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Original Article

HLA-B27 STATUS AND ITS ASSOCIATION WITH ANKYLOSING SPONDYLITIS (AS) IN CLINICALLY MANIFESTED AXIAL SPONDYLOARTHRITIS PATIENTS IN BANGLADESH

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Abstract:

Background: *Axial spondyloarthritis (axSpA) is a chronic inflammatory disease strongly associated with HLA-B27. Data from Bangladesh on its clinical relevance are limited. This study evaluated the association between HLA-B27 and ankylosing spondylitis (AS) among axSpA patients.*

Methods: *This cross-sectional study was conducted at the National Institute of Laboratory Medicine and Referral Centre (NILMRC), Dhaka, from March to December 2023. A total of 300 patients with suspected axSpA were included based on ASAS criteria. Demographic, clinical, and laboratory data were collected. HLA-B27 was detected using real-time PCR. ESR and CRP were measured using the Westergren method and nephelometry, respectively. Data were analyzed using SPSS version 27.*

Results: *Among the participants, 23.7% were HLA-B27 positive and 19.7% were clinically diagnosed with AS. HLA-B27 showed a strong association with AS (OR=20.08; 95% CI: 11.56–34.86). Male gender, positive family history, and shorter disease duration were significantly associated with both AS and HLA-B27 positivity (p<0.001). CRP levels were significantly higher in AS patients (p<0.001), while ESR showed elevated mean values. The systemic immune-inflammation index (SII) also demonstrated significant association with disease status.*

Conclusion: *HLA-B27 is significantly associated with ankylosing spondylitis in Bangladeshi axSpA patients. Combined evaluation of clinical features and inflammatory markers may aid in early identification and management, particularly in resource-limited settings.*

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Axial spondyloarthritis, Ankylosing spondylitis, HLA-B27, CRP, ESR, SII, Bangladesh

Introduction

Axial spondyloarthritis (axSpA) is a long-term inflammatory condition that primarily involves the axial skeleton (spine and sacroiliac joints). It belongs to the broader group of spondyloarthritides, which also includes psoriatic arthritis, arthritis linked to inflammatory bowel disease, and reactive arthritis. This term encompasses both patients who show structural changes in the sacroiliac joints or spine on imaging (known as radiographic axial spondyloarthritis or

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ankylosing spondylitis) and those who do not yet have visible structural damage, referred to as non-radiographic axial spondyloarthritis[1]. The disease typically presents in early adulthood and has a significant impact on quality of life and socioeconomic productivity due to its chronic and disabling nature[2].

A systematic review has shown that the prevalence of HLA-B27 among axSpA patients meeting various classification criteria, including the New York (NY), Amor, ESSG, and ASAS criteria, ranges from 26.2% to 91%[3,4]. Furthermore, among patients with ankylosing spondylitis (radiographic axSpA), HLA-B27 positivity rates were reported as 94.8% in South Korea, 83% in Europe, 71% in Latin America, and 79% in Canada. These variations are likely attributable to differences in genetic backgrounds[5,6,7,8]. Furthermore, HLA-B27 positivity has been associated with earlier disease onset, male predominance, and more severe radiological and clinical manifestations, including sacroiliitis and extra-articular features[9].

The prevalence and clinical presentation of axial spondyloarthritis (axSpA) vary significantly across different geographic regions, largely due to differences in the distribution of HLA-B27 among populations. In South-East Asia, including Bangladesh, the overall prevalence of spondyloarthritis is comparatively lower than in Western countries; however, it continues to be a significant contributor to chronic inflammatory back pain. In Bangladesh, available studies demonstrate a substantial proportion of HLA-B27 positivity among patients with suspected or confirmed spondylo-arthropathy. For instance, hospital-based studies have reported HLA-B27 positivity rates ranging from approximately 49% to over 70% among patients, with a strong association with disease severity and clinical manifestations[10]. Moreover, a markedly high prevalence of HLA-B27—reaching up to 92%—has been reported among patients with confirmed ankylosing spondylitis, underscoring its important diagnostic and prognostic relevance in the Bangladeshi population[10].

