

## Comparison of Clinical Features in Hla-B27 Positive and Negative Patients with Axial Spondyloarthritis

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### ABSTRACT

**Objective:** To compare the clinical features of HLA-B27 positive and negative patients having axial spondyloarthritis.

**Study Design:** Quasi-experimental study.

**Place and Duration of Study:** Department of Rheumatology, Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan, from Oct 2022 to Apr 2023.

**Methodology:** Patients with axial spondyloarthritis who were diagnosed by consultant rheumatologist on the basis of Assessment of Spondyloarthritis International Society were recruited. All baseline investigations and HLA typing were performed on the study participants. They were further divided into two groups for comparison on the basis of HLA-B27 positivity or negativity. Relevant clinical features were compared in both the groups.

**Results:** A total of 150 patients of axial spondyloarthritis were recruited in this study, with mean age being 42.78±10.2 years, among whom 41(27.3%) patients were female while 109(72.7%) were male, while 104(69.3%) patients of axial spondyloarthritis were HLA-B27 positive and 46(30.7%) were HLA-B27 negative. It was noted that positive family history of axial spondyloarthritis, hip joint involvement, uveitis, inadequate response to NSAIDs and good response to biological therapy were statistically significant among patients who were HLA-B27 positive as compared to those who were HLA-B27 negative.

**Conclusion:** Positive family history, hip joint involvement, uveitis, inadequate response to NSAIDs and good response to biological therapy was noted among patients who were HLA-B27 positive.

**Keywords:** Axial Spondyloarthritis, HLA-B27, Rheumatology.

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### INTRODUCTION

Rheumatology is an emerging medical specialty in our part of the world with wide range of diseases.<sup>1</sup> Axial Spondyloarthritis is not an uncommon diagnosis in rheumatology setups<sup>2</sup> but it does not confine itself to joints, usually presents as a multisystem disorder warranting multidisciplinary teamwork in order to manage patients effectively.<sup>3</sup> Recent advances in molecular typing revolutionized the diagnosis and management strategies of immune based disorders<sup>4</sup> with HLA typing now performed in routine clinical practice.<sup>5</sup> HLA-B27 must be performed in cases who are diagnosed with axial Spondyloarthritis to determine appropriate treatment plan and determining course of illness in the patients.<sup>6</sup> Existing literature has highlighted the role of this molecular marker in etiology, pathology and management of this rheumatological illness<sup>7</sup> with family history, presence of peripheral joint involvement and presence of psoriasis having an association with presence of

HLA-B27 and altered clinical course of axial Spondyloarthritis.<sup>8</sup> Factors such as earlier onset of axial spondyloarthritis, higher axial involvement and presence of uveitis were seen more in patients who were HLA-B27 positive as compared to those who were negative.<sup>9</sup> As limited health care resources are available in Pakistan, a balance needs to be achieved between carrying out necessary investigations and saving the patient from financial stress. A recent study from Pakistan concluded that subtypes were not different among patients and controls recruited in their study<sup>10</sup> but limited local data is available regarding difference in clinical spectrum of patients who are positive or negative for HLA-B27, thus, this study was planned with the rationale to compare the clinical features in HLA-B27 positive and negative patients with axial spondyloarthritis.

### METHODOLOGY

This quasi-experimental study was carried out at Department of Rheumatology, Pak Emirates Military Hospital (PEMH), Rawalpindi Pakistan from October 2022 to April 2023, after taking permission from Ethics Review Board of the hospital via letter

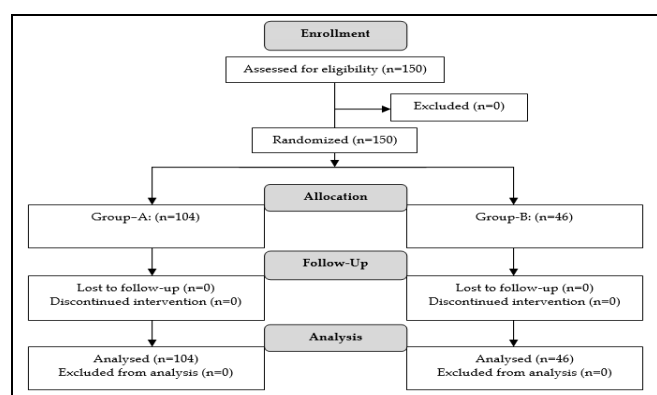
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A/28/226/EC/521/23. Sample size was calculated by using the World Health Organization (WHO) sample size calculator and keeping the population prevalence proportion of Group-I (HLA-B27 positive patients) as 25% and Group-II (HLA-B27 negative patients) as 17%.<sup>11</sup> Non probability consecutive sampling technique was used to gather the required sample size for this study. Patients were only enrolled if they met full inclusion criteria otherwise, they were excluded.

**Inclusion Criteria:** Patients of belonging to either gender, between the age of 18 and 60 years, diagnosed with axial spondyloarthritis by consultant rheumatologist at PEMH.

**Exclusion Criteria:** Patients with any type of cancers (solid or hematopoietic), in whom HLA-B27 testing could not be performed due to any reason or who refused treatment (NSAIDs or biological therapy) were excluded.



