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Report

High prevalence of metabolic syndrome in patients with psoriasis in Lebanon: a prospective study

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Abstract

Background Psoriasis is a chronic inflammatory disease that affects not only the skin but also other organs as well. Genetic factors play an important role in individual predisposition. Lately, a positive association has been confirmed between psoriasis and metabolic syndrome (MBS), in western as well as in Middle Eastern countries.

Aim Assess the prevalence of MBS in Lebanese patients with psoriasis and the differential effect according to types and disease severity.

Methods This was a case-control study including 150 psoriasis patients and 150 age- and gender-matched controls admitted to the dermatology clinics at the American University of Beirut–Medical Center, a tertiary care center in Beirut. Psoriasis severity was assessed by the Psoriasis Area Severity Index (PASI). Blood samples were collected from fasting subjects and tested for glucose, HDL cholesterol, triglycerides, and C-reactive protein (CRP). Multivariate binary logistic regression models were built to assess the relationship between MBS and psoriasis, after adjustment for smoking as a possible confounding variable.

Results Patients with psoriasis were two times more likely to have MBS as compared to controls (35.3% vs 18.0%, $P < 0.001$) with an odds ratio (OR) of 2.4. All components of MBS were more prevalent in psoriasis patients than in controls. PASI score was greater in patients with MBS than those without MBS (10.5 ± 11.5 vs. 7.0 ± 8.1, $P = 0.05$). MBS prevalence tended to be higher in the inverse type than in others (52.2% versus 32.3%; $P = 0.06$) and in patients with nail pitting versus those without (45.3% vs. 28.2%; $P = 0.03$).

Conclusions This was the first study to assess the prevalence of MBS in Lebanese subjects with psoriasis and, to our knowledge, the first study that showed a higher likelihood of MBS in patients with inverse psoriasis and with nail pitting.

Introduction

Psoriasis is a chronic systemic autoimmune skin disorder affecting multiple organs, associated with several comorbidities, and necessitating lifelong treatment. Two to 3% of Caucasians are affected with varying prevalence depending on the region and ethnicity.[1–3] Genetic factors play a crucial role in individual predisposition, labeling this disease as hereditary. It is characterized by proliferation and abnormal differentiation of keratinocytes associated with infiltration of T cells in the epidermis and dermis.[4] It can have several presentations, the most common being plaque type and affecting 80% of the psoriasis population.[5]

A strong positive association between psoriasis and known risk factors for metabolic syndrome (MBS) including central obesity, insulin resistance, and dyslipidemia, has been described.[6] This association was found to be most valid in patients with moderate to severe psoriasis.[7] Moreover, young patients with severe psoriasis were specifically prone to develop myocardial infarction.[8] MBS is a well-known disorder characterized by the presence of a number of cardiometabolic risk factors, including central obesity, hyperglycemia, abnormal triglycerides, and high-density lipoprotein (HDL) levels, and elevated blood pressure. MBS is associated with increased risk of coronary heart disease, sudden death, and stroke. The National Cholesterol Education Program-Adult Treatment Panel III 2001 definition was adopted in this study because this definition has been validated the most as well as the impact on morbidity and mortality is lower with newer definitions.[9] Mancia *et al.*[10] demonstrated that regardless of the definition of MBS, the risk of cardiovascular events and death is significantly greater in those with as compared to those without MBS.

Numerous studies have shown a correlation between psoriasis and MBS in many developed and developing countries, including Middle Eastern countries.[6,7,11–14] Indeed, one recent study conducted in Kuwait and a few others in Israel found a strong association between psoriasis and MBS, in addition to other inflammatory comorbid diseases.[13–16] As psoriasis is a genetic disorder and as both environmental and genetic factors play a role in the development of MBS, the relationship between psoriasis and MBS may not be the same between different ethnicities or between populations of the same ethnic group in different countries because of the different environmental exposure. Thus extrapolating data and results across countries is not always reasonable. Although the relationship between MBS and psoriasis was widely investigated, data on the relationship with different types or with the severity of psoriasis are very scarce. Thus, in this study, we assessed the prevalence of MBS in Lebanese patients with psoriasis and the differential effect according to types and disease severity.

