Curr Rheumatol Rep (2014) 16:438
DOI 10.1007/s11926-014-0438-3

Seronegative Arthritis in Latin America: A Current Review

Carla Gonçalves Schain Saad · Célio Roberto Gonçalves · Percival D. Sampaio-Barros

Published online: 15 July 2014
© Springer Science+Business Media New York 2014

Abstract In many Latin American countries seronegative arthritis, especially the spondyloarthritides (SpA), is commonly characterized by associated axial and peripheral involvement. In this article, the authors review the ethnic distribution of the population and the different SpA in 10 Latin American countries, and the main characteristics of the Ibero-American Registry of Spondyloarthropathies (RESPONDIA) compared with other international registries. The peripheral component of SpA is more frequent in mixed-race populations, whereas psoriatic arthritis is significantly more frequent in countries with predominantly white populations.

Keywords Spondyloarthritis · Ankylosing spondylitis · Psoriatic arthritis · Argentina · Brazil · Colombia · Mexico · Latin America · Seronegative arthritis · RESPONDIA · Reactive arthritis · Undifferentiated spondyloarthritis · Spondyloarthropathy · HLA-B27 · Prevalence

Introduction

Knowledge about the peculiarities of seronegative arthritis, especially the spondyloarthritides (SpA), in Latin American countries has increased because of the large number of articles published recently. Important aspects, for example the greater prevalence of peripheral involvement (even among patients with predominantly axial disease), the characteristics of the different SpA in countries with strong miscegenation (interbreeding involving persons of different races) with blacks and Amerindians, "female aspects" of SpA, and the importance of extra-articular manifestations, can now be discussed in the setting of newly published data. Different clinical and demographic aspects of Latin American SpA patients may be a consequence of the diverse processes of colonization observed in the last five centuries. This miscegenation may help explain the characteristics of SpA in countries with predominantly white populations (for example Argentina) and in those with highly miscegenated populations (for example Brazil, Colombia, and Mexico).

Psoriasis and psoriatic arthritis (PsA) are also important concerns in Latin American countries. Because both manifestations are prevalent in predominantly white populations, it seems that both the prevalence and incidence of psoriasis and PsA are lower in Latin America than in other parts of the world, for example Europe and the United States. PsA data from several Latin American countries presented at the 2010 Spondyloarthritis Research and Treatment Network (SPARTAN) meeting showed that although PsA is highly prevalent in countries such as Argentina (60.2 %), its prevalence is much lower in Brazil (13.7 %) and Guatemala (10 %). However, these data may be biased and may not accurately represent the frequency of psoriatic disease in each region, a matter that must also account for disease distribution based on ethnicity [1].

Because of this ethnic diversity, in this article the authors describe data from the Ibero-American Registry of Spondyloarthropathies (RESPONDIA), then present data from the individual countries.

RESPONDIA

The RESPONDIA registry has fostered study of the demographic characteristics of the Latin American population during the past decade, because many university centers in

This article is part of the Topical Collection on *Spondyloarthritis*

C. G. S. Saad · C. R. Gonçalves · P. D. Sampaio-Barros (✉)
Disciplina de Reumatologia, Faculdade de Medicina, Universidade de São Paulo, Av. Dr Arnaldo, 455 – 3°. Andar – Cerqueira César, São Paulo, SP, Brasil CEP: 01246-903
e-mail: pdsampaiobarros@uol.com.br

Argentina, Brazil, Chile, Costa Rica, Ecuador, Mexico, Peru, Uruguay, and Venezuela have used a standardized protocol, adapted from the Registry of Spondyloarthropathies of the Spanish Society of Rheumatology (REGISPONSER), for investigation of many patients classified as having SpA according to the European Spondyloarthropathies Study Group (ESSG) from 2006 to 2009.

A study comparing a large European series with 2,356 patients from the REGISPONSER and Belgian (ASPECT) registries with 1,083 Latin American SpA patients (from RESPONDIA) revealed a significantly higher frequency of peripheral arthritis (57 % vs 42 %) and enthesitis (54 % vs 38 %) in the Latin American patients, and a greater frequency of HLA-B27 positivity (83 % vs 71 %) among European patients. An assessment of extra-articular manifestations found greater prevalence of inflammatory bowel disease (IBD) in the European group (7 % vs 4.5 %), but there were no differences in the prevalence of uveitis or cutaneous psoriasis. With regard to treatment, except for the use of anti-tumor necrosis factor (anti-TNF) therapy (15 % in Europe vs 14 % in Latin America), all other medications were prescribed significantly more often for Latin American patients: nonsteroidal anti-inflammatory drugs (89 % vs 75 %), corticosteroids (19 % vs 8 %), methotrexate (MTX; 34 % vs 10 %), sulfasalazine (32 % vs 19 %), and anti-TNF + MTX (8 % vs 3.5 %) [2•]. In a study analyzing 847 Belgian (ASPECT), 1,405 Spanish (REGISPONSER), and 466 Ibero-American (RESPONDIA) SpA patients, hip disease also was more frequent among Latin American patients (36 % vs 24 %). Most patients requiring hip-replacement surgery in this series were included in the study. Functional status, measured by use of the Bath Ankylosing Spondylitis Functional Index (BASFI), was significantly worse among patients with hip involvement. The need for hip-replacement surgery was associated with early-onset, entheseal, and axial disease [3].

