

Global Partnering Opportunities and Challenges of Psoriasis and Psoriatic Arthritis in Latin America: A Report from the GRAPPA 2010 Annual Meeting

LUIS R. ESPINOZA, SERGIO M.A. TOLOZA, RAFAEL VALLE-ONATE, and PHILIP J. MEASE

ABSTRACT. Documenting the disease burden of psoriasis and psoriatic arthritis (PsA) in Central and South America is difficult. The most conclusive data have come from the Iberoamerican Registry of Spondyloarthritis (RESPONDIA), which registered patients with a diagnosis of spondyloarthritis in a multinational, multicenter (Argentina, Brazil, Costa Rica, Chile, Mexico, Peru, Uruguay, Venezuela, Spain, and Portugal) cross-sectional study conducted between 2006 and 2007. Compared with elsewhere in the Western world, patients with PsA from RESPONDIA were older at study visit, at onset of symptoms, and at diagnosis of spondyloarthritis (SpA); had longer mean disease duration from onset of symptoms to diagnosis; and were more likely to have dactylitis, nail involvement, enthesitis, and peripheral arthritis in lower and upper extremities. It is critical to understand the biologic basis, estimate the disease burden, and determine the clinical treatment of PsA in Latin America. The Group for Research and Assessment of Psoriasis and PsA (GRAPPA) has an increasing number of members from this region. In a coordinated effort, GRAPPA, the Latin American Psoriasis and PsA Society (LAPPAS), and the Pan American League of Associations for Rheumatology (PANLAR) are supporting clinician researchers with educational initiatives in Latin America to understand these conditions. (J Rheumatol 2012;39:445–7; doi:3899/jrheum.111246)

Key Indexing Terms:

SPONDYLOARTHRITIS EPIDEMIOLOGY PSORIATIC ARTHRITIS LATIN AMERICA

Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) in Latin America

In 2003, GRAPPA's founding members were primarily from Europe and North America; however, an increasing number are from Latin America. At the 2010 GRAPPA annual meeting, historical perspectives, epidemiology, and current research on psoriasis and psoriatic arthritis (PsA) in Latin America were reviewed.

Historical Perspective on PsA and Spondyloarthritis (SpA) in Latin America

Psoriasis and its related clinical manifestations including PsA are prevalent disorders in the Western world, particularly among whites. The clinical and epidemiological study of these disorders in Latin America, however, lags far

behind the study of other rheumatic disorders such as rheumatoid arthritis and systemic lupus erythematosus¹.

From the scarce evidence available, it appears that both the prevalence and incidence of psoriasis and PsA are lower in Latin America than in other parts of the Western world. Although confirmatory epidemiological studies are lacking, psoriasis and PsA are almost negligible among native populations from the Andean region. Further, genetic studies are complicated by the racial and ethnic heterogeneity of the Latin American population: most countries, with few exceptions, such as Argentina and Uruguay, have large native populations. Since the discovery of America in 1492, genetic admixture between natives and whites, mostly Spaniards, has occurred, but the influence of this admixture on the clinical expression and frequency of PsA or psoriasis has not been determined.

The presence of PsA in Latin America before the arrival of the Spaniards is not well established. However, skeletal remains have been analyzed to determine the presence of rheumatologic disorders during the pre-Columbian era and suggest that spondyloarthritis (SpA) as well as diffuse idiopathic skeletal hyperostosis (DISH) were already present among 504 human remains housed at the Universidad de Tarapaca in Arica, Chile, with a frequency of 7% and 4%, respectively, in prehistoric Amerindians > 40 years old². In another study, bones from 65 humans who lived at coastal Mayan sites in northern Belize during the years 1350-1600 AD were analyzed to determine the relationship of disease

From the Section of Rheumatology, Louisiana State University Health Sciences Center, New Orleans, Louisiana, USA; Hospital San Juan Bautista, Catamarca, Argentina; Division of Rheumatology, Military Hospital, Universidad de la Sabana, Bogota, Colombia; and Swedish Medical Center, University of Washington, Seattle, Washington, USA.

L.R. Espinoza, MD, Professor and Chief, Section of Rheumatology, Louisiana State University Health Sciences; S.M.A. Toloza, MD, Rheumatologist, Hospital San Juan Bautista; R. Valle-Onate, MD, Professor of Medicine, Division of Rheumatology, Military Hospital, Universidad de la Sabana; P.J. Mease, MD, Director of Rheumatology Research, Swedish Medical Center, and Clinical Professor of Medicine, University of Washington.

Address correspondence to Dr. L.R. Espinoza, Section of Rheumatology, Louisiana State University Health Sciences Center, 1542 Tulane Avenue, New Orleans, LA 70112-2822. E-mail: lespin1@lsuhsc.edu

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2012. All rights reserved.

to diet, culture, and the environment³. The frequency of SpA in these human remains was about 10%, which is similar to the frequency of the modern Mayan population. The increased frequency in Mayans compared with Amerindians may be a consequence of overcrowding and poor sanitation, especially exposure to water contaminated with fecal bacteria.

