Zahedan J Res Med Sci. 2015 July; 17(6):e983. DOI: http://sx.doi.org/10.17795/zjrms983

Published online 2015 July 18. **Short Communication**

A Survey on the Frequency of HLA-B27 in Patients Engaged With Seronegative Spondyloarthropathies in Kashan, Iran

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Received: February 17, 2014; **Accepted:** April 12, 2014

Background: Seronegative Spondyloarthropathies (SNSAs) are referred to a group of diseases with same clinical and genetic features.
Objectives: Due to lack of data about HLA-B27 prevalence in patient with SNSA in Kashan this study was conducted to determine the status of HLA-B27 in these patients.
Patients and Methods: This cross sectional study was conducted on 294 patients suffered from SNSA. Presence or absence of HLA-B27 was checked by serological method using Greener kit. Results were analyzed with SPSS-16 software using t-test and χ^2 test.
Results: Of all 26.5% of subjects were HLA-B27 positive. HLA-B27 was significantly more frequent in male patients (34.1% vs. 16.5%, $P < 0.001$). Prevalence of HLA-B27 was 69% in ankylosing spondylitis, 31.5% in psoriatic arthritis, 18.2% in entropathic arthropathy, 17.9% in undifferentiated spondyloarthropathies, 16.1% in reactive arthritis and 12.5% in juvenile rheumatoid arthritis ($P < 0.001$).
Conclusions: HLA-B27 has highest prevalence in ankylosing spondylitis and least prevalence in juvenile rheumatoid arthritis. HLA-B27 prevalence was in relation with gender, type of disease, family history, peripheral, and axial joints engagement.

Keywords: Seronegative; Spondyloarthropathies; HLA-B27

1. Background

Seronegative Spondyloathropathies (SNSAs) are defined as a group of diseases with the same clinical demonstrations and genetic characteristics [1]. There is six subtype of SNSAs contains Ankylosing Spondylitis (AS), psoriatic arthritis, entropathic arthropathy, reactive arthritis, Juvenile Rheumatoid Arthritis (JRA) and undifferentiated spondyloarthropathies [1].

Human leukocyte antigen system or HLA refers to four gene families (know with A - D letters) that codify a series of polymorphic proteins on most nucleated cell surfaces in human body [2]. The role of HLA system in many rheumatologic disorders has been known [3]. HLA-B27 is a type of these genetic factors that have different prevalence in various rheumatologic diseases [3]. In SNSAs presence of HLA-B27 is very prevalent but the exact prevalence is unknown [4, 5]. Different values have been reported in previous studies for example in one study 43% of SNSAs patients were HLA-B27 positive while in another study it was 90% [4, 6]. HLA-B27 prevalence varies among different races. In a 2009 US national survey 7.5% of non-Hispanic whites, 4.6% of non-Hispanic blacks and 1.1% of Mexican-Americans were HLA-B27 positive [7]. In general, an individual's risk of developing AS is increased 5.6-fold to 16-fold if there is a first degree relative with AS. This risk depends partly upon the presence of HLA-B27; 10 - 20% of HLA-B27 positive individuals with affected first degree relatives develop AS [8]. According to importance of HLA-B27 prevalence determination, controversies in different articles and cross racial varieties this study was conducted on Kashan's SNSA patients.

2. Objectives

Due to lack of data about HLA-B27 prevalence in patient with SNSA in Kashan this study was conducted to determine the status of HLA-B27 in these patients.

3. Patients and Methods

In this cross sectional study 294 patients suffered from SNSAs were evaluated. Patients were selected from hospitalized known cases or outpatient referrers of Kashan's rheumatology clinic, randomly. All patients were diagnosed during 2005 to 2010 years and were under standard treatment of SNSAs.

After providing details on how to conduct the study, patient's consent was obtained to participate in the study. Demographic information such as age, gender, disease duration and family history was obtained and were recorded in a questionnaire. Type of disease was extracted from medical records and recorded in questionnaire.

All patients were examined by a rheumatologist and disease manifestations (such as peripheral and axial joints engagement) were recorded. Five milliliters venous blood was obtained from patient's cubital fossa and HLA-B12 were determined by flow cytometery method using BD™ HLA-B27 Kit produced by United Kindom. Data were analyzed by windows SPSS-16 using t-test and χ^2 tests. Results reported as Mean ± Standard Deviation. Statistical significance was set at $P < 0.05$.

