



# Taibah University

## Journal of Taibah University Medical Sciences

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Original Article

## Clinical patterns of seronegative spondyloarthropathies in a tertiary centre in Pakistan



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Received 12 February 2018; revised 3 March 2018; accepted 6 March 2018; Available online 29 March 2018

### المخلص

**أهداف البحث:** لالتهاب الفقرات والمفاصل أنماط مختلفة في مناطق مختلفة من العالم. وتعتبر معرفة النمط الإقليمي مهمة للتشخيص الصحيح. تهدف هذه الدراسة لتقييم الأعراض والنمط السريري لالتهاب الفقرات والمفاصل بين شريحة المجتمع المنخفضة اقتصاديا واجتماعيا في الباكستان.

**طرق البحث:** خلال الفترة من يوليو ٢٠١٦ إلى يونيو ٢٠١٧، تم إجراء دراسة ملاحظة سريرية في مستشفى تعليمي جامعي للرعاية الثالثة. وكانت العينة التي تم الاختيار منها ٥٠٠٠ شخص في البداية من عيادة الروماتيزم. وتم اختيار ١١٤ شخص وإدراجهم في هذه الدراسة على النحو المحدد في معايير الاشتمال. كما تم تسجيل جميع المتغيرات الديموغرافية وعمل الفحوصات السريرية الأساسية. وتم تجميع معلومات المريض بناء على المشاهدات الدارجة لالتهاب الفقرات والمفاصل. واستخدمت معايير تشخيص مجموعة الدراسة الأوروبية لالتهاب الفقرات والمفاصل لتشخيص وتصنيف المشاركين بالدراسة.

**النتائج:** من بين ١١٤ حالة تم تشخيصها في هذه الدراسة، ضمت الدراسة ٣٦٪ (٤١) من الإناث و ٦٤٪ (٧٣) من الذكور. وكان متوسط العمر للمرضى بين ٢٥-٦٥ عاما. وكان الذكور أكثر تضررا بمرتين تقريبا عن الإناث بمعدل ٢:١.٤. وكان الذكور في العمر ٣٠-٦٠ عاما الأكثر ضررا. وكانت الأنواع الفرعية الأكثر تشخيصا في كثير من الأحيان التهاب الفقار اللاصق، والتهاب المفاصل التفاعلي والتهاب المفاصل الصدفي. وكانت أكثر الأعراض انتشارا هي التهاب المفصل العجزي الحرقفي، وآلم التهاب العمود الفقري والتهاب المفصل الزليلي.

**الاستنتاجات:** وجدت الدراسة الهيمنة الذكورية لالتهاب الفقرات والمفاصل، ومن بين جميع المرضى الذين شملتهم هذه الدراسة؛ تم تشخيص التهاب الفقار

اللاصق، والتهاب المفاصل الصدفي والتهاب المفاصل التفاعلي مع الأنواع الفرعية السائدة لالتهاب الفقرات والمفاصل.

**الكلمات المفتاحية:** التهاب الفقرات والمفاصل؛ التهاب المفاصل الروماتويدي؛ التهاب المفاصل الصدفي؛ التهاب الفقار اللاصق؛ التهاب المفاصل التفاعلي

### Abstract

**Objectives:** The patterns of spondyloarthropathies (SpA) differ across regions globally, and an understanding of these patterns is important for the correct diagnosis of this condition. The aim of this study was to evaluate the presenting symptoms and clinical patterns of SpA in a community of low socioeconomic status in Pakistan.

**Methods:** This clinical observational study was conducted in a tertiary care teaching hospital from July 2016 to June 2017. Five thousand patients were initially recruited in the rheumatology clinic. A total of 114 patients were finally selected and enrolled in this study, as defined by the inclusion criteria. All demographic variables were recorded and baseline clinical investigations were performed. The European Spondyloarthropathy Study Group (ESSG) diagnostic criteria were used to diagnose the condition and classify the study participants.

**Results:** Of the 114 patients, 64% (73 patients) were men and 36% (41 patients) were women. The mean age of the patients ranged 25–65 years. The men were affected twice as much as women with a ratio of 2:1.4. Men in the age group of 30–60 years constituted a large proportion of the study population. The most frequently diagnosed subtypes were ankylosing spondylitis, reactive arthritis, and psoriatic arthritis. The most common presenting symptoms were sacroiliitis, inflammatory spinal pain, and synovitis.

