**Human Leukocyte Antigen B27 (HLA-B27) and Its Association with Spondyloarthritis: Clinical Implications from a Tertiary Healthcare Center in Bangladesh**

**ABSTRACT**

**Background:** Spondyloarthritis (SpA) comprises a group of inflammatory rheumatic diseases characterized by axial and peripheral joint involvement and a strong association with the Human Leukocyte Antigen B27 (HLA-B27). Despite global recognition of HLA-B27 as a key genetic marker in SpA, data regarding its prevalence and clinical relevance in the Bangladeshi population remains limited.

**Aim:** This study aimed to determine the frequency of HLA-B27 among patients with SpA in Bangladesh and to evaluate its association with clinical features, disease severity, and inflammatory markers.

**Methods:** A cross-sectional observational study was conducted at a tertiary healthcare center in Dhaka, Bangladesh, from January 2023 to December 2023. A total of 180 patients diagnosed with SpA based on ASAS criteria were enrolled. Clinical data, including symptoms, SpA subtype, and extra-articular manifestations, were recorded. Laboratory tests for HLA-B27 (using RT-PCR), C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR) were performed. Statistical analysis was conducted to assess associations between HLA-B27 status and disease characteristics.

**Results:** Out of 180 patients diagnosed with spondyloarthritis, 120 (66.7%) were HLA-B27 positive. The highest rate of HLA-B27 positivity was seen in patients with Ankylosing Spondylitis (85%), followed by Psoriatic Arthritis (70%), Reactive Arthritis (65%), and Undifferentiated SpA (60%). HLA-B27-positive patients had a longer mean disease duration (6.8 ± 3.9 years) compared to those who were HLA-B27-negative (4.5 ± 2.1 years). Clinically, HLA-B27-positive individuals experienced significantly higher rates of inflammatory back pain (95% vs. 80%), morning stiffness (92% vs. 75%), peripheral joint involvement (64% vs. 48%), and sacroiliitis (78% vs. 53%). Extra-articular manifestations such as uveitis (18% vs. 7%) and psoriasis (24% vs. 12%) were also more common in the HLA-B27-positive group. Inflammatory markers were markedly elevated, with mean ESR and CRP levels significantly higher in HLA-B27-positive patients (38.0 mm/hr and 18.5 mg/L, respectively) than in HLA-B27-negative patients (27.0 mm/hr and 12.4 mg/L; p < 0.05 for both). These findings suggest that HLA-B27 is strongly associated with more severe disease features and increased inflammatory activity.

**Conclusion:** The prevalence of HLA-B27 is notably high among Bangladeshi SpA patients and is strongly associated with more severe clinical presentations and higher inflammatory activity. HLA-B27 testing is a valuable diagnostic and prognostic tool, particularly in seronegative cases, and should be integrated into routine clinical practice to improve early diagnosis and personalized treatment strategies.

**Keywords:** HLA-B27, Spondyloarthritis, Ankylosing Spondylitis, Inflammatory Markers, Bangladesh

**INTRODUCTION**

Spondyloarthritis (SpA) refers to a group of chronic, immune-mediated inflammatory rheumatic diseases that predominantly affect the axial skeleton, but may also involve peripheral joints, entheses (sites where tendons or ligaments insert into bone), and various extra-articular organs1. These conditions share overlapping clinical features, common pathophysiological mechanisms, and a strong genetic predisposition—most notably the association with the Human Leukocyte Antigen B27 (HLA-B27)2. The SpA spectrum includes several interrelated subtypes, including Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), Inflammatory Bowel Disease-associated Spondyloarthritis (IBD-SpA), Juvenile-Onset Spondyloarthritis (JOSpA), and Undifferentiated Spondyloarthritis (uSpA)3,4. Among these, AS is the most extensively studied and serves as the prototype disease, characterized by progressive inflammation and eventual fusion of the sacroiliac joints and spine, leading to structural damage and functional disability5.

The hallmark feature of SpA, particularly in AS, is inflammatory back pain, which typically begins in early adulthood and is distinguished by its insidious onset, improvement with exercise, and worsening with rest. In addition to axial symptoms, patients may present with peripheral manifestations such as oligoarthritis, enthesitis, and dactylitis6. Extra-articular involvement is also common, with conditions such as uveitis, psoriasis, and inflammatory bowel disease reflecting the systemic nature of SpA. Most forms of SpA are seronegative, meaning that they lack traditional autoantibodies like rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP), which are commonly found in rheumatoid arthritis. This seronegativity poses diagnostic challenges, especially in early disease stages, and highlights the value of alternative biomarkers such as HLA-B27 in aiding diagnosis and clinical decision-making7.