HLA class I molecules, encoded by MHC genes on chromosome 6, regulate immune responses by presenting antigens and influencing T-cell activity. Among them, HLA-B27 is strongly associated with spondyloarthritis (SpA), a group of immune-mediated rheumatic diseases including AS, reactive, psoriatic, and enteropathic arthritis. First linked in 1973, HLA-B27 prevalence varies across SpA subtypes and ethnic groups[11,12,13,14].

AS, the most common spondyloarthritis, affects ~16.7 per 10,000 in Asia and millions globally. It is a chronic inflammatory disease of the sacroiliac joints and axial skeleton, with possible peripheral and extra-articular involvement. Typically starting in young adults, AS has a strong genetic basis, notably linked to HLA-B27, which may trigger disease by antigen mimicry or binding [15].

HLA allele distribution varies by ethnicity, making population-specific data crucial. The Bangladeshi population has a mixed Indo-Aryan, Austro-Asiatic, Dravidian, Mughal, Arab, Persian, Turkic, and British ancestry[14]. HLA-B27 prevalence also differs globally: ~8% in Caucasians, 4% in North Africans, 2–9% in Chinese, and 0.1–0.5% in Japanese[16].

HLA-B27 can be detected by CDC or DNA-based genotyping, but both are costly and time-consuming, with CDC prone to cross-reactivity. Flow cytometry using anti-HLA-B27 antibodies is efficient and widely used, while PCR, offering higher sensitivity, has increasingly supplemented or replaced it since 1997[17,18].

Biomarkers related to inflammation and immunity are essential for diagnosing, assessing disease activity, and predicting the prognosis of axial spondyloarthritis (axSpA) and ankylosing spondylitis (AS). Within this group, acute-phase reactants like C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) serve as common indicators of systemic inflammation and are incorporated in the Assessment of Spondylo Arthritis International Society (ASAS) classification criteria[4]. In AS patients, high CRP levels have been consistently linked to greater disease activity, radiographic progression, and worse functional outcomes[19]. Likewise, ESR is often increased in active disease, but its sensitivity is not as high as that of CRP[20].

Other inflammatory and serological markers, such as rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), are typically negative in spondyloarthritis, which helps distinguish ankylosing spondylitis (AS) from rheumatoid arthritis[21]. Aside from traditional markers, new hematological indices like the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII) are being recognized as economic indicators of systemic inflammation. Recent research indicates that these indices are linked to disease activity and could act as additional markers in inflammatory rheumatic conditions, such as axSpA[22].

Although the prevalence and subtype distribution of HLA-B27 have been extensively studied worldwide, data from Bangladesh remain scarce. Moreover, comprehensive information on its association with specific clinical manifestations is limited. Understanding this relationship is crucial for early diagnosis, risk stratification, and targeted management, particularly in resource-limited settings where advanced imaging facilities may not be readily available. Therefore, this study—conducted at the Virology Department of the National Institute of Laboratory Medicine, Dhaka—aims to evaluate the distribution of HLA-B27 and its association with ankylosing spondylitis in clinically manifested axial spondyloarthritis patients in the Bangladeshi population, thereby contributing to improved clinical insight and patient care in this region.

Materials and Methods

Study population and place

This cross-sectional prospective study was conducted at department of virology, NILMRC from 1st March 2023 to 31st December 2023. By following the ASAS criteria, patients with suspected axial spondyloarthritis who came for testing HLA-B27 at NILMRC, all were included irrespective of age and sexes. The selection criteria patients who had symptoms of a sacroiliitis or low back pain for more than 3 months and age ranged between 18-44 years came to do test in NILMRC. The study excluded patients who had age <18 and >45 years and those who did not have sacroiliitis or low back pain for more than 3 months, refused to participate. Following the selection criteria, a total of 300 patients were included in the study.

