

PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH PSORIASIS AT MOSTAR CLINICAL HOSPITAL

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SUMMARY – Psoriasis is a chronic inflammatory skin disease. Metabolic syndrome is composed of obesity, hyperglycemia, hypertension and dyslipidemia. Previous reports have shown higher prevalence of metabolic syndrome in patients with psoriasis. It is believed that similar inflammatory changes lie in the pathophysiological background of psoriasis and metabolic syndrome. The main objective of this study was to assess the prevalence of metabolic syndrome and its components in patients with psoriasis, as well as to investigate the presence of systemic signs of inflammation such as erythrocyte sedimentation rate and C-reactive protein. The study included 60 patients with psoriasis and the same number of control subjects. We measured anthropometric and laboratory parameters; metabolic syndrome was defined according to the National Cholesterol Education Program-Adult Treatment Panel III criteria and Psoriasis Area and Severity Index was determined in all patients with psoriasis. This study showed a statistically significant presence of obesity (48.3%) and hyperglycemia (23.3%) in patients with psoriasis, while the prevalence of metabolic syndrome was 46.7%. These findings should encourage practitioners to screen psoriasis patients, especially when the disease is severe, for metabolic disorders and introduce appropriate prevention strategies.

Key words: *Psoriasis – diagnosis; Metabolic syndrome – prevalence; Inflammation – C-reactive protein*

Introduction

Psoriasis is a chronic inflammatory skin disease that affects 1%-3% of the population. Recent advances in the understanding of the immunopathogenesis and genetics of psoriasis have shifted the focus from a single organ disease confined to dermal structures to a systemic inflammatory condition analogous to other inflammatory immune disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and Crohn's disease^{1,2}.

The concomitant occurrence of abdominal obesity, dyslipidemia, hypertension and glucose intolerance or insulin resistance constitutes the metabolic syndrome.

An increased prevalence of metabolic syndrome in psoriasis patients compared to non-psoriasis subjects has been recently reported^{1,3-5}. Patients with inflammatory autoimmune diseases are characterized by an increased prevalence of metabolic syndrome, accelerated atherosclerosis, and consequently higher cardiovascular morbidity and mortality rates compared with those without these conditions⁶. The mode of action underlying this phenomenon has been uncertain so far, but may be related to the induction of insulin resistance by proinflammatory cytokines, which are elevated in chronic inflammatory diseases^{2,7}. It seems therefore that chronic inflammation may be involved in the association of psoriasis with chronic metabolic and cardiovascular disorders, just as it is known to be involved in RA, SLE and Crohn's disease².

The main objective of this study was to assess the prevalence of metabolic syndrome and its components in patients with psoriasis, as well as to investigate the

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presence of systemic signs of inflammation such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

Patients and Methods

This study included 60 patients with psoriasis and the same number of control patients suffering from other noninflammatory conditions in which metabolic syndrome has no influence on the pathogenesis, such as actinic keratosis, basal cell carcinoma, viral warts, lipoma, fibroma and stretch marks. The study was conducted at the Department of Dermatology and Venereology, Mostar Clinical Hospital in Mostar. The study was a hospital-based case-control study involving a series of 120 patients. Patients with autoimmune diseases, malignant diseases, acute infection and pregnant women were excluded from the study. An informed consent was obtained from all patients. The study was approved by the institutional ethics committee.

Relevant data on study patients included age, sex, weight, height, body mass index, waist circumference, blood pressure, and severity of psoriasis. Serum biochemical parameters included concentrations of glucose (4.2–6.4 mmol/L), triglycerides (0.6–2.2 mmol/L), HDL cholesterol (men: 0.8–1.7 mmol/L; women: 0.90–1.90 mmol/L), CRP (0.0–5.0 mg/L) and ESR (3.6–28 mm). Body mass index (BMI) was calculated as weight in kilograms/height in square meters ($BMI = kg/m^2$). To determine waist circumference, we located the upper hip bone and placed the measuring tape at the level of the upper most part of the hip bone around the abdomen (ensuing the tape measure was horizontal). The tape measure was snug but did not cause compression on the skin. Blood pressure was recorded as the average of two measurements after subjects had been sitting for five minutes. The severity of psoriasis was assessed according to the Psoriasis Area and Severity Index (PASI). Metabolic syndrome was diagnosed by the presence of three or more of the five criteria set by the National Cholesterol Education Program Adult Panel III (NCEP-ATP III): waist circumference >102 cm in men and >88 cm in women; triglycerides >1.7 mmol/L (150 mg/dL); high density lipoprotein (HDL) cholesterol <1.0 mmol/L (40 mg/dL) in men and <1.3 mmol/dL (50 mg/dL) in women;

blood pressure >130/85 mm Hg; fasting plasma glucose >6.1 mmol/L (100 mg/dL)⁸. Venous blood samples were collected at enrolment after overnight fast (at least 8 h).

