyceridemia, 29.5% patients had altered fasting blood glucose, 58.1% presented low HDL serum levels, and 61% patients had hypertension. The prevalence of MetS was 46.7% with 49 patients fulfilling at least three criteria.

IR was found in 35 (33%) patients. There was no difference in the prevalence of MetS and IR between men and women.

Differences between groups with and without MetS regarding disease duration were not found (Man–Whitney test, p = 0.72, z = -0.36) (Table 1).

Higher proportion of patients with MetS in the group of patients with severe psoriasis in comparison with mild psoriasis patients is statistically significant ($p < 0.05$, χ^2 test = 5.92) (Table 2).

In patients with PsA, MetS was more frequently detected, in comparison with psoriasis patients without PsA, and this difference is of marginal statistical significance ($p = 0.05$, χ^2 test = 3.75) (Table 3, Figure 1).

Table 1. Disease duration in groups with and without metabolic syndrome (MetS)

MetS presence	Disease duration			
		Min	Max	SD
Absent	15.2	1	50	14.7
Present	17.3	0.6	52	15.6

Table 2. The presence of the metabolic syndrome in relation to the psoriasis severity

Psoriasis severity		Metabolic syndrome presence		Total
		Absent	Present	
Mild psoriasis	n	26	9	35
	% Group	74.3	25.7	100
Moderate/severe psoriasis	n	16	19	35
	% Group	45.7	54.3	100
Total	n	42	28	70
	% Group	60	40	100

Table 3. The presence of metabolic syndrome in relation to the psoriatic arthritis

Presence of arthritis		Metabolic syndrome presence		Total
		Absent	Present	
Absent	n	42	28	70
	%	60%	40	100
Present	n	14	21	35
	%	40%	60	100
Total	n	56	49	105
	%	53.3%	46.7	100

Higher proportion of patients with IR in severe psoriasis in comparison with mild psoriasis patient group was of marginal statistical significance ($p = 0.05$, χ^2 test = 3.81) (Table 4).

In patients with PsA IR was more frequently detected in comparison with psoriasis patients without arthritis ($p < 0.01$, χ^2 test = 7.74) (Table 5, Figure 2).

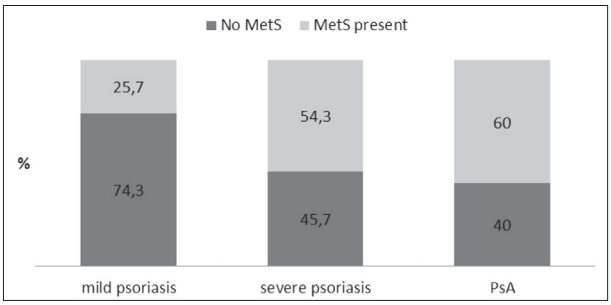


Figure 1. Presence of metabolic syndrome (MetS) in patients with mild psoriasis, severe psoriasis, and psoriatic arthritis (PsA), as percentage of MetS-positive patients in the group

Table 4. The presence of insulin resistance in relation to the psoriasis severity

Psoriasis severity		Insulin resistance presence		Total
		Absent	Present	
Mild psoriasis	n	30	5	35
	% Group	85.7	14.3	100
Severe psoriasis	n	23	12	35
	% Group	65.7	34.3	100
Total	n	53	17	70
	% Group	75.7	24.3	100

Table 5. The presence of insulin resistance in relation to the psoriatic arthritis

Psoriatic arthritis presence		Insulin resistance presence		Total
		Absent	Present	
Absent	n	53	17	70
	%	75.7	24.3	100
Present	n	17	18	35
	%	48.6	51.4	100
Total	n	70	35	105
	%	66.7	33.3	100

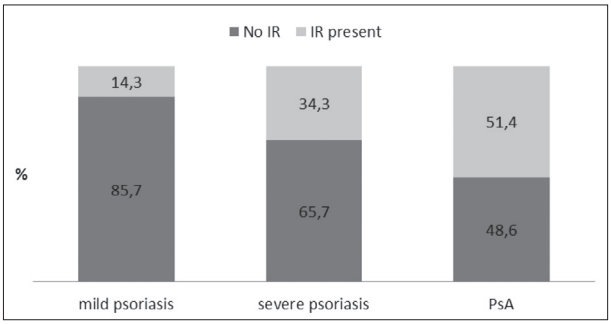


Figure 2. The presence of insulin resistance (IR) in patients with mild or severe psoriasis and in patients with psoriatic arthritis (PsA)

To evaluate psoriasis severity as a risk factor for IR that is independent of MetS, after excluding all patients with MetS, proportions of patients with IR were similar in the rest of the mild and severe psoriasis groups, the difference was not significant ($p = 1.0$, χ^2 test = 5.34) (Table 6).

Positive correlation between PASI score and HOMA B index in psoriasis patients after excluding patients with MetS is statistically significant (Table 7).

No statistically significant difference between HOMA indices in patients without MetS regarding psoriasis severity was found (Mann–Whitney test) (Table 8).