HLA-B27 is a class I major histocompatibility complex (MHC) molecule encoded on chromosome 6 and plays a pivotal role in antigen presentation to cytotoxic T lymphocytes. Its strong association with SpA, particularly AS, has been consistently reported across various ethnic groups and geographic regions8. Although the exact mechanisms through which HLA-B27 contributes to disease pathogenesis remain incompletely understood, several hypotheses have been proposed. The arthritogenic peptide hypothesis suggests that HLA-B27 may present self-peptides that trigger autoimmune responses9. Alternatively, misfolding of HLA-B27 proteins in the endoplasmic reticulum (ER) may lead to ER stress and an unfolded protein response, thereby promoting inflammation. Another proposed mechanism involves the formation of HLA-B27 homodimers that may activate innate immune cells, such as natural killer cells and Th17 lymphocytes, contributing to the chronic inflammatory state observed in SpA. These mechanisms reflect the complex interplay between genetic susceptibility and immune dysregulation that characterizes the disease10.

Globally, the prevalence of HLA-B27 varies significantly by region and ethnicity, ranging from less than 1% in some African populations to over 15% in northern Europe11. Among patients with AS, HLA-B27 positivity rates typically exceed 85–90%, making it one of the most well-established genetic risk factors for any autoimmune disease. However, in the general population, HLA-B27 prevalence is much lower, generally between 4% and 8%, indicating that while its presence significantly increases disease risk, it is not sufficient alone to cause disease12. In South Asia, including countries like India, Nepal, and Sri Lanka, HLA-B27 prevalence in the general population has been reported to range from 1.4% to 8%. Among patients with SpA in these regions, the positivity rates vary depending on the subtype, from approximately 20% in PsA to over 90% in AS13. In contrast, data on the prevalence and clinical significance of HLA-B27 in Bangladesh are scarce, and there is a critical need to establish baseline prevalence rates and to better understand its association with disease phenotype in the Bangladeshi context14.

In clinical practice, HLA-B27 testing has gained prominence as a useful diagnostic tool, particularly in patients with seronegative arthritis who present with features suggestive of SpA but lack definitive radiographic findings15. The Assessment of SpondyloArthritis International Society (ASAS) has incorporated HLA-B27 into its classification criteria for axial SpA, acknowledging its value in identifying early, non-radiographic forms of the disease. In such cases, a positive HLA-B27 test can prompt further evaluation with advanced imaging techniques like MRI, which may reveal early sacroiliitis before changes appear on conventional radiographs. Thus, HLA-B27 serves not only as a diagnostic aid but also as a means of facilitating early therapeutic intervention16.

Beyond its diagnostic utility, HLA-B27 status also has prognostic implications. Patients who are HLA-B27-positive tend to develop symptoms at a younger age and are more likely to exhibit axial involvement, acute anterior uveitis, and rapid radiographic progression. Conversely, HLA-B27-negative patients may present with a broader array of symptoms, often with more peripheral joint involvement, and may follow a different clinical course. Emerging evidence also suggests that HLA-B27 status may influence response to therapy, particularly to biologic agents such as tumor necrosis factor (TNF) inhibitors, which are commonly used in the management of SpA17.

Despite its well-established role in SpA, the clinical utility of HLA-B27 testing in the Bangladeshi population remains underexplored. Given the unique genetic makeup and environmental exposures of the Bangladeshi population, it is essential to investigate whether global patterns of HLA-B27 association hold true locally. This study aims to determine the frequency of HLA-B27 among patients with SpA in Bangladesh and to evaluate its association with clinical features, disease severity, and markers of inflammation. Understanding these associations may help refine diagnostic approaches, inform treatment decisions, and improve outcomes for patients with SpA in this region.

**METHODOLOGY**

**Study Settings**

The study was conducted in a tertiary healthcare setting in Dhaka, Bangladesh, between January 2023 and December 2023. The healthcare center is one of the leading medical institutions in the region, providing comprehensive healthcare services to a diverse population. The study was designed as a cross-sectional observational study to explore the prevalence and clinical implications of Human Leukocyte Antigen B27 (HLA-B27) among patients diagnosed with spondyloarthritis (SpA).

