

Metabolic syndrome and psoriasis: a study in 97 patients

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SUMMARY

BACKGROUND: Psoriasis is associated with higher prevalence of metabolic syndrome (MS). The prevalence of MS varies according to the studied population as it suffers influence of genetics, aging, sedentary behaviour and diet.

OBJECTIVE: To study the prevalence of MS in local psoriasis patients and the influence of psoriasis variables on its appearance.

METHODS: A group of 97 psoriasis patients were studied for MS and compared with 97 controls. Psoriasis type, nail involvement, psoriasis extension measured by PASI (Psoriasis Area and Severity Index) were obtained through physical examination and history of previous myocardial infarction, angina and stroke were obtained through chart review.

RESULTS: Comparison of MS prevalence in psoriasis patients (49.4%) with controls (35.0%) showed difference with $p=0.04$; $OR=1.8$ ($95\%CI=1.02-3.23$). Patients with psoriasis had higher body mass index ($p=0.02$), higher systolic blood pressure ($p=0.007$), lower HDL cholesterol ($p=0.01$), higher glucose ($p=0.04$), higher waist circumference ($p=0.003$) and more angina pectoris ($p=0.03$; $OR=2.5$; $95\%CI=1.04-6.15$) than controls. When psoriasis sample with and without MS were compared, those with MS were older ($p=0.0004$), had disease onset at older age ($p=0.02$), more tobacco exposure ($p=0.02$), and a tendency to have less scalp involvement ($p=0.06$) in univariate analysis. Logistic regression showed that only age and scalp involvement were independently associated with MS in the psoriasis sample.

CONCLUSION: In our psoriasis sample, MS prevalence is high and the items that deserve more attention are central obesity, low HDL, hypertension and smoking habits. In the psoriasis group, MS was associated independently with older age and less scalp involvement.

KEYWORDS: Psoriasis. Metabolic syndrome X. Metabolic diseases.

INTRODUCTION

Psoriasis is a chronic and complex immune-mediated skin disorder.¹ The systemic nature of the inflammatory process involved in its etiopathogenesis is responsible for several co-morbidities, which themselves have a considerable impact on the patient's quality of life and mortality.¹ Myocardial infarction and stroke are considered to be increased in

patients with psoriasis when compared with the general population.² Hence, the effective treatment of this disease includes not only care with the skin and nail manifestations but also attention to the associated conditions. A meta-analysis including 12 other studies showed that patients with psoriasis were 2.2 times more likely to have metabolic syndrome (MS) than the general population² and some authors found that there is a positive correlation between severity of

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psoriasis and the presence of MS.³ The exact mechanism for this interaction remains uncertain but the link between them may be the effects of pro-inflammatory cytokines and adipocytes on glucose regulation, lipid status, and endothelial function.¹

MS is a clustering of several medical conditions such as central obesity, arterial hypertension, glucose intolerance, high serum triglycerides and low high-density lipoprotein (HDL) levels (4). It has been recognized as a pro-inflammatory, prothrombotic state associated with elevated levels of C-reactive protein (CRP), interleukin (IL)-6, and plasminogen activator inhibitor (PAI)-1.^{5,6} This syndrome lies in the background of the association of psoriasis, cardiovascular risk and type 2 diabetes mellitus. The prevalence of MS varies according to the studied population as it suffers influence of genetics, aging, sedentary behaviour and diet.^{7,8}

In the present study, we aimed at identifying the prevalence of MS in psoriasis patients from a single dermatology centre in Southern Brasil, and its relationship to the clinical profile of the skin disease.

METHODS

The local Committee of Ethics in Research approved this study and all participants signed a consent form. It is a cross sectional observational study that includes a convenience sample of 97 individuals formed by all psoriasis patients that came for regular consultations during a twelve-month period and that agreed to participate. All of them were from a single Dermatology Outpatient Clinic of a Tertiary Care Hospital. Patients under 18 years of age, pregnant women and patients with uncontrolled hypothyroidism were excluded. As control, 97 individuals were included, paired according to gender and age that came for an ophthalmologic appointment to test refraction and for routine gynaecological exams without chronic inflammatory diseases.

