METABOLIC SYNDROME PREVALENCE IN PSORIASIS PATIENTS

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Summary

Psoriasis is a chronic auto-immune disease that affects 2-3% of the general population. It is associated with a series of conditions such as psoriasis arthritis, metabolic syndrome, cardiovascular disease, inflammatory bowel disease, psychiatric manifestations. This review aims to highlight the common pathogenic pathway of psoriasis and comorbidities, especially metabolic syndrome (MetS) and, according to the literature, their evolution with systemic therapy.

We conducted an observational study on 51 patients with psoriasis. The metabolic syndrome defined according to National Cholesterol Education și ATP III criteria (Adult Treatment Panel guidelines), was seen in 54,90% of cases.

The common pathogenic pathway of psoriasis and metabolic syndrome is represented by chronic inflammation and cytokines as TNF α and IL 6, IL 17 are seen in both cases. Despite the numerous efforts to elucidate the pathogenesis of MetS, the relation between psoriasis and its different components remains complex and fairly unclear.

Keywords: *psoriasis, metabolic syndrome, treatment.*

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Introduction

Psoriasis is a chronic, inflammatory, immune-mediated condition that affects approximately 2-3% of the population worldwide[1].

The chronic inflammation involved in psoriasis pathogenesis is responsible for several comorbidities with major impact on patients' quality of life and on mortality. Recently, progresses on pathogenesis of this condition were made, proinflammatory cytokines such as TNF, Il-1, Il-6, Il-8, IL-17, IL-22, Il-23, vascular endothelial growth factor (VEGF), interferon-γ etc. were involved and released into systemic bloodstream depending on the severity of psoriasis. It is proven that myocardial infarction and AVC are more frequent in psoriasis patients than the general population[2].

Numerous studies showed an increase in prevalence of MetS and its components in psoriasis patients. A meta analysis of 63 observational studies, published in 2020 by Caudhary S. et. al, revealed that psoriasis patients have a 2,077 OR: 2.077 [95% CI, 1.84 - 2.34] higher risk to develop MetS in comparison with the general population. [3].

The exact mechanism of this interaction remains unknown but the connection between these conditions can be explained by pro-inflammatory cytokines and adipocytes that regulate glucose and lipids levels and endothelial function. [2]

Conventional systemic treatment should be used carefully in psoriasis patients with MetS due to potential negative impact on coexistent metabolic manifestations, especially long term therapy. The biologic treatment seems to have a different safety profile compared to conventional therapy therefore the former is usually well

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tolerated. Dermatologists should pay special consideration to recognizing coexistent metabolic manifestations and offering proper pharmacologic and nonpharmacologic recommendations (hypocaloric diet and regular exercise).

The etiopathogenic mechanisms remain fairly unclear but chronic inflammation is present in both conditions and proinflammatory cytokines and immunological mediators have an important role.

Aim

The aim of the study was to determine the prevalence of MetS and its components in a group of psoriasis patients and to evaluate the impact of systemic treatment for psoriasis on these comorbidities, shown in research.

Patients and methods

We conducted an observational study on 51 psoriasis patients who checked-in at the Dermatology Department of Emergency County Hospital of Slatina between January 2020-December 2021. Clinical data (age, sex, height, weight, type of psoriasis, PASI and DLQI scores) and associated comorbidities (dyslipidemia, hypertension, diabetes mellitus and obesity), cardiovascular disease (congestive heart failure (CHF), ischemic heart disease (IHD), vascular stroke (VS)), alcohol intake and smoking were collected.

The study was conducted according to the international norms (the **Declaration** of **Helsinki**, reviewed in 2013) and national norms (the law of patient's rights, np46/2003). The access to the patient's data was made respecting the patient's confidentiality. The data did not contain patients' name, address and phone numbers. The patients were informed regarding the medical diagnostic tools and available treatment options and a written consent was signed.

For statistical analysis of data used software IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM and the results are presented as mean ±SD; in order to compare groups we used t-test and Pearson/Fisher's coefficient for evaluating correlations. A level of $p<0.05$ was considered statistically significant.

Psoriasis severity was based on PASI and DLQI scores.

The clinical criteria for the diagnosis of metabolic syndrome, as defined in the National Cholesterol Education Program's Adult Treatment Panel III (ATP III) report, include:

1. waist circumference of more than 102 cm (40 in) in men and more than 88 cm (35 in) in women;
2. triglyceride levels of at least 150 mg per dL (1.70 mmol per L); high-density lipoprotein cholesterol levels of less than 40 mg per dL (1.04 mmol per L) in men and less than 50 mg per dL (1.30 mmol per L) in women;
3. blood pressure of at least 130/85 mm Hg;
4. fasting glucose levels of at least 110 mg per dL (6.10 mmol per L).[4]

Results

The study group was formed by 51 patients clinically diagnosed with psoriasis and 51 healthy subjects.