Normality of distribution of continuous variables was tested by Kolmogorov-Smirnov test. For the analysis of nominal variables, χ^2 -test was used. The median and interquartile range was used for continuous variables whose distribution deviated significantly from the normal. Differences between groups in these variables were tested by Mann-Whitney U test. P value <0.05 was considered significant. The SPSS for Windows software (version 13.0; SPSS Inc., Chicago, Illinois, USA) was used on statistical data analysis.

Results

The case group included 60 patients with psoriasis, 33 (55%) men and 27 (45%) women, mean age 49.9 ± 14.8 (range 16–79) years. Patients of the 50–59 age group prevailed ($n=23$; 38.3%) (Fig. 1). Control group included 53.3% of men and 46.6% of women, mean age 53.7 ± 14.9 years. There were no significant between-group differences according to age and sex.

Control group included subjects with anti-inflammatory skin disease (seborrheic keratosis 25%, viral warts 33.3%, fibromas 18.27%, solar lentigo 9.99%, basalioma 6.67%, lipomas 3.33% and stretch marks 3.33%).

Patients most commonly ($n=31$; 51.7%) had a mild form of the disease as defined by PASI index (χ^2 -test=9.100; $df=2$; $p=0.011$).

In the psoriasis group, hyperglycemia was found in 14 (23.3%), hypertension in 24 (40.0%), dyslipidemia

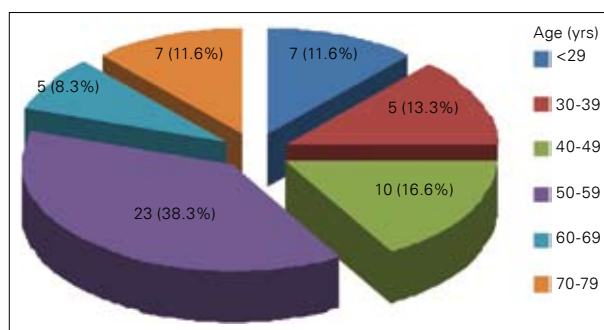


Fig 1. Distribution of patients with psoriasis according to age groups.

Table 1. Prevalence of metabolic syndrome and its components in patients with psoriasis and control group

Variable	Number of patients according to groups (%)		χ^2 -test	p-value
	Patients with psoriasis	Controls		
Metabolic syndrome				
Present	28 (46.7)	27 (45.0)	0.034	0.855
Absent	32 (53.3)	33 (55.0)		
Hyperglycemia				
Present	14 (23.3)	4 (6.7)	6.536	0.011
Absent	46 (76.7)	56 (93.3)		
Hypertension				
Present	24 (40.0)	34 (56.7)	3.337	0.068
Absent	36 (60.0)	26 (43.3)		
Dyslipidemia				
Present	26 (43.3)	19 (31.7)	1.742	0.187
Absent	34 (56.7)	41 (68.3)		
Obesity				
Present	29 (48.3)	15 (25.0)	7.033	0.008
Absent	31 (51.7)	45 (75.0)		

in 26 (43.3%), and obesity in 29 (48.3%) patients. Comparison of patients with psoriasis and control subjects revealed an almost equal presence of metabolic syndrome ($n=28$; 46.7% *vs.* $n=27$; 45.0%) (χ^2 -test=0.034; $df=1$; $p=0.855$). The components of the metabolic syndrome hyperglycemia (χ^2 -test=6.536; $df=1$; $p=0.011$) and obesity (χ^2 -test=7.033; $df=1$; $p=0.008$) were significantly more common in the case group, while other components of the ratio were approximately equal in the two groups (Table 1).