Epidemiological information (age, ethnic background, disease duration, tobacco use and age at disease onset), clinical aspects of psoriasis (psoriasis type, nail involvement, treatment), history of diabetes mellitus and high blood pressure treatment, previous history of myocardial infarction, angina and stroke were obtained through chart review and upon direct questioning. Data on PASI (Psoriasis Area and Severity Index) (9), arterial blood pressure, body mass index (BMI) and abdom-

inal circumference were obtained through physical examination. Blood was drawn for fasting glucose (by automated enzymatic method), total cholesterol, HDL (high-density lipoprotein) cholesterol, LDL (low-density lipoprotein) cholesterol and triglycerides (by enzymatic/colorimetric methods); ESR (erythrocyte sedimentation rate by the Westergren method), uric acid (by fasting automated enzymatic method) and CRP (C reactive protein by immunoturbidimetry) were determined.

The metabolic syndrome diagnosis was done according to the guidelines developed by the 2001 NCEP ATP III and updated in 2005 in a statement from the American Heart Association (AHA)/National Heart, Lung, and Blood Institute (NHLBI) (4,10). Current ATP III criteria define metabolic syndrome as the presence of any three of the following five traits:

- Abdominal obesity, defined as a waist circumference in men ≥ 102 cm and in women ≥ 88 cm ;
- Serum triglycerides ≥ 150 mg/dL or drug treatment for elevated triglycerides;
- HDL cholesterol < 40 mg/dL in men and < 50 mg/dL in women or drug treatment for low HDL cholesterol;
- Blood pressure $\geq 130/85$ mmHg or drug treatment for elevated blood pressure;
- Fasting plasma glucose ≥ 100 mg/dL or drug treatment for elevated blood glucose.

STATISTICAL ANALYSIS

Data was collected in frequency and contingency tables. Data distribution was studied through the Kolmogorov Smirnov test. Central tendency was expressed in mean and standard deviation (SD) for parametrical data and median and interquartile range (IQR) for non-parametric data. Comparison studies were carried out through Fisher and chi-squared test when data were nominal and Mann Whitney and unpaired t test when data were numeric. Correlation studies were carried out through the Spearman test.

Data that showed association/correlation with $p < 0.1$ with MS in univariate analysis were further studied through logistic regression (MS as dependent variable) to access the variables independence.

The adopted significance level was 5%. Calculations were done with the help of the software Medcalc 12.0.

RESULTS

Pairing data and sample description:

In the 97 psoriasis patients, 48/97 (49.4%) were female with age range between 20 and 80 years old (median=52; IQR=42-59 years); in the 97 individuals from the control group, 49/97 (50.5%) were female (p=0.94); with age range between 20 and 81 years old (median=52; IQR=31.5-60; p=0.44).

In the psoriasis group, the age of disease onset varied from 6-72 years old (mean 30.9±16.2 years) and the disease duration was of 1-43 years (median 13.0; IQR=8-21.5 years). Tobacco exposure was found in 61.8% of them. Tobacco use was more common in psoriasis patients (28.8% smokers and 32.2% former smokers) than controls (6.2% smokers and 23.7% former smokers) with p<0.0001.

In 81/97 (83.5%) the psoriasis was in plaques; in 10/97 (10.3%) it was gutatta; in 5/97 (5.1) it was pustular, in 4/97(4.1%) involved genital area; in 33/97 (34.0%) involved scalp; in 10/97 (10.3%) had articular involvement. Nail involvement was found in 27/97 (27.8%) ranging from 1 to 20 fingers (median 5.0; IQR=2-12). PASI varied from 0 to 49.8 (median=3.4; IQR=1.6-10.0). This sample was treated with cyclosporine in 3.0%; acitretin in 7.2%; methotrexate in 28.8%; ustekinumab in 7.2% and anti TNF-α drugs in 17.5%. About 34.0% used just topical treatment.

