ORIGINAL RESEARCH

Metabolic Syndrome in Psoriasis and Psoriatic Arthritis in a Mixed Race Population: Comparison of Their Prevalences

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Background: There is a growing body of evidence suggesting the association between psoriasis (PsO) and psoriatic arthritis (PsA) separately with metabolic syndrome (MS) in different populations. The literature is relatively scarce in terms of comparing the prevalence of MS in PsO and PsA with controls without systemic inflammatory diseases.
Objective: We aimed to assess the prevalence of MS among patients with PsO, PsA, and a control group without systemic inflammatory disease, in addition to investigating the risks of MS occurrence and its different components in each group.
Methods: This is a cross-sectional case-control study with three groups of patients: PsO, PsA, and control. The diagnosis of MS was defined according to the modified 2009 NCTEP ATP III criteria. Patients underwent thorough physical examination and fasting blood samples.
Results: A total of 195 patients were included in this analysis (PsO = 50; PsA = 64, and controls = 81). The prevalence of MS in the control, PsO, and PsA groups was 37%, 56%, and 57.8%, respectively (p < 0.001). Waist circumference (p = 0.013) and arterial hypertension (p < 0.001) were the most significant components of MS in patients with PsO and PsA. Multivariate analysis confirmed an independent risk of MS in women, elderly patients, obese patients, patients with hyperglycemia, and patients with psoriasis, especially PsA (OR = 6.2 [CI 95% 2.4–16.2], p < 0.001).
Conclusion: MS is more prevalent in patients with PsA, which can be determined by the increase in inflammatory pathways.
Keywords: metabolic syndrome, obesity, prevalence, psoriasis, psoriatic arthritis

Introduction

Psoriasis (PsO) is a chronic, immune-mediated, inflammatory disease with an important genetic predisposition, which may be expressed by skin lesions, joint disease, or both. It affects about 2 to 3% of the world's population.[1–4] Approximately 30% of patients might have joint disease, which is characterized by chronic inflammation of the peripheral and axial joints leading to an inflammatory type of arthritis, called psoriatic arthritis (PsA).[4–6] Cutaneous involvement generally precedes articular disease in about 10 years, especially in patients affected by moderate to severe PsO who are at increased risk of developing arthritis.[5,7]

Several studies have shown the relationship between psoriasis and metabolic syndrome (MS), which encompasses a set of cardiovascular risk factors, such as central obesity, altered glucose metabolism, systemic arterial hypertension (SAH), and dyslipidemia, thereby conferring an overall increase in mortality in comparison to the general population.[8] The prevalence of MS may vary in different populations around the world according to the criteria used, but it is estimated that a quarter of the world's population is affected by the condition.[9]

123

MS is significantly more prevalent in PsO affecting 30% to 55.9% of the studied patients.[10–15] In general, the diagnosis of PsO increases by twice the risk of MS development.[11,16] Considering that PsA confers an exacerbated systemic inflammatory state,[17] it would be expected to increase the risk of MS. However, the literature is relatively controversial on this issue with an estimated prevalence of 46% and an increased risk of 1.66 times for MS development in PsA.[18]

Studying the prevalence of MS in patients with PsO and PsA, in comparison to a control group without systemic inflammatory diseases is relatively scarce in the literature. In this study, we aimed to assess the prevalence of MS among patients with PsO, PsA, and a non-inflammatory control group, in addition to investigating the risks of MS occurrence and its different components in each group.

Methods

Study Design, Setting, and Participants

Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist was used for the preparation of this manuscript.[19] This study was carried out by the tenets of the Declaration of Helsinki and was approved by the institutional research ethics board (CAAE 01001218.1.0000.5257/2018). Written informed consent was obtained from all patients. This is a prospective cross-sectional case-control study from the dermatology outpatient clinic of the Clementino Fraga Filho University Hospital/ Federal University of Rio de Janeiro. Three groups of patients were included from January 2019 to March 2021. Inclusion criteria were patients aged between 30–74 years old with a confirmed diagnosis of PsO for more than 10 years, a second group of patients affected by PsA (CASPAR criteria), and a control group, which was randomly selected from our outpatient clinic.

Exclusion criteria for patients and controls comprised previous symptomatic or asymptomatic coronary heart disease, previous stroke, and other systemic inflammatory diseases, such as hidradenitis suppurativa, systemic lupus erythematosus, and rheumatoid arthritis, among others. Controls who have had the diagnosis or those having first-degree relatives with the diagnosis of PsO were excluded.

