Prevalence of Psoriatic Arthritis in a Large Cohort of Brazilian Patients with Psoriasis

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ABSTRACT. ***Objective.*** To determine the prevalence of psoriatic arthritis (PsA) in a large cohort of Brazilian patients with psoriasis (PsO) being seen at dermatology centers.

Methods. A multicenter study was conducted in 4 university dermatology clinics. In each center, consecutive patients with confirmed diagnoses of PsO were evaluated by a rheumatologist. Individuals were classified as having PsA according to the ClASsification criteria for Psoriatic ARthritis (CASPAR). Laboratory tests and radiographs were performed, as needed, based on the clinical judgment of the rheumatologist.

Results. A total of 524 patients with PsO were evaluated. The mean age was 48.5 ± 14.5 years, 50% were women, and the mean PsO duration was 15.4 ± 11.7 years. A diagnosis of PsA was documented in 175 patients (33%), of whom 49% were newly identified by the rheumatologist. Most individuals with PsA (72%) had peripheral involvement, 11% had isolated axial involvement, and 17% had both peripheral and axial involvement. Dactylitis occurred in 20% and clinical enthesitis in 30% of the patients. Laboratory and/or radiograph tests were necessary for a definitive diagnosis of PsA in 42 of 175 individuals (24%).

Conclusion. In our study, one-third of Brazilian patients with PsO, followed in dermatology settings, were diagnosed with PsA by a rheumatologist. Almost half of subjects with PsA had no previous diagnosis. A collaboration between dermatologists and rheumatologists is greatly needed to establish earlier PsA diagnoses and adequate multidisciplinary management. (J Rheumatol First Release March 1 2015; doi:10.3899/jrheum.140474)

Key Indexing Terms:
PSORIATIC ARTHRITIS PSORIASIS PREVALENCE

Psoriatic arthritis (PsA) is a manifestation of psoriatic disease that could affect up to 48% of patients with psoriasis (PsO)[1,2,3,4,5]. In the vast majority of cases, cutaneous involvement precedes PsA by more than 10 years[2], and the initial musculoskeletal manifestations can occur during followup at the dermatology clinic. Dermatologists managing PsO are well placed to identify PsA. However, they are usually not trained to perform musculoskeletal examinations and the diagnosis of PsA is based on clinical recognition of musculoskeletal inflammatory features[6]. Additionally, dermatologists might be more focused on managing cutaneous PsO and the presentation of PsA can be subtle or limited with a fluctuating course, making diagnosis even more difficult[3]. Different classification criteria have been used in epidemiological investigations so that the real prevalence of PsA among patients with PsO

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worldwide remains a matter of discussion[7,8,9]. Recent studies, applying the widely used ClASsification criteria for Psoriatic ARthritis (CASPAR)[6], have shown that the PsA incidence is increasing[10] and that a reliable prevalence value is about 30%[11]. In Brazil, the occurrence of PsA in patients with PsO is unknown; therefore, the aim of our study was to determine the prevalence of PsA among Brazilian patients followed at PsO dermatology clinics.

MATERIALS AND METHODS

A cross-sectional, multicentric study was conducted in dermatology settings at public university hospitals in 4 different states of Brazil: Universidade de Brasilia, Distrito Federal; Universidade Estadual do Rio de Janeiro, Rio de Janeiro; Universidade de São Paulo, São Paulo; and Universidade Federal de Uberlândia, Minas Gerais. At all 4 of these academic centers, regular cooperation between dermatologists and rheumatologists had been previously established. Over a 3-month period, from January to March 2011, all consecutive patients from each center with a confirmed diagnosis of PsO were invited to participate in our study after informed consent assignment and local ethical committee approval. All of the included patients were initially evaluated at the dermatology unit by a dermatologist who recorded their clinical manifestations related to cutaneous disease, including the Psoriasis Area and Severity Index (PASI) score[12]. Thereafter, on the same day, all of the patients were assessed by a rheumatologist who took a detailed medical history and performed a physical examination focused on musculoskeletal involvement, allowing for classification into 3 main groups: PsO only, PsO and osteoarthritis (OA) and/or chronic myofascial pain (CMP) syndrome, and PsA with or without OA and CMP. The diagnosis of PsA was established according to CASPAR criteria[6]. The Leeds Enthesitis Index was used to assess enthesitis clinically[13]. Dactylitis was reported as absent or present. Complementary laboratory and radiograph tests were used to define the diagnosis, as needed, according to the clinical judgment of the rheumatologist. Descriptive statistics were performed using the Student t test, Mann-Whitney U test, and binomial test as appropriate. The association of clinical variables (age, sex, PsO duration and type, nail involvement, PASI score, systemic treatment for PsO, PsA predominant pattern) with previous or new diagnosis of PsA was investigated using univariate and multivariate logistic regression. A level of 0.05 was considered significant.