Extra-articular manifestations were analyzed in two studies from RESPONDIA. The first study analyzed 1,264 patients (1,072 with primary ankylosing spondylitis (AS), 147 with psoriasis, and 45 with IBD) and showed that primary AS was associated with a younger age at onset, male gender, inflammatory back pain, and sacroiliac pain, whereas psoriatic spondylitis was associated with dactylitis, enthesitis, and peripheral arthritis; functional capacity, disease activity, and quality of life were comparable among the different groups [4]. The second study investigated anterior uveitis in a group of 2,012 patients in 85 centers in 10 Ibero-American countries. The occurrence of anterior uveitis (in 372 patients; 18.5 %), was associated with inflammatory low back pain, radiographic sacroiliitis, enthesopathies, urethritis and/or acute diarrhea, balanitis, hip involvement, HLA-B27 positivity, and higher C-reactive protein (CRP) levels. Another interesting aspect was the negative association with the number of painful and swollen peripheral joints, PsA, psoriasis, nail involvement, and dactylitis (trend). No association with gender, race, or disease indices (activity, functionality, and quality of life) was observed. Logistic regression showed that AS ($P=0.001$) and HLA-B27 positivity ($P=0.083$; trend) were significantly associated with anterior uveitis, whereas extra-articular manifestations (predominantly psoriasis) were negatively associated ($P=0.016$) [5].

The different aspects of SpA in RESPONDIA participants from Ibero-American countries are described in a recent review [6].

Argentina

With approximately 40 million inhabitants, Argentina has a predominantly white population (86.4 %, of Spanish and Italian origin), with 13.6 % regarded as nonwhite (including Indians and blacks; National Institute of Statistics and Census of Argentina, 2005). Recent studies focusing on SpA in Argentina reflect this ethnic distribution, with a significant proportion of patients having PsA. A group of 402 Argentinian patients classified as having SpA according to the ESSG criteria were included in a prospective, observational, multicenter study. The patients were predominantly male (59 %) and belonged to two major groups: white (70.8 %) and white-native (22.8 %). Among these patients, 242 (60.2 %) had PsA, 86 (21.4 %) had AS, 33 (8.2 %) had undifferentiated SpA (uSpA), 25 (6.2 %) had reactive arthritis (ReA), 10 (2.5 %) had IBD-associated SpA, and 6 (1.5 %) had juvenile AS. A family history of SpA was found for 16.8 % of patients. With regard to social subgroups, 74.3 % were in the middle (35.3 %) or lower (39 %) social classes. Mean BASFI and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores were 2.6 (0.8–5.4) and 3.8 (1.9–5.7), respectively. Patients from the lower (4.8 vs 2.8) and middle classes (3.9 vs 2.8) had significantly higher mean BASDAI scores than those in the upper classes. Unemployed people made up 18.3 % of the patients, and most of these had AS (25.9 %). Permanent labor disability was found for 15.7 % of patients with AS, 16.7 % with juvenile AS, and 6.9 % with PsA. Although the predominance of patients with PsA could be expected considering the general population of Argentina, it is important to emphasize that these data can be biased by the characteristics of some Argentinian centers, more focused in the study of PsA. Nevertheless, the observed lower frequency of AS and juvenile AS may be an underestimate, because of the insidious and oligosymptomatic onset of AS among this group of patients. The poorer functional capacity and higher disease activity observed in the lower social classes also was expected [7].

The incidence and prevalence of PsA in Argentina are similar to those observed in Europe and the United States. PsA incidence and prevalence were determined in Buenos

Aires, the capital of Argentina, in a six-year study by a university hospital-based health-management organization. Among 138,288 persons who participated, for a total of 558,878 person-years, 35 developed PsA (IR 6.26; 95 % CI 4.2–8.3 cases per 100,000 person-years). The prevalence was 74 cases per 100,000 persons [8].

A study analyzing 59 patients with AS (43 (72.9 %) were male, with a median age of 47 years (33–57 years) and median disease duration of 120 months (33–57 months)) and 53 patients with rheumatoid arthritis (RA) (37 (69.8 %) were female, with a median age of 56 years (44–60 years) and a median disease duration of 156 months (96–288 months)) focused on the level of adherence to treatment. Although the adherence of AS patients to pharmacologic treatment was acceptable, it was lower than that observed for RA patients. According to multivariate logistic analysis, lack of adherence to treatment was not associated with gender, age, disease duration, education, health insurance, depressive status, or disease activity in either group. Lack of adherence to exercise was similar for both groups [9].

Brazil

Brazil, the largest country in Latin America, has more than 190 million inhabitants, 48.7 % of whom are white (predominantly European ancestry, with Portuguese, Spanish, or Italian origin) and 50.6 % African-Brazilian (43.6 % with mixed white and black ancestry, and 7 % pure blacks), according to the last national demographic census (National Institute of Geography and Statistics, 2010). A study analyzing 1, 318 patients from the Brazilian Registry of Spondyloarthritis (RBE) and conducted in 29 centers in the five main geographic regions of the country showed that white race (65 % of patients) was significantly associated with psoriasis and HLA-B27 positivity. Patients of African–Brazilian descent had higher percentages of hip involvement, axial inflammatory pain, and radiographic sacroiliitis than white patients. It is important to note that most African–Brazilian patients in the study were biracial, products of miscegenation between whites and blacks; only a few were regarded as black only [10]. Analysis of the effect of gender on characterization of the group revealed that female gender was associated with peripheral SpA, upper limb arthritis, dactylitis, psoriasis, nail involvement, and a family history of SpA. Importantly, the number of painful and swollen joints was significantly higher among females, who also had higher BASDAI, BASFI (trend), ankylosing spondylitis quality of life (ASQoL), Maastricht ankylosing spondylitis enthesitis score (MASES), and patients' global assessment scores [11]. A study analyzing age at onset for 1,424 Brazilian patients showed that disease onset for 259 (18.2 %) occurred after 40 years, for 151 (10.6 %) after 45 years, and for 81 (5.8 %) after 50 years; mean age at disease onset was 28.5±12.3 years. Later age at onset was associated with female gender, peripheral arthritis, dactylitis, nail involvement, and psoriasis [12].

