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Original Research Article.

A Cross Sectional Study of Sero-prevalence of HLA-B27 among Spondyloarthritis Patients Attending SMS Hospital, Jaipur, Rajasthan

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ABSTRACT

Introduction: Spondyloarthropathies are a heterogeneous group of inflammatory interrelated diseases involving peripheral joints and spine. All forms of spondyloarthropathies are known to have a strong association with HLA-B27 gene in various studies done. There was a paucity of literature about clinical and demographic characteristics of the HLA-B27 positive arthritis patients in Rajasthan. So this study was planned to know the seropositivity of HLA-B27 among seronegative spondyloarthritis patients and to find out association between socio-demographic and clinical characteristics and HLA-B27 seroprevalence.

Materials and Methods: A cross sectional observational study was carried out from May 2017 to April 2018 in Department of Pathology, SMS Medical College, Jaipur (Rajasthan). A total of 100 cases of spondyloarthritis disease were enrolled in the study to find out seroprevalence of HLA-B27 and to differentiate the clinical and demographic characteristics in HLA-B27 positive and negative patients.

Results: In the present study 29% seroprevalence of HLA-B27 was observed. Seropositivity of HLA-B27 was significantly associated with age (P-value < 0.05) while sex, religion, caste, family history, raised ESR, Positive C-reactive protein, RA factor etc. were showed no significant association (P-value > 0.05).

Conclusion: This study confirms the previously reported association in ankylosing spondylitis patients between HLA-B27 and earlier disease onset with male preponderance & family aggregation.

Keywords: Spondyloarthritis, Sero-prevalence, HLA-B27.

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INTRODUCTION

The spondarthropathies are a group of conditions affecting the spine and peripheral joints, which cluster in families and are, linked to certain type-1 HLA antigens. These disorders include ankylosing spondylitis, reactive arthritis, psoriatic arthritis and spondylitis, enteropathy associated arthritis and spondylitis, juvenile-onset spondyloarthritis and undifferentiated spondyloarthritis. The course of the disease is extremely variable, ranging from the individual with mild stiffness and radiographically equivocal sacroilietis to the patient with a totally fused spine and severe bilateral hip arthritis, accompanied by severe peripheral arthritis and extra articular manifestations.[1,2]

Genetic studies have contributed the most significant information to understanding of ankylosing spondylitis. A strong genetic predisposition was confirmed by the discovery of a remarkably high association between ankylosing spondylitis and the human leukocyte antigen HLA-B27 in 1973. A proportion of ankylosing spondylitis cases that do not involve HLA-B27 have been reported, however, it is still regarded as one of the most important factors for the development of ankylosing spondylitis with a high association (>100), and is present in up to 90% of patients in the majority of ethnic groups that present with the disease.[3]

The HLA class-I molecules, HLA-B27, is encoded at the B locus of the major histocompatibility complex located in the short arm of chromosome 6.The traditional function of HLA class-I is to present the peptides to CTLs to initiate immune responses. Furthermore, the HLA-B27shows a high degree of polymorphism resulting from nucleotide substitutions in exons 2 and 3, which encode the α1 and α2 domains of the B27's heavy chain. This high polymorphism may not only influence the specificity of binding antigenic peptides but also can play a role in the pathogenicity and susceptibility of ankylosing spondylitis. There is evidence that the distribution of HLA-B27subtypes worldwide is widely influenced by the race and the ethnicity with different strengths of association with ankylosing spondylitis.[4]

About 80–90% of patients with ankylosing spondylitis show presence of HLA-B27. However, only a small proportion of people

in the general population who harbour HLA-B27 (5–6% in white people) develop ankylosing spondylitis, and HLA-B27 explains only 20–40% of the genetic susceptibility to ankylosing spondylitis suggesting the contribution of additional genes[1]. The frequency of HLA-B27 with ankylosing spondylitis or other related spondyloarthropathies among Indian population varies from 30 to 94% as compared to 1.4 - 8% of the generalpopulation.[5]

There has been no study done in Rajasthan till now, which describes the clinical and demographic characteristics of the HLA-B27 positive arthritis patients. So, present study was conducted to provide an overview of the demographic and clinical characteristics of HLA-B27 positive arthritis as compared to HLA-B27 negative arthritis.

MATERIALS AND METHODS

A cross sectional observational study wascarried out in Department of Pathology, SMS Medical College, Jaipur (Rajasthan) from March 2017 to April 2018.After taking approval from institutional ethics committee and informed consent from the patients of low back pain, heal pain or knee joint pain, blood samples were collected in advance hematology lab. Total 100 samples were included in the study. Clinical data along with personal details of all cases were noted in a predesigned and semi-structured performa. The HLA-B27 detection will be done using sequence specific primers for HLA-B27. These primers are known to detect all the known polymorphisms of HLA-B27. Data were entered in Microsoft Excel Spreadsheets 2010 and analyzed using chi square test of significance by Primer. P-value < 0.05 was considered as the level of significance.