RESULTS

Data related to epidemiological and dermatological characteristics of 524 patients with PsO from each center are presented in Table 1. Half of the patients were women with a mean age of 48.5 ± 14.5 years and a mean PsO duration of 15.4 ± 11.7 years. White ethnicity was the most prevalent at 71%, followed by mulatto at 20%, and black at 8%. Cutaneous involvement revealed that most of the subjects had plaque PsO (78.8%) with a mean PASI score of 8.2 ± 8.9 and almost 60% were receiving systemic treatment for their dermatological condition. Psoriatic nail involvement was found in 50.8% of the patients.

After a detailed clinical evaluation by the rheumatologist, including a meticulous anamnesis and physical examination, no rheumatic condition was observed in 233 patients with PsO (44.5%), while OA and/or CMP were documented in 116 (22.1%). A diagnosis of PsA was detected in 175 patients (33.3%), in association with OA and/or CMP in 38 (7.2%). In 42 of 175 patients (24%), laboratory and/or radiograph tests were performed to establish the diagnosis of PsA. Notably, a new diagnosis of PsA was established in our study, after rheumatological assessment, in 86 subjects with PsO (16.4% of the total and 49.1% of the patients with PsA). In 89 patients, our approach confirmed a previous PsA diagnosis; 63 (70.8%) of these were taking disease-modifying drugs as part of their PsA treatment. Concerning articular symptoms, most of the patients with PsA (72%) had isolated inflammatory peripheral involvement, whereas in 17%, peripheral disease was associated with axial manifestations, and a pure axial pattern was documented in 11%. Dactylitis (20%) and clinical enthesitis (30.2%) were quite frequent.

The comparison of patients with PsO with and without PsA revealed similar sex distributions and skin involvement characteristics. In contrast, the patients with PsA were older (50.6 ± 12.9 yrs vs 47.5 ± 15.2, p = 0.015), were less frequently of white ethnicity (78% vs 65%, p = 0 .017), and had a higher frequency of nail involvement (59.2% vs 46.8%, p = 0.008; Table 2). Interestingly, a multivariate regression model applied to the variables in Table 2 showed that male sex was a protective factor for PsA (OR 0.416, 95% CI 0.201–0.861, p = 0.018). The comparison with univariate analysis of previously and newly diagnosed patients with PsA showed that the former group had more predominant peripheral involvement (p = 0.01), longer cutaneous disease duration (p < 0.001), higher PASI scores (p = 0.005), and was more frequently receiving systemic treatment for PsO (p = 0.003). Predominant axial involvement was the only variable associated with a new PsA diagnosis (p = 0.01; Table 3). In a multivariate model, predominant peripheral involvement remained associated with a prior PsA diagnosis (OR 7.91, 95% CI 3.05–20.5, p < 0.001) while predominant axial involvement showed a strong negative association (OR 0.10, 95% CI 0.03–0.31, p < 0.001; Table 4).

DISCUSSION

We report herein, to our knowledge for the first time, a 33% prevalence of PsA in a large cohort of Brazilian patients with PsO, mostly associated with older age and nail involvement. The prevalence of inflammatory musculoskeletal manifestations in PsO is quite variable across the literature, which might be related to specific geographical characteristics of the disease, as well as to genetic backgrounds and the different criteria used for study population selection and for PsA case definition[8,9]. In our study, we chose to apply the CASPAR classification criteria for PsA case definition because these criteria are internationally agreed upon as a result of their high sensitivity (91.4%) and specificity (98.7%) in established disease[6] and their validity in early PsA[14]. To avoid selection bias, including PsO severity, we evaluated unselected consecutive patients with definitive diagnosis

Table 1. General and dermatological characteristics of the 524 psoriatic patients. Values are n (%) unless otherwise specified.