Another important aspect of Brazilian SpA patients in the RBE is the entheseal component. A study analyzing the effect of enthesitis among 1,505 SpA patients, as assessed by MASES, showed that 54 % of the patients were affected by at least one enthesis. The presence of enthesitis was significantly associated with axial (buttock, cervical, and hip pain) and peripheral (lower limb arthritis, number of painful and swollen joints) symptoms, and with higher mean BASDAI, BASFI, and ASQoL scores. Importantly, multivariate logistic regression showed that BASFI ($P<0.0001$; OR 74.839), ASQoL ($P=0.0001$; OR 14.645), and Achilles tendinitis ($P=0.0059$; OR 7.593) were associated with work incapacity [13•].

Among 1,505 SpA patients, PsA affected 271 (18.4 %), who were characteristically older and had a shorter disease duration than patients with other SpA. PsA was associated with female gender, white ethnicity, upper limb arthritis, lower limb arthritis, enthesitis, dactylitis, positive family history, and use of MTX. Joint pain and swelling also occurred more frequently among patients with PsA, which was negatively associated with axial symptoms and HLA-B27 positivity [14]. Another recent study evaluating 158 patients with PsA in a single tertiary university center found that cardiovascular disease was frequent among patients with PsA, and that it was associated with arterial hypertension (OR 21; $P<0.001$) and diabetes mellitus (OR 5.4; $P<0.001$) [15].

Arthritis associated with IBD was described in two recent articles. Among 130 Brazilian patients with IBD in a single referral center, enteropathic arthritis was diagnosed for 41 (31.5 %); there was a predominance of peripheral involvement (22 patients). Most patients had oligoarticular (86.5 %) or asymmetric (65.6 %) involvement; the most commonly affected joints were the knees (56.1 %), ankles (29.1 %), and hips (29.3 %), with enthesitis reported for seven patients (5.4 %) [16]. According to the Brazilian Registry of SpA, only 3.2 % of the patients had a diagnosis of IBD, with 2.5 % presenting with spondylitis and 0.7 % with peripheral arthritis, associated with a higher prevalence of female gender and enthesitis [17].

A study analyzing the long-term follow-up (2, 5, 7, and 10 years) of 111 Brazilian patients (predominantly male (81.1 %), white (78.4 %), and HLA-B27-positive (61.3 %)) with diagnosis of uSpA, fulfilling ESSG and Amor criteria, revealed that 27 patients (24.3 %) developed AS and three (2.7 %) developed PsA, whereas 25 patients (22.5 %) went into remission during follow-up. Multivariate logistic regression analysis showed that progression to AS was associated with HLA-B27 positivity ($P=0.035$; OR 6.720; 95 % CI 11.45–39.43) and buttock pain ($P=0.009$; OR 6.211; 95 % CI 1.591–24.25) [18]. Another study analyzing the eight-year

follow-up of 40 patients with diagnosis of uSpA, also fulfilling ESSG criteria, showed a predominance of female gender (58 %), African–Brazilian ethnicity (60 %), and HLA-B27 negativity (55 %). Ten patients (27.8 %) had AS progression during the eight-year follow-up; buttock pain (OR 10.55; $P=0.006$) and low-grade radiographic sacroiliitis (OR 11.50; $P=0.025$) at baseline were associated with definite SpA [19].

Peripheral involvement is an important and frequent characteristic among Brazilian SpA patients and may be associated with intense miscegenation. Analysis of the five geographic regions of the Brazilian Registry of SpA led to important arguments in this discussion. In a series with 1,505 SpA patients, 762 (68 % white and 20.1 % African–Brazilian) were from the southeast, 272 (49.4 % white and 43.7 % African–Brazilian) from the midwest, 126 (66.7 % white, 16.7 % African–Brazilian, and 16.6 % mixed, including Indian) from the north, and 87 (32.1 % white and 56 % African–Brazilian) from the northeast. Purely axial involvement and the occurrence of anterior uveitis were significantly more frequent in the south whereas combined axial and peripheral involvement and higher mean erythrocyte sedimentation rate (ESR) and CRP values were more common in areas with a strong component of miscegenation (northeast and north). A greater frequency of male gender, hip involvement, and work incapacity was associated with higher MASES, BASFI, and ASQoL scores in the northeast region [20]. Table 1 shows the "south–north gradient," demonstrating that the a peripheral component is more frequent in the northern regions (with high incidence of miscegenation), as are higher BASDAI, BASFI, and ASQoL scores and higher mean values on inflammatory tests (ESR and CRP), compared with the southern region (with a predominantly white population).

A study evaluating serum sclerostin levels and inflammatory markers among AS patients receiving anti-TNF therapy showed that persistently low sclerostin levels were associated with continuous inflammation after treatment for 12 months [21].

In 2013, the second update of the Guidelines for the Diagnosis and Treatment of Ankylosing Spondylitis [22] and the Guidelines for the Diagnosis and Treatment of Psoriatic Arthritis [23] of the Brazilian Society of Rheumatology were published. These guidelines follow the Brazilian Medical Association's strict rules for evidence-based medicine.

Chile

Chile is a Latin American country with a significant white population (59 %, predominantly of Spanish origin), although it also has a large indigenous population (25 % European–Native American and 8 % Native American; National Institute of Statistics, 2005). A study including 109 Chilean SpA patients from five university centers revealed a predominance of male gender (58.4 %) and white–indigenous ethnicity (81.4 %), with 58.7 % of the patients having diagnosis of AS, 25.6 % PsA, and 7.3 % uSpA. Inflammatory low back pain (74.3 %) and arthritis of the lower extremities (59.3 %) were frequent symptoms, and uveitis was reported for 18.6 % of cases [24].