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**Conclusion:** Males had a higher prevalence of SpA. Ankylosing spondylitis, psoriatic arthritis, and reactive arthritis were the most commonly diagnosed subtypes.

**Keywords:** Ankylosing spondylitis; Psoriatic arthritis; Reactive arthritis; Rheumatoid arthritis; Spondyloarthropathies

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## Introduction

Spondyloarthropathies (SpA) refer to a family of diseases that share several clinical features. The most distinguishing features are inflammation of axial joints, asymmetric oligoarthritis, dactylitis, and enthesitis.<sup>1</sup> Concurrent genital and skin lesions, and eye and bowel inflammation might be observed.<sup>2</sup> Many patients also experience eye disorders and entheses with joint and systemic manifestations. Several subtypes of spondyloarthropathy occur, including ankylosing spondylitis, psoriatic arthritis, autoimmune arthritis related to juvenile idiopathic arthritis, inflammatory bowel disease, and reactive arthritis. Clinical features include axial arthritis, enthesopathy, peripheral arthritis, and extra-articular manifestation, including psoriasis, uveitis, and inflammatory bowel disease.<sup>3</sup>

An important aspect of management of these patients was the clinical approach, for which several classification criteria were proposed to categorize the patients. In the 1970s, several specific subtypes of spondyloarthritis were defined, such as those in the modified New York criteria.<sup>4</sup> However, these had certain restrictions and focused mainly on axial features. In 1990, the first set of classification criteria for the entire group of spondyloarthritis was proposed by Amor and Colleagues. A different set of criteria were specified by the European Spondyloarthropathy Study Group (ESSG), with inflammatory back pain and peripheral arthritis as the main entry criteria.<sup>5</sup>

The overall prevalence of SpA is approximately 1% in the United States of America. The prevalence of the spondyloarthropathy subtypes is 0.1% for psoriatic arthritis, 0.2–0.5% for ankylosing spondylitis, and <0.1% for both enteropathic peripheral arthritis and enteropathic axial arthritis.<sup>6</sup> A recent Canadian retrospective study reported an increasing prevalence of ankylosing spondylitis.<sup>8</sup> In northern European countries, psoriatic arthritis, ankylosing spondylitis, undifferentiated arthritis, and autoimmune arthritis associated with inflammatory bowel disease accounted for 54.0%, 21.4%, 17.8%, and 2.3% of cases, respectively. The remaining patients had some form of a combination of spondyloarthritis diagnoses.<sup>7</sup> The prevalence of SpA in the Caucasian population is estimated to be approximately 2%; however, there is considerable variation worldwide, depending on geographical location.<sup>8</sup>

To our knowledge, to date, no data have been published regarding the pattern of this disease in developing countries, including Pakistan (where all spondyloarthropathy subtypes

are observed in the population). The objective of the present study was to evaluate the pattern and prevalence of SpA and its presenting symptoms in patients of low socioeconomic status in a tertiary center in Karachi, Pakistan.

## Materials and Methods

A hospital-based clinical observational study was carried out for one year (July 2016 to June 2017) at Jinnah medical college hospital, Karachi, Pakistan. Approximately 5000 patients presented with back pain complaints. Of these patients, 114 were included in this study based on the ESSG criteria. Patients diagnosed with any subtype or characteristics of spondyloarthropathy according to the ESSG criteria including, inflammatory spinal pain, synovitis (asymmetric or predominantly in the lower limbs) and one or more of the following features were included in the study: a positive family history, psoriasis, inflammatory bowel disease, urethritis, gluteal pain, enthesopathy, and sacroiliitis [9].

A detailed history of the patient was recorded, and a thorough physical examination and specific tests were performed and further reviewed. Written informed consent was obtained where possible and verbal consent was obtained if the participants were illiterate. The privacy of the patient was maintained during the history taking and examination. Confidentiality is an essential aspect of our administrative procedures as we understand the importance of protecting the personal information of patients. Therefore, the patients were assured that their personal information including name, age, occupation, and gender, would not be disclosed.