Characteristics	Total, n = 524	Brasilia, n = 148	Rio de Janeiro, n = 118	São Paulo, n = 104	Uberlândia, n = 154
Female	262 (50.0)	83 (56.1)	51 (43.2)	44 (42.3)	84 (54.5)
Age, yrs, mean (SD)	48.5 (14.5)	47.0 (13.4)	50.4 (15.7)	48.5 (15.9)	48.5 (13.52)
PsO duration, yrs, mean (SD)	15.4 (11.7)	16.3 (11.5)	17.3 (12.2)	16 (12.1)	12.5 (10.7)
PsO plaque	413 (78.8)	122 (84.1)	104 (88.1)	75 (72.1)	122 (72.7)
PsOgutate	27 (5.2)	9 (6.2)	5 (4.2)	3 (2.9)	10 (6.5)
PsOpalmoplantar	40 (7.6)	4 (2.8)	3 (2.5)	12 (11.5)	21 (13.6)
PsOpustular	21 (4.0)	5 (3.4)	1 (0.8)	8 (7.7)	7 (4.5)
PsOerithrodermic	19 (3.6)	5 (3.4)	4 (3.4)	6 (5.8)	4 (2.6)
PASI, mean (SD)	8.2 (8.9)	8.1 (6.9)	14.6 (11.3)	6.6 (7.5)	4.7 (6.7)
Nail involvement	266 (50.8)	70 (47.9)	63 (53.4)	69 (66.3)	64 (41.6)
Systemic treatment for PsO	301 (57.8)	76 (52.4)	97 (82.2)	79 (76.0)	49 (31.8)

PsO: psoriasis; PASI: Psoriasis Activity Severity Index.

Table 2. Comparison between patients with and without PsA. Values are n (%) unless otherwise specified.

Characteristics	PsA, n = 175	Non-PsA, n = 349	p
Age, yrs, mean (SD)	50.6 (12.9)	47.5 (15.2)	0.015
Female sex	92 (52.6)	170 (48.7)	0.405
PsO duration, yrs, mean (SD)	16.0 (11.0)	15.06 (12.0)	0.140
Ethnicity white	115 (65.7)	261 (74.8)	0.017
Ethnicity black	17 (9.7)	27 (7.7)	0.663
Ethnicity mulatto*	42 (24)	59 (16.9)	0.063
PsO plaque	138 (79.3)	275 (79.3)	0.987
PsOgutate	5 (2.9)	22 (6.3)	0.092
PsOpalmoplantar	11 (6.3)	29 (8.4)	0.415
PsOpustular	9 (5.2)	12 (3.5)	0.348
PsOerithrodermic	10 (5.7)	9 (2.6)	0.070
PASI score, mean (SD)	7.92 (8.6)	8.85 (9.5)	0.716
Nail involvement	103 (59.2)	163 (46.8)	0.008

* Asian ethnicity [1 patient (0.6%) in the PsA and 2 patients (0.6%) in the non-PsA group]. PsA: psoriatic arthritis; PsO: psoriasis; PASI: Psoriasis Activity Severity Index.

Table 3. Comparison of demographic and clinical features in 175 patients with previous and new diagnosis of PsA. Values are n (%) unless otherwise specified.

Characteristics	Previous Diagnosis, n = 89 (51)	New Diagnosis, n = 86 (49)	p
Age, yrs, mean (SD)	51.3 (13.8)	50.1 (11.9)	0.62
Female sex	47 (52.8)	45 (52.3)	0.94
PsO duration, yrs, mean (SD)	18.9 (9.9)	12.9 (11.2)	< 0.001
PsO plaque	75 (84)	65 (75.6)	0.23
PASI score, mean (SD)	10.6 (9.9)	7.1 (8.8)	0.005
Nail involvement	50 (56.2)	53 (61.6)	0.52
PsO systemic treatment	68 (76.4)	48 (55.8)	0.003
Predominant peripheral involvement, total 144	79 (88.8)	65 (75.6)	0.01
Predominant axial involvement, total 31	10 (11.2)	21 (24.4)	0.01

PsA: psoriatic arthritis; PsO: psoriasis; PASI: Psoriasis Activity Severity Index.

of PsO confirmed by the dermatologist and followed in dermatology clinics[5].

It is relevant to emphasize that Brazil is a continent-sized country with a heterogeneous population in which particular environmental and genetic differences are found. Therefore, carrying out our study in 4 centers located in different geographical areas was proposed to provide a representative picture for the whole country. To our knowledge, the only

Table 4. Statistical predictors of previous diagnosis of PsA by multivariate regression analysis*.

