ORIGINAL ARTICLES

A study of clinical profile in female spondyloarthropathy

Patil LN[1], Oak JL[2]

[1,2]Kokilaben Dhirubhai Ambani Hospital,Andheri, Mumbai, India

Abstract

Objective: To assess the clinical features of SpA including BATH indices and to compare clinical data of male and female spondyloarthropathy patients.

Methods: The study included male and female patients (60 each) fulfilling the European Spondyloarthropathy Study Group (ESSG) or assessment of ankylosing spondylitis (ASAS) criteria for SpA and the CASPER criteria for PsA or the modified New York criteria for AS. The subjects completed initial clinical evaluation and radiological and laboratory assessment.

Results: The mean age of presentation was found to be higher in females (34.6± 9.6 years). Backache was the most common features identified in both the groups. Peripheral arthritis was present in 51.7% of total patients (56.7% males and 46.7% females). Asymmetrical lower limb arthritis was found to be more predominant; however, 10% of the patients reported involvement of wrist. Psoriasis and inflammatory bowel disease, and uveitis were noted in 13 (7 males and 6 females), three (1 male and 2 females) and 14 patients (9 males and 5 females) respectively. Dorsal and neck pain were frequently prevalent among the patients.

Conclusion: Though the severity of symptoms and disability are comparable across both the genders, females have increasingly been diagnosed with SpA. Most common symptom of presentation is low back pain followed by gluteal pain. Peripheral arthritis, predominantly lower limb oligoarthritis is common in Indian population when compared to their western counterparts.

Keywords: Spondyloarthropathy, BASDAI, BASFI

Introduction

The spondyloarthropathies (SpAs) encompass a group of linked clinical syndromes in terms of disease manifestations and genetic susceptibility. The clinical subset includes ankylosing spondylitis (AS), reactive arthritis (ReA), psoriatic arthritis (PsA), enteropathic arthritis (EA) associated with Crohn's disease or ulcerative colitis and juvenile onset SpA. There is a male preponderance in the disease with male to female ratio of 2.5:1 to 5:1.[1] Review of literature shows that epidemiological data pertaining to the prevalence of SpA in India is not available. All types of cost burden associated with AS result from loss of function and disease activity. Early diagnosis and treatment are necessary to prevent/reduce functional decline and improve patient outcome. There has been a great resurgence of interest in AS in recent years because of the availability of novel, imaging techniques and highly effective newer therapies such as the tumor necrosis factor inhibitors.[2,3] Therefore, it has become extremely important that the patients be correctly diagnosed early in the disease course for obtaining full benefit of the advanced therapeutics. [4]

AS being more common in males, it is usually not considered as differential diagnosis in females with similar complaints, which leads to a delay in the diagnosis and treatment. The interval between the first complaints of the disease and the time of definite diagnosis may be as long as 4-9 yrs.[5] There are few studies from the Indian

subcontinent on female patients with SpA and clinical characterization of AS.[6-9]

The present study was carried out with the primary objective of prospectively analyzing the clinical patterns along with the occurrence of HLA B27 in spondyloarthropathy in female patients. Secondary objectives included analysis of the differences in clinical manifestations according to patient's gender and the evaluation of severity of disease based on BATH indices in the study population. i.e. BATH Ankylosing Spondylitis Disease Activity Index (BASDAI) and BATH Ankylosing Spondylitis Functional Index (BASFI).

Materials and methods

The prospective observational study was carried out at a tertiary care hospital and research centre in Mumbai. Subjects with any disease spectrum of SpA and within the age group of 19-45 years were considered. Those fulfilling the European Spondyloarthropathy Study Group (ESSG) or assessment of ankylosing spondylitis (ASAS) criteria for SpA and the CASPER criteria for PsA or the modified New York criteria for AS were included.[10] Patients with mechanical backache like spondylolisthesis, prolapsed intervertebral disc, degenerative spine disease, and lumbar strain or sprain were excluded. The juvenile SpA patients were excluded from the study.

Informed consent was obtained from the study participants and the ethics committee approval was from Institutional Scientific and Ethics Committee (ISEB) of Kokilaben Dhirubhai Ambani Hospital and Medical Research Centre. An investigator-administered questionnaire was used to gather demographic details. Initial clinical evaluation, radiological and laboratory assessment were also completed. HLA-B27 was done for all patients using flow cytometry method. BASDAI, BASFI, BASMI, and BAS-G indices were included for functional assessment of the patients who were within the first year of their presentation. Besides spinal assessment, the number of joints affected by peripheral arthritis and the presence of enthesitis were noted. Other aspects of the disease were noted such as the disease course and status of the disease.