The mean age was 50.35 ±13.42 and the average duration of the disease was 9.94±6.25 years. It was noticed a slight predominance of males (29(56.9%) M vs 22 (43.1%) W).

Regarding metabolic syndrome, this was seen in 29 psoriasis patients who met at least 3 out of 5 diagnostic criteria while in the control group it was observed in 18 persons.

Dyslipidemia was present in 38 cases and 29 from the control group. Cholesterol level was increased in 38 cases vs 29 in healthy patients; HDL cholesterol was decreased in 64.7 % vs 33.3% in control group; LDL cholesterol was increased in 29.4 % vs 19.6%.

Glucose level was higher in psoriasis patients but without being statistically significant (p= 0,618) with a mean value of 96.80 mg/dl ±16.97 mg/dl compared to healthy subjects, 94.84 mg/dl. Diabetes mellitus being noted in 14 patients from the study group while in the control group only in 10 cases.

Body mass index (BMI) in psoriasis cases was on average 27.42 ±3.39; 23 patients were obese, 9 overweight in comparison with the control lot where 18 were obese and overweight was seen in 11 cases.

Hypertension was noted in 38 psoriasis cases (74.51%) in comparison to 19 cases (37.25%) in the control lot. The majority were under treatment prescribed by the cardiologist.

Regarding smoking, 21 patients with psoriasis were identified in contrast to only 9 in healthy subjects.

Patients' general data are presented in the table 1.

Discussions

Metabolic syndrome (MetS) has become a worldwide important health issue and therefore it is prominently studied due to its association with type II diabetes mellitus and cardiovascular events. This syndrome actually represents a sum of risk factors for developing diabetes mellitus and ischemic heart diseases.

The correlation between Pso and MetS or any of its components (dyslipidemia, type II diabetes mellitus, obesity or cardiovascular events) is frequently reported by research but remains partly unknown.

Table 1. General data about the study group

Number of patients (N)	**51**
Sex F (N/%)	22 (43.13%)
Sex M (N/%)	29 (56.86%)
Age (years)	50.35
Evolution (years)	9.94
Type of psoriasis (N/%)	
Vulgar	45 (88.23%)
Arhtropathic	5 (9.80%)
Pustular	1 (1.96%)
PASI	13.65
DLQI	17
BMI (kg/m2)	28.03
Current medication	
Local therapy (N/%)	3 (5.88%)
Conventional systemic therapy (N/%)	13 (25.49%)
Biologic therapy (N/%)	35 (68.62%)
HTA (N/%)	38 (74.51%)
Diabetes mellitus (N/%)	14 (27.45%)
Smoking (N/%)	21 (41.17%)
Alcohol intake (N/%)	4 (7.84%)
Dyslipidemia (N/%)	38 (74.50%)