In a study from the 16th century of the skeletal remains of 443 Amerindians in Mexico, however, only 2 cases of SpA were found, most likely ankylosing spondylitis or DISH⁴. Similar findings were reported in a study of the remains of more than 700 humans from over 8000 years ago in the Andean region of southern Peru and northern Chile, in which no case of SpA was found⁵. These findings appear to correlate with the very low frequency (< 1%) of HLA-B27 previously reported among these native populations⁶.

It is well established that SpA existed in both New and Old World populations for at least 5000 years, likely related to agropastoral activities and village formation as well as poor sanitation. It is unknown, however, whether PsA in Latin America was underreported or nonexistent. Although arthritis mutilans has been described in ancient white populations, it has not been described in Latin American human remains, and neither psoriasis nor PsA were present in South America until the settlement of America by the Spanish. The first reported case of PsA in Latin America was described in a priest born in Spain: Fra Pedro de Urraca lived in Lima, Peru, and died as a consequence of a chronic debilitating disease, resembling severe PsA, which affected both skin and joints⁷. Not established, however, was whether psoriasis and PsA were brought to Latin America by this Spanish priest or other European settlers.

Therefore, it is not possible to make strong inferences regarding disease frequency and causation from archeological studies. It can be concluded that SpA was already present in the New World, but it is unknown if PsA was represented among the human remains with SpA.

Epidemiology of Psoriasis and PsA in Latin America

Today, the burden of psoriatic disease in Latin America remains largely unknown. At a symposium held in Dallas, Texas, in 2009, 26 psoriasis experts from Latin American countries estimated the average regional prevalence of psoriasis in their countries at 2.14% (SD 0.92, range 1.13%–2.9%) and that of PsA at 15.25% (SD 3.88, range 10%–18%)⁸. Although the authors agreed their estimations were not robust, they believed them to be comparable between Latin American countries and the United States and Europe.

At a more recent symposium held in Houston, Texas, in 2010 by the Spondyloarthritis Research and Treatment Network (SPARTAN), data on PsA from several Latin American countries were also presented. PsA was shown to be highly prevalent in patients with SpA in Argentina (60.2%), but much lower in Brazil (13.7%) and Guatemala

(10%)^{9,10,11}. Given the small number of physicians in each country who estimated these figures, the data may be biased and may not accurately represent the frequency of psoriatic disease in each region. They may more accurately represent physician knowledge of worldwide prevalence figures in relation to the practices in which they work. Moreover, the data do not include disease distribution based on ethnicity.

RESPONDIA Study

The Iberoamerican Registry of Spondyloarthritis (RESPONDIA)¹² study included consecutive patients with a diagnosis of SpA according to European Spondylarthropathy Study Group criteria and/or Amor criteria in a multinational, multicenter (Argentina, Brazil, Costa Rica, Chile, Mexico, Peru, Uruguay, Venezuela, Spain, and Portugal) cross-sectional study conducted between 2006 and 2007. In the RESPONDIA database, 100 rheumatologists from 10 Iberoamerican countries collected demographic, clinical, clinimetric, treatment, function, radiographic, and quality-of-life data. The number of PsA patients and the ethnicities differed between countries. PsA patients had predominantly axial involvement. Overall, compared with elsewhere in the Western world, PsA patients from RESPONDIA were older at study visit, at onset of symptoms, and at diagnosis of SpA; had a longer mean disease duration from onset of symptoms to diagnosis; and were more likely to have dactylitis, nail involvement, enthesitis, and peripheral arthritis in lower and upper extremities¹². Longitudinal data of PsA patients are not available.

Genetic Studies

Very few genetic studies have been performed in Latin American patients with PsA. All reports have studied the relationship between HLA-C*06 and HLA-B*27 and disease expression in whites, but none have been performed in other ethnicities including native populations. In a study of Brazilian patients with PsA, HLA-B*27 was shown to be associated with axial disease, most frequently the HLA-B*2705 allele (90.5%)¹³.

GRAPPA Latin American Members

GRAPPA has members from several Latin American countries, including Argentina, Brazil, Chile, Colombia, Peru, and Venezuela, but lacks representation from others, particularly from Central America. This overrepresentation from South American countries may reflect the predominant Caucasian ethnicity of participant physicians and thus, their particular interest in PsA. Although the exact burden and disease expression of psoriasis and PsA in Latin America are unknown, it is thought that the prevalence and incidence of psoriatic disease in the native population is low. The role of ancestry genes and genetic admixture on the occurrence of psoriasis and PsA — and their influence on disease outcomes, particularly mortality and quality of life — among

Latin American natives and mestizos has not been established. Thus, the need for a proper assessment of psoriatic disease (epidemiologic, genetic, and biomarker studies) in Latin America is obvious. GRAPPA, as an umbrella organization for Latin American experts in psoriasis and PsA, may help determine both the frequency and the phenotype of psoriatic disease in Latin America.