The parameters of systemic inflammation ESR (median 10.0 mm *vs.* 10.0 mm) and CRP (median 2.45 mg/L *vs.* 3.20 mg/L) were not elevated in either group (Table 2).

Discussion

This case-control study included a total of 120 patients. Among 60 patients with psoriasis 55% were men and 45% women. A similar sex ratio in the case group (52%:48%) was found in a study conducted in Brazil⁹. Previous available studies included slightly more men than women but without statistically significant differences^{2,10}.

Metabolic syndrome is a disorder that presents a significant risk for the cardiovascular system and human health. Synonymous with metabolic syndrome are syndrome X, syndrome X plus, the insulin resistance syndrome, plurimetabolic syndrome, or deadly quartet. Metabolic syndrome is composed of obesity, insulin resistance (hyperinsulinemia), which leads to impaired glucose tolerance, abnormal lipid levels (dyslipidemia) and elevated blood pressure (hypertension). It is believed that the pathophysiological background of this syndrome involves inflammatory changes which, along with genetic susceptibility and exposure to environmental factors, lead to the expression of the metabolic syndrome components. Chronic inflammatory changes, in particular secretion of proinflammatory cytokines induced by chronic systemic inflammation characteristic of psoriasis, may be responsible for the development

of metabolic syndrome particularly in patients with severe longstanding psoriasis^{2,11,12}.

According to the literature, the incidence of metabolic syndrome in patients with psoriasis varies in a range from 23.8% to 44%^{2,9,11,13,14}. These results are different in different countries, e.g., 23.8% in Egypt, 30.1% in northern Italy, 40%, in the United States and 44% in Brazil^{2,11,14}. By comparing available studies, we found that the incidence of metabolic syndrome in

Table 2. Serum levels of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in patients with psoriasis and control group

Variable	*C [Q] of laboratory values according to groups		Mann-Whitney U test	p-value
	Patients with psoriasis	Controls		
ESR	10.0 [11]	10.0 [5]	1771.000	0.879
CRP	2.45 [3.1]	3.20 [2.2]	1680.000	0.529

*C [Q] - median [interquartile range]

patients with psoriasis in a study conducted in Brazil was 44%⁹, which is consistent with the results (46.7%) recorded in our study.

The prevalence of metabolic syndrome in general population depends on the diagnostic criteria of the population (ethnic groups), age and sex. The largest differences occur in the age-specific prevalence. In the Third National Health and Nutrition Examination Survey (NHANES III), the prevalence increased from 6.7% in subjects aged 20–29 to 43.5% in those aged 60–69, while in the ≥ 70 age group it was 42%¹⁵. The prevalence of metabolic syndrome in general population is rapidly increasing after the age of 60², and in our study, most patients were aged over 50. Their age is a potential reason for more internal disorders.

The results of the present study showed an approximately equal share of metabolic syndrome in patients with psoriasis ($n=28$; 46.7%) and in control subjects ($n=27$; 45.0%). The lack of statistically significant between-group difference in the prevalence of metabolic syndrome is in accordance with the results of a study conducted in Tunisia¹⁶, and in contrast to the results of a number of other available studies^{2,8,11,13,14,17,18}. Differences in genetics, level of physical activity, age, sex, diet (our eating habits are similar to those in the eastern Balkans)^{11,17,19}, may explain deviations from the comparative study. There are reports on a significantly higher prevalence of metabolic syndrome in patients with psoriasis compared to control group^{10,11,17,20}. The high prevalence of the metabolic syndrome components in psoriasis patients was exclusively due to the effects of chronic inflammation and secretion of proinflammatory cytokines^{10,17,20}.

A case-control study conducted in Taiwan showed a significantly higher prevalence of obesity, a component of the metabolic syndrome, in patients with psoriasis¹⁴, which is consistent with the results of our study. In this study, hyperglycemia (23.3%) and obesity (48.3%) were significantly more common in the case group, while the ratio of other components (hypertension and dyslipidemia) was approximately equal in both groups^{14,21}.