## Results

Among 114 confirmed cases 73 (64%) were males and 41 (36%) were females. The mean age of the patients was 45 ± 20.2 years. The male to female ratio was 2:1.4. Out of 114 cases of sero-negative spondyloarthropathies, 36% had psoriatic arthritis, 29% ankylosing spondylitis, 25% reactive arthritis, 8% undifferentiated arthritis and 2% had inflammatory bowel of disease associated arthritis. The highest percentage of patients belonged to psoriatic arthritis followed by ankylosing spondylitis and reactive arthritis. The highest percentage of the patients diagnosed as a case for study belonged to the age group ranging (30–60 years) with some cases of age below 30 years and above 60 years (Table 1). The diagnosis was highest (42.8 years) for psoriatic arthritis followed by 39.5 years for reactive arthritis, 32.8 years ankylosing spondylitis, 31.7-year undifferentiated arthritis and 29.5 years inflammatory bowel of disease-associated arthritis. Male dominance was seen in ankylosing spondylitis showing 81.8% and 66.7% in

**Table 1: Demographic data for patients with seronegative spondyloarthropathies according to age group and sex.**

	Male (n = 73)	Female (n = 41)	Total = 114
Sex	64%	36%	
Age group			
<30	20	11	31
30–60	45	25	70
>60	8	5	13

**Table 2: Descriptive results for 114 patients with Seronegative Spondyloarthropathies.**

	Ps.A.	A.S.	RE.A.	UN.A.	I.B.D.A.
Number of cases (no.)	41	33	29	9	2
Age at diagnosis (years)	42.8	32.8	39.5	31.7	29.5
Sex					
Male (%)	58.5%	81.8%	55.2%	66.7%	0%
Female (%)	41.5%	18.2%	44.8%	33.3%	100%
Disease duration (years)					
Mean	63.4	60.0	5.8	18.0	26.5
Mode	6.0	1.0	1.0	1.0	24.0

Ps.A. – Psoriatic Arthritis, A.S. – Ankylosing Spondylitis, RE.A. – Reactive Arthritis, UN.A. – Undifferentiated Arthritis, I.B.D.A. – Inflammatory Bowel Disease Associated Arthritis.

**Table 3: Descriptive results for seronegative spondyloarthropathies with reference to specific variables.**

	PS.A.	A.S.	RE.A.	UN.A.	I.B.D.A.
Inflammatory spinal pain	7.3%	93.9%	3.4%	44.4%	50%
Synovitis	87.8%	21.2%	82.8%	66.7%	–
Positive family history	4.9%	–	–	–	–
Enthesopathy	2.4%	–	–	22.2%	–
Sacroiliitis	12.2%	66.7%	–	22.2%	50%

Ps.A. – Psoriatic Arthritis, A.S. – Ankylosing Spondylitis, RE.A. – Reactive Arthritis, UN.A. – Undifferentiated Arthritis, I.B.D.A. – Inflammatory Bowel Disease Associated Arthritis.

undifferentiated arthritis whereas female dominance was seen in inflammatory bowel disease-associated arthritis with 100% occurrence. The disease duration of psoriatic arthritis and ankylosing spondylitis was 63.4 years and 60.0 years, respectively (Table 2). The inflammatory spinal pain was dominantly seen in ankylosing spondylitis (93.9%) followed by 50% and 44.4% in inflammatory bowel disease-associated arthritis and undifferentiated arthritis respectively. Synovitis was a prominent feature in large number of patients with psoriatic arthritis (87.8%) and reactive arthritis (82.8%), whereas, in patients with ankylosing spondylitis, only about 21.25% had synovitis. Positive family history was only seen in psoriatic arthritis patients. Enthesopathy was noticed in patients with undifferentiated arthritis (22.2%). Sacroiliitis was seen dominantly in patients with ankylosing spondylitis (66.7%), followed by inflammatory bowel disease associated arthritis and undifferentiated arthritis with 50% and 22.2%, respectively (Table 3).

## Discussion

To the best of our knowledge, this was the first study to analyze the pattern of SpA in Pakistan. We believe SpA are frequently observed in this part of the world, but are often overlooked. There are many reasons for this, including symptoms not always occurring simultaneously, in addition to the primary and secondary care settings in this region, because patients with back pain are first observed by primary care physicians.<sup>10</sup> Hence, better techniques and strategies for early diagnosis are still a major challenge for the future. The results

of this study showed that diagnosis of SpA in patients with specific disease combinations is more useful than focusing on a single specific type of spondyloarthropathy. Furthermore, all the important spondyloarthropathy subtypes frequently observed in a Pakistani population are reported.