**Figure: Patient Flow Diagram (n=150)**

Patients of axial spondyloarthritis who were diagnosed by consultant rheumatologist on the basis of Assessment of Spondyloarthritis International Society were recruited<sup>12</sup> with all baseline investigations and HLA typing performed on the study participants from Department of Immunology, Armed Forces Institute of Pathology via set protocols.<sup>13</sup> They were divided into two groups for the sake of comparison on the basis of HLA-B27 positivity. All the patients underwent detailed history and clinical examination at time of diagnosis along with all relevant investigations. They were followed up on two weeks' intervals for assessing the course of illness and seeing extra articular manifestations. Treatment options were given by the team according to international guidelines including both NSAIDs and biological therapy.<sup>14</sup> Response to treatment was observed by same team. Statistical Package for the

Social Sciences (SPSS) version 23.0 was used to analyze the data collected. Frequency and percentages were calculated for the qualitative variables while mean and standard deviation were calculated for the age of the patients. Pearson chi-square test and Fischer exact test were used to assess for comparison of different clinical variables among patients with positive and negative HLA-B27 where *p*-value of  $\leq 0.05$  was set to be statistically significant.

## RESULTS

A total of 150 patients of axial spondyloarthritis were recruited with mean age of the participants being  $42.78 \pm 10.2$  years, of which 41(27.3%) patients were female while 109(72.7%) were male. The clinical findings observed in study participants during course of illness are summarized in Table-I. On analysis, statistical significance was noted in positive family history of axial spondyloarthritis (*p*-value-0.037), hip joint involvement (*p*-value-0.036), uveitis (*p*-value-0.006), inadequate response to NSAIDs (*p*-value<0.001) and good response to biological therapy (*p*-value<0.001) among patients who were HLA-B27 positive but diagnosis of psoriasis was not significantly different in both the study groups.

**Table-I: Characteristics of Patients with Axial Spondyloarthritis (n=150)**

Study parameters	n(%)
<b>Age (years)</b>	
Mean±SD	42.78±10.2 years
<b>Gender</b>	
Male	109(72.7%)
Female	41(27.3%)
<b>Psoriasis</b>	
No	135(90.0%)
Yes	15(10.0%)
<b>Uveitis</b>	
No	90(60.0%)
Yes	60(40.0%)
<b>Hip joint involvement</b>	
No	137(91.3%)
Yes	13(8.7%)
<b>HLA-B27</b>	
Positive	104(69.3%)
Negative	46(30.7%)

## DISCUSSION

Axial Spondyloarthritis is diagnosed in routine in clinical settings and patients are managed usually on long term basis. HLA-B27 status of patients diagnosed with axial Spondyloarthritis becomes important because there are a lot of characteristics including response to treatment which may differ in HLA-B27

positive and negative patients. A study from Pakistan reported that 77% patients were HLA-B27 positive and peripheral arthritis and uveitis were seen more in patients who were HLA-B27 positive<sup>15</sup> which is supported by our findings. Another study found that disease activity was less severe in these patients as compared to patients who were negative.<sup>16</sup> We did not study the disease activity status in both groups but our results summarized that clinically HLA-B27 positive and negative patients were different in many aspects such as positive family history, hip joint involvement, uveitis, inadequate response to NSAIDs and good response to biological therapy was found more in patients who were HLA-B27 positive. Another study concluded that more axial symptoms were found in HLA-B27 positive patients with no laboratory or imaging related differences were observed between the two groups.<sup>17</sup> A cohort study comprising of over 4000 patients concluded that male gender, lesser age, greater family aggregation, and more incidence of uveitis were found more frequently in HLA-B27 positive patients.<sup>18</sup> Our results supported these findings but more studies on our own population from different hospitals of the country would be more beneficial for patients of this relatively uncommon disorder.

**Table-II: Comparison of Different Clinical Variables Among Two Study Groups (n=150)**

Clinical parameters	HLA-B27 positive (n=104)	HLA-B27 negative (n=46)	p-value
<b>Positive family history</b>			0.037
No	81(77.8%)	42(91.3%)	
Yes	23(22.2%)	04(8.7%)	
<b>Psoriasis</b>			0.100
No	91(87.5%)	44(95.6%)	
Yes	13(12.5%)	02(4.4%)	
<b>Hip joint involvement</b>			0.036
No	92(88.4%)	45(97.8%)	
Yes	12(11.6%)	01(2.2%)	
<b>Uveitis</b>			0.006
No	55(52.8%)	34(73.9%)	
Yes	49(44.2%)	11(26.1%)	
<b>Response to NSAIDs</b>			<0.001
No	71(68.2%)	14(30.4%)	
Yes	33(31.1%)	32(69.6%)	
<b>Response to biological therapy</b>			<0.001
No	77(74.1%)	42(91.3%)	
Yes	27(25.9%)	04(8.7%)	

\*NSAID: Non-steroidal Anti Inflammatory Drugs

## LIMITATION OF STUDY

Difference in clinical picture may be dependent on number of factors other than HLA-B27 status. Strict control

of these factors by higher powered studies may generate more precise results. Being a single center study is also a limitation of this as study as sample population may not be actual representative of rest of Pakistani population. Enrolling multiple public sector hospitals may cater for this limitation.

## CONCLUSION

Positive family history, hip joint involvement, uveitis, inadequate response to NSAIDs and good response to biological therapy was found more in patients who were HLA-B27 positive in this study.

**Conflict of Interest:** None.

**Funding Source:** None.

## Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

HS & AF: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZT & GAN: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AK & FH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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