Characteristics	OR	95% CI	p
Age	1.01	0.98–1.04	0.458
Female sex	0.60	0.27–1.35	0.222
PsO duration	1.03	0.99–1.08	0.08
PsO plaque	1.09	0.99–1.21	0.093
PASI score	1.04	1.00–1.09	0.051
Nail involvement	0.60	0.281–1.29	0.195
PsO systemic treatment	1.69	0.76–3.77	0.193
Predominant peripheral involvement	7.91	3.05–20.5	< 0.001
Predominant axial involvement	0.10	0.03–0.31	< 0.001

* Values are expressed as OR with 95% CI in 175 patients with PsA comparing 89 previously diagnosed and 86 newly diagnosed during this study. PsA: psoriatic arthritis; PsO: psoriasis; PASI: Psoriasis Activity Severity Index.

data published on the prevalence of PsA in PsO in Brazil appeared in a 2012 paper by Carneiro, *et al* from Brasilia[15]. Based on the CASPAR criteria, a rheumatologist identified 47 PsA cases in 133 psoriatic patients (35%) followed up in a dermatology clinic. A new diagnosis was established in 17 (36%). These data were similar to ours, but importantly, about half of the patients in that study were included in the Brasilia series of our investigation. Three studies have been published on PsA epidemiology in other Latin American countries[16,17,18], but only 1 of them was conducted using a methodology comparable to ours[18]. The first, from the Andean Mountains of Peru, showed that PsA was present in the aboriginal population, identifying 16 PsA cases in 8191 patients attending an arthritis clinic[16]. The second, from Buenos Aires, Argentina, was based on health insurance data, and estimated the PsA prevalence in the general population and found 74 cases per 105 with an estimated incidence rate of 6.3 per 105 person-years[17]. The third and most recent study, also from Buenos Aires, Argentina, screened 100 consecutive, unselected patients with PsO attending a dermatology clinic, all of whom were evaluated by a rheumatologist[18]. Despite patient selection being quite similar to ours and the use of the CASPAR criteria, a PsA prevalence of only 17% was found, considerably lower than our estimate of 33%, which was in accordance with those reported in other studies conducted outside Latin America, using comparable methodologies and study populations[11,19]. In the PREPARE multicenter study (Prevalence of Psoriatic Arthritis in Adults with Psoriasis: an Estimate from Dermatology Practice) conducted in European and North American dermatology clinics, Mease, *et al* found a 30% prevalence of rheumatologist-diagnosed PsA in the 949 subjects with PsO screened[11]. Haroon, *et al* in Dublin, Ireland, diagnosed 29 patients with PsA among 100 subjects with PsO attending a dermatology clinic who had no known diagnosis of arthritis[19]. In contrast, confirming that genetic and environmental background is critical, 2 studies with similar methodologies but from Asian countries found a much lower prevalence of PsA. Only 5.8% out of 1928 consecutive Chinese patients[20] and 8.7% out of 1149 consecutive Indian psoriatic patients had PsA[21].

Other investigators have also described a lower prevalence, but in scenarios with different study population selection criteria[3,4,5]. Ibrahim, *et al* in the UK reported PsA in 13.8% of patients with PsO, although only a sample of patients with PsO selected by questionnaires was evaluated by a rheumatologist[4]. Reich, *et al* in Germany detected PsA in 20.6% out of 1511 patients with plaque-type PsO using the Moll and Wright criteria; in their study, the rheumatologist evaluated only patients who were referred by a dermatologist and who manifested joint symptoms, and spine involvement was not evaluated[3]. De Marco, *et al* in Italy in a 3-year study reported on 110 patients with PsA among 1200 patients with PsO followed at a PsO-dedicated dermatology clinic, and again, only a proportion of the subjects (23%) were referred by a dermatologist to the rheumatologist because of the presence of musculoskeletal complaints[5].

Our cohort of patients with PsA was similar to those found in the literature in terms of the 1:1 male-to-female ratio[1]. Plaque PsO was the most common cutaneous involvement (80%), similar to what has been found in other series worldwide[5,22,23,24], although the psoriatic nail involvement in 60% of our patients was lower than the 80% prevalence reported by other authors[23], but still similar to the 62% described by Mease, *et al* in their study[11]. In our series, nail involvement and older age were both associated with the development of arthritis ($p = 0.015$ and 0.008, respectively). White ethnicity was significantly correlated with the absence of arthritis (78% vs 65%, $p = 0.017$), while mulatto ethnicity, although not reaching statistical significance, was more frequent among patients with PsA (24% vs 17%, $p = 0.063$).