A cross-sectional, observational, analytical study of 153 patients with psoriasis was conducted at the dermatology department of the University of Chile. Mean patient age was 42.7 years, and 60.1 % of the patients were male. The most frequent disease subtype was plaque psoriasis (71.9 %), followed by guttate psoriasis (17.7 %). Less than 10 % of the body surface area was affected among 38.6 % of the patients. Joint involvement was reported by 28.8 % of the patients. Those with early onset of disease (before 30 years of age) were more likely to have a family history of psoriasis. Hypertension and diabetes were present among 20.3 % and 11.1 % of patients, respectively. A greater impact of the

Table 1 Clinical instruments and laboratory evaluation of 1,505 Brazilian SpA patients, according to main geographic region

	Region (%)				
	South (N=258)	Southeast (N=762)	Center west (N=126)	Northeast (N=87)	North (N=126)
Swollen joints*	0.81±2.68	1.72±5.75	1.44±3.77	1.03±2.77	3.06±4.72
Painful joints*	2.63±5.56	3.68±8.03	3.69±5.27	3.76±6.81	7.14±11.32
MASES*	1.69±2.69	1.90±2.85	1.96±2.82	3.41±3.46	3.69±3.51
BASDAI*	4.28±2.39	3.92±2.37	4.32±2.25	4.84±2.60	5.08±2.24
BASFI*	4.39±2.88	4.53±2.73	4.20±2.72	5.74±2.99	4.93±2.66
ASQoL*	6.48±5.67	7.46±5.16	8.59±5.57	10.47±4.77	8.30±5.21
ESR, mm*	21.72±20.46	22.26±21.17	25.80±21.77	32.70±23.32	40.15±26.32
CRP (mg L^{-1})*	9.93±17.91	8.62±15.33	9.53±28.53	21.90±26.62	17.15±34.77
Physician VAS*	4.03±2.67	3.36±2.47	3.81±2.55	5.09±2.94	5.61±2.64
Patient VAS*	4.81±2.80	4.56±2.90	5.27±2.70	5.55±3.02	5.42±2.96

*$P<0.005$.

ASQoL, ankylosing spondylitis quality of life; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; CRP, C-reactive protein; ESR, erythocyte sedimentation rate; MASES, Maastricht ankylosing spondylitis enthesitis score; SpA, spondyloarthritis; VAS, visual analogue scale.

disease on quality of life was associated with male gender, young age at onset, newly diagnosed disease, facial involvement, and widespread disease. Chilean patients with psoriasis had clinical characteristics and quality of life comparable to those of patients from other countries, except for the greater impact of psoriasis on men's quality of life [25].

Colombia

Colombia, with a population of 46 million, is another highly miscegenated Latin American country; 37 % of the population is regarded as white, 49 % as Amerindian (mixed white and Indian), and 10.6 % as African–Colombian (mixed white and black) (national census, 2005). A prospective study assessing clinical and radiographic features, and disease activity and severity, among 218 Colombian patients with suspected SpA identified 71 patients (32.5 %) with uSpA. There was a predominance of male gender, and the mean age was 29 years. Inflammatory back pain, lower limb arthritis, and enthesopathy was a common clinical picture in this series. Radiographic evidence of sacroiliitis (mostly unilateral and/or asymmetric) was detected in 55 % of the cases, and HLA-B27 was found in 39 % of the patients tested. During the follow-up, only 7 % of the patients fulfilled the ESSG criteria for SpA. The authors regard uSpA a distinct subset of SpA in Colombia, and, because of the low frequency of HLA-B27 in the series, suggest inclusion of other genetic factors [26].

A more recent study examined the clinical and immunologic variables associated with disease progression to AS for a series of 139 consecutive Colombian patients with SpA, classified in accordance with ESSG criteria, and treated by the rheumatology service of the Military Hospital in Bogota. In this group, 55 patients had AS, 49 uSpA, 22 ReA, and 13 PsA. Mean age at onset was 26.8 years, mean disease duration was 8.5 years, and 18 % of the patients had a family history of SpA. Musculoskeletal and systemic symptoms, for example fever, weight loss, and fatigue, were common clinical complaints, especially among patients with uSpA and AS. HLA-B27 was positive for 60 % of the tested patients whereas uveitis was reported by fewer patients (7.2 %) compared with other Latin American countries. Follow-up of 51 of these patients revealed that 22 % (11 patients, with ReA initially diagnosed for six and uSpA for five) developed AS. Interestingly, autoantibodies against cyclic citrullinated peptide were observed in 9.7 % of the psoriatic patients with joint involvement whereas they were absent from patients without joint involvement [26].

A study comparing the frequency of promoter polymorphism of TNFα-308A among Colombian patients with different types of SpA revealed significant differences between the control group and patients with SpA, especially uSpA and ReA. Furthermore, there was no significant correlation with activity and functional indices, serum TNFα level, or HLA-B27 status [27].

A study analyzing several serum biomarkers (TNFα, interleukin (IL)-1α, IL-6, IL-17, IL-23, and ultrasensitive CRP (US-CRP)) and factors associated with clinical activity and poor prognosis was performed among 62 Colombian patients (30 with uSpA, 19 with AS, and 13 with ReA). Mean age at onset was 26.9 years, and 69.4 % of the patients were male. Clinical and laboratory data revealed 42 patients had inflammatory back pain (67.7 %), 44 had arthritis (71.0 %), and 34 had enthesitis (54.8 %), with positive HLA-B27 for 26 patients (41.9 %). Patients with SpA had significantly higher levels of IL-17, IL-23, TNFα, IL-6, IL-1α, and US-CRP compared with controls. An increase in serum levels of US-CRP, IL-6, IL-1α, and LBP was associated with HLA-B27, inflammatory back pain and arthritis, and was correlated with poor prognosis in SpA [28].