Data Collection and Variables

Patients were evaluated clinically by an experienced medical team in dermatological diseases. The interviews were carried out on a face-to-face basis with a structured questionnaire, in which patients were questioned about their medical and family history, current and past medications, as well as their comorbidities. The diagnosis of PsO was clinically determined, and occasionally by skin biopsy. PsO physical severity was assessed by Psoriasis Area and Severity Index (PASI) scores. Patients with a PASI score > 10 were enrolled for systemic therapy.[7] The diagnosis of PsA was performed in patients who fulfilled the classification criteria (CASPAR).[20]

Blood pressure was measured with an adequate cuff size suitable for arm circumference after 10 minutes of resting. Bodyweight, body height, and waist circumference were also measured. Overweight and obesity were defined by a body mass index (BMI) between 25 and 30 kg/m^2 and greater than 30 kg/m^2, respectively. Besides BMI, we used waist circumference as a parameter for obesity, since BMI does not consider differences between genders and body composition, which might exclude those within the weight range adequate for height, but with excessive centripetal abdominal fat.[21]

Fasting blood within the last six months was taken for assay of glucose, and lipid levels (high-density lipoprotein [HDL], and triglycerides). MS was defined according to the modified 2009 NCTEP ATP III criteria.[22] Criteria comprised the occurrence of three or more of the following: 1) fasting blood sugar over 100 mg/dL (or under treatment for hyperglycemia); 2) blood pressure over 130/85 mmHg (or under treatment for hypertension); 3) fasting triglyceride levels over 150 mg/dL (or under treatment for hypertriglyceridemia); 4) fasting HDL cholesterol levels less than 40 mg/dL (men) or 50 mg/dL (women) (or under treatment for dyslipidemia), and 5) waist circumference over 102 cm (men) or 88 cm (women).

Statistical Analysis

For categorical variables, such as blood pressure, and fasting HDL cholesterol, glucose, and triglyceride levels, as well as waist circumference, and BMI, descriptive statistics were used to summarize proportions, and mean ± standard deviation.

The Student's *t*-test and the Chi-square test were used to compare differences and associations between the three groups (PsO, PsA, and control group). Uni- and multivariate logistic regression models were used to calculate the odds ratio (Odds Ratio [OR]). Univariate statistical tests were initially tested for each variable. By convention, only predictors with $p < 0.20$ are entered into the multivariate logistic models. Data analysis was performed using SPSS 22.0 software (Statistical Package for the Social Science [SPSS Inc., Chicago, IL, USA]). A significance level of 5% was considered significant.

Results

Descriptive and Outcome Data

This cross-sectional study included 195 patients (control group, n = 81; PsO = 50; and PsA = 64). The main demographic characteristics are detailed in Table 1. The main reasons for seeking medical care in the control group were actinic (10 patients, 12.3%) and seborrheic (8 patients, 9.9%) keratoses; basal cell carcinoma (7 patients, 8.6%), and soft fibroma (7 patients, 8.6%). The female-to-male ratio was 45/36, 22/28, and 43/21 in the control group, PsO and PsA (p = 0.046), respectively. Patients in the control group were significantly younger (p = 0.043), even though they were distributed in the sixth decade of life in all studied groups.

Waist circumference and BMI were significantly higher in PsA (p = 0.013, p = 0.05, respectively), while the occurrence of arterial hypertension was significantly higher in PsO (p < 0.001). No significant differences were observed in fasting HDL, glucose, and triglyceride levels between the groups. The use of immunosuppressants and/or immuno-biologic agents was significantly higher in PsA (p < 0.001).