Ethical Consideration

The Institutional Review Board (IRB) of the NILMRC granted ethical permission for the study (2024:0201). The participants were informed in detail about the procedure and plan of the study. All participants provided their written, fully informed consent, as well as assent together with the parents of any minors. The doctors and the medical technologist collected personal information and other relevant medical data by face-to-face interview.

Procedures and measures

A semi-structured questionnaire was used to record the socio demographic characteristics like age sex, and clinical features of the patients. After selecting the patients, positive family history and duration of disease was collected from the patients' medical record and face-to-face interview. In this study arthritis and uveitis are diagnosed by the physicians. ESR, CRP, HLA-B27 and other lab reports were collected from the laboratory section. After collecting all the data, ASAS criteria was followed to diagnose ankylosing spondylitis patient. According to ASAS criteria, other SpA features like presence of arthritis, enthesitis, uveitis, positive family history and elevated CRP was recorded. Among the patients, those who showed ≥ 2 other SpA features positive and positive HLA-B27 in lab test, were categorized as ankylosing spondylitis patients.

Laboratory markers

CRP, ESR with CBC were measured during the study. CRP<6 was regarded as normal. Normal limit of ESR was estimated based on the gender. In case of male >10 mm and female>20 in 1st hour was categorized as raised ESR. ESR was estimated using the "Automated Starrsed RS system" based on the Westergren (gold standard) method. C-reactive protein (CRP) was measured using the Atellica® NEPH 630 System, based on nephelometry.

HLA B27 Real Time PCR

Genomic DNA was extracted from whole blood samples using a commercial kit (e GeneJET™ Genomic DNA Purification Kit). HLA-B27 was typed using polymerase chain reaction (gb GENETIC HLA-B*27). This genotyping was undertaken using the Quant studio 5 real-time Detection System. In case of PCR result interpretation, manufacturers instruction is used.

Statistical analysis

After collecting data, data were analyzed by the Statistical Package for the Social Sciences (SPSS- 27). Categorical data were summarized into percentage. Numerical data were presented with either Mean (±SD) as per needed. Independent t test and Mann-Whitney test was done for Chi-square test was done to find out the relationship of HLA with AS and other variables such as clinical features and laboratory markers.

Results:

Among the Axial spondyloarthritis patients, the mean age of the patients was 30.64 years. There were almost equal proportion of male and female patients, where ratio of man was slight higher than female (M: F = 1.10:1). Only 18 people (6.0%) had positive family histories of AS, and the duration of disease was found predominantly between 1-3 years and <1 years (46.7% and 37.0% respectively). Among the patient, 71 (23.7%) was HLA-B27 positive and 59 (19.7%) clinically diagnosed AS patients (Table I).

Table-I

Sociodemographic, presence of HLA B27, family history and duration of disease of the axial spondyloarthritis patients (n=300)

Variables	Frequency(f)	Percentage (%)
Age (years)		
18-25 years	81	27.0
26-35 years	139	46.3
36-45 years	80	26.7
Sex		
Male	157	52.3
Female	142	47.2
Presence of HLA-B27		
Positive	71	23.7
Negative	229	76.3
Family History		
Positive	18	6.0
Negative	282	94.0
Clinically diagnosed AS		
Positive	59	19.7
Negative	241	80.3
Duration of diseases		
d”1 years	111	37.0
1-3 years	140	46.7
4-5 years	24	8.0
5-10 years	18	6.0
>10 years	7	2.3

AS= ankylosing spondylitis

Both ankylosing spondylitis and HLA-B27 was significantly associated with gender, positive family history and duration of diseases. AS positive patients were found in higher proportion at the age group 26-35 years and 18-25 years. The mean age of AS positive was lower (29.15 years) than AS negative individual. AS positive was also significantly higher in male than female. Positive family history also showed significant relationship with AS positive. Above two third of the patients had duration of AS within <1 year (20.3%) and 1-3 years (45.8%). Similarly, proportion of HLA-B27 was found higher in early age group 26-35 years and 18-25 years. Male gender, positive family history was showed significant association with HLA-B27 positive individual. HLA-B27 also showed higher proportion in lower duration of disease such <1 year (19.7%) and 1-3 years (40.8%) (Table II).