Comparison of psoriasis patients and controls according to metabolic profile:

The MS prevalence, its components as well as its cardiovascular repercussions in the psoriasis group compared with controls are shown in **Table 1**. In this table, it is possible to see that psoriasis patients had higher rate of MS, higher BMI and waist circumference, higher systolic blood pressure and glucose level, lower HDL cholesterol and higher number of individuals with angina pectoris.

Comparison between psoriasis patients with and without MS:

When psoriasis patients with and without MS were compared, we noticed that those with MS were older, had higher exposure to tobacco, disease onset at older age and tendency towards less involvement of scalp as shown in **Table 2**.

When psoriasis variables associated with MS with p <0.1 were studied through logistic regression, age (OR=1.08; 95% CI=1.06-1.16) and scalp involvement (OR=0.23; 95%CI=0.06-0.87) were independently related to MS.

DISCUSSION

The results of the present study have shown that psoriasis patients from our region have 1.8 times

TABLE 1 - COMPARISON OF METABOLIC SYNDROME, ITS COMPONENTS AND ITS CONSEQUENCES BETWEEN PSORIASIS PATIENTS (N=97) AND CONTROLS (N=97).

Variable	Psoriasis patients	Controls	P
Metabolic syndrome - n (%)	48/97 (49.4)	34/97 (35.0)	0.04* §
Mean body mass index and SD - (kg/m ²)	28.4±5.09	26.8±4.68	0.02*
Median systolic blood pressure and IQR - (mm Hg)	130(120-140)	120(110-130)	0.007**
Median diastolic blood pressure and IQR - (mm Hg)	80 (70-90)	80 (70-90)	0.99**
Median waist circumference and SD (cm)	99 (92-108)	94 (86-104)	0.003#
History of hypertension - n (%)	37 (38.1)	43 (44.3)	0,38*
History of dyslipidemia- n (%)	23 (23.7)	23 (23.7)	1.00*
History of diabetes mellitus	10 (10.3)	10 (10.3)	1.00*
History of angina pectoris	18 (18.5)	8 (8.2)	0.003*§§
History of stroke	0	1 (1.03)	1.00##
History of myocardial infarction	4 (4.1)	5 (5.1)	1.00*
Median fasting blood glucose and SD (mg/dL)	89 (80-98.5)	91.7 (87-101)	0.04##
Median total cholesterol and IQR (mg/dL)	181(160-203)	180(160-212)	0.52**
Median HDL cholesterol and IQR (mg/dL)	42 (37.0-50.5)	47 (39.0-59.5)	0.01**
Median LDL Cholesterol and IQR (mg/dl)	196.4(84-129.9)	104 (86-126)	0.37 **
Median triglycerides and IQR (mg/dL)	118 (78-164.5)	119.2(87-168)	0.39**

*- chi squared test; ** Mann Whitney test; # unpaired t test; ## - Fisher test; SD= standard deviation; IQR= interquartile rate;n=number. § - OR = 1.8 (95%CI=1.02-3.23); §§ - OR=2.5, 95%CI=1.04-6.15).

more chances of having MS than controls, a result similar to the findings of a meta-analysis done by Armstrong et al² that included 41,853 patients. When comparing psoriatic patients with controls, the MS components that predisposed to this finding were body weight, waist circumference and high systolic blood pressure. Low HDL cholesterol and higher glucose levels were also a finding. Studies of the relationship between the individual components of MS with psoriasis are contradictory. Madanagobalane and Anandan³ reported a higher prevalence of obesity in psoriasis patients than in controls as we did, but Nisa and Qazi¹¹, contrasting with our findings, did not observe a difference in the occurrence of central obesity. Finding a higher prevalence of central obesity is important in this context because it has become clear that the distribution and function of adipose tissue, rather than the amount of fat per se, exerts an important impact in MS.¹² A strong genetic component influencing fat distribution has been described and

may be responsible for the contradictory findings in populations with different ethnic backgrounds.¹³

Hypertension is another component of MS. While some studies have shown an association between hypertension and psoriasis, others have not^{3,14-18}. In our study, the number of patients with hypertension was the same in controls and psoriasis but systolic blood pressure was higher in the psoriatic group.