Materials and methods

Study subjects

This was a case–control study, including 150 patients with psoriasis and 150 age- and gender-matched controls admitted to the dermatology clinics at the American University of Beirut–Medical Center, a tertiary care center in Beirut. The controls were subjects referred during the study period for various dermatologic complaints other than psoriasis, such as acne, rosacea, epidermal inclusion cysts, and tinea pedis. Individuals who were less than 18 years, pregnant, or receiving systemic corticosteroids were excluded from the study. In addition, all subjects known to have serious and chronic diseases such as cancer, kidney, liver, and heart diseases were excluded from the study.

Data collection

Data collected from enrolled subjects included age, gender, medical history, smoking and alcohol drinking habits (defined as yes or no), personal history of psoriasis and psoriatic arthritis, dermatologic condition for controls, age onset of psoriasis, and type of psoriasis. Weight and height were measured barefooted. Waist circumference was measured by placing a measuring tape at the level of the iliac crest. Psoriasis severity was assessed by the psoriasis area severity index (PASI). Psoriasis was considered mild to moderate if the PASI score was ≤10 and severe if the PASI score was >10.

Venous blood samples were collected from fasting subjects and tested for glucose, HDL cholesterol, triglycerides, and C-reactive protein (CRP). MBS was diagnosed in the presence of three or more criteria of the National Cholesterol Education Program's Adult Panel III (ATP III): (i) fasting blood sugar ≥100 mg/dl or treatment for hyperglycemia; (ii) serum HDL level <40 mg/dl in men or <50 mg/dl in women or treatment for low HDL; (iii) serum triglyceride level ≥150 mg/dl or treatment for elevated triglycerides; (iv) obesity, defined by waist circumference ≥102 cm in men or ≥88 cm in women; and (v) blood pressure ≥130/85 or treatment for hypertension.[17] Measurement of the levels of HDL, triglycerides, fasting blood sugar, and CRP was done at the American University of Beirut – Medical Center Laboratory using the Cobas machine 6000 (Mannheim, Germany), Module c501 (Germany), through an enzymatic calorimetric process.

Ethics

The study was approved by the institutional review board of the American University of Beirut, and written informed consents were obtained from all participants before enrollment in the study.

Statistical analyses

Statistical analyses were made using SPSS (Chicago, IL, USA) version 19.0 software package. Continuous variables are presented as means ± SD, unless stated otherwise. Data were considered statistically significant if $P < 0.05$. Chi-squared test and binary logistic regression were used to assess the relationship between two categorical variables. Independent *t*-test was used to compare mean values of continuous variables such as age and body mass index between patients and controls and to compare mean of age, disease duration, age at onset, and PASI score between patients with psoriasis with MBS and those without MBS. All these variables were normally distributed.

Multivariate binary logistic regression models were built to assess the relationship between MBS and psoriasis, after adjustment for smoking as a possible confounding variable.

Results

Baseline characteristics

Baseline characteristics of patients with psoriasis and controls are shown in Table 1. The mean age was 42.1 ± 16.5 years in patients and 41.9 ± 16.4 years in controls without a difference between groups. Patients with psoriasis had a higher body mass index (29.1 ± 6.0 vs. 26.2 ± 5.1; $P < 0.001$), higher CRP levels ($P = 0.005$), and were more likely to be ever or current smokers, as compared to controls ($P < 0.05$). There was no difference between cases and controls regarding the presence of coronary artery disease and polycystic ovary syndrome.

Psoriasis and metabolic syndrome

Patients with psoriasis were two times more likely to have MBS as compared to controls (35.3 vs. 18.0%, $P < 0.001$) with an OR of 2.4 (95% CI 1.4–4.2). This relationship persisted after adjustment for smoking (Table 2).

Table 1 Baseline characteristics of psoriasis and control patients

	Patients (n = 150)	Controls (n = 150)	P value*
Gender			
Male	67 (44.7%)	68 (45.3%)	0.908
Female	83 (55.3%)	82 (54.7%)	
Age (years)	42.14 ± 16.53	41.91 ± 16.46	0.905
Body mass index (kg/m^2)	29.18 ± 6.09	26.23 ± 5.14	<0.001
Coronary artery disease	4 (2.7%)	3 (2.0%)	0.702
Smoking status			
Ever smoker	96 (64.0%)	71 (47.3%)	0.004
Current smoker	84 (56.0%)	62 (41.3%)	0.011
Alcohol intake	27 (18.0%)	28 (18.8%)	0.860
CRP (mg/dl)	5.55 ± 9.38	3.05 ± 5.42	0.005

*P-value for difference between groups by chi-squared test (for proportions) or t-test (for continuous variables), where applicable.