In this study all patients had sacroilitis. Uveitis and enthesitis both were found slightly higher proportion in AS positive and HLA-B27 positive patients (25.4% and 21.1% respectively in both symptoms). (Figure 1)

RA/RF and anti-CCP did not showed any association with AS and HLA-B27. Raised CRP showed association with both AS positive and HLA-B27 positive. Mean value of CRP was 20.33 in AS and 17.19 in HLA-B27 positive patients. Mean ESR value

Table-II

Relationship of ankylosing spondylitis and HLA B27 with age, sex, family history and duration of disease (n=300)

	Ankylosing spondylitis			HLA B27		
Variables	Positive	Negative	p-value	Positive	Negative	p-value
Age						
18-25 years	19 (32.2)	62 (25.7)		20 (28.2)	61 (26.6)	
26-35 years	29 (49.2)	110 (45.6)	0.27#	33 (46.5)	106 (46.3)	0.94#
36-45 years	11 (18.6)	69 (28.6)		18 (25.4)	62 (27.1)	
Mean ± SD	29.15±6.22	31.01±6.87	0.05**	30.24±6.49	30.77±6.87	0.56**
Sex						
Male	42 (71.2)	115 (47.7) OR:2.71	0.001#	51 (71.8)	106 (46.32) OR:2.95	<0.001#
Female	17 (28.8)	126 (52.3) CI:1.5-5.0		20 (28.2)	123 (53.7) CI:1.7-5.3	
Family History						
Positive	17 (28.8)	1 (0.4) OR:97.14	<0.001#	17 (23.9)	1 (0.4) OR:71.7	<0.001#
Negative	42 (71.2)	240 (99.6) CI:12.59-749.52		54 (76.1)	228 (99.6) CI:9.34-551.17	
Duration of diseases						
≤1 years	12 (20.3)	99 (41.1)		14 (19.7)	97 (42.4)	
1-3 years	27 (45.8)	113 (46.9)		29 (40.8)	111 (48.5)	
4-5 years	5 (8.5)	19 (7.9)	<0.001#	9 (12.7)	15 (6.6)	<0.001#
5-10 years	11 (18.6)	7 (2.9)		13 (18.3)	5 (2.2)	
>10 years	4 (6.8)	3 (1.2)		6 (8.5)	1 (0.4)	

Here, ** indicates independent t test was done. # indicates chi-square test was done.

Table-III

Relationship of ankylosing spondylitis and HLA B27 with lab markers (n=524)

Variables	Ankylosing spondylitis Present	Absent	p-value	HLA B27 Positive	Negative	p-value
CRP						
Raised	27 (45.8)	56 (23.2)	<0.001 OR=2.78	27 (38.0)	56 (24.5)	0.25# OR=1.89
Normal	32 (54.2)	185 (76.8)	CI=1.54-5.04	44 (62.0)	173 (75.5)	CI=1. 1-3.33
Mean	20.33	5.67	<0.001*	17.19	5.87	0.008*
ESR						
Raised	31 (52.5)	126 (52.3)	0.97	36 (50.7)	121 (52.8)	0.75#
Normal	28 (47.5)	115 (47.7)		35 (49.3)	108 (47.2)	
Mean	30.92	20.79	0.02*	29.48	20.70	0.002*
NLR 2.26	1.93	0.07*	2.23	1.9	0.08*	
SII index	684.89	503.01	0.018*	660.81	500	0.011*

Here, RA/RF= Rheumatoid Factor, CRP= C-reactive protein, ESR=Erythrocyte sediment ratio, * indicates Mann-Whitney U test. # indicates chi-square test.