We showed that the frequency of SpA was slightly higher in males (64%) than in females (36%). The incidences of SpA reported in a previous study in American population were slightly higher. Further, those authors showed that the frequency of reactive arthritis was 47% and undifferentiated arthritis was 33%. With respect to the subtypes, 10% of patients had ankylosing spondylitis, and 9% had psoriatic arthritis.<sup>11</sup> In our study, 36% of the patients had psoriatic arthritis, 25% had reactive arthritis, and 29% had ankylosing spondylitis.

The study conducted in Japan clearly showed that the prevalence of SpA was higher in males than in females (760 males versus 227 females), which supports the findings of our work.<sup>11</sup> It is also important to notice the percentage distribution of the subtypes, which was 4.0% for reactive arthritis, 68.3% for ankylosing spondylitis and 12.7% for psoriatic arthritis.<sup>12</sup> A study conducted in Spain over a one year period showed similar results, with SpA predominance in male patients. A total of 1385 patients were included in the study, 939 males (68%) and 440 females (32%). The (mean  $\pm$  standard deviation) age at diagnosis of our patients was  $43 \pm 10$  years, which is similar to the findings of the study conducted in Spain.<sup>13</sup> Similarly, a Canadian retrospective study showed that a higher proportion of males were being diagnosed with ankylosing spondylitis. However, the incidence of SpA was increasing in females, especially with ankylosing spondylitis.<sup>8</sup>

The mean duration of disease in our patients was  $52 \pm 10$  months, and it was higher in patients with psoriatic arthritis and ankylosing spondylitis. The German Spondyloarthritis Inception Cohort reported that in patients with expert-diagnosed axial SpA, the mean duration of symptoms was 5.2 years.<sup>14</sup> However, we believe ankylosing spondylitis can occur earlier in the disease as shown by our study. In longstanding cases, a plain radiograph of the spine, sacroiliac joints, and involved peripheral joints might be helpful. These changes are used in the classification criteria for SpA. A plain radiograph of the pelvis is recommended in patients with SpA. A diagnosis of ankylosing spondylitis can be made on the basis of a plain radiograph.

In this study, we used the ESSG criteria, which offer greater simplicity with respect to the diagnosis of SpA, as they are based on the results obtained from 140 patients with SpA and 1829 controls, recruited from seven countries. They were also observed by rheumatologists who specialized in diagnosis and treatment of spondyloarthropathy.<sup>15</sup> Although the patients were European, the validity of the ESSG criteria has been demonstrated in other populations. This was the basis on which our study was conducted and evaluated.

## Conclusions

In conclusion, our study revealed a male predominance in the pattern of SpA; psoriatic arthritis, ankylosing spondylitis, and reactive arthritis were the predominantly noticed

subtypes in our study population. The inflammatory spinal pain was usually a symptom of ankylosing spondylitis, and the other features observed were related to psoriatic arthritis, ankylosing spondylitis, and reactive arthritis.

As diagnosing seronegative SpA can be challenging, it is recommended that the physician have a high index of suspicion. Patients generally present with joint symptoms, related comorbidities, or a combination of both. There are also no single clinical features or laboratory tests that can be used to diagnose SpA. Early diagnosis depends on awareness of population-specific patterns of SpA that would determine effective treatment. This study is important as it involved patients of low socioeconomic status from a developing country (Pakistan). Knowledge of the pattern of the disease and its early diagnosis might contribute to more favorable treatment outcomes.

### Funding

This work was self-funded by the authors and external funding was not received.

### Authors' contributions

JSM and MI conceived and designed the study, coordinated data collection and entry, performed the statistical analysis, and wrote the manuscript. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

### Conflict of interest

The authors have no conflict of interest to declare.

### Acknowledgments

We wish to thank Mohamad Shahzeb Ali and Farhan Khalid for their contributions to data collection and entry. We also acknowledge the involvement of all the study subjects at Jinnah Medical College Hospital, Karachi, Pakistan.

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**How to cite this article:** Muhammad JS, Ghauri MI. Clinical patterns of seronegative spondyloarthropathies in a tertiary centre in Pakistan. *J Taibah Univ Med Sc* 2018;13(3):298–301.