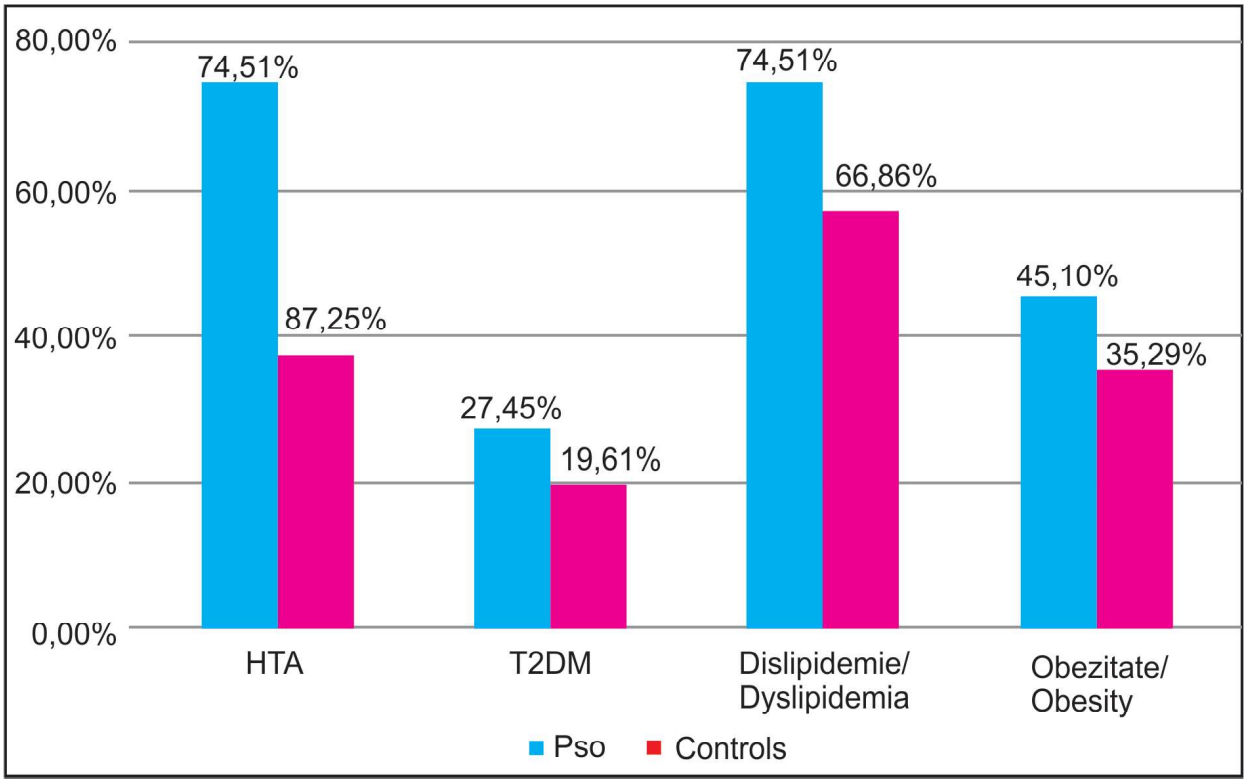

Figure 1. Comparative clinical data Pso/control group

Table 2. Comparative clinical and laboratory data Pso/control group

	Psoriasis group		Control group		P
	Mean	SD	Mean	SD	
Age	50,35	0,89	41,23	11,8	0.321
BMI (kg/m^2)	27,42	3,39	27,57	3,63	0.835
Systolic BP (mmHg)	140,61	13,05	131,71	12,09	0.001
Diastolic BP (mmHg)	83,76	7,31	80,76	8,81	0.064
Glucose (mg/dl)	96,8	16,97	94,84	22,22	0.618
Cholesterol total (mg/dl)	230,90	34,97	227,63	43,55	0.676
HDL (mg/dl)	43,41	6,07	49,18	8,18	<0,001
LDL (mg/dl)	91,96	12,00	98,96	9,80	0.006
Triglycerides (mg/dl)	181,53	33,14	172,98	37,47	0.225
Waist circumference (cm)	94,37	12,74	93,29	13,37	0.678

According to research, in MetS proinflammatory cytokines (IL-6, TNF-α) level, pro-oxidant status markers (OxLDL, uric acid) and prothrombotic factors (PAI-1) are high. Furthermore, leptin concentrations are also increased probably due to leptin resistance. In contrast, the level of anti-inflammatory cytokines (IL-10), ghrelin, adiponectin and antioxidant factors (PON-1) are low [5].

Our study results showed a higher prevalence of metabolic syndrome and its components in the psoriasis group in comparison with the control group, respectively 28 vs 19.

A recent study by Fernández-Armenteros et al. shows that psoriasis pacients have a significant shigher prevalence, in comparison to control group, to develop cardiovascular risk factors such as: type II diabetes mellitus (13.9% vs 7.4%, OR 2.01), dyslipidemia (28.8% vs 17.4%, OR 1.92), hypertension (31.2% vs 19.0%, OR 1.93), obesity (33.7% vs 28.1%, OR 1.30), increased fasting glucose (21.4% vs 15.1%, OR 1.54), low HDL cholesterol (38.1% vs 32.3%, OR 1.29), hypertrygliceridemia (45.7% vs 35.2%, OR 1.55) and high waist circumference (75.7% vs 72.3%, OR 1.19). MetS had a higher prevalence in psoriasis group (28.3% vs 15.1%, OR 2.21) while de risk factors were seen with a similar frequence regardless of the severity of psoriasis. Psoriasis patients have a increased prevalence to develop ischemic heart disease (3.3% vs 1.8%, OR 1.87) and vascular stroke(1.8% vs 1.2%, OR 1.55). [6]

Another study published in 2021 by Aalemi KA et al revealed an important higher prevalence of MetS in psoriasis cases in comparison to the control group (36.8% vs 21.1%). More than half of the cases had moderate to severe psoriasis (62.3%), while 37,7% had mild psoriasis. Also, overweight and obesity were more common in the study group (65.8% vs 41.2%), and cholesterol, triglyceride and glucose levels were much higher in the psoriasis group compared to the control group [7].

The latest data suggest that local overproduction of proinflammatory mediators in psoriasis patients can migrate into the bloodstream. That might determine insulin resistance, endothelial dysfunctions, increased oxidative stress, increased angiogenesis and hypercoagulation that can be responsible for cardiovascular damage [7].