Table-IV

Relationship of HLA B27 with AS in ankylosing spondylitis patients (n=190)

Ankylosing Spondylitis	HLA B27 Present	Absent	p-value
Present	59 (100)	0 (0.0)	<0.001, OR=20.08 CI=11.56-34.86
Absent	12 (5.0)	229 (95.0)	

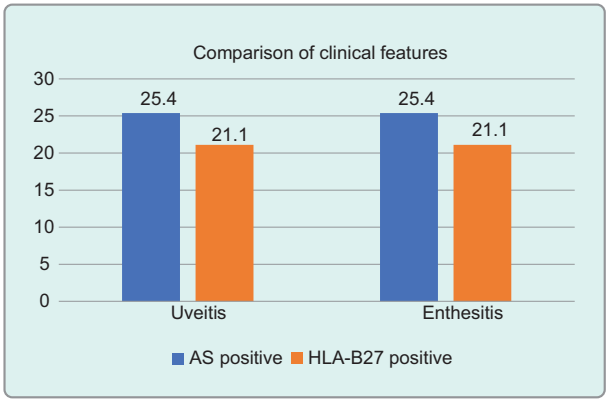

Figure 1: *Showing comparison of clinical features between AS positive and HLA-B27 Positive patients.*

was found significantly higher in AS and HLA-B27 positive patient. Inflammatory marker like NLR and SII index was also found higher in both AS positive and HLA-B27 positive where SII index showed significant association with HLA-B27 patients and AS positive patients. (Table III)

Table III, AS was diagnosed from HLA-B27 and presence of other SpA features. HLA-B27 showed significant association with ankylosing spondylitis. Odds ratio 20.08 indicates that AS is 20 times more associated with HLA-B27 markers (Table IV).

Discussion

The present study investigated the relationship between HLA-B27 status and ankylosing spondylitis (AS) among patients with clinically manifested axial spondyloarthritis (axSpA) in Bangladesh. The results revealed that 23.7% of the study population tested positive for HLA-B27, while 19.7% were clinically diagnosed with AS. These proportions are comparatively lower than those reported in several international studies, where HLA-B27 positivity among axSpA patients ranges widely from approximately 26.2% to 91%. Such variation across studies may be attributed to differences in ethnic and genetic backgrounds, which are known to influence the distribution of HLA-B27 in different populations. Additionally, disparities in study design, patient selection criteria, and the use of varying diagnostic and classification approaches—such as ASAS, New York, or other criteria—may also contribute to these differences. Previous studies have shown that HLA-B27 distribution varies significantly

across regions, with higher prevalence in European and East Asian populations compared to South Asian populations [23,24].

Table II demonstrates the relationship of ankylosing spondylitis (AS) and HLA-B27 with age, sex, family history, and duration of disease among axial spondyloarthritis (axSpA) patients. In this study, AS and HLA-B27 positivity were more frequently observed in younger individuals, particularly in the 18–35 years' age group, with mean ages of 29.15 and 30.24 years respectively. Although the association with age was not statistically significant, but the trend aligns with existing literature indicating that axSpA typically presents in early adulthood.[20] Similar findings have been reported in studies from Asia and Europe, where the peak onset occurs before 40 years of age[1].

A statistically significant association was observed between male sex and both AS and HLA-B27 positivity (p=0.001 and p<0.001 respectively), with males showing approximately three times higher odds of disease. This is consistent with previous studies that have reported male predominance in AS, possibly due to genetic, hormonal, and immunological differences [5,24]. However, recent evidence suggests that female cases may be underdiagnosed, which could influence observed sex distribution[25].

One of the most striking findings of this study is the strong association between positive family history and both AS and HLA-B27 positivity (p<0.001), with extremely high odds ratios (OR: 97.14 and 71.7 respectively). This supports the well-established genetic predisposition of AS, where HLA-B27 plays a central role in familial aggregation. Previous studies have similarly demonstrated that first-degree relatives of HLA-B27 positive individuals have a significantly increased risk of developing AS[26,27].