Another study was designed to distinguish responders from nonresponders to three standard pulses of infliximab at week 6 among a series of 47 AS patients. Although 22 different cytokines were measured as potential biomarkers, only higher levels of serum IL-1 helped distinguish the responders, with sensitivity of 84.9 % and specificity of 23.8 % [29].

Costa Rica

A small Central American country, Costa Rica has 4 million inhabitants, with a large white population (80 %), followed by white–Native American (15 %) and black (4 %) (national census, 2000). A study analyzed 33 patients with SpA in Costa Rica, predominantly men (58.5 %) and white–Native Americans (61.7 %) with a mean age of 41.3 years. Most patients had AS (45 %) or uSpA (45 %), and HLA-B27 was positive for 57.1 % of cases [30].

Guatemala

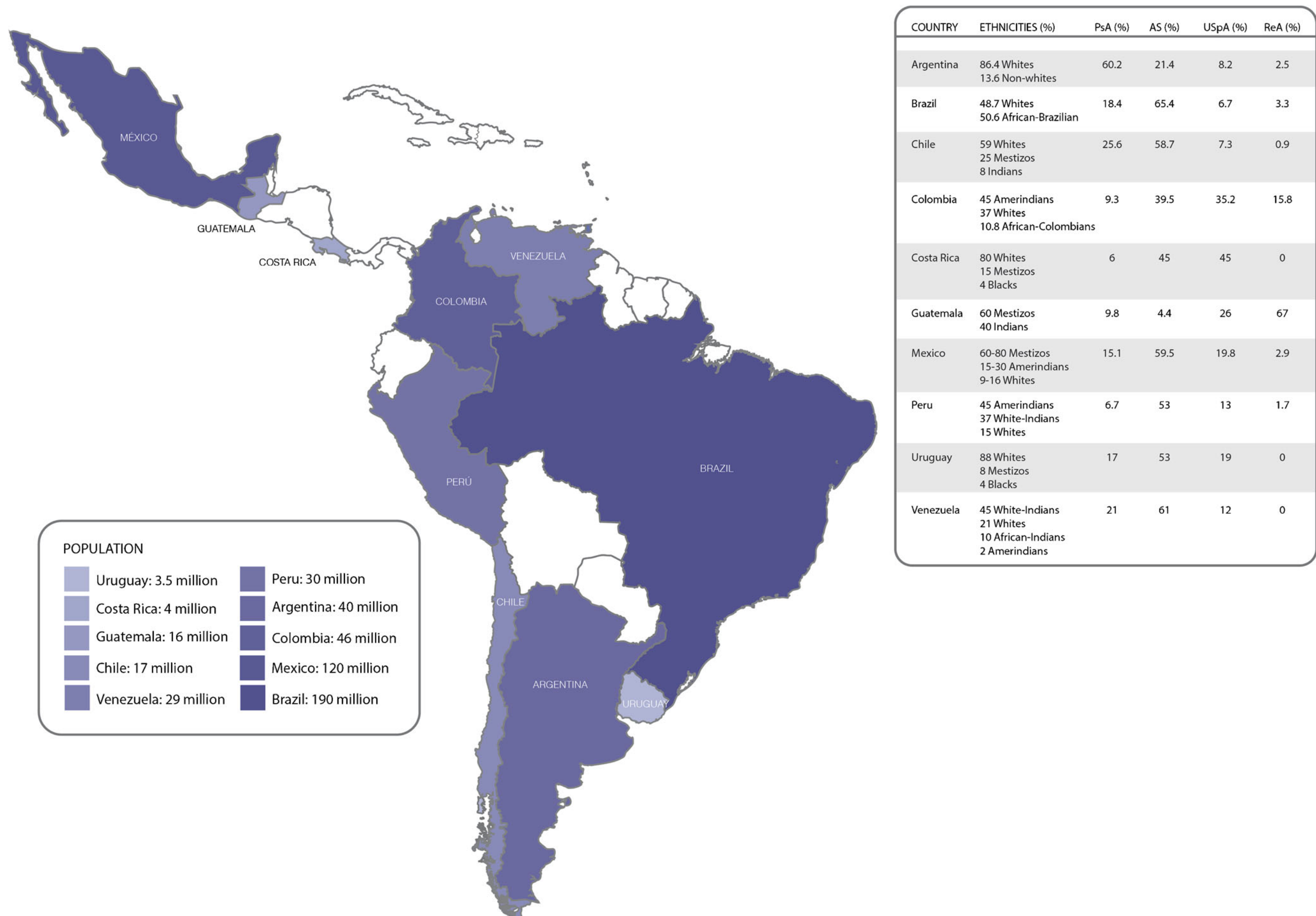
Another Central American country, Guatemala has a population of 16 million, predominantly of white–Native American (60 %) and Native American (especially Mayan, 40 %) ethnicity (National Institute of Statistics of Guatemala, 2000). A recent publication describing 183 SpA patients from Guatemala revealed female predominance (60 %). Axial and peripheral components were observed frequently, and the most common diseases in the group were ReA (67 %) and uSpA (26 %) [31].

Mexico

The Mexican population (120 million) is composed predominantly of European–Native Americans (60–80 %), with lower percentages of Native Americans (descendants of Indians who inhabited Mesoamerica; 15–30 %), whites (European ancestry; 9–16 %), and others (Asians, blacks; 1 %). The prevalence of HLA-B27 was 5 %. The prevalence of nontraumatic back pain in Mexico is 14.6 % (95 % CI, 13.6–15.8), more than 10 times greater than that of inflammatory back pain, which is 1.3 % (95 % CI, 1.0–1.7). In this setting, the prevalence of SpA in Mexico is 0.6 % (95 % CI, 0.4–0.9) and that of AS is 0.1 % (95 % CI, 0.02–0.2) [32•]. In previous studies, the relative frequencies of the different SpA were 60 % for AS, 20 % for uSpA, 15 % for PsA, 3 % for ReA, and 2 % for Crohn's disease and/or ulcerative colitis, with a high proportion of juvenile-onset patients among those with AS (35 %). Another important aspect was the association of HLA-B27 with AS: HLA-B27 was positive for approximately 90 % of the juvenile-onset AS cases, and B*2705 was the HLA-B27 subtype for >95 % of the AS patients. Overall, the initial combination of axial and peripheral symptoms in the juvenile patient, followed by axial disease, and then peripheral arthritis and enthesitis in the adult patient is the classical clinical pattern most frequently observed in the Mexican population [33].