Table 1 Patient Demographics.*

Characteristics	Control	PsO	PsA	*p-value*
Gender (n;%)				
Female	45 (55.6)	22 (44.0)	43 (67.2)	0.046
Male	36 (44.4)	28 (56.0)	21 (32.8)	
Age (yr.; Mean ± SD)	53.3 (11.5)	55.2 (13.4)	57.9 (10.9)	0.043
Race (n;%)				
White	40 (49.4)	22 (44.0)	35 (55.6)	0.414
Black	7 (8.6)	9 (18.0)	8 (12.7)	
Interracial	34 (42.0)	19 (38.0)	20 (31.7)	
Immunosuppressants (n;%)				
None	81 (100)	19 (38)	7 (10.9)	<0.001
Immunobiologic agents	0	8 (16)	38 (59.4)	
Mtx	0	26 (52)	45 (70.3)	
Both	0	3 (6)	27 (42.9)	
Waist Circumference (n;%)				
Normal	33 (46.5)	17 (34.7)	14 (22.2)	0.013
≥ 88 cm (women) e 102 cm (men)	38 (53.5)	32 (65.3)	49 (77.8)	
BMI (n;%)				
Normal	26 (32.1)	20 (40)	10 (15.7)	0.05
Over 25	32 (39.5)	15 (30)	30 (46.9)	
Over 30	23 (28.3)	15 (30)	24 (37.5)	
Blood Pressure (n;%) (mmHg)				
Over 130/85 or under treatment	30 (37.0)	36 (72.0)	39 (60.9)	<0.001
Fasting glucose over 100 mg/dL (n;%)	25 (31.3)	22 (44.0)	29 (45.3)	0.165
Fasting triglyceride over 150 mg/dL (n;%)	17 (22.4)	20 (40.0)	19 (29.7)	0.105
Fasting HDL (mg/dL) (n;%)				
Women under 50 and men under 40	25 (32.1)	22 (44)	17 (26.6)	0.140

Notes: * BMI – body mass index; cm – centimeters; HDL – high-density lipoprotein; Mtx – Methotrexate; PsA – psoriatic arthritis; PsO – psoriasis; SD – standard deviation.

Main Results

Overall, ninety-five patients were diagnosed with MS (48.7%). The prevalence of MS was significantly higher in PsA (57.8%), compared with the control group (37%), and the PsO group (52%) (p < 0.001) (Table 2). In the univariate analysis, multiple demographic characteristics were significant for the occurrence of MS, including gender (female), age, BMI, and hyperglycemia. Women were 2.3 times more likely to develop MS than men (p = 0.007). Advancing age (per year) increased by 5% the risk of developing MS (p < 0.001). In addition, there was an increase of 4.6-fold in the risk of MS for every one-unit increase in BMI (p < 0.001). Hyperglycemia was also associated with a higher prevalence of MS (OR 8.53 [IC 95% 4.03–18.1, p < 0.001]).

The multivariate models confirmed gender (female), age, BMI, and hyperglycemia as independent predictors for the occurrence of MS. It is worth mentioning that the diagnosis of PsO and PsA per se was also independently correlated with a higher prevalence of MS when compared to controls (OR 2.44 [IC 95% 1.05–5.69, p = 0.038]; OR 6.23 [IC 95% 2.4–16.2, p < 0.001], respectively) (Table 3).

Discussion

Key Results

In this study, we observed a significantly higher prevalence of MS in the patients affected by PsA, compared to patients with PsO and controls. A closer look at the different components of MS revealed a significantly higher prevalence of obesity and hypertension, especially for PsA and PsO, respectively. It is worth noting that 62% of patients with PsO and approximately 90% of patients with PsA were classified as having moderate to severe disease because they were under systemic treatment with immunobiologic agents, methotrexate, or both. In the univariate analysis, multiple demographic

Table 2 Metabolic Syndrome Prevalence Among Different Groups.*

| | Groups | | | | | | Total | |
| | Control | | PsO | | PsA | | | |
	n	%	n	%	n	%	n	%
Metabolic Syndrome								
Yes	30	37.1	28	52	37	57.8	95	48.7
No	51	62.9	22	48	27	42.2	100	51.3
Total	81	100	50	100	64	100	195	100

Notes: * n - number of patients; PsA – psoriatic arthritis; PsO – psoriasis.

Table 3 Metabolic Syndrome Predictive Factors.*

	Odds Ratio (OR)	CI 95%	P value	Odds Ratio (OR)	CI 95%	P value
Female (ref: male)	2.33	(1.26–4.33)	0.007	2.23	(1.09–4.54)	0.028
Age, per unit increase	1.05	(1.02–1.08)	<0.001	1.04	(1.00–1.07)	0.034
Race (ref: white)						
Black	1.06	(0.42–2.73)	0.879	—	—	—
Mixed-race	0.78	(0.41–1.51)	0.465	—	—	—
Asian	0.35	(0.20–3.46)	0.369	—	—	—
BMI, per unit increase	4.61	(2.09–10.2)	<0.001	4.07	(1.64–10.1)	0.003
Hyperglycemia (ref: no hyperglycemia)	8.54	(4.03–18.1)	<0.001	5.93	(2.64–13.3)	<0.001
Study group (ref: controls)						
Psoriasis	—	—	—	2.44	(1.05–5.69)	0.038
Psoriatic Arthritis	—	—	—	6.23	(2.40–16.2)	<0.001