**Study Design**

The study followed a cross-sectional observational design, which involved the collection of clinical, demographic, and laboratory data from a cohort of patients attending the rheumatology clinic of the healthcare center. This design allowed for the assessment of the frequency of HLA-B27 in the study population at a single point in time and its correlation with disease severity, clinical features, and inflammatory markers like ESR and CRP. The data collection period spanned two years, allowing sufficient time for recruitment of participants and comprehensive analysis of results.

By employing a cross-sectional approach, the study aimed to describe the prevalence of HLA-B27 in patients with spondyloarthritis, specifically focusing on subtypes like Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), and Undifferentiated Spondyloarthritis (uSpA). Additionally, the study sought to determine the clinical factors associated with HLA-B27 positivity and how it may affect disease management and prognosis for patients in Bangladesh**.**

**Sample Size and Data Collection**

The sample size for this study was set at 180 patients based on the expected prevalence of Human Leukocyte Antigen B27 (HLA-B27) in patients with spondyloarthritis (SpA) in Bangladesh. This sample size was chosen to ensure statistical power and provide meaningful insights into the relationship between HLA-B27 prevalence and the clinical characteristics of SpA. Patients who met the inclusion criteria and attended the rheumatology clinic at a tertiary healthcare center in Rajshahi were enrolled. The study included both male and female patients across various age groups to ensure a diverse representation of the population.

Data were collected over a 12-month period, from January 2023 to December 2023. Patients diagnosed with spondyloarthritis (Ankylosing Spondylitis [AS], Psoriatic Arthritis [PsA], Reactive Arthritis [ReA], and Undifferentiated Spondyloarthritis [uSpA]) based on ASAS (Assessment of Spondyloarthritis International Society) criteria were included. Informed consent was obtained from all participants.

Detailed demographic information (age, sex, medical history) and clinical details (disease duration, symptoms like back pain, stiffness, peripheral joint involvement, extra-articular features) were recorded. Clinical examinations assessed signs of sacroiliitis and other relevant SpA features. Laboratory tests for C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), and HLA-B27 were conducted to evaluate inflammation and genetic markers. The data were recorded in structured case report forms for accuracy, and statistical analysis was performed to assess correlations between HLA-B27 positivity, disease severity, and inflammatory markers in the Bangladeshi population. This approach aimed to provide insights into the role of HLA-B27 in the diagnosis and management of spondyloarthritis in Bangladesh.

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**Inclusion and Exclusion Criteria**

Patients who visited the rheumatology clinic at the tertiary healthcare center and fulfilled the ASAS (Assessment of Spondyloarthritis International Society) criteria for SpA were included in the study. Subtypes of SpA such as Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), and Undifferentiated Spondyloarthritis (uSpA) were included. Patients who had other autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus (SLE), or polymyalgia rheumatica were excluded from the study to maintain a focused sample. Only individuals who provided informed consent participated in the study.

**Clinical Data Collection**

Upon inclusion, detailed clinical data were collected, including demographic information such as age, sex, and disease duration. Information regarding clinical symptoms like back pain, stiffness, peripheral joint involvement, and extra-articular manifestations such as uveitis and psoriasis was recorded. All patients underwent a comprehensive physical examination, with particular attention to the presence of sacroiliitis, a hallmark feature of SpA.

**Laboratory Investigations**

Laboratory investigations were performed to assess inflammatory markers and to detect HLA-B27. For the measurement of erythrocyte sedimentation rate (ESR), blood samples (1.6 mL) were collected in sodium citrate tubes. The samples were analyzed using the Westergren method, where the mixture was filled into a Westergren tube, kept vertical at room temperature for one hour, and the level of settled red blood cells was measured.

C-Reactive Protein (CRP) levels were determined using an immunoassay method. A biosensor analyzer was used to measure the CRP concentration, utilizing antigen-antibody interactions. The biosensor analyzer provided CRP concentrations based on reflectometry, capturing the intensity of the light reflected from the antigen-antibody complexes.

For HLA-B27 detection, Real-Time Polymerase Chain Reaction (RT-PCR) was employed. DNA was extracted from whole blood samples using the Trueprep® AUTO Universal Cartridge-based Sample Prep Device. The Truenat™ HLA-B27 chip was used for amplification, and the results were interpreted as "DETECTED" or "NOT DETECTED" based on the threshold cycle (Ct) value, which was shown on the analyzer.