Queries pertaining to the following were included in the questionnaire: time/ age of disease onset and the diagnosis, and the presence of buttock pain, backache, foot pain, hip pain and eye inflammation as initial symptoms. For patients who could not answer this questionnaire format, visual analogue scale (VAS) was used for the evaluation of pain, wellbeing, disease activity and function for the past week and past six months.

Statistical analysis

Based on the literature, it was observed that BASDAI score for females was 6.32 with standard deviation as ± 2. Expecting BASDAI score to be 5 with standard deviation of ± 3.5, the sample size was calculated to be 58 subjects to achieve 80% power with 5% level of significance. Data was presented as mean ± SD. Unpaired T test was used for continuous data and chi square test for categorical data. P <0.05 was considered as significant.

Results

The study considered patients of both the genders (60 each). Women had greater mean age of presentation (34.6±9.6 years versus 32.7±9.14years) and age of onset of symptoms of SpA (28.3 ±9.9 years versus 25.7±7.3 years). Age at first diagnosis of SpA in females was (31.2±10.8 years versus males 30.2 ±6.8 years). There was no statistical difference between male and female patients (Fig. 1.)

Low back pain was the most common presenting symptom in both the groups (58 out of 120 patients), followed by gluteal pain in 25 out of 120 patients. Other symptoms noted were peripheral joint pain, swelling, effusion, polyarthritis and uveitis. Uveitis was seen in females (2 patients), while none of the males had uveitis as a presenting symptom. (Fig. 2).

The family history was elicited for all patients with SpA features and was positive in 26.6% of the cohort (19 females and 13 males). Peripheral arthritis was present in 51.7% of total patients (56.7% males and 46.7% females). Arthritis was predominantly asymmetrical lower limb arthritis. However, 10% of the patients reported involvement of wrist. Ankylosing spondylitis was the most frequent in the group (52 males and 52 females), followed by psoriatic arthritis (7 males and 6 females), and arthritis associated with inflammatory bowel disease (1 male and 2 female, Table 1). Uveitis was present in 14 patients (9 males and 5 females). Dorsal pain and neck pain were frequently prevalent among patients (Table 2). BATH indices (BASDAI, BASFI, BAS-G) showed similar scores for males and females without any significant difference (Table 3), indicating that females suffer from equally severe disease as males. BASMI indices of male and

Fig.1: Comparison of age (in years) in male and female patients at presentation, symptom onset, at first diagnosis and diagnostic delay