Table 6. The presence of insulin resistance in relation to the psoriasis severity in patients without metabolic syndrome

Psoriasis severity		Insulin resistance presence		Total
		Absent	Present	
Mild psoriasis	n	23	3	26
	% Group	88.5	11.5	100
Severe psoriasis	n	15	1	16
	% Group	93.8	6.3	100
Total	n	38	4	42
	% Group	90.5	9.5	100

Table 7. Psoriasis Area Severity Index (PASI) score and Homeostatic Model Assessment (HOMA) indices correlation in patients without metabolic syndrome

HOMA		PASI num
HOMA_IR	Correlation coefficient	0.185
	p	0.173
	n	56
HOMA_S%	Correlation coefficient	-0.212
	p	0.117
	n	56
HOMA_B%	Correlation coefficient	0.355**
	p	0.007
	n	56

In patients without MetS, association between IR and PsA was found ($p < 0.05$, χ^2 test = 5.34) (Table 9, Figure 3).

Table 9. The presence of insulin resistance in relation to the psoriatic arthritis in patients without metabolic syndrome

Arthritis presence		Insulin resistance presence		Total
		Absent	Present	
Absent	n	38	4	42
	%	90.5	9.5	100
Present	n	9	5	14
	%	64.3	35.7	100
Total	n	47	9	56
	%	83.9	16.1	100

Table 8. Homeostatic Model Assessment (HOMA) indices in patients without metabolic syndrome regarding psoriasis severity

HOMA	Mild psoriasis group					Moderate/severe psoriasis group					p
	AM	Min	Max	SD	Median	AM	Min	Max	SD	Median	
HOMA_IR	1.5	0.5	6.35	1.09	1.26	1.63	0.67	6.85	1.45	1.28	0.97
HOMA_S%	89	42	200.9	39.4	81.1	82.3	14.6	149.2	34.3	78.7	0.85
HOMA_B%	127.2	64.9	218.1	41.2	119.3	153.3	69.4	373.5	67.5	142.7	0.16

AM – arithmetic mean; SD – standard deviation

Table 10. Homeostatic Model Assessment (HOMA) indices in patients with psoriasis and patients with psoriatic arthritis, after excluding patients with metabolic syndrome

HOMA	Group in relation to arthritis										p
	No arthritis					With arthritis					
	AM	Min	Max	SD	Median	AM	Min	Max	SD	Median	
HOMA_IR	1.55	0.5	6.85	1.22	1.26	1.64	0.37	3.41	0.86	1.7	0.29
HOMA_S%	86.4	14.6	200.9	37.3	81.1	87.5	29.3	267.3	66.7	58.7	0.21
HOMA_B%	137.1	64.9	373.5	53.5	129.7	152.5	56.1	271.6	64.1	161.6	0.33

AM – arithmetic mean; SD – standard deviation

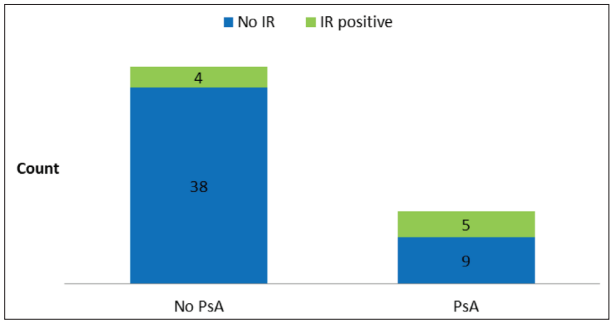


Figure 3. The presence of insulin resistance (IR) in relation to the psoriatic arthritis (PsA) in patients without metabolic syndrome

Differences between HOMA indices in patients with psoriasis (both mild and severe group) and patients with PsA, after excluding patients with MetS, were not statistically significant (Mann–Whitney test) (Table 10).

DISCUSSION

The mean age of psoriatic patients was 50 (± 15.21) years, similar to other previous studies [1, 14, 15].

The prevalence of MetS in our study was 46,7% with 49 of 105 patients fulfilling at least three criteria. Similar results were obtained in a study by Souza et al. [16] conducted in Brazil, in which prevalence of MetS was 50%. Slightly lower prevalence was obtained in a study by Gissondi et al. [17], where prevalence of MetS was 30.1%, in a study by Özkul et al. [2] (36%) conducted in Turkey, and a study by Singh Bhati S et al. [1] (38%) conducted in Central India.

No differences in the prevalence of MetS between man and women was found, which was also the case with the study by Costa et al. [2] and by Özkul et al. [2, 4]. MetS was directly positively correlated with age of the patients, as was as in the study by Gissondi et al. [17].

Differences between groups with and without MetS regarding duration of the disease ($p = 0.72$, $z = -0.36$) were not found, which coinsides with the Singh Bhati et al. [1] study, quite opposite compared to the Gissondi et al. [17] study, in which prevalence of MetS was directly correlated to psoriasis duration.