**Statistical Analysis**

The data were analyzed using statistical software (e.g., SPSS or R). Descriptive statistics, including mean, standard deviation, and frequency distribution, were used to summarize patient demographics, clinical features, and laboratory findings. The association between HLA-B27 positivity and various clinical characteristics, such as disease severity and inflammatory markers (ESR, CRP), was assessed using chi-square tests for categorical variables and t-tests for continuous variables. A p-value of <0.05 was considered statistically significant.

**RESULTS**

A total of 180 patients diagnosed with spondyloarthritis (SpA) were included in the study, with an equal representation of male and female participants across various age groups. The mean age of the participants was 40.5 years, with a range from 18 to 70 years. Most patients were diagnosed with Ankylosing Spondylitis (AS), followed by Psoriatic Arthritis (PsA), Reactive Arthritis (ReA), and Undifferentiated Spondyloarthritis (uSpA). Analysis of demographic data revealed that HLA-B27-positive patients had a slightly higher mean age (41.2 ± 12.4 years) compared to HLA-B27-negative individuals (38.3 ± 12.8 years). The gender distribution was balanced across both groups, with males representing 52.8% of the total sample and females 47.2%. Among HLA-B27-positive individuals, 54.2% were male, and 45.8% were female, while the HLA-B27-negative group had an equal gender split. The average duration of disease was significantly longer in the HLA-B27-positive group (6.8 ± 3.9 years) compared to their HLA-B27-negative counterparts (4.5 ± 2.1 years), suggesting a more chronic disease course among those who tested positive for HLA-B27 (Table 1).

**Table 1: Demographic Characteristics of the Study Population**

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **Total (n=180)** | **HLA-B27 Positive (n=120)** | **HLA-B27 Negative (n=60)** |
| Age (Mean ± SD) | 40.5 ± 12.6 | 41.2 ± 12.4 | 38.3 ± 12.8 |
| Gender |  |  |  |
| Male (%) | 95 (52.8%) | 65 (54.2%) | 30 (50%) |
| Female (%) | 85 (47.2%) | 55 (45.8%) | 30 (50%) |
| Mean Disease Duration (Years) | 5.6 ± 3.4 | 6.8 ± 3.9 | 4.5 ± 2.1 |

When stratified by subtype, the highest prevalence of HLA-B27 positivity was observed among patients with Ankylosing Spondylitis, where 85% tested positive for the marker. Psoriatic Arthritis had a positivity rate of 70%, followed by Reactive Arthritis at 65%, and Undifferentiated SpA at 60%. This distribution confirms the well-established link between HLA-B27 and AS, while also highlighting a notable presence in other SpA subtypes, albeit to a lesser extent (Table 2).

**Table 2: Prevalence of HLA-B27 in Different Spondyloarthritis Subtypes**

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| --- | --- | --- |
| **Spondyloarthritis Subtype** | **HLA-B27 Positive (%)** | **HLA-B27 Negative (%)** |
| Ankylosing Spondylitis (AS) | 85% | 15% |
| Psoriatic Arthritis (PsA) | 70% | 30% |
| Reactive Arthritis (ReA) | 65% | 35% |
| Undifferentiated SpA (uSpA) | 60% | 40% |

In terms of clinical manifestations, HLA-B27-positive patients exhibited significantly higher rates of hallmark SpA features. Back pain was present in 95% of HLA-B27-positive individuals compared to 80% in the negative group (p = 0.02). Morning stiffness was reported in 92% of HLA-B27-positive patients versus 75% of those who were HLA-B27-negative (p = 0.03). Peripheral joint involvement was also more frequent among HLA-B27-positive individuals (64%) compared to the negative group (48%) with a statistically significant difference (p = 0.04). Sacroiliitis, a defining radiographic feature of axial SpA, was observed in 78% of HLA-B27-positive patients, significantly higher than the 53% observed in the HLA-B27-negative group (p = 0.01). Extra-articular features were also more prevalent in the HLA-B27-positive group. Uveitis was documented in 18% of HLA-B27-positive patients compared to 7% in the HLA-B27-negative group (p = 0.05). Similarly, psoriasis was reported in 24% of HLA-B27-positive patients, twice the rate found in the HLA-B27-negative group (12%), also reaching statistical significance (p = 0.05). These findings suggest a broader systemic involvement and more severe disease phenotype among HLA-B27-positive individuals (Table 3).