Low HDL serum levels contribute to cardiovascular risk in this context as this particle has multiple anti-atherogenic properties.^{15,19} Low serum HDL level may result in decreased activity of lipoprotein lipase, secondary to insulin resistance²⁰. HDL anti-atherogenic properties are believed to be mediated by its role in the elimination of cholesterol from macrophages in a mechanism called "macrophage cholesterol efflux".¹⁹ It also hinders the thrombotic component of atherosclerosis²¹ and helps maintain the endothelial function.²² Its serum levels are inversely related to stroke risk, need for coronary revascular-

TABLE 2 - COMPARISON OF PSORIASIS PATIENTS WITH (N=48) AND WITHOUT (N=49) METABOLIC SYNDROME (MS).

Variable	With MS	Without MS	P
Gender (female/male)	23/25	25/24	0.75 *
Mean age and SD (years)	54.9±10.6	45.9±13.3	0.0004#
Median age at disease onset and IQR (years)	44 (33-63)	31 (16-43.5)	0.002**
Median disease duration and IQR (years)	12(4.5-22.5)	13 (8-21.5)	0.72**
Ethnic background (A/C)	6/42	9/40	0.57*
Tobacco users - n (%)	35 (72.9)	25 (51)	0.02*
Median ESR and IQR (mm)	25 (10-42)	20 (9-33)	0.39**
Median CRP and IQR (mg/dL)	11.6 (6-17.5)	9.5 (5,2-19.3)	0.65**
Mean uric acid and SD (mg/dL)	5.2±1.1	4.9±1.1	0.14#
Presence of nail psoriasis - n (%)	16 (33.3)	12 (24.4)	0.33*
Median number of involved nails and IQR	5 (3.2-11.2)	6 (2-12)	0.76###
Vulgar psoriasis - n (%)	40 (83.3)	41 (83.6)	0.96*
Psoriasis guttata - n (%)	3 (6.2)	7 (14.2)	0.31 ###
Pustular psoriasis - n (%)	4 (8.3)	1 (2.0)	0.20###
Genital involvement - n (%)	1 (2.0)	3 (6.1)	0.61 ##
Scalp involvement - n (%)	12 (25)	21 (42.8)	0.06 *
Articular involvement - n (%)	5 (10.4)	5 (10.2)	1.0 ##
Median PASI and IQR	3.4(1.2-7.3)	3.5(1.6-10.0)	0.51**
Treatment			
Cyclosporine - n (%)	1 (2.0)	2 (4.0)	1.0 ##
Acitretin - n (%)	4 (8.3)	3 (6.1)	0.71 ##
Methotrexate - n (%)	16 (33.3)	12 (24.4)	0.33*
Ustekinumab - n (%)	2 (4.1)	5 (10.2)	0.43###
Anti TNF- α - n (%)	8 (16.6)	9 (18.3)	0.82*
Only topic treatment - n (%)	16 (33.3)	17 (34.6)	0.88*

* - chi squared test; ** Mann Whitney test; # unpaired t test; ## - Fisher test; SD= standard deviation; IQR= interquartile rate; n=number; ESR= erythrocyte sedimentation rate; CRP= S reactive protein; A/C= Afrodescendants/Caucasians; PASI =Psoriasis Area Severity Index.

ization, myocardial infarction and death from cardiovascular causes.^{15,19} Beneficial effects of psoriasis treatment on HDL composition and function were observed in a small uncontrolled study.²³

Smoking habits have a close relationship with psoriasis: it is associated with higher prevalence and severity of this skin disease.²⁴ The present study shows that, not only psoriasis patients smoke more than controls, but also that the prevalence of this practice was more common in psoriatic patients with MS. This practice certainly worsens the scenario. Smoking increases levels of triglycerides (TG) and lowers HDL cholesterol²⁵; it also releases large amounts of free radicals causing oxidative stress.²³ Smokers were found to have the largest waist circumference and reduced insulin sensitivity.²⁶ The effect of smoking on metabolic disorders lasts up to 20 years after quitting the habit.²⁷

