



## A STUDY ON THE INCIDENCE & CLINICAL PROFILE OF SUBSETS OF SPONDYLOARTHRITIS AND ITS ASSOCIATION WITH HLA-B27

### Biochemistry

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### ABSTRACT

**Objective:** To study the incidence, clinical profile & HLA association of subsets of spondyloarthritis patients in eastern India. Results: Ankylosing spondylitis (AS) constitutes maximum number of cases followed by undifferentiated spondyloarthropathy (USpA) and others. 59% of AS cases presented with both axial & peripheral arthritis whereas 41% have only axial presentation. Reactive arthritis (ReA) cases had only peripheral involvement of 87.5%. Enthesitis was seen in 41.3%, 72%, 75% cases of AS, USpA, & ReA groups respectively. HLA-B27 was positive in 88.3% of AS and 78.3% of USpA & 60% of psoriatic arthritis (PsA) cases. But only 50% positive in ReA & inflammatory bowel disease (IBD) associated arthritis groups. Conclusion: our study suggests a strong association of HLA-B27 with the subsets of spondyloarthritis. HLA Typing would help in the diagnosis of spondyloarthritis mainly ankylosing spondylitis where clinical features are unclear and it can help in identifying the family members who are at risk.

### KEYWORDS:

Spondyloarthritis, Ankylosing spondylitis, undifferentiated spondyloarthropathy, HLA-B27

### INTRODUCTION:

Seronegative spondyloarthropathy (SpA) patients lack detectable rheumatoid factors in serum and include a group of diseases like ankylosing spondylitis (AS), reactive arthritis (ReA), arthritis associated with psoriasis (PsA) and inflammatory bowel disease (IBD) & undifferentiated spondyloarthropathy (USpA).

Prevalence of spondyloarthropathy around the world has been estimated to range from 0.01% - 2.5%<sup>[1]</sup>. Indian data on the epidemiology of spondyloarthropathy are scarce. Prevalence data from the first Indian COPCORD (Community Oriented Programme for Control of Rheumatic Disease) survey showed the rural prevalence of back pain to be 17.3%. This includes both inflammatory and mechanical back aches. Of all the people with low backache, about 1-2% are likely to have SpA. From this rural cohort the SpA prevalence can be estimated about 0.17-0.34%<sup>[2]</sup>

Association of HLA-B27 to inflammatory SpA was first recognized in 1973<sup>[3]</sup>. In UK, HLA-B27 is present in 90-95% of patients with AS, 60-90% patients with reactive arthritis, 50-60% of patients with psoriatic arthritis or inflammatory bowel disease associated arthritis and 80-90% of children with juvenile ankylosing spondylitis.

HLA-B27 associations with seronegative spondyloarthritis in different Indian populations vary from 18-94% as compared to 1.4-8% of the general population<sup>[4]</sup>

None of the diseases under spondyloarthropathy requires a positive HLA-B27 test for a definite diagnosis. All diagnosis are based on the appearance of certain clinical signs and symptoms, and for AS the demonstration of radiological sacroiliitis is mandatory for diagnosis.

Positive predictive value of HLA-B27 lies between 0.95% to 9.5% which indicates that the overwhelming majority of HLA-B27 positive persons do not suffer from AS. However, the negative predictive value is exceptionally high which shows the chance of having AS for a person without HLA-B27 is extremely low. A negative test result should be interpreted as an exclusion criterion for the diagnosis of AS.

Earlier reports have shown wide discrepancy in the seropositivity among the Indian population. Hence the present study was undertaken to compare the HLA association in seronegative spondyloarthritis patients and their different clinical manifestations in eastern India.

### MATERIAL & METHODS:

This study was conducted by taking all total 90 cases of SpA diagnosed as per ESSG criteria presented to Dept. of Medicine, SCB Medical College during 1 yr period. They were assessed for clinical profile and extraarticular manifestation. All the cases below 16 yrs (juvenile SpA) were excluded from the study.