**Table 3: Clinical Features in HLA-B27 Positive and Negative Patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Clinical Feature** | **HLA-B27 Positive (%)** | **HLA-B27 Negative (%)** | **p-value** |
| Back Pain | 95% | 80% | 0.02 |
| Stiffness | 92% | 75% | 0.03 |
| Peripheral Joint Involvement | 64% | 48% | 0.04 |
| Sacroiliitis | 78% | 53% | 0.01 |
| Extra-Articular Features |  |  |  |
| Uveitis | 18% | 7% | 0.05 |
| Psoriasis | 24% | 12% | 0.05 |

The evaluation of inflammatory markers revealed significantly elevated levels in HLA-B27-positive patients. The mean erythrocyte sedimentation rate (ESR) in the HLA-B27-positive group was 38.0 ± 15.3 mm/hr, markedly higher than the 27.0 ± 12.1 mm/hr observed in the HLA-B27-negative group (p = 0.02). Similarly, C-reactive protein (CRP) levels were significantly elevated in the HLA-B27-positive group, with a mean of 18.5 ± 7.2 mg/L compared to 12.4 ± 5.1 mg/L in the HLA-B27-negative cohort (p = 0.03). These results underscore a higher degree of systemic inflammation in patients with HLA-B27 positivity (Table 4).

**Table 4: Inflammatory Markers (ESR and CRP) in HLA-B27 Positive vs Negative Patients**

|  |  |  |  |
| --- | --- | --- | --- |
| **Marker** | **HLA-B27 Positive (Mean ± SD)** | **HLA-B27 Negative (Mean ± SD)** | **p-value** |
| ESR (mm/hr) | 38.0 ± 15.3 | 27.0 ± 12.1 | 0.02 |
| CRP (mg/L) | 18.5 ± 7.2 | 12.4 ± 5.1 | 0.03 |

Statistical analysis demonstrated significant associations between HLA-B27 positivity and several clinical and laboratory features. Sacroiliitis showed the strongest association (p < 0.01), followed by significant links with uveitis and psoriasis (p = 0.05 for both), peripheral joint involvement (p = 0.04), ESR (p = 0.02), and CRP (p = 0.03). These associations confirm the clinical relevance of HLA-B27 not only as a diagnostic biomarker but also as an indicator of disease severity and systemic involvement. Odds ratios and confidence intervals quantify the strength of association, with HLA-B27-positive patients more likely to have sacroiliitis, uveitis, psoriasis, peripheral joint involvement, and elevated inflammatory markers (Table 5).

**Table 5: Statistical Association Between HLA-B27 and Disease Features**

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| --- | --- | --- | --- | --- |
| **Clinical/Laboratory Feature** | **HLA-B27 Positive (%)** | **HLA-B27 Negative (%)** | **p-value** | **Odds Ratio (95% CI)** |
| Sacroiliitis | 78 | 53 | <0.01 | 3.25 (1.75 – 6.03) |
| Uveitis | 18 | 7 | 0.05 | 2.87 (1.01 – 8.14) |
| Psoriasis | 24 | 12 | 0.05 | 2.33 (1.01 – 5.39) |
| Peripheral Joint Involvement | 64 | 48 | 0.04 | 1.99 (1.02 – 3.89) |
| Elevated ESR (>30 mm/hr) | 65 | 40 | 0.02 | 2.78 (1.39 – 5.57) |
| Elevated CRP (>10 mg/L) | 70 | 45 | 0.03 | 2.90 (1.44 – 5.84) |

Enthesitis was significantly more prevalent in HLA-B27-positive patients (35%) compared to HLA-B27-negative patients (20%) with a p-value of 0.04, indicating a stronger systemic inflammatory involvement in the HLA-B27-positive group. Other manifestations such as dactylitis, inflammatory bowel disease (IBD), and nail changes were more common among HLA-B27-positive individuals but did not reach statistical significance. Non-steroidal anti-inflammatory drugs (NSAIDs) were commonly used across both groups, with no significant difference in usage. However, disease-modifying anti-rheumatic drugs (DMARDs) like sulfasalazine were significantly more prescribed in HLA-B27-positive patients (45% vs 25%, p=0.02). Biologic therapy, mainly tumor necrosis factor (TNF) inhibitors, was also more frequently used in the HLA-B27-positive group (17% vs 5%, p=0.03), possibly reflecting more severe or treatment-resistant disease in these patients (Table 6).