Dyslipidemia (38.1% had hypertriglyceridemia, 58.1% presented with low HDL serum levels) was the most prevalent comorbidity, followed by hypertension (61%), obesity (57.1%), while 29.5% of the patients had altered fasting blood glucose. The result in the study conducted by Souza et al. [16] were similar – dyslipidemia (74.5%) was the most prevalent comorbidity, followed by hypertension (61.8%), obesity (52.5%), and 30.9% had type 2 diabetes mellitus.

A statistically significant association between severity of psoriasis and MetS was found, as in many other studies [10, 18, 19], in contrast to some other studies where that association was not found [1].

Association between PsA and MetS was statistically significant, as in other previously done studies [4, 6, 20], as well as association between PsA and IR – a higher percentage of patients with PsA had IR, as in the study by Abogamal et al. [21].

IR was found in 35 (33%) patients. There was no difference in the prevalence of IR between men and women.

When comparing the group with mild and more severe form of the disease, there was no statistically significant association between psoriasis severity and IR, although there was a positive correlation between PASI and HOMA B index in patients without MetS, which can be explained as a tendency for IR development, as IR in addition to high β-cell function (HOMA B index increased) is most frequently observed in individuals with prediabetes [22]. Results were similar to a study by Polic et al. [10], conducted in Croatia, in which results suggest that disease severity is an independent factor for IR irrespective of the Mets presence [10].

Association between PsA and IR in patients without MetS was statistically significant, as in the study conducted by Abogamal et al. [21] and these findings explain the role of inflammatory arthritis through inflammatory cytokines on developing IR in PsA patients. However, when comparing association between PsA and HOMA indices in patients without MetS using the Mann–Whitney test, this significance is not proven most likely due to the small number of participants.

Psoriasis promotes IR, which increases the demand for insulin secretion from pancreatic β-cells to maintain the glucose homeostasis and even in normoglycemic patients can lead to atherosclerosis, myocardial dysfunction, and major cardiovascular events [23, 24].

The question is whether all patients with psoriasis and PsA should be tested for IR. It is well known that obesity is one of the major factors, but not all obese patients are insulin resistant so obesity is not the only predictor of increased risk for cardiovascular diseases, as proven in this study.

CONCLUSION

MetS and IR prevalence increases in patients with PsA and in patients with moderate and severe form of chronic plaque psoriasis. Both psoriasis severity and PsA are independent predictors for IR regardless of the MetS presence. These conclusions support the great role of dermatologists in prevention and early diagnosis of cardiovascular diseases in psoriasis patients.

Considering the chronic nature of psoriasis and frequent onset in adolescence, dermatologists are frequently the first healthcare providers in younger patients that do not have established comorbidities yet, and who are suitable for the possible lifestyle intervention aimed for the prevention of MetS and IR, and subsequent cardiovascular diseases.

Study limitations

Our study has several limitations including its cross-sectional design and relatively small number of participants.

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Conflict of interest: None declared.

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Псоријазни артритис и тежина клиничке слике псоријазе као предиктори метаболичког синдрома и инсулинске резистенције

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САЖЕТАК

Увод/Циљ Циљ ове студије је евалуација тежине клиничке слике псоријазе и присуства псоријазног артритиса као предиктора за развој метаболичког синдрома (МетС) и инсулинске резистенције (ИР) код болесника са хроничном плак псоријазом, као и да се евалуира да ли су тежина клиничке слике и предиктори псоријазног артритиса за развој ИР, независно од присуства МетС-а.

Методе Ова проспективна, опсервационо дескриптивна студија спроведена је на Клиници за кожно-венеричне болести Универзитетског клиничког центра Војводине. У студију је укључено 105 болесника са хроничном плак псоријазом који су подељени у три групе. Група са благим обликом псоријазе (Индекс раширености и тежине псоријазе – *PASI* (*Psoriasis Area Severity Index*) < 10), група са умереним и тешким обликом (*PASI* ≥ 10) и група са псоријазним артритисом, дијагностикованим на основу критеријума *CASPAR*.

Резултати Проценат болесника који су имали МетС је био виши у групи са тежим обликом псоријазе ($p < 0,05$), као и проценат болесника са ИР ($p = 0,05$). Такође, преваленција МетС-а ($p = 0,05$) и ИР ($p < 0,01$) већа је код болесника са псоријазним артритисом. Код болесника без МетС-а није утврђена повезаност између тежине клиничке слике псоријазе и ИР ($p = 1,0$), међутим постојала је позитивна корелација између индекса *PASI* и индекса секреторног капацитета β-ћелија панкреаса % (*HOMA B*), што потврђује тенденцију развијања ИР. Повезаност псоријазног артритиса и ИР код болесника без МетС-а је била статистички значајна ($p < 0,05$).

Закључак Преваленција метаболичког синдрома и инсулинске резистенције је већа код болесника са псоријазним артритисом и код болесника са умереним и тешким обликом хроничне плак псоријазе. Тежина клиничке слике и псоријазни артритис су предиктори инсулинске резистенције, независно од присуства метаболичког синдрома.

Кључне речи: псоријаза; тежина клиничке слике псоријазе; псоријазни артритис; инсулинска резистенција; метаболички синдром