The Institute Ethics Committee was approached for Ethical Clearance. An informed consent was obtained from all the participants before collecting the blood samples.

Routine tests like complete blood count, renal function test & liver function test, ESR (erythrocyte sedimentation rate), CRP (C-Reactive Protein) were done during presentation. X-rays of pelvis & other involved joints were undertaken if required. HLA B-27 assay was done by the method of flow cytometry.

All statistical analysis was done in SPSS software version 20.

### RESULTS:

After studying the age and sex distribution of total 90 spondyloarthropathy patients, most cases were found to be presented in 3<sup>rd</sup> & 4<sup>th</sup> decades of life. In USpA, patients presented early in their 2<sup>nd</sup> & 3<sup>rd</sup> decades but in psoriatic arthritis 60% cases present in 5<sup>th</sup> to 6<sup>th</sup> decades.

Males outnumber the females in each group with M:F of 3.5:1 & highest male to female ratio observed in AS which was 7:1.

Out of total 90 cases, ankylosing spondylitis constitutes maximum number of cases followed by undifferentiated spondyloarthropathy and others.

According to Table 1, out of 46 cases of AS, 59% presented with both axial & peripheral arthritis whereas 41% have only axial presentation. ReA cases had only peripheral involvement of 87.5%.

**Table 1: Types of articular involvement**

categories	Axial	Percentage (%)	Peripheral	Percentage (%)	Axial + Peripheral	Percentage (%)
AS	19	41.0	-	-	27	59.0
USpA	2	6.9	5	17.2	22	75.9

ReA	-	-	7	87.5	1	12.5
PsA	-	-	2	40.0	3	60.0
IBD with arthritis	-	-	1	50.0	1	50.0
Total (n=90)	21	23.33	15	16.67	54	60.0

Enthesitis was seen in 41.3%, 72%, 75% cases of AS, USpA, & ReA groups respectively. Plantar fasciitis being the most common presentation followed by Achilles tendinitis. (Table 2)

**Table 2: Prevalence of enthesitis among study population**

Categories	No. Of enthesitis	Percentage (%)	Plantar Fasciitis	Percentage (%)	Achilles Tendinitis	Percentage (%)
AS (n=46)	19	41.3	14	73.7	5	26.3
USpA (n=29)	21	72.4	18	85.7	3	14.3
ReA (n=8)	6	75.0	5	83	1	17
PsA (n=5)	1	20.0	1	100	-	-
IBD with arthritis (n=2)	-	-	-	-	-	-

Among the extraarticular manifestations, uveitis was most common that occur in 17.4% cases of AS & 6.7% cases of USpA.

On examining various inflammatory parameters, we observed ESR & CRP was highest among ReA patients followed by AS patients. Hb% was lowest in IBD with arthritis group.

Association of HLA-B27 with subsets of spondyloarthritis was revealed in Table 3. According to this HLA-B27 was found to be positive in 88.3% cases of AS and 78.3% in USpA & 60% in PsA groups. But it was only 50% positive in ReA & IBD with arthritis groups.

**Table 3: association of HLA-B27 in the study population**

Categories	No of HLA-B27 done	HLA-B27 positivity	Percentage	HLA-B27 negativity	Percentage
AS (n=46)	43	38	88.3	5	11.7
USpA (n=29)	23	18	78.3	5	21.7
ReA (n=8)	6	3	50.0	3	50.0
PsA (n=5)	5	3	60.0	2	40.0
IBD with arthritis (n=2)	2	1	50.0	1	50.0
Total (n=90)	79	63	79.74	16	20.26

## DISCUSSION:

Spondyloarthritis is a group of chronic disorder that are characterised by presence of asymmetrical peripheral arthritis, inflammatory back pain, sacroiliitis, peripheral enthesitis with absence of rheumatoid factor and its association with HLA-B27<sup>[5]</sup>

The data regarding true incidence and prevalence of SpA is scarce in India. Indirect evidence by S Prakash et al showed a prevalence of 0.17 to 0.34%.<sup>[6]</sup>

However there are few studies regarding its epidemiology & different clinical manifestations in India limiting better understanding of this disease pattern in this part of this world. Also there are few reports regarding its association with HLA-B27.