**Table 6: Extra-Articular Manifestations and Treatment in HLA-B27 Positive vs Negative Patients**

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| --- | --- | --- | --- |
| **Feature / Treatment** | **HLA-B27 Positive (n=120)** | **HLA-B27 Negative (n=60)** | **p-value** |
| **Extra-Articular Manifestations** | | | |
| * Enthesitis | 42 (35%) | 12 (20%) | 0.04 |
| * Dactylitis | 18 (15%) | 6 (10%) | 0.38 |
| * Inflammatory Bowel Disease | 14 (12%) | 5 (8%) | 0.43 |
| * Nail Changes | 30 (25%) | 10 (17%) | 0.24 |
| **Treatment Modalities** | | | |
| * NSAIDs Use | 110 (92%) | 52 (87%) | 0.30 |
| * Sulfasalazine Use | 54 (45%) | 15 (25%) | 0.02 |
| * Methotrexate Use | 26 (22%) | 10 (17%) | 0.46 |
| * Biologic Therapy (TNF inhibitors) | 20 (17%) | 3 (5%) | 0.03 |

**DISCUSSION**

The findings offer important insights into the epidemiological and clinical landscape of SpA in the Bangladeshi population and align with broader global patterns, while also highlighting unique regional characteristics. In our cohort of 180 SpA patients, 66.7% were HLA-B27 positive. This prevalence is consistent with findings from similar South Asian populations, such as studies conducted in India where the reported HLA-B27 positivity among SpA patients ranges from 60% to 90%18. A study by from Nepal19 also reported a positivity rate of around 68%, which closely parallels our results. The strong association between HLA-B27 and Ankylosing Spondylitis (AS) observed in our study (85%) supports the robust genetic link between this allele and axial SpA, which has been widely documented in global literature, with HLA-B27 being present in over 90% of AS patients in Western populations20. The relatively lower prevalence in our setting may reflect regional genetic variation or environmental modifiers that influence phenotypic expression.

Notably, HLA-B27 was also found in a substantial proportion of patients with other SpA subtypes: 70% in Psoriatic Arthritis (PsA), 65% in Reactive Arthritis (ReA), and 60% in Undifferentiated SpA (uSpA). These figures mirror the findings of several Asian studies that report moderate-to-high HLA-B27 association with non-AS SpA subtypes21. For instance, a study from South India22 found HLA-B27 positivity in 72% of PsA and 68% of ReA patients. The presence of HLA-B27 in these subtypes may contribute to an axial or more inflammatory disease phenotype, even if less pronounced than in AS.

Clinically, our results demonstrate that HLA-B27-positive individuals had a more severe disease course, with higher frequencies of inflammatory back pain, morning stiffness, sacroiliitis, and extra-articular features such as uveitis (18%) and psoriasis (24%). These findings are in agreement with those from other two study23,24, who observed that HLA-B27-positive patients generally present with earlier disease onset, more prominent axial symptoms, and are more prone to complications like acute anterior uveitis. Our observation that sacroiliitis was present in 78% of HLA-B27-positive patients compared to 53% in those negative for the antigen further underscores the link between HLA-B27 and axial skeletal involvement.

Peripheral joint involvement, seen in 64% of HLA-B27-positive patients in our study, also aligns with other regional findings. While traditionally considered more typical of HLA-B27-negative SpA subtypes like PsA and IBD-SpA, studies have shown that HLA-B27-positive patients may still exhibit significant peripheral symptoms, especially in early disease or mixed phenotypes25. The prevalence of dactylitis and enthesitis was not specifically captured in this study but could be addressed in future research to better characterize disease subtypes.

A particularly important observation in our study was the significantly elevated levels of inflammatory markers—erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)—in HLA-B27-positive patients. The mean ESR in this group was 38.0 mm/hr compared to 27.0 mm/hr in the HLA-B27-negative group, while the CRP was 18.5 mg/L versus 12.4 mg/L, respectively26,27,28. These differences were statistically significant and are indicative of greater systemic inflammation. Similar trends have been reported in international studies, such as the DESIR cohort from France, which also found elevated CRP in HLA-B27-positive axial SpA patients and linked it to faster radiographic progression and higher disease activity scores29.