An interesting aspect related to juvenile-onset SpA is associated with its long-term follow-up. A follow-up study showed that 75 % of the Mexican juvenile-onset SpA cases fulfilled the modified New York criteria for AS 5 to 10 years after onset. Similarly, 42 % of the uSpA patients developed AS within 3 years. Radiographic sacroiliitis, grade 2 bilateral or grade 3 unilateral (OR, 11.18; 95 %CI, 2.59–48.16; P=0.001), and previous uveitis (OR, 19.25; 95 %CI, 1.72–214.39; P=0.001) were the most important prognostic factors affecting this transition. Although patients with peripheral arthritis, particularly juvenile-onset SpA, may receive an early diagnosis because of early referral to a rheumatologist, those with axial disease may be diagnosed late in the course of the disease [34].

In Mexico, patients rarely receive standard treatment for SpA from their general physicians or orthopedic surgeons. However, once they are referred to a rheumatologist, their SpA is more likely to be treated appropriately and in



COUNTRY	ETHNICITIES (%)	PsA (%)	AS (%)	USpA (%)	ReA (%)
Argentina	86.4 Whites 13.6 Non-whites	60.2	21.4	8.2	2.5
Brazil	48.7 Whites 50.6 African-Brazilian	18.4	65.4	6.7	3.3
Chile	59 Whites 25 Mestizos 8 Indians	25.6	58.7	7.3	0.9
Colombia	45 Amerindians 37 Whites 10.8 African-Colombians	9.3	39.5	35.2	15.8
Costa Rica	80 Whites 15 Mestizos 4 Blacks	6	45	45	0
Guatemala	60 Mestizos 40 Indians	9.8	4.4	26	67
Mexico	60-80 Mestizos 15-30 Amerindians 9-16 Whites	15.1	59.5	19.8	2.9
Peru	45 Amerindians 37 White-Indians 15 Whites	6.7	53	13	1.7
Uruguay	88 Whites 8 Mestizos 4 Blacks	17	53	19	0
Venezuela	45 White-Indians 21 Whites 10 African-Indians 2 Amerindians	21	61	12	0

Fig. 1 Ethnicities and profile of the spondyloarthritides in 10 Latin American countries. The sum of the ethnicities is not 100 % due to the heterogeneity of the populations

agreement with the Assessment of Spondyloarthritis International Society (ASAS) and the European League Against Rheumatism (EULAR) recommendations for treatment of AS [33].

Peru

Peru is a South American country with approximately 30 million inhabitants, predominantly Native American (45 %), followed by white–Native American (37 %), white (15 %), and other (3 %) (national census, 2000). A group of 60 Peruvian patients with SpA according to the ESSG criteria were predominantly male (65 %) and white–Native American (93 %). Mean age was 40 years, and HLA-B27 positivity was less frequent than expected (31 %). The most frequent SpA were AS (53 %), juvenile SpA (25 %), and uSpA (13 %), and patients reported significant peripheral involvement, notably arthritis of the lower limbs (43 %) and dactylitis (30 %) [35].

Consecutive patients with psoriasis and PsA living in the Peruvian Andes were evaluated by the CASPAR (Classification of Psoriatic Arthritis) criteria, currently used to classify PsA. Diagnosis of psoriasis was confirmed by a dermatologist. Seventeen patients (11 (65 %) men and 6 (35 %) women) fulfilled classification criteria for PsA. One patient was of European ancestry and was not included in the analysis; among the 16 Indian patients in the group, five had Quechua ancestry and one was a native Aymara. At the time of their first visit to a clinic, no native patient with PsA had a family history of psoriasis or PsA, and all patients had established disease of long duration and severity. In contrast with literature reports, both psoriasis and PsA were present in aboriginal people from the Peruvian Andes [36].

Uruguay

Uruguay is a South American country with 3.5 million inhabitants, predominantly white (88 %), followed by white–Native American (8 %), and black (4 %) (National Institute of Statistics of Uruguay, 2011). The Uruguayan branch of RESPONDIA included 53 SpA patients, predominantly male (66 %) and white (87 %), with a mean age at onset of 31.6 years. Inflammatory back pain (41 %) and peripheral arthritis (41 %) were the most common initial symptoms, and AS (53 %), uSpA (19 %), and PsA (17 %) were the most frequent diseases [37].

Venezuela

Venezuela is another South American country in which there has been significant miscegenation among the population, which is 67 % white–Native American, 21 % white, 10 % African–Native American, and 2 % Native American (national census, 2001). A recent analysis of 69 SpA patients in Venezuela revealed male predominance (62.3 %), and the most frequent SpA were AS (61 %), PsA (21 %), and uSpA (12 %). Axial and peripheral involvement was reported by 51 % of the patients, and anterior uveitis by 22 % of cases [38].

A map of Latin America with the percentages of the different ethnicities in the population and the diverse SpA in 10 countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Guatemala, Mexico, Peru, Uruguay, and Venezuela) is shown in Fig. 1.