This study is an attempt to profile various manifestations of spondyloarthritis and correlation of different groups with HLA-B27.

Among total 90 patients observed, ankylosing spondylitis was the most common disease which constituted 51% of total cases followed by USpA (31%) being the 2nd most common. The Collantes study<sup>[7]</sup> reported a similar incidence of AS (61%) followed by PsA (21%) &

USpA (15%). Kim et al observed a 49.2% incidence of AS and 13% incidence of USpA in their study<sup>[8]</sup>.

In our study males outnumber the females in each group. M:F ratio in AS was 7:1 whereas in USpA 1.5:1. Though in most studies from western countries, M:F in AS was 2-3:1<sup>[9,10]</sup>, but our study showed a higher frequency which may be due to the under reporting of female cases in our society as they tend to regard back pain as an insignificant physical sign of their daily lives.

SpA affects both axial and peripheral joints. In our study, 60% of patients were found to have peripheral arthritis. 23.3% had only axial involvement and 16.7% had both axial and peripheral involvement. Collantes study reported a 17% incidence of peripheral arthritis. We had a higher incidence of peripheral arthritis in our study, and this is in consistent with another study by Emam SJ et al who also found similar incidence of peripheral arthritis<sup>[11]</sup>. In case of AS, we observed peripheral arthritis in 59% of cases. Another study in India also reported similar incidence of peripheral arthritis (65.7%)<sup>[12]</sup>. Lee et al reported 70% incidence of peripheral arthritis in their study.

Enthesitis in the form of Achilles tendinitis & Plantar fasciitis was presented in 41% cases of AS, 72% CASES OF USpA, 75% in ReA and 20% in PsA in our study. Lee et al<sup>[13]</sup> in 2002 reported 53% incidence of enthesitis among AS patients with Achilles tendinitis being the most common site (88%) followed by Plantar fasciitis (31%). But Collantes study<sup>[7]</sup> reported 25% incidence of enthesitis in AS patients. Our study was quite similar to the study by Lee et al but we observed plantar fasciitis being the most common site of affection in 73% followed by Achilles tendinitis in 27% of cases.

Incidence of enthesitis was 82% among USpA patients according to Kim et al<sup>[8]</sup> from Korea which was very similar to our study. We observed a higher incidence of enthesitis among reactive arthritis patients which was against the finding by Immann et al<sup>[14]</sup> and Collantes et al who reported 30% & 19% incidence of enthesitis among ReA patients respectively.

HLA-B27 association with SpA was found to be 79.74% in our study. It was positive in 88.3% cases of AS, 78.3% cases of USpA, 60% in PsA, 50% in ReA & IBD associated arthritis patients. Also similar data was obtained from Collantes study that reported 84% association of HLA-B27 with AS, 71% among USpA, 64% among ReA & 22% in PsA patients & 40% in IBD associated arthritis groups. Baek et al reported 98.5% HLA-B27 association among AS patients in Singapore. Also similar association of HLA-B27 by Prakash et al from India was observed to be 84% among USpA patients<sup>[15]</sup>. In contrast, some other studies from India<sup>[16,17,18]</sup> and another study in Bangladesh reported lesser frequency of HLA-B27 association among spondyloarthritis patients<sup>[19]</sup>

## CONCLUSION:

Our study suggests higher association of HLA-B27 with spondyloarthritis in this eastern zone of India than that reported by others from this country. However many factors like geographic variance, ethnic background and environmental factors have to be considered before making any definite conclusion. We suggest HLA Typing would help in the diagnosis of spondyloarthritis mainly in AS where clinical features are unclear and it can help in identifying the family members who are at risk. Further extensive studies taking larger population are needed to assess the prevalence of HLA-B27 among different groups of spondyloarthritis patients in this zone of India.

## CONFLICT OF INTEREST:

The authors declare that there is no conflict of interests regarding the publication of this paper.

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