Several authors have noted an association of progression of skin involvement^{2,3,28} and presence of the arthropathic form²⁹ with SM. In our sample, it was not possible to link the presence of MS neither with the extension of the skin disease nor with articular manifestations. Our sample of patients with psoriatic arthritis was small and may not have had the strength to prove such association. Psoriatic arthritis occurs in 33% of psoriasis patients in our region³⁰ but it was present in roughly 10% of the studied sample. Concerning the occurrence of MS, according to the degree of skin involvement, it is important to note that categorizing severity of disease based on the percentage of affected body surface area may be a poor marker of the degree of systemic inflammation¹⁸, especially when all types

of psoriasis are studied together. Most studies in the literature were done exclusively in patients with psoriasis vulgaris not including others forms as we did.

A curious feature in the present analysis was the negative association of scalp psoriasis with MS. In our sample, only one patient had isolated scalp involvement; all others had association with plaque psoriasis. We did not find data from others studies to compare with and this finding is a contribution of the authors to this issue.

In the current study, it was also not possible to prove that the medications used for treatment modified the scenario, including the use of biologic agents. Biological drugs may have a beneficial effect in this context³¹. The low sample number may have precluded this finding.

This is a transversal study with a small number of patients and all the limitations that this type of study has but it does show the urgent need for a holistic view in the care of psoriatic patients.

Concluding, in the studied sample, MS prevalence is high in the psoriasis patients and findings that deserve more attention are central obesity, low HDL, hypertension and smoking habits. As psoriasis is quite a common disease, with estimated prevalence of 2.5% in the general population in our country³², this brings a great opportunity for the dermatologist to act as a transforming agent by improving the survival rate of this group of patients.

CONFLICT OF INTEREST

None.

RESUMO

OBJETIVO: Estudar a prevalência de SM (Síndrome metabólica) em pacientes com psoríase de nossa localidade, assim como a influência das variáveis da psoríase no seu aparecimento.

MÉTODOS: Noventa e sete pacientes com psoríase foram estudados para SM e comparados com 97 controles. Dados sobre o tipo de psoríase, envolvimento de unhas e extensão da lesão cutânea medida pelo PASI (Psoriasis Area and Severity Index) foram obtidas por meio de exame físico. Dados de infarto do miocárdio, angina pectoris e acidente vascular cerebral prévios foram coletados por meio de revisão de prontuários e questionamento direto.

RESULTADOS: A comparação da prevalência de SM em pacientes com psoríase (49,4%) com controles (35,0%) apresentou diferença com $p = 0,04$; OR = 1,8 (IC95% = 1,02-3,23). Pacientes com psoríase apresentaram maior índice de massa corporal ($p = 0,02$), maior pressão arterial sistólica ($p = 0,007$), menor colesterol HDL ($p = 0,01$), maiores valores de glicose ($p = 0,04$), maior circunferência da cintura ($p = 0,003$) e mais angina pectoris ($p = 0,03$; OR = 2,5; IC95% = 1,04-6,15) do que controles. Quando os pacientes de psoríase com e sem SM foram comparados entre si, aqueles com SM eram mais velhos ($p = 0,0004$), apresentaram início da doença em idade mais avançada ($p = 0,02$), tinham maior exposição ao fumo ($p = 0,02$) e tendência a ter menor envolvimento no couro cabeludo ($p = 0,06$) quando comparados com os sem SM na análise univariada. A regressão logística mostrou que apenas a idade e o envolvimento do couro cabeludo foram independentemente associados à SM na amostra de psoríase.

CONCLUSÃO: Na presente amostra de pacientes com psoríase, a prevalência de SM é alta e os itens que merecem mais atenção são obesidade central, baixo HDL, hipertensão e hábito de fumar. No grupo da psoríase, a SM foi associada de forma independente com idade mais avançada e menor envolvimento no couro cabeludo.

PALAVRAS-CHAVE: Psoríase. Síndrome metabólica. Doenças metabólicas.

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