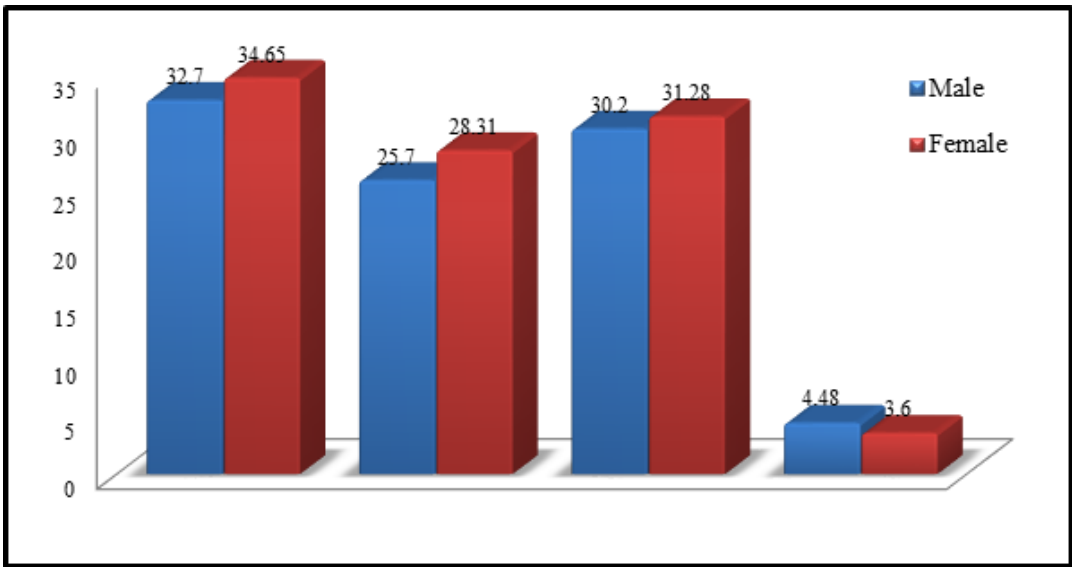
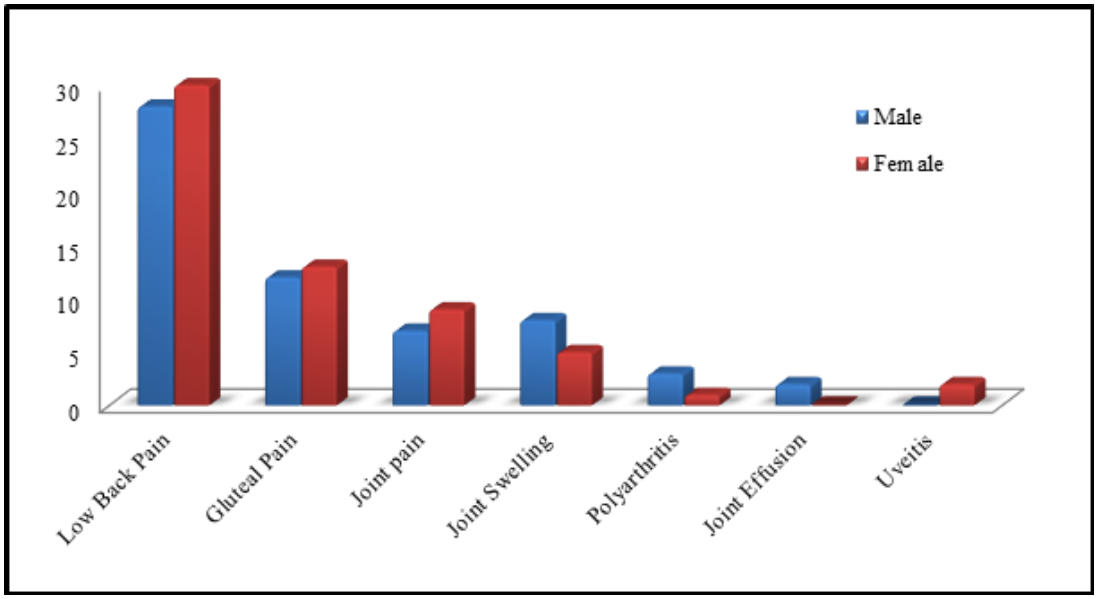


Fig. 2: Comparison of presenting symptoms in male and female patients



female patients showed significant difference suggesting males have severe restriction in movements compared to females. (Table 3). HLA-B27 was done in all patients with clinical diagnosis of SpA and was positive in 95 of 120 patients (51 male and 44 female) (Table 4).

Discussion

There is a perception that the diagnosis of SpA is often delayed, underdiagnosed or overlooked in women than men. The current study examined the presenting symptoms, the disease activity and the functioning indices of the patients to better understand the reasons pertaining to these disparities.

The corresponding mean ages of disease onset noted in males and females were 25.7±7.3 years and 28.3± 9.9 years, and were higher than that reported by Malviya *et.al* (23.6 years) in ankylosing spondylitis patients in India.[13] Although the age of onset could be much lower in patients belonging to developing countries, the present work did not confirm the same.[13] In concurrence with the previous literature findings, maximum number of patients had onset

Table 1: Distribution of clinical subsets of spondyloarthropathy in the cohort

Gender	Ankylosing Spondylitis	Psoriatic arthritis	Reactive arthritis	IBD-related arthritis
Males	52	7	0	1
Females	52	6	0	2
Total	104	13	0	3

Table 2: Symptoms in patients of spondyloarthropathy

Symptomatology							
Gender	**Low back pain**	**Dorsal pain**	**Neck pain**	**Peripheral arthritis**	**Psoriasis**	**IBD**	**Uveitis**
Male	57	14	12	34	7	1	9
Female	55	17	5	28	6	2	5
Total	112	31	17	62	13	3	14

Table 3: Comparison of BATH indices in male and female patients

BATH indices/ Gender	Values	Pvalue
BASDAI		0.298
Male	5.456	
Female	5.0958	
BASFI		0.154
Male	5.3342	
Female	4.7725	
BASMI		0.04
Male	3.5167	
Female	2.5333	
BAS-G		**0.17**
Male	**6.3333**	
Female	**5.8683**	

of symptoms before the age of 45 years.