Numerous epidemiological studies show an increased prevalence of cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, obesity or metabolic syndrome in psoriasis patients.[8]

Psoriasis, comorbidities and therapeutic implications

The cardio-metabolic associated comorbidities in moderate to severe psoriasis call for prudence and it determines a series of consequences in choosing a certain systemic treatment.

1. High blood pressure

According to the specialty literature, psoriasis patients have a higher prevalence of developing hypertension, especially uncontrolled hypertension, depending on the severity of psoriasis. [9,10]. The prevalence of hypertension varies, according to a meta analysis from 1.30 rate in a mild psoriasis to 1,49 rate in severe psoriasis[11]. In our study the percentage was 74.51% vs 37.25% in the control group.

2. Diabetes mellitus

Psoriasis is associated with increased risk for diabetes mellitus regardless of the conventional risk factors. The risk of diabetes mellitus, the probability of insulin resistance and development of diabetes complications increases accordingly to psoriasis severity (based on BSA score). A meta analysis shows that the risk for diabetes is 1.53 for

mild forms and goes up to 1.97 for severe forms[12,13]. Also, the patients with psoriasis and diabetes have higher risk for micro and macrovascular complication compared to patients with diabetes without psoriasis [14].

In our study the percentage was 27.45% vs 19.61% in the control group.

3. Dyslipidemia

It is recorded at a higher prevalence among the psoriasis patients. They also have high cholesterol levels with low HDL and high LDL. The direct relation between the two conditions remains unclear but some studies suggest that dyslipidemia can be a risk factor for psoriasis [15].

4. Obesity

Obesity represents an independent risk factor for psoriasis. There is a direct correlation between psoriasis and BMI, obese patients being more prone to developing a severe psoriasis[16]. Obese patients with psoriasis supraexpress α-TNF which induces monocytes differentiation and indirectly promotes native T cells differentiation in Th1 and Th17. Also, psoriasis patients have a high IL-6 level produced mainly by adipocytes and macrophages but also by IL-17. There is a bidirectional relation between psoriasis and obesity, both conditions presenting chronic inflammation [17]. It was demonstrated that weight loss of obese patients with psoriasis is beneficial and improves the cutaneous eruption[18].

Management of moderate to severe psoriasis associated with cardio-metabolic manifestations

Conventional systemic therapies used for moderate to severe psoriasis associated with cardio metabolic manifestations require special attention of the physician. For such, (MTX) methotrexate needs monitoring for liver fibrosis and hepatotoxicity and nefrotoxicity in cases of diabetes mellitus, obese, hepatic diseases and alcohol intake patients. Cyclosporine needs precaution when used for psoriasis with metabolic syndrome since it can aggravate HTA, increase lipids and uric acid levels. Also, this is an absolute contraindication for patients with chronic renal disease. Acitretin can cause hypercholesterolemia and hypertriglyceridemia[19].

In psoriasis associated with diabetes mellitus/insulin resistance there is no absolute contraindication for any of systemic therapies. It can be safely used conventional systemic therapies like acitretin, fumaric acid; biologic therapies like anti TNF agents: infliximab, adalimumab, certolizumab pegol, etanercept decrease insulin resistance; anti IL-17 (secukinumab, ixekizumab), anti Il-12/23 (ustekinumab), anti Il23/p19: guselkumab, risankizumab, tildrakizumab. Can also be used cyclosporine and methotrexate but with precaution [20]. Some studies showed that obese patients with psoriasis under treatment with anti TNF-α agents can gain weight [20].

According to the latest studies, biologic therapies have a beneficial effect on psoriasis with MetS or any other of its components. It was proven that anti TNF-α agents: infliximab, adalimumab, certolizumab pegol, and etanercept decrease insulin resistance[21]. Furthermore, anti TNF-α agents should be the first line treatment for psoriasis with cardiovascular risk factors, considering that adalimumab determines decrease of endothelial biomarkers activation, decrease of selectin E level and significantly reduces intima's thickness. Still, in case of psoriasis and congestive heart failure, anti TNF-α agents are contraindicated (adalimumab, infliximab, certolizumab) and need precaution in mild congestive heart failure class I/II. [20]. Secukinumab (anti IL17) improves endothelial function in psoriasis patients with benefits on cardiovascular conditions [22]. An observational study regarding the use of biologic therapy on severe psoriasis with cardiovascular risk factors, suggests that this treatment induces a good response on coronary plaques based on computed tomography angiogram [23].

Conclusions

Despite numerous studies on different models and locations regarding the relation between psoriasis and metabolic syndrome, this matter still remains partly unknown. The result of our study shows a higher prevalence of metabolic syndrome and its component among psoriasis patients in comparison to the control group.

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Conflict of interest
NONE DECLARED

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