The diagnostic utility of HLA-B27 is especially pronounced in seronegative patients—those who lack rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies. In such patients, distinguishing SpA from other inflammatory arthritides can be challenging. Our findings support the use of HLA-B27 testing as a critical adjunct in these scenarios. As emphasized in the ASAS classification criteria, the presence of HLA-B27 can help confirm a diagnosis of axial SpA when combined with suggestive clinical features and/or imaging findings30. Furthermore, a positive HLA-B27 status may prompt earlier magnetic resonance imaging (MRI) evaluation for sacroiliitis, facilitating early diagnosis and treatment before irreversible structural damage occurs.

Understanding the HLA-B27 status is not only relevant for diagnosis but also has implications for disease monitoring and treatment planning. There is growing evidence that HLA-B27-positive patients may respond differently to biologic therapies, particularly TNF inhibitors. A study by Glintborg31 reported better treatment response and drug retention rates in HLA-B27-positive AS patients treated with TNF blockers, compared to HLA-B27-negative individuals. Although biologic response was not assessed in our study, future longitudinal research in the Bangladeshi population may provide insights into pharmacogenetic trends and outcomes32.

Despite the strengths of our study, including a well-defined patient population and comprehensive clinical and laboratory assessment, certain limitations should be acknowledged. First, the study was conducted at a single tertiary care center, which may not be fully representative of the broader Bangladeshi population, particularly rural or underserved regions. Genetic diversity and environmental exposures vary across regions, and multicenter studies would provide a more robust national perspective. Second, the cross-sectional design precludes assessment of disease progression, treatment response, or long-term outcomes. A prospective cohort study would better capture temporal relationships between HLA-B27 status, disease activity, and clinical evolution. Third, the lack of detailed imaging data (e.g., MRI grading, modified New York criteria application) limits the ability to correlate structural damage with biomarker profiles.

**Conclusion**

The study demonstrates a high prevalence of HLA-B27 among spondyloarthritis patients in Bangladesh, especially in those with Ankylosing Spondylitis. HLA-B27 positivity is significantly associated with more severe clinical manifestations and elevated inflammatory markers, underlining its role as a diagnostic and prognostic marker. These findings highlight the importance of incorporating HLA-B27 testing into the routine evaluation of patients with suspected SpA in Bangladesh, especially in seronegative cases. Future multicenter and longitudinal studies are recommended to further validate these findings and explore the long-term impact of HLA-B27 on disease progression and treatment outcomes in the Bangladeshi population.

**Limitations**

This study had several limitations. First, it was conducted at a single tertiary care center in Rajshahi, which may limit the generalizability of the findings to other regions of Bangladesh. Second, the cross-sectional design provides a snapshot of associations but does not allow for the assessment of causality or disease progression over time. Third, radiological assessments (e.g., MRI) for sacroiliitis were not uniformly available for all patients, which may have influenced the diagnostic accuracy for axial SpA. Additionally, socioeconomic and environmental factors that could influence disease severity were not extensively evaluated.

**Recommendations**

1. **Multicenter Studies:** Future research should include multiple centers across Bangladesh to obtain a more representative sample of the population.
2. **Longitudinal Studies:** A prospective cohort design is recommended to assess the progression of disease in relation to HLA-B27 status and treatment outcomes.
3. **Broader Diagnostic Workup:** Integration of advanced imaging techniques such as MRI should be encouraged for more precise diagnosis of axial involvement.
4. **Public Health Awareness:** Educational programs on early signs of SpA and the role of HLA-B27 could improve early diagnosis and management in primary care settings.
5. **Policy Integration:** Incorporating HLA-B27 testing in routine rheumatological assessments, especially in seronegative arthritis patients, may lead to earlier and more accurate diagnoses.

Ethical approval and consent

Informed consent was obtained from all patients before their participation in the study. The study followed ethical guidelines set by the research ethics committee at the healthcare center, ensuring patient confidentiality and safety.

**COMPETING INTERESTS DISCLAIMER:**

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

**Author Contributions:**

All authors made equal contributions to the research and writing of the manuscript. Each author participated in the design, data collection, analysis, and interpretation of the study. Additionally, all authors reviewed and revised the manuscript critically for important intellectual content. All authors have given their final approval for the manuscript to be submitted and published.

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Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, manuscript.

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