Table 2 Odds ratio (95% CI) for having metabolic syndrome in patients with psoriasis versus controls, before and after adjustment for smoking

	Unadjusted	Adjusted for smoking
Obesity (WC ≥102 cm in males or ≥88 cm in females)	3.10 (1.93–4.98)	3.03 (1.88–4.90)
FBS ≥100 mg/dl	1.47 (0.83–2.60)	1.32 (0.73–2.37)
HDL <40 mg/dl in males or <50 mg/dl in females	1.66 (1.04–2.66)	1.51 (0.93–2.44)
Triglycerides ≥150 mg/dl or on fibrates or niacin	1.83 (1.08–3.10)	1.64 (0.95–2.81)
SBP ≥130 mmHg or DBP ≥85 mmHg or on antihypertensives	2.49 (1.49–4.16)	2.42 (1.44–4.07)
Metabolic syndrome[a]	2.49 (1.46–4.25)	2.30 (1.34–3.95)

DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; SBP, systolic blood pressure; WC, waist circumference.
[a]Metabolic syndrome was diagnosed by the presence of ≥3 criteria of the National Cholesterol Education Programs Adult Panel III (ATP III).

All components of MBS were more prevalent in patients with psoriasis than in controls (P < 0.05), but the difference did not reach statistical significance for fasting blood sugar (Fig. 1). When the analyses were done in males and females separately, similar results were obtained regarding the prevalence of MBS, obesity, and high blood pressure in both genders.

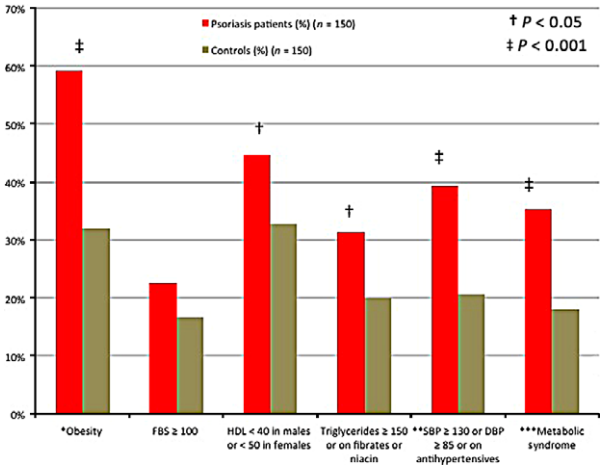

Figure 1 Prevalence of metabolic syndrome and its components in patients and controls. *Waist circumference ≥102 cm in males or ≥88 cm in females. Metabolic syndrome was diagnosed by the presence of ≥3 criteria of the National Cholesterol Education Programs Adult Panel III (ATP III). DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; SBP, systolic blood pressure

Effect of disease duration

Within patients with psoriasis, subjects with MBS were older (49.0 ± 15.6 years vs. 38.3 ± 15.8 years, P < 0.001) and had longer disease duration (13.0 ± 14.4 years vs. 8.3 ± 8.6 years, P = 0.03) compared to those without MBS (Table 3). Moreover, the risk of MBS was 40% higher for each 10-year increase in disease duration (OR 1.4; 95% CI 1.1–1.3), and 20% higher for each 10-year increase in age of onset (OR 1.2; 95% CI 1.1–1.2) (Table 4).

Table 3 Characteristics of psoriatic patients with and without MBS

	Patients with MBS (n = 53)	Patients without MBS (n = 97)	P value
Gender (male/female)	1 : 1.12	1 : 1.31	0.649**
Disease duration (years)	13.04 ± 14.45	8.39 ± 8.68	0.037*
Age (years)	49.08 ± 15.67	38.35 ± 15.81	<0.001*
Age of onset (years)	36.37 ± 18.55	29.96 ± 17.47	0.039*
C-reactive protein (mg/dl)	7.21 ± 9.32	4.64 ± 9.33	0.109*
Disease severity			
PASI score	10.56 ± 11.56	7.06 ± 8.14	0.054*
PASI ≤10	33 (62.3%)	76 (78.4%)	0.035**
PASI >10	20 (37.7%)	21 (21.6%)	

MBS, metabolic syndrome; PASI, psoriasis area severity index.
P value for difference between groups by *t-test or **chi-squared test.