RESULTS

Out of 100 subjects included in the present study, 70%were male and 30% were female with male to female ratio of 2.3:1. The mean age of males was 33.44 ± 12.14 years while it was 38.40 ± 18.02 years.

Majority of subjects (91%) were belonged to Hindu religion and rest (9%) were Muslims. Knee joint was most common (41%) joint involved in the present study followed by lumber spine (24%), sacroiliac joint (24%), ankle joint (17%) and wrist joint (11%). (Table-1)

In the present study, duration of symptoms was more than 12 months in 49% subjects, less than 6 months in 27% subjects and between 6-12 months in 22% subjects. In 2%subjects duration of symptoms could not be find out. History of trauma was present in 18% cases and family history of similar disease was found positive only in 14% cases. In majority of cases (84%) no associated medical illness was seen.

ESR was raised in 79.22% cases(61 out of 77), CRP was positive in 33.77% (26 out of 77), RA factor was positive in 15.38% (12 out of 78), abnormal X-ray findings were seen in 25% (13 out of 52) and abnormal MRI finding were seen in 59.46% (22 out of 37). Overall seroprevalence of HLA-B27 in spondyloarthritis cases was 29% (28 positive while 1 case is borderline positive) in this study.

In the present study, significant association was observed between HLA-B27 positivity and age in spondyloarthritis cases (P value < 0.05) while sex, religion caste, duration of symptom, history of trauma, family history, raise ESR, positive CRP, positive RA factor, abnormal X-ray and MRI finding did not show significant association (P-value > 0.05). (Table-2)

Table 1: Distribution of study subject according to joint involvement

S. No.	Joint Involved	Unilateral	Bilateral	Total*
1	**Multiple Joints**	-	11	11
2	**Ankle Joint**	8	15	23
3	**Knee Joint**	15	26	41
4	**Hip Joint**	1	1	2
5	**Wrist Joint**	7	10	17
6	**Elbow Joint**	3	5	8
7	**Shoulder Joint**	1	4	5
8	**Metacarpal Joint**	3	2	5
9	**Spine-Cervical Joint**	8	-	8
10	**Spine-Lumber Joint**	24	-	24
11	**Sacroiliac Joint**	22	2	24
12	**Great Toe**	1	0	1
13	**Proximal Interphalangeal Joint**	1	0	1
14	**Scapula**	1	1	2

*Multiple responses

Table 2: Association of HLA-B27 with socio-demographic and clinical parameters

Socio-demographic or clinical parameters		HLA B27 +ve		HLA B27 -ve		P-Value*
		(n)	(%)	(n)	(%)	
Age Groups (Years)	**≥ 20**	8	8	6	6	0.045
	21-40	16	16	40	40	
	41-60	3	3	21	21	
	61-80	2	2	4	4	
	Male	23	23	47	47	0.290
Sex	**Female**	6	6	24	24	
Religion	**Hindu**	27	27	64	64	0.932
	Muslim	2	2	7	7	
Caste	**Sharma**	3	3	8	8	0.890
	Meena	4	4	6	6	
	Muslim	2	2	7	7	
	Jat	1	1	7	7	
	Agarwal	2	2	4	4	
	Saini	2	2	2	2	
	Jain	1	1	1	1	
	Rajpoot	0	0	1	1	
	Others	14	14	35	35	
Duration of Symptoms	**< 6 Months**	5	5	22	22	0.342
	6-12 Months	7	7	15	15	
	> 12 Months	17	17	32	32	
History of Trauma	**Present**	5	5	13	13	0.872
	Absent	24	24	58	58	
Family History	**Present**	5	5	9	9	0.780
	Absent	24	24	62	62	
ESR	**Raised**	19	19	42	42	0.936
	Normal	3	3	9	9	
CRP	**Positive**	12	12	14	14	0.166
	Negative	14	14	37	37	
RA factor	**Positive**	6	6	6	6	0.266
	Negative	19	19	47	47	

*Chi square test

DISCUSSION

The term spondyloarthritis represents a condition characterised by a broad spectrum of clinical manifestations, laboratory abnormalities and imaging features that genetically tend to be associated with the major histocompatibility complex class-1 antigen, HLA-B27. In particular, spondyloarthritis is an inflammatory condition in which both peripheral and axial joints might be affected. Chronic back pain is the leading symptom of an axial involvement, with pronounced stiffness and improvement of pain and stiffness with exercise. Other musculoskeletal manifestations are arthritis, enthesitis and dactylitis. Extraarticular manifestations such as anterior uveitis, psoriasis and inflammatory bowel disease are also characteristic for spondyloarthritis.[6]