Insight into the current research shows that of all components of the metabolic syndrome obesity is most strongly associated with psoriasis^{22,23}. Obesity is associated with other components of metabolic syndrome and appears to be a precursor for the de-

velopment of insulin resistance (hyperglycemia), dyslipidemia and hypertension^{6,24,25}. Obese patients with psoriasis have a five times greater risk of developing diabetes. Unlike other inflammatory diseases, in previous clinical trials it was observed that nearly half of the patients with moderate to severe psoriasis were obese^{11,23,26}. The pathophysiology of psoriasis and obesity involves the same cytokines that are known to contribute to the development of the components of metabolic syndrome^{25,27}. Literature data suggest that obesity is associated with a twofold risk of early psoriasis, and the present study confirmed that obesity was more frequent in patients with psoriasis than in control group.

In recent years, psoriasis has been considered an immune system disorder like RA, SLE and Crohn's disease²⁸. These phenotypically different states share common pathologic changes such as chronic inflammation, angiogenesis, and oxidative stress^{28,29}. Inflammation has emerged as a key factor in atherogenesis by providing a unique mechanism of association between atherosclerosis and chronic inflammatory immune diseases. In these diseases, inflammation results in an increase of CRP and ESR, signs of systemic inflammation^{2,30,31}.

Most of the study patients with psoriasis had a mild form of the disease as a result of random selection of patients presenting for treatment at Department of Dermatology and Venereology, Mostar Clinical Hospital, who were willing to enroll in the study. A smaller area of the skin affected by the psoriatic inflammatory process may explain the lack of statistically significant differences in ESR and CRP levels between the case group and control group. In addition, in patients with psoriasis, again due to the mild forms of the disease, the parameters of systemic inflammation, ESR (median 10.0 mm) and CRP (median 2.45 mg/L), were not elevated. In a study conducted in Portugal and in other similar studies available, CRP remained significantly higher in patients with psoriasis despite treatment, and it was concluded that CRP along with PASI could be used as a "global severity index"³⁰⁻³³. Our study did not confirm that both ESR and CRP levels were elevated in patients with psoriasis.

Conclusion

This study indicated obesity and hyperglycemia to be significantly frequent in patients with psoriasis.

Practitioners are encouraged to screen psoriasis patients, especially when the disease is severe, for metabolic disorders and cardiovascular risk factors and to develop appropriate prevention strategies. Based on this study, CRP along with PASI could not be considered as a global index of disease severity. Additional studies investigating the role of psoriasis activity and severity as an independent risk factor for developing metabolic disorders, atherosclerosis and myocardial infarction, and the role of psoriasis treatment in altering the risk of developing these serious comorbidities are urgently needed.

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Sažetak

UČESTALOST METABOLIČKOG SINDROMA U BOLESNIKA S PSORIJAZOM U KLINIČKOJ BOLNICI MOSTAR

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Psorijaza je kronična upalna kožna bolest. Metabolički sindrom se sastoji od pretilosti, hiperglikemije, hipertenzije i dislipidemije. U prethodnim istraživanjima uočena je povećana učestalost metaboličkog sindroma u bolesnika s psorijazom. Smatra se da su u patofiziološkoj podlozi psorijaze i metaboličkog sindroma slične upalne promjene. Glavni cilj istraživanja je bio utvrditi učestalost metaboličkog sindroma i njegovih sastavnica u oboljelih od psorijaze, kao i ispitati prisutnost sistemskih znakova upale, sedimentacije i C-reaktivnog proteina. Istraživanje je uključilo 60 bolesnika s psorijazom i jednak broj bolesnika ispitne skupine. Određeni su antropometrijski i laboratorijski parametri, dijagnoza metaboličkog sindroma je postavljena na osnovi kriterija koje je definirao NCEP-ATP III (National Cholesterol Education Program-Adult Treatment Panel III), a PASI indeks (Psoriasis Area and Severity Index) je određen svim bolesnicima s psorijazom. Istraživanje je pokazalo statistički značajno učestaliju pretilost (48,3%) i hiperglikemiju (23,3%) u skupini bolesnika s psorijazom, a učestalost metaboličkog sindroma iznosila je 46,7%. Ovi rezultati trebali bi liječnike potaknuti na probir bolesnika s psorijazom, naročito onih s teškim oblikom bolesti, na metaboličke poremećaje i uvođenje odgovarajuće prevencije.

Ključne riječi: Psorijaza – dijagnoza; Metabolički sindrom – učestalost; Upala – C-reaktivni protein