Table 4 Odds ratio (95% CI) for having MBS or its components according to disease severity, age of onset, and disease duration

	PASI >10 vs. PASI ≤ 10	PASI score[a]	Age of onset[b]	Duration[b]
Obesity (WC ≥102 cm in men or ≥88 cm in women)	1.46 (0.69–3.09)	1.00 (0.87–1.17)	1.26† (1.02–1.21)	1.34 (0.99–1.31)
FBS ≥100	1.64 (0.72–3.71)	1.05 (0.86–1.21)	1.35† (1.04–1.25)	1.49† (1.04–1.36)
HDL <40 mg/dl in men or <50 mg/dl in women	1.10 (0.53–2.26)	1.03 (0.88–1.17)	1.00 (0.92–1.08)	1.54 (0.90–1.15)
Triglycerides ≥150 mg/dl or on fibrates or niacin	1.19 (0.56–2.56)	1.14 (0.91–1.23)	1.21 (1.00–1.18)	1.38† (1.01 –1.31)
SBP ≥130 mmHg or DBP ≥85 mmHg or on antihypertensive	2.59† (1.24–5.40)	1.65† (1.06–1.47)	1.32† (1.04–1.23)	1.30 (0.98–1.27)
MBS[c]	2.19† (1.05–4.58)	1.45† (1.01–1.37)	1.22† (1.00– 1.18)	1.43† (1.03–1.34)

DBP, diastolic blood pressure; FBS, fasting blood sugar; HDL, high-density lipoprotein; MBS, metabolic syndrome; OR, odds ratio; PASI, psoriasis area severity index; SBP, systolic blood pressure; WC, waist circumference.
[a]OR for each 10 points increase in PASI score.
[b]OR for each 10-year increase in age of onset and duration of disease.
[c]MBS was diagnosed by the presence of ≥3 criteria of the National Cholesterol Education Programs Adult Panel III (ATP III).
†OR with $P \leq 0.05$.

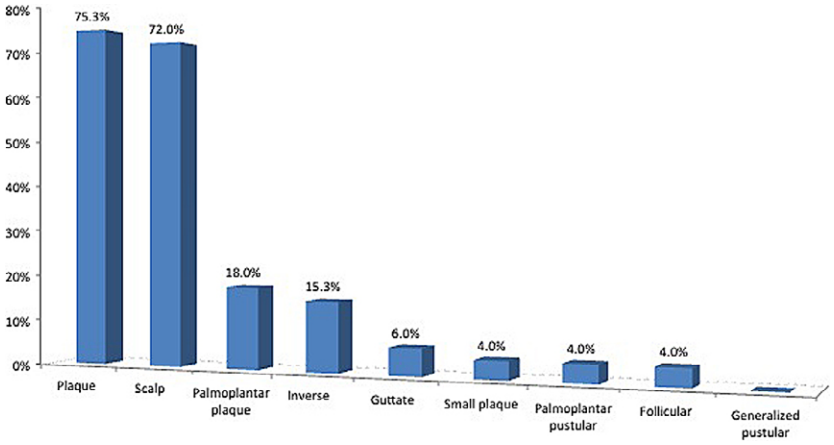

Figure 2 Patient distribution according to psoriasis subtypes

Effect of disease severity

PASI score was greater in patients with MBS than those without (10.5 ± 11.5 vs. 7.0 ± 8.1, $P = 0.05$) (Table 3). Additionally, patients with severe psoriasis (PASI >10) were two times more likely to have MBS: OR 2.1 (95% CI 1.1–4.5). Moreover, each 10-point increase in the PASI score was associated with 40% higher risk of MBS (Table 4).

Effect of psoriasis subtypes

Plaque and scalp psoriasis were the most common presentations (Fig. 2); 42.7% of patients with psoriasis had nail pitting.