The present study on seroprevalence of HLA-B27 among spondyloarthritis patients was done on 100 cases. The male preponderance (M:F ratio 2.3:1) in the present study was similar to various authors like, Kennedy et al[7] (M:F ratio 2.6:1), Nazarinia et al[8] (M:F ratio 2.5:1) while very close to the results by Vaidya et

al[2] 64.7% with sex ratio 1.8:1, Tipu and Bashir[9] 76.6% with 3.3:1, Behera et al[10] 77.7% with sex ratio 3.5:1 and Arevalo et al[11] 74.8% with sex ratio 3:1. The age range was 5-82 years with maximum cases in the age group 21-40 years with a mean of 34.93±14.25 years. This was similar to Tipu and Bashir[9] (age distribution of 5-80 years with mean age 40±10 years), Vaidyaet al[2] (15-75 years with mean 39.1±14.9 years), Behera et al[10] (20-60 years with maximum age group 30-40 years) and Romero-Sanchez et al[12] (19-45 years with mean 31.9±9.9 years). In the present study 91% patients were Hindu and 9% patients were Muslim by religion. This difference in religion may be due to difference in geographic location.

In this study the distribution of joint involvement were predominantly knee joint 41% followed by sacroiliac 24%, lumber spine 24%, ankle joint 23%, and wrist joint 17%. Similar results were observed by Parasannanavar et al[5] who also reported that knee joint 54%, hip joint 46%, cervical spine 43%, multiple joint 40 %, lumber spine 38%, ankle joint 30%, sacroiliac 25%, wrist joint 11% and shoulder joint 7%.In the present study there were 14% patients who presented with a positive family history. This finding was similar to Nazarinia et al[8] and Arevalo et al[11] who found a family history in 14.3% and 21% respectively.

About 79.22% subjects showed raised ESR which was very close to findings observed by Sonkar and Usha[13] and Mirjam et al[14] (raised ESR in 77.55% & 73% patients respectively). Beheraet al[11] and Prajzlerova et al[15] also found that ESR value was raised in spondyloarthritis patients. The acute-phase reactants are a class of serum proteins, mainly glycoproteins, whose concentration in the blood increases after various stimuli such as trauma or inflammation. The magnitude of the acute-phase protein response is roughly proportional to the severity of the stimulus. Serial measurements of these proteins can therefore be used, like the erythrocyte sedimentation rate (ESR), which is largely a measure of fibrinogen, to monitor the progress of an inflammatory disorder.[16]

C-Reactive Protein (CRP) in present study was found positive in 33.77% cases. Sonkar and Usha[14] and McGonagle et al[17] were found CRP value raised by 63.63% and 100% respectively. Behera et al[10] and Prajzlerova et al[15] also found that CRP value was raised in spondyloarthritis patients. The disease activity was significantly associated with serum concentration of CRP in HLA-B27 positive patients.[18] CRP is a commonly used acute-phase protein that reflects systemic inflammation. In general, the level of CRP is higher in patients with the full-blown radiographic form of the disease compared with Non-radiographic- axial spondyloarthritis (nr-axSpA). Although CRP is not elevated in a large proportion of patients with active axial spondyloarthritis (axSpA), it is widely used as a reliable parameter of disease activity. CRP levels are moderately correlated with MRI inflammation, which is presently the best tool for assessing disease activity. In addition, CRP has been demonstrated to be a reliable biomarker for the monitoring of treatment response and the prediction of further structural progression of the disease. Several studies and clinical practice have demonstrated that elevated CRP levels decrease significantly during anti-TNF therapy.[15]

In the present study we found that out of 78 patients 12 patients (15.38%) had positive RA factor. Out of them 6 patients showed HLA-B27 seropositivity (6%), 7 patients were male and 5 were female. Two female patients showed HLA-B27 seropositivity with positive RA factor. Toussirot et al[19] found 8.3 % cases had RF positive in Ankylosing Spondylitis and 6.6 % of patients with Rheumatoid arthritis may have positive HLA-B27. These findings were concordant to present study. In the general population, RA and AS occur with a comparable frequency from 0.3 to 1.5%. Pathogenesis of these diseases has not yet been fully clarified. Epidemiological data, as well as higher incidence of both RA and AS in certain families and identical twins, support the significance of genetic factors.[20]

In our study overall seroprevalence of HLA-B27 in spondyloarthritis patients was 29%. This was concordant with earlier studies by Tipu and Bashir[9] and Romero- Sanchez et al[12] they found 23.4%, 12.1% respectively.

However, contrary results were seen in other studies done by Nazarinia et al[8], Behera et al[10],Sonkarand Usha[13] and McGonagle et al[17] in which HLA-B27 seropositivity were 73.4%, 79.74%, 43.63% and 53% respectively. These differences may be due to the different geographic location.

CONCLUSION

Spondyloarthritis is a chronic disease with typical onset at a young age with male preponderance. Present study suggests the association of HLA-B27 with spondyloarthropathy. So, HLA-B27 typing would be helpful in the diagnosis of spondyloarthritis patients mainly in ankylosing spondylosis.

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