Both ankylosing spondylitis (AS) and HLA-B27 positivity were more commonly identified in patients with a shorter duration of disease (<3 years). This suggests that HLA-B27 may be associated with the early phase of disease onset and could aid in prompt diagnosis when interpreted alongside clinical features. Early detection is crucial, as it allows timely intervention, which may help slow disease progression and improve long-term clinical outcomes.

Table III illustrates the relationship between ankylosing spondylitis (AS), HLA-B27, and various laboratory markers, highlighting important inflammatory and immunological patterns. Among the conventional markers, C-reactive protein (CRP) showed a strong association with AS (p<0.001), with significantly higher mean CRP levels in AS patients compared to non-AS individuals. This finding is consistent with previous studies that have identified CRP as a reliable indicator of disease activity and inflammation in axial spondyloarthritis (axSpA), and it is incorporated into the ASAS classification criteria[4,28]. Although CRP was elevated in HLA-B27 positive patients, the association was not statistically significant, suggesting that while HLA-B27 contributes to disease susceptibility, CRP more directly reflects inflammatory activity.

Similarly, erythrocyte sedimentation rate (ESR) showed significantly higher mean values in both AS and HLA-B27 positive patients (p=0.02 and p=0.002, respectively), indicating ongoing systemic inflammation. However, the categorical comparison (raised vs normal ESR) did not show a significant association, which is consistent with previous literature suggesting that ESR is less sensitive and more variable compared to CRP in reflecting disease activity[20].

An important aspect of this study is the evaluation of emerging inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR) and systemic immune-inflammation index (SII). Although NLR was higher in AS and HLA-B27 positive patients, it did not reach statistical significance. However, SII index showed a significant association with both AS (p=0.018) and HLA-B27 positivity (p=0.011), suggesting its potential role as a novel marker of systemic inflammation. Recent studies have indicated that SII, which integrates neutrophil, lymphocyte, and platelet counts, may better reflect the overall inflammatory burden and immune response compared to traditional markers[22].

A major strength of this study is the use of PCR-based genotyping for HLA-B27, which offers higher sensitivity and specificity compared to conventional diagnostic methods. In addition, the application of ASAS criteria for patient selection and diagnosis ensures a standardized and clinically relevant classification of axial spondyloarthritis. The combination of laboratory confirmation of HLA-B27 with clinical diagnosis of ankylosing spondylitis enhances the reliability of the observed association between HLA-B27 and AS. Furthermore, the inclusion of both conventional inflammatory markers and emerging

indices such as NLR and SII adds depth to the analysis and provides valuable insights into disease assessment within the Bangladeshi population.

Conclusion

In conclusion, this study demonstrates a significant association between HLA-B27 and ankylosing spondylitis among axSpA patients in Bangladesh. The findings highlight the importance of clinical, and inflammatory markers in disease diagnosis and assessment. The incorporation of novel indices such as SII may further enhance disease evaluation. These results underscore the need for early detection strategies and population-specific research to improve the management of axSpA in resource-limited settings.

Recommendations

Early screening for HLA-B27 in patients with suspected axial spondyloarthritis, along with assessment of inflammatory markers such as CRP and SII, may improve timely diagnosis and disease evaluation. Incorporation of imaging modalities like MRI alongside ASAS criteria is recommended to enhance diagnostic accuracy. Further large-scale, multicenter studies are needed to validate these findings in the Bangladeshi population.

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Limitations

In this study, the diagnosis of AS was based on HLA-B27 positive and presence of other clinical features of SpA. Radiological or MRI criteria for AS diagnosis could give a better perspective regarding the relationship of AS and HLA-B27.

Conflict of interest statement

There is no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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The Institutional Review Board (IRB) of the NILMRC granted ethical permission for the study (2024:0201).

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