MBS prevalence tended to be higher in the inverse type than in others (52.2 vs. 32.3%; $P = 0.06$). In addition, 65.4% of patients with inverse psoriasis had high blood pressure compared to 34.6% of patients with other subtypes ($P = 0.006$).

Patients with nail pitting were more likely to have MBS than others (45.3 vs. 28.2%; $P = 0.03$). A similar trend was observed with high triglyceride (39.1 vs. 25.9%) and low HDL levels (53.1 vs. 38.8%), but these differences did not reach statistical significance ($P = 0.08$).

Discussion

This case–control study showed a high prevalence of MBS, as well as a higher prevalence of each component of MBS in patients with psoriasis compared to healthy controls. Moreover, MBS prevalence was higher in subjects with nail pitting and tended to be higher in the inverse type than in other types. This is to our knowledge the first study that assessed the association between psoriasis subtypes and MBS.

The prevalence of MBS observed in the current study was similar to what was reported in North African and Western populations.[18,19] Conversely, reports from Asian populations such as Japan and Korea showed a lower prevalence of MBS, suggesting a possible role of ethnicity and environmental factors.[12,20] Indeed, in our study, the

unadjusted OR of MBS in patients with psoriasis was 2.4. This OR was higher than that reported in the Israeli population[14] but much lower than that reported in the Indian population (OR of 6.09).[21] The association between psoriasis and MBS has been attributed to inflammatory markers shared by both psoriasis and MBS, such as Th1 cytokines (TNF-α), CRP, and IL-6.[20–22] Furthermore, IL-17 is involved in the pathogenesis of psoriasis and is elevated in patients with unstable coronary arterial disease.[23] Recently, other emerging markers of inflammation, atherogenesis, and cardiovascular events such as sCD40L and complement C3 have been shown to be increased in patients with psoriasis.[23,24] In addition, specific genetic loci have been identified in patients with psoriasis and in those who display features of MBS. For instance, CDKAL1 gene has been identified in patients with psoriasis as well as in those with type II diabetes mellitus. Apolipoprotein E-4, a well-known cardiovascular risk factor, has been implicated in patients with psoriasis.[20,25,26]

The association between psoriasis and MBS was observed in both genders in the current study. On the contrary, in a case–control study (consisting of 164 cases and 216 controls) done in Tunisia, Mebazaa *et al.* found a significant relationship in women only.[18] The authors of that study ascribed this finding to the high fertility rate and reduced physical activity in women.

The prevalence of MBS was higher in patients with severe psoriasis defined as PASI score >10, and the risk of MBS increased as the PASI score increased. This association with disease severity was previously reported by a case–control study in a Korean population where patients with moderate to severe psoriasis, defined as use of systemic therapies, had an increased risk of MBS.[20] Conversely, other studies did not find any association between severity of psoriasis and MBS.[21,22,27] Some inflammatory markers were shown to be higher in severity when compared to mild to moderate psoriasis, particularly leptin. This proinflammatory peptide hormone, which is secreted by adipose tissue, is known to play a role in MBS features.[26,28]

Longer disease duration was associated with increased risk of MBS. This was consistent with some[21] but not all studies.[20] The chronic inflammatory status in patients with psoriasis might be a plausible explanation of this finding. The older age of onset was associated with increased risk of MBS in line with the findings of Kutlu *et al.*[29] and Rosa *et al.*[22] who demonstrated that age of onset greater than 40 years was more common in psoriatic patients with MBS than those without MBS.

Our study was the first to exhibit a relationship between inverse and nail pitting and MBS. Choi *et al.*[20] did not show any association between some types of psoriasis and MBS; however, that study did not include inverse subtype and nail pitting in the analysis. It is possible that obesity may predispose patients to the development of an inverse subtype of psoriasis. However, the mechanisms underlying the difference in the relationship between MBS and psoriasis subtypes are not clear and need to be further evaluated in a larger study.

In conclusion, this was the first study to assess the prevalence of MBS in Lebanese subjects with psoriasis and, to our knowledge, the first study that showed a higher likelihood of MBS in patients with inverse psoriasis and with nail pitting. Additional studies are needed to explore the mechanisms behind this higher prevalence of MBS in these types of psoriasis.

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