Gender bias in SpA is an interesting aspect of the study. The male preponderance reported in literature has varied from 2.5:1 to 5:1.[1] There has been increasing recognition that AS is not infrequent in females and the severity of the symptoms are similar across them, although females have less structural changes in spine and this was highlighted by Feldtkeller *et al*.[14,15] Previous studies from India has reported very high male to female ratio of 16.[18] The present study has considered equal number of male and female patients over a period of 2 years, considering the fact that the disease is not uncommon in women. Another factor for relatively less recognition of AS in females could be their high threshold in seeking medical attention, which is secondary to cultural and socioeconomic environment in India.[16] Most of the data available from Indian settings are for AS patients and not SpA patients as a group.

Association of HLA-B27 with familial aggregation is a well-known characteristic of SpA and the same has also been reported in India.[9] In the present study, HLA B27 was positive in 79% patients, and family history was positive in 26.6% of the patients. The genetic susceptibility was reported to be low when compared to the study by Malaviya *et.al.* (90%). No specific reason could be ascertained for

Table 4: Prevalence of HLA-B27 in male and female patients

Gender	HLAB27		Total
	Positive	Negative	
Male	51 (85%)	9 (15%)	60
Female	44 (73.3%)	16 (26.6%)	60
Total	95 (79.1%)	25 (20.8%)	120

this finding.

The most common presenting symptom was low back pain (58 out of 120 patients) and this is in line with the study by Roussou *et.al*.[17] Gluteal pain was seen as second most common presenting symptom (5 out of 120 patients) in the current study. This pain represents sacroiliac joint involvement and could be severe in the early phase of the disease; it can be associated with low back stiffness.[18] Peripheral joint pain, as a presenting symptom, was reported less frequently in Indian patients than in western population.[19]

Two patients had anterior uveitis as a presenting symptom and developed other features of SpA in the following years. A study by Linder *et.al.* detected SpA in 10% of the patients with uveitis. Hence uveitis patients must be evaluated or followed up for SpA.[20]

Prevalence of peripheral arthritis was found to be higher (51.6%, 62 out of 120 patients) in the present study when compared to the western population, thereby corroborating the findings by Malaviya *et.al* in Indian AS patients (65.7%).[16,19] The pattern of peripheral arthritis was typical as described in SpA, i.e., inflammatory asymmetric oligoarthritis, predominantly involving the large joints in the lower extremity.[21] An unusual presentation of acute large joint polyarthritis involving both upper limbs and lower limbs was also observed in four patients.

The overall disease activity in females was similar to males as observed with BASDAI and BASFI indices, and no statistical difference was noted. This finding was consistent with study by Roussou *et.al.* Upon considering BASMI indices for joint flexibility, indices for cervical rotation were significantly severe in men along with lumbar side flexion and dorsal kyphosis. This difference could be because of genetic predisposition for severe disease in males.

Conducting the study in SpA group and not in AS patients exclusively is one of the major limitations of the study. In summary, back pain was reported as the first and main symptom by 91% of the female patients during the disease course. Since pain is a common musculoskeletal complaint, it can be easily perceived as spondylitis, muscle spasm, gynecological problem or osteomalacia in female patients. The other clinical features of SpA like morning stiffness, enthesitis, peripheral arthritis or dactylitis should be given due attention. Similarly, careful assessment of sacroiliac joints, both clinical as well as radiological, should be done whenever symptoms of back pain prevail for a longer duration. The imaging should include both spine and sacroiliac joints, to identify features like bone marrow edema, joint space narrowing or joint erosions.

Conclusion

SpA needs to be considered as a differential diagnosis in female patients with long-standing back pain. Attention should be given to SpA features like early morning stiffness, enthesitis, peripheral arthritis and dactylitis. Imaging of sacroiliac joints needs to be done in suspected cases for early diagnosis and treatment of SpA.

Competing interests
The authors declare that they have no competing interests.

Citation
Patil LN, Oak JL. A Study of clinical profile in female spondyloarthropathy. IJRCI. 2019;7(1):OA2.

Submitted: 15 July 2019, **Accepted:** 17 October 2019, **Published:** 19 November 2019

*Correspondence: Dr. Jyotsna Oak, Kokilaben Dhirubhai Ambani Hospital.Andheri, Mumbai. India
jyotsnaoak@gmail.com

References

1. Goldmann L., Scafer AI, Goldman's Cecil Medicine, 24th ed., New York: Elsevier; 2012. Chapter 273, Spondyloarthropathy; p.1690-1697
2. Gorman JD, Sack KE, Davis JC. Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor alpha. N Engl J Med [Internet]. 2002 May 2 [cited 2015 Jun 15];346(18):1349–56.