Notes: * BMI – body mass index; CI – confidence interval; ref – reference.

characteristics were significant for the occurrence of MS, namely female gender, age, BMI, and hyperglycemia. In the multivariate model, all of these characteristics and the diagnosis of PsO or PsA were confirmed as independent risk factors associated with MS development.

Interpretation and Generalization

The association between PsO or PsA with MS is relatively well established in the literature, considering that numerous studies have separately identified this correlation.[10–15,18,23,24] On the other hand, literature is relatively scarce in identifying the prevalence of MS and its components among PsO, PsA, and a control group without systemic inflammatory disease. It would be expected a higher occurrence of comorbidities in PsA, would confer greater cardiovascular and metabolic risks. Besides, the concept of "psoriatic march" has been proposed to explain the effect of PsO severity on the development of cardiovascular diseases and MS.[25]

Our study advances the understanding by comparing the prevalence of MS and its different components in each group individually. Previous studies have mostly used patients with PsO or arthritis rheumatoid, as a control group.[26,27] Choosing an adequate control group is of utmost importance, considering that joint inflammation superimposed on skin inflammation confers a significant change in the systemic inflammatory state which can ultimately modify cardiovascular risk.[28]

In our PsA group, we observed a significant prevalence of female patients with advancing age in comparison to PsO and controls. This is in line with previous observations that menopausal women have imbalanced sexual hormones, influencing the development of obesity, insulin resistance, diabetes mellitus, systemic blood hypertension, and MS.[25] The age factor should be analyzed, not only in the context of advancing age per se but also could indirectly represent the time of inflammatory exposure. Gisondi et al demonstrated an association between longer PsO duration and a higher prevalence of MS, mostly because of a long-lasting inflammatory state.[12] These results are supported by an Indian study that showed a greater prevalence of MS in older psoriatic patients.[29]

In general, PsO is a recognized disease of Caucasians. Even though race had no impact on MS prevalence in our studied population, it is important to emphasize that Brazil is a continental country with a heterogeneous population, in terms of the ethnic composition that considers local distinct colonizations. On the other hand, it should be noted that there is a dissociation between skin color and ancestry and the influence of environmental issues. In Brazil, PsO is more prevalent in the South and Southeast,[30] having a similar distribution among whites, blacks, and interracials.[31]

Regarding obesity, we observed a significantly higher prevalence in PsA in comparison to the other two groups, both in waist circumference and BMI. On the other hand, it is important to note that waist circumference better reflects the distribution of fat body weight compared to BMI.[6] Corroborating our findings, a systematic review that included 201,831 patients with PsO demonstrated a greater risk of obesity, which could be even higher in patients with severe PsO.[16] Obesity also affects PsA patients, in the way that higher occurrence was found (22.68%), in comparison to PsO (16.75%).[32] Our obesity rates were three to four times higher, which can be reflected by our research scenario in a tertiary referral hospital, while that study used only patients from health primary attention.

The next relevant MS component in our study was hyperglycemia. Although it was similarly distributed among groups, it comprised an independent risk factor for the development of MS in multivariate analysis. This is a well-established risk factor in the literature for the occurrence of MS, especially in severe PsO and PsA.[33]

Psoriasis, Psoriatic Arthritis, and Metabolic Syndrome

As aforementioned, the association of MS with PsO and PsA was previously demonstrated in the literature. Overall, the prevalence of MS in PsO is up to 55.9% of the patients, while for PsA, the prevalence is even higher, reaching up to 59% of the patients.[14,24,34] Our findings are in line showing the occurrence of MS in 56% and 57.8%, respectively. Generally speaking, patients with PsO experience a 2–2.5 times greater risk of developing MS in comparison to the general population.[1,35] Our multivariate model indicated a greater risk of MS in women, in advancing age, in obese, and in patients with hyperglycemia. Of note, the diagnosis of PsO and PsA resulted in an independently increased risk of MS (OR = 2.44, p = 0.038; and OR = 6.2; p < 0.001, respectively).