Conclusions

Analysis of patients with SpA in the Latin American population showed that significant prevalence of the peripheral component seems to be associated with the frequent miscegenation observed in this region. In countries with significant miscegenation (between whites and blacks and/or Native Americans), for example Brazil, Colombia, and Mexico, the authors observed significantly higher prevalence of the peripheral component, associated with the axial component in AS or in predominantly peripheral diseases, for example uSpA and ReA. PsA, however, a disease more common in predominantly white populations, was more frequent in Argentina, a South American country with a more homogeneous ethnic distribution.

Compliance with Ethics Guidelines

Conflict of Interest Carla Gonçalves Schain Saad, and Percival D. Sampaio-Barros declare that they are recipients of a research grant from the Federico Foundation. Célio Roberto Gonçalves declares that he has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular importance, published recently, have been highlighted as:
- • Of importance

1. Espinoza LR, Toloza SM, Valle-Onate R, Mease PJ. Global partnering opportunities and challenges of psoriasis and psoriatic arthritis in Latin America: a report from the GRAPPA 2010 annual meeting. J Rheumatol. 2012;39:445–7.

2.• Benegas M, Muñoz-Gomariz E, Font P, Burgos-Vargas R, Chaves J, Palleiro D, et al. Comparison of the clinical expression of patients with ankylosing spondylitis from Europe and Latin America. J Rheumatol. 2012;39:2315–20. *This article, comparing 1,083 Latin American (from nine countries) and 2,356 European patients (from Spain and Belgium), shows that the Latin American patients were characterized by a higher frequency of peripheral involvement and enthesitis whereas the European patients had a significantly higher percentage of positive HLA-B27*.
3. Vander Cruyssen B, Muñoz-Gomariz E, Font P, Mulero J, de Vlam K, Boonen A, et al. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery. Rheumatology (Oxford). 2010;49:73–81.
4. Pérez Alamino R, Maldonado Cocco JA, Citera G, Arturi P, Vazquez-Mellado J, Sampaio-Barros PD, et al. Differential features between primary ankylosing spondylitis and spondylitis associated with psoriasis and inflammatory disease. J Rheumatol. 2011;38: 1656–60.
5. Sampaio-Barros PD, Pereira IA, Hernández-Cuevas C, Berman A, Burgos-Vargas R, Gutierrez MA, et al. An analysis of 372 patients with anterior uveitis in a large Ibero-American cohort of spondyloarthritis: the RESPONDIA group. Clin Exp Rheumatol. 2013;31:484–9.
6. Gallinaro AL, Ventura C, Sampaio Barros PD, Gonçalves CR. Spondyloarthritis: analysis of a Brazilian series compared with a large Ibero-American registry (RESPONDIA group). Braz J Rheumatol. 2010;50:581–9.
7. Buschiazzo E, Maldonado-Cocco JA, Arturi P, Citera G, Berman A, Nitsche A, et al. Epidemiology of spondyloarthritis in Argentina. Am J Med Sci. 2011;341:289–92.
8. Soriano ER, Rosa J, Velozo E, Schpilberg M, Imamura PM, Diaz J. Incidence and prevalence of psoriatic arthritis in Buenos Aires, Argentina: a 6-year health management organization-based study. Rheumatology (Oxford). 2011;50:729–34.
9. Arturi P, Schneeberger EE, Sommerfleck F, Buschiazzo E, Ledesma C, Maldonado Cocco JA, et al. Adherence to treatment in patients with ankylosing spondylitis. Clin Rheumatol. 2013;32: 1007–15.
10. Skare TL, Bortoluzzo AB, Gonçalves CR, Braga da Silva JA, Ximenes AC, Bértolo MB, et al. Ethnic influence in clinical and functional measures of Brazilian patients with spondyloarthritis. J Rheumatol. 2012;39:141–7.
11. de Carvalho HM, Bortoluzzo AB, Gonçalves CR, da Silva JA, Ximenes AC, Bértolo MB, et al. Gender characterization in a large series of Brazilian patients with spondyloarthritis. Clin Rheumatol. 2012;31:687–95.
12. Skare TL, Leite N, Bortoluzzo AB, Gonçalves CR, da Silva JA, Ximenes AC, et al. Effect of age at disease onset in the clinical profile of spondyloarthritis: a study of 1424 Brazilian patients. Clin Exp Rheumatol. 2012;30:351–7.
13.• Carneiro S, Bortoluzzo AB, Gonçalves CR, da Silva JA, Ximenes AC, Bértolo MB, et al. Effect of enthesitis on 1505 Brazilian patients with spondyloarthritis. J Rheumatol. 2013;40:1719–25. *This article reveals that when the MASES was applied to a group of 1,505 Brazilian patients with SpA, 54 % had at least one affected enthesis. Achilles enthesitis also was associated with work incapacity in the multivariate logistic regression analysis*.
14. Bonfiglioli R, Carneiro S, Bortoluzzo AB, Gonçalves CR, da Silva JA, Ximenes AC, et al. Characteristics of psoriatic arthritis in a large cohort of Brazilian patients with spondyloarthritis. Braz J Rheumatol. 2014; submitted to publication.
15. Favarato MH, Mease P, Gonçalves CR, Gonçalves Saad C, Sampaio-Barros PD, Goldenstein-Schainberg C. Hypertension and diabetes significantly enhance the risk of cardiovascular disease in patients with psoriatic arthritis. Clin Exp Rheumatol. 2014; 32:182–7.
16. Lanna CC, Ferrari ML, Rocha SL, Nascimento E, de Carvalho MM, da Cunha AS. A cross-sectional study of 130 Brazilian patients with Crohn's disease and ulcerative colitis: analysis of articular and ophthalmologic manifestations. Clin Rheumatol. 2008;27:503–9.
17. Resende GG, Lanna CC, Bortoluzzo AB, Gonçalves CR, Braga da Silva JA, Ximenes AC, et al. Enteropathic arthritis in Brazil: data from the Brazilian Registry of Spondyloarthritis. Braz J Rheumatol. 2013;53:452–6.
18. Sampaio-Barros PD, Bortoluzzo AB, Conde RA, Costallat LT, Samara AM, Bértolo MB. Undifferentiated spondyloarthritis: a long-term follow-up. J Rheumatol. 2010;37:1195–9.
19. Lage RC, Bomtempo CAS, Kakehasi AM, de Carvalho MA. Undifferentiated spondyloarthritis in a heterogeneous Brazilian population: an eight-year follow-up study. Rheumatol Int. 2013 Jun 14 (E-pub ahead of print).
20. Sampaio-Barros PD, Santiago MB, Bortoluzzo AB, Ximenes AC, Braga da Silva JA, Bértolo MB, et al. Combined axial and peripheral involvement is associated with miscegenation in a large and heterogeneous Brazilian cohort of 1505 patients with spondyloarthritis. Arthritis Rheum. 2013;65:S1056.
21. Saad CG, Ribeiro AC, Moraes JC, Takayama L, Gonçalves CR, Rodrigues MB, et al. Low sclerostin levels: a predictive marker of persistent inflammation in ankylosing spondylitis during anti-tumor necrosis factor therapy? Arthritis Res Ther. 2012;14:R216.
22. Sampaio-Barros PD, Keiserman M, Meirelles ES, Pinheiro MM, Ximenes AC, Azevedo VF, et al. Recommendations for the management and treatment of ankylosing spondylitis. Braz J Rheumatol. 2013;53:242–57.
23. Carneiro S, Azevedo VF, Bonfiglioli R, Ranza R, Gonçalves CR, Keiserman M, et al. Recommendations for the management and treatment of psoriatic arthritis. Braz J Rheumatol. 2013;53:227–41.
24. Gutierrez MA, Pérez C, Saavedra J, Silva F, Fuentealba C, Pozo P, et al. Registro Iberoamericano de Espondiloartritis: Chile. Reumatol Clin. 2008;4 Suppl 4:S41–7.
25. Valenzuela F, Silva P, Valdés MP, Papp K. Epidemiology and quality of life of patients with psoriasis in Chile. Actas Dermosifiliogr. 2011;102:810–6.
26. Valle-Oñate R, Candia L, Romero-Sánchez C, Iglesias-Gamarra A, Caballero-Uribe CV, Santos-Moreno P, et al. Epidemiology of spondyloarthritis in Colombia. Am J Med Sci. 2011;341:293–4.
27. Romero-Sánchez C, Londoño J, Delgado G, Jaimes DA, De Avila J, Mora A, et al. Association of tumor necrosis factor alpha-308 promoter polymorphism with spondyloarthritides patients in Colombia. Rheumatol Int. 2012;32:2195–7.
28. Londoño J, Romero-Sanchez MC, Torres VG, Bautista WA, Fernandez DJ, Quiroga JA, et al. The association between serum levels of potential biomarkers with the presence of factors related to the clinical activity and poor prognosis in spondyloarthritis. Braz J Rheumatol. 2012;52:536–44.
29. Romero-Sánchez C, Robinson WH, Tomooka BH, Londoño J, Valle-Oñate R, Huang F, et al. Identification of acute phase reactants and cytokines useful for monitoring infliximab therapy in ankylosing spondylitis. Clin Rheumatol. 2008;27:1429–35.
30. Saenz-Castro R. Registro Iberoamericano de Espondiloartritis: Costa Rica. Reumatol Clin. 2008;4 Suppl 4:S36–40.
31. Garcia-Kutzbach A, Montenegro A, Iraheta I, Bará C, Saenz R. Epidemiology of spondyloarthropathies in Central America. Am J Med Sci. 2011;341:295–7.
32.• Peláez-Ballestas I, Navarro-Zarza JE, Julian J, Lopez A, Flores-Camacho R, Casasola-Vargas JC, et al. A community-based study on the prevalence of spondyloarthritis and inflammatory back pain in Mexicans. J Clin Rheumatol. 2013;19:57–61. *This study analyzed the results of a door-to-door nurse survey applying the Community Oriented Program for the Control of Rheumatic Diseases (COPCORD) to 4,059 individuals in Mexico City. The*