3. Braun J, Sieper J. Ankylosing spondylitis. Lancet [Internet]. 2007 Apr 21 [cited 2015 Jun 16];369(9570):1379–90
4. Rudwaleit M, Listing J, Brandt J, Braun J, Sieper J. Prediction of a major clinical response (BASDAI 50) to tumour necrosis factor alpha blockers in ankylosing spondylitis. Ann Rheum Dis. 2004;63(6):665–70.
5. Prasad P, Singh RP. Ankylosing spondylitis in tribal belt of Chhotanagpur region. J Indian Med Assoc [Internet]. 1982 Apr 1 [cited 2015 Jun 16];78(7):108–12.
6. Khan MA. Ankylosing spondylitis and HLA-B27 in Punjabis. Lancet [Internet]. 1977 Sep 3 [cited 2015 Jun 16];2(8036):504.
7. Prasad P, Singh RP. Ankylosing spondylitis in tribal belt of Chhotanagpur region. J Indian Med Assoc [Internet]. 1982 Apr 1 [cited 2015 Jun 16];78(7):108–12
8. Prakash S, Mehra NK, Bhargava S, Vaidya MC, Malaviya AN. Ankylosing spondylitis in North India: a clinical and immunogenetic study. Ann Rheum Dis [Internet]. 1984 Jun [cited 2015 Jun 16];43(3):381–5.
9. Achuthan K, Porkodi R, Ramakrishnan S, Krishnamurthy V, Madhavan R, Parthiban M, et al. Pattern of rheumatic diseases in south India. V. Ankylosing spondylitis. A clinical and radiological study. J Assoc Physicians India [Internet]. 1990 Oct [cited 2015 Jun 16];38(10):774–6.
10. Dougados M, van der Linden S, Juhlin R, Huitfeldt B, Amor B, Calin A, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondylarthropathy. Arthritis Rheum [Internet]. 1991 Oct [cited 2015 May 19];34(10):1218–27.
11. Feldtkeller E, Khan MA, van der Heijde D, van der Linden S, Braun J. Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis. Rheumatol Int [Internet]. 2003 Mar [cited 2015 May 18];23(2):61–6.
12. Carette S, Graham D, Little H, Rubenstein J, Rosen P. The natural disease course of ankylosing spondylitis. Arthritis Rheum [Internet]. 1983 Feb [cited 2015 Jun 24];26(2):186–90.
13. Aggarwal R, Malaviya AN. Clinical characteristics of patients with ankylosing spondylitis in India. Clin Rheumatol [Internet]. 2009 Oct [cited 2015 Jun 24];28(10):1199–205.
14. Zink A. The national database of the German Collaborative Arthritis Centres: I. Structure, aims, and patients. Ann Rheum Dis [Internet]. 2001 Mar 1 [cited 2015 May 28];60(3):199–206
15. Feldtkeller E, Braun J. Impact of sex on inheritance of ankylosing spondylitis. Lancet (London, England) [Internet]. 2000 Mar 25 [cited 2015 Jun 24];355(9209):1096–7; author reply 1098
16. Aggarwal R, Malaviya AN. Diagnosis delay in patients with ankylosing spondylitis: factors and outcomes--an Indian perspective. Clin Rheumatol [Internet]. 2009 Mar [cited 2015 Jun 16];28(3):327–31.
17. Roussou E, Sultana S. Spondyloarthritis in women: differences in disease onset, clinical presentation, and Bath Ankylosing Spondylitis Disease Activity and Functional indices (BASDAI and BASFI) between men and women with spondyloarthritides. Clin Rheumatol [Internet]. 2011 Jan [cited 2015 Jun 24];30(1):121–7.
18. Firestein G S., Budd R C, Gabriel S E, O'Dell J.R., MnInnes I.B., Kelly's Textbook of Rheumatology, 9th ed.,Philadelphia: Elsevier; 2013. Chapter 75, Ankylosing Spondylitis; p.1202-1220.
19. Singh G, Lawrence A, Agarwal V, Misra R, Aggarwal A. Higher prevalence of extra-articular manifestations in ankylosing spondylitis with peripheral arthritis. J Clin Rheumatol [Internet]. 2008 Oct [cited 2015 Jun 24];14(5):264–6.
20. Linder R, Hoffmann A, Brunner R. Prevalence of the spondyloarthritides in patients with uveitis. J Rheumatol [Internet]. 2004 Nov 1 [cited 2015 Jun 23];31(11):2226–9.
21. Kanga U, Mehra NK, Larrea CL, Lardy NM, Kumar A, Feltkamp TE. Seronegative spondyloarthropathies and HLA-B27 subtyes: a study in Asian Indians. Clin Rheumatol [Internet]. 1996 Jan [cited 2015 Jun 24];15 Suppl 1:13–8.