These results support the hypothesis that joint inflammation confers additional risk for the development of MS and increased cardiovascular risk, in comparison to patients with PsO and the general population.[34] PsA has been considered a marker of severity in the PsO spectrum, with additional degrees of systemic inflammation.[36] Furthermore, a "dose-response" effect is relatively well known between MS and severe PsO.[1,36,37] In our study, about 60% of patients with PsO and 90% of patients with PsA met the criteria for moderate to severe disease because of the need for systemic medication. On the other hand, Bostoen et al found a significantly higher prevalence of MS in patients with PsO (44.9% vs 25.5% in PsA) and attributed their results to the use of systemic treatment (40.8% and 81.8%, respectively), which could reduce the degree of inflammation justifying their findings.[26]

In general, immunobiologic agents could reduce the occurrence of comorbidities and MS, and ultimately the cardiovascular risk, by decreasing the inflammatory burden.[38] Patients using methotrexate also have a lower prevalence of hyperglycemia, obesity, dyslipidemia, and cardiovascular events, suggesting a protective effect of systemic treatment.[39]

In this regard, it is important to emphasize that obesity promotes a negative effect on the induction and maintenance of disease remission with systemic treatment, regardless of the type of treatment, both in PsO[40] and PsA.[41,42] In quantitative means, a recent meta-analysis with 11,873 patients showed a 50% higher risk of non-response to treatment with TNF-alpha inhibitors in patients with PsO and PsA (OR 1.57 [CI 95% 1.30–1.89]).[40] It is still unclear whether dose adjustment, which would be possible for some immunobiologic agents, such as infliximab, golimumab, and ustekinumab, would be related to a better response in obese patients.[39] Our results could appear initially conflicting, since waist circumference, BMI, and MS prevalence were significantly higher in PsA. On the other hand, a closer look at the prevalence of additional comorbidities in this group indicates that an even higher prevalence of MS would be expected in our PsO and PsA patients if they were not using systemic medication.

Limitations

First, there is a certain difficulty in classifying groups of patients with PsO and PsA, considering that the diagnosis of both diseases is clinical and there are no serological tests available for adequate distinction. Thus, less symptomatic patients in terms of joint disease could be erroneously included in the PsO group. To address this limitation, we included patients with long-lasting PsO diagnoses of more than 10 years. This interim would differentiate patients having fewer chances of developing arthritis over time.

Second, our study was carried out in a tertiary university hospital, which is a referral center for medium and high-complexity diseases. Therefore, our controls could be potentially more affected by comorbidities. In addition, mild PsO was diagnosed in solely one-third of the patients. Also, our sample size is small which limits generalizability. Third, the impact of the use of systemic immunosuppressive medications, such as methotrexate and immunobiologic agents, on the prevalence of MS cannot be excluded from our group. Also, methotrexate may be associated with an increased risk of liver disease, which could have some effect on the development of MS, while using immunobiologic agents could exert a protective effect, concerning cardiovascular risk.

Fourth, in our study, we did not assess sedentary lifestyle and routine physical exercises, which can contribute to both obesity and MS. In addition, eating habits and alcohol intake were not included in our analysis. Considering that our population mostly consisted of low socioeconomic levels, we could expect on beforehand an unbalanced diet and irregular practice of physical exercises. Finally, as this is a cross-sectional study, we cannot determine whether risk factors such as abdominal obesity, hypertension, dyslipidemia, and hyperglycemia occurred before PsO and PsA diagnosis or if they occurred in the context of these diseases.

Conclusions

The prevalence of MS was significantly higher in PsA, in comparison to PsO and controls. Moderate to severe disease criteria were met in about two-thirds of the patients with PsO, while patients affected by PsA were mostly under treatment with immunosuppressants. Patients in all groups had a consistent increase in waist circumference, reaching obesity levels according to BMI criteria in about a third. Gender, age, BMI, and hyperglycemia were confirmed in the

multivariate model as independent risk factors for the occurrence of MS. Of note, the diagnosis of PsO or PsA also carried an independent risk of MS development.

Data Sharing Statement

The data underlying this article cannot be shared publicly due to the privacy of individuals who participated in the study. The data will be shared on reasonable request to the corresponding author.

Acknowledgments

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest involved in the production of this manuscript.

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