prevalence of back pain was 14.6 %, whereas the prevalence of inflammatory back pain was 1.3 % and that of AS was 0.6 %.
33. Burgos-Vargas R, Peláez-Ballestas I. Epidemiology of spondyloarthritis in Mexico. Am J Med Sci. 2011;341:298–300.
34. Huerta-Sil G, Casasola-Vargas JC, Londoño JD, et al. Low-grade radiographic sacroiliitis as prognostic factor in patients with undifferentiated spondyloarthritis fulfilling diagnostic criteria for ankylosing spondylitis throughout follow up. Ann Rheum Dis. 2003;65:642–6.
35. Chavez-Corrales JE, Jauregui MM, Linares MA, Mora C, Valencia PR, Garcia E, et al. Registro Iberoamericano de Espondiloartritis: Peru. Reumatol Clin. 2008;4 Suppl 4:S63–7.
36. Toloza SM, Vega-Hinojosa O, Chandran V, Valle-Onate R, Espinoza LR. Psoriasis and psoriatic arthritis in Peruvian aborigines: a report from the GRAPPA 2011 annual meeting. J Rheumatol. 2012;39:2216–9.
37. Palleiro D, Spangenberg E. Registro Iberoamericano de Espondiloartritis (RESPONDIA): Uruguay. Reumatol Clin. 2008;4 (Suppl 4):S73–8.
38. Chacón R, Granados Y, Esteva MH, Martinez Y, Maldonado T, Rondón J, et al. Registro Iberoamericano de Espondiloartritis (RESPONDIA): Venezuela. Reumatol Clin. 2008;4 (Suppl 4): S79–86.