Disease Phenotypes of PsA and Psoriasis Patients in Latin America: Physician Estimations from PANLAR and SOLAPSO

With the above objective in mind, a group of Latin American rheumatologists have established the Latin American Psoriasis and Psoriatic Arthritis Society (LAPPAS) as an offshoot of GRAPPA, with goals of phenotyping patients with psoriasis and PsA, identifying genetic factors and biomarkers related to the development of PsA among patients with psoriasis, and identifying risk factors associated with disease phenotypes and comorbidities in patients with psoriasis and PsA in their countries.

Latin American rheumatologists and dermatologists lack clinical experience with PsA and psoriatic patients. The LAPPAS study group performed an online survey among Latin American rheumatologists from PANLAR (Pan American League of Associations for Rheumatology) with an interest in PsA and among dermatologists belonging to SOLAPSO (Sociedad Latino-Americana de Psoriasis)¹⁴. Of the physicians who completed the online survey, 40% of the dermatologists and half the rheumatologists serve populations of over 1 million in public academic medical settings. Specialized PsA and psoriasis clinics in Latin America are not available. Both dermatologists and rheumatologists manage comorbidities with referrals to appropriate specialists and most frequently treat their patients with methotrexate, nonsteroidal antiinflammatory drugs, and topical agents; they rarely use biologics despite accessibility of these drugs.

GRAPPA Activities in Latin America

In September 2010, 10 GRAPPA members participated in the Brazilian Rheumatology Congress in Porto Alegre, Brazil, where they discussed psoriasis and PsA disease states, epidemiology, classification, assessment, and management. A 2-part followup meeting will be held in 2011 in Fortaleza, Brazil. In the first part, participants will learn standard physical examination methods for joints, enthesitis, dactylitis, spine, skin, and nail assessments in patients with PsA in preparation for clinical registry work in Latin America. In the second part, rheumatologists and dermatologists will attend an educational session on psoriasis and PsA pathophysiology, clinical features, assessment, and management; it is

hoped that this session will be a model for future educational modules as part of GRAPPA's global outreach initiative to increase understanding of psoriasis and PsA.

Conclusions

Knowledge of psoriatic disease burden in Central and South America is limited, and available data most likely underestimate the frequency of this disorder. Data from the LAPPAS survey may be biased, and no formal classification criteria have been applied. GRAPPA is partnering with rheumatology and dermatology thought leaders, including LAPPAS and PANLAR, to conduct educational initiatives to investigate the biologic basis, estimate the disease burden, and determine the clinical treatment of PsA and psoriasis in Latin America.

REFERENCES

1. Nestle FO, Kaplan DH, Barker J. Psoriasis. *N Engl J Med* 2009;361:496-509.
2. Arriaza BT. Seronegative spondyloarthropathies and diffuse idiopathic skeletal hyperostosis in ancient northern Chile. *Am J Phys Anthropol* 1993;91:263-78.
3. White C, Maxwell J, Dolphin A, Williams J, Longstaffe F. Pathoecology and paleodiet in postclassic: historic Maya from northern coastal Belize. *Mem Inst Oswaldo Cruz* 2006;101 Suppl 2:35-42.
4. Aceves-Avila FJ, Baez-Molgado S, Medina F, Fraga A. Paleopathology in osseous remains from the 16th century. A survey of rheumatic diseases. *J Rheumatol* 1998;25:776-82.
5. Gerszten PC, Gerszten E, Allison MJ. Diseases of the spine in South American mummies. *Neurosurgery* 2001;48:208-13.
6. Stastny P. HL-A antigens in mummified pre-Columbian tissues. *Science* 1974;183:864-6.
7. Castillo-Ojugas A. Description of psoriatic arthropathy in the 17th century. *Arthritis Rheum* 1991;32:812-3.
8. International Psoriasis Council Psoriasis Review. Dallas, Texas; IPC. [Internet. Accessed October 28, 2011]; Available from: www.psoriasis-council.org/publications/newsletters
9. 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.
10. Sampaio-Barros PD. Epidemiology of spondyloarthritis in Brazil. *Am J Med Sci* 2011;341:287-8.
11. Garcia-Kutzbach A, Montenegro A, Iraheta I, Bara C, Saenz R. Epidemiology of spondyloarthropathies in Central America. *Am J Med Sci* 2011;341:295-7.
12. Vázquez-Mellado J, Font-Ugalde P, Muñoz-Gomález E, Collantes-Estévez E. Registro iberoamericano de espondiloarthritis (RESPONDIA): ¿qué es, cómo surgió, quiénes somos y qué hacemos? *Metodología general. Reumatología Clínica* 2008;4 Suppl 14:S17-22.
13. Bonfiglioli R, Conde RA, Sampaio-Barros PD, Louzada-Junior P, Donadi EA, Bertolo MB. Frequency of HLA-B27 alleles in Brazilian patients with psoriatic arthritis. *Clin Rheumatol* 2008;27:709-12.
14. Toloza SM, Valle-Onate R, Espinoza LR. Psoriatic arthritis in South and Central America. *Curr Rheumatol Rep* 2011;13:360-8.