Interestingly, and in accordance with recent reports[22], the majority of our patients with PsA (72%) had isolated inflammatory peripheral involvement, 17% had peripheral and axial patterns, whereas only 11% manifested isolated axial disease. Similarly, Hoff, *et al* showed that 96.2% of their overall PsA cohort had peripheral involvement with a 26.9% concomitant presence of axial disease[25]. The prevalence rates of dactylitis and enthesitis have been quite variable across the literature because most studies have been cross-sectional; our estimates of 20% and 30%, respectively, were lower than those reported in longterm followup series[1,26], but similar to those observed in comparable studies[20,22,27].

It is important to emphasize that in our study, to establish a definite diagnosis of PsA, complementary laboratory and/or radiology examinations were requested by the rheumatologists in 24% of the patients. In our experience, this rate was in agreement with what is usually done in

clinical practice and it is particularly relevant in axial involvement definition. In addition, the CASPAR criteria includes 1 serologic item and 1 radiographic item[6]. In the PREPARE study, about 20% of the patients also had radiograph or laboratory test information; nevertheless, according to their analysis, a change in PsA diagnosis was found in only 3.8% and 1.2% of cases when radiograph and laboratory tests were, respectively, added to the rheumatological clinical evaluation[10].

A further relevant finding of our study was that, in our dermatology settings, almost half of patients who had PsA were not recognized and treated appropriately for joint disease, representing 16.4% of the whole PsO population. A substantial proportion of these subjects were at high risk for developing joint damage with impaired function and even reduced life expectancy[1,26]. Some recent studies have shown comparable or even worse figures. In the PREPARE study, Mease, *et al* reported that 41% of patients in the dermatology clinic identified by a rheumatologist as having PsA did not have a previous diagnosis of inflammatory arthritis[11]. More importantly, in the prospective, cross-sectional cohort study of Reich, *et al*, 85% of PsA diagnoses were made for the first time[3]. In the 2 studies from China and India, 92% and 83% of PsA cases, respectively, were newly diagnosed by a rheumatological evaluation[20,21].

Taken together, all of these data demonstrate the magnitude of PsA underdiagnosis in different dermatology settings worldwide, and therefore represent strong arguments for the need for a more intense collaboration between dermatologists and rheumatologists to achieve a timely and accurate diagnosis of PsA. In this sense, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis has broadly proposed that this goal could be achieved with the establishment of combined rheumatology/dermatology clinics or with specific training programs; this approach could also include the use of patient self-administered screening questionnaires that could help dermatologists to identify patients with a high probability of having PsA and who require rheumatology referrals[28]. Therefore, we aimed to determine which clinical elements could be associated with a delayed diagnosis of PsA in our PsO series. Notably, the presence of more prolonged and severe cutaneous disease and predominant peripheral involvement were associated with a previous PsA diagnosis. A study demonstrated a relationship between polyarthritis and previous PsA diagnosis[19]. Interestingly, predominant axial involvement was more frequent among patients with newly diagnosed PsA, as observed by other authors[19]. This finding suggests that, in some patients, the lack of attention for possible axial disease could be a reason for delayed diagnosis.

We recognize that our study has strengths along with some limitations. The major strengths were the following: (1) it was a multicentric study involving a big sample of patients in a continent-sized country with balanced centers and populations, and a unique diagnostic criteria for PsA; (2) all enrolled patients with PsO were consecutive subjects to avoid selection bias; and (3) the patients' clinical evaluations were performed by experienced rheumatologists who were well trained in this study protocol. In contrast, the limitations were the following: (1) partial information on musculoskeletal involvement was collected to keep the protocol simple; (2) imaging studies to confirm enthesopathies or OA diagnoses were performed only if considered necessary by the evaluating rheumatologist; and (3) all of the patients with PsO were under treatment for their skin disease, with a significant number receiving systemic medications that could have influenced skin and articular disease expression. Additionally, it was a cross-sectional study that might not reflect the true prevalence of PsA in patients with PsO.

We demonstrated a high 33% prevalence of PsA among our patients with PsO in different representative dermatology settings in Brazil. Importantly, half of these patients had not been previously diagnosed and properly treated. Therefore, our major effort must be to shorten the time until PsA diagnosis to allow for adequate and appropriate care and specific therapy to preserve functional capacity, reduce associated morbidity, and improve the quality of life of patients with PsA.

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