4. Results

Of all patients 26.8% (167 subjects) were male and 43.2% (127 subjects) were female. Average age of the patients was 29.5 ± 13.5 years. Average disease duration was 3.5 ± 3.2 years. Antrropathic arthropathy was observed in 22.4% (66 subjects) of the patients. Then, reactive arthritis, psoriatic arthritis, juvenile rheumatoid arthritis, ankylosing spondylitis and finally undifferentiated spondiloarthropathies were observed in 19.1% (56 subjects), 18.4% (54 subjects), 16.3% (48 subjects), 14.3% (42 subjects) and 9.5% (28 subjects) patients, respectively. First degree relative background was positive in 12.6% (37 subjects) patients.

In 84.4% (248 subjects), peripheral joint engagement was observed. Of all patients 34.7% (120 patients) had axial joint engagement. Extra articular engagement was also observed in 59.2% (147 patients). HLA-B27 was reported positive in 26.5% of patient with seronegative spondyloarthropathies. The study findings are reported in Table 1.

Table 1. Abundance Distribution of HLA-B27 in Patients With Seronegative Spondyloarthropathies, According to the Patients Profiles in Kashan From 2005 to 2010

Variable	Positive [a]	Negative [a]	Sum Patients	P-Value
Gender				< 0.001
Male	57 (34.1)	110 (65.9)	167	
Famale	21 (16.5)	106 (83.5)	127	
Total	78 (26.5)	216 (73.5)	294	
Type of disease				< 0.001
Juvenile rheumatoid arthritis	6 (12.5)	42 (87.5)	48	
Reactive arthritis	9 (16.1)	47 (83.9)	56	
Undifferentiated SpA[b]	5 (17.9)	23 (82.1)	28	
Entropathic arthropathy	12 (18.2)	54 (81.8)	66	
Psoriatic arthritis	17 (31.5)	37 (68.5)	54	
Ankylosing spondylitis	29 (69)	216 (73.5)	45	
Total	78 (25.6)	216 (73.5)	294	
Family background				< 0.001
Yes	26 (70.3)	11 (29.7)	37	
No	52 (20.2)	205 (79.8)	257	
Total	78 (26.5)	216 (73.5)	294	
Peripheral joint engagement				< 0.001
Yes	55 (22.2)	193 (77.8)	248	
No	23 (50)	23 (50)	46	
Total	78 (26.5)	216 (73.5)	294	
Axial joint engagement				< 0.001
Yes	53 (52)	49 (48)	102	
No	25 (13)	167 (87)	192	
Total	78 (26.5)	216 (73.5)	294	
Extra articular joint engagement				0.4
Yes	49 (28.2)	125 (71.8)	174	
No	29 (24.2)	91 (75.8)	120	
Total	78 (26.5)	216 (73.5)	294	

[a] Values are presented as No. (%).
[b] Abbreviation: SpA: Spondyloarthropathy.

The study results show that HLA-B27 was positive in one-fourth of the patients with one of seronegative spondyloarthropathies. HLA-B27 was more prevalent in males than females. Among seronegative spondyloarthropathies, HLA-B27 was the most prevalent and ankylosing spondilits (69%) was the least prevalent one in juvenile rheumatoid arthritis (5-12%). Prevalence of HLA-B27 amongst patients with positive family background was more than those with no background.

5. Discussion

In this study we found that prevalence of HLA-B27 in Kashan's SNSAs patients were 26.5%. Prevalence of this kind of HLA was twice in males than females which was statistically significant. Wu et al. [9] reported prevalence of HLA-B27 in patients with SNSAs about 40%, Buschiazzo et al. reported 45% without sexual separation [10]. Mijiyawa et al. reported positive HLA-B27 in of African patients with SNSAs [11]. They reminded that HLA-B27 is not a suitable marker to diagnose these diseases in Africans while others consider the relation between HLA-B27 and serongative spondyloarthropathies as an obvious example of relation between a group of diseases and a special heritage marker [11].

Adib et al. reported prevalence of HLA-B27 in general population of Iran about 3% in their study [12]. They noted that prevalence level of HLA-B27 is limited to Caucasians and is similar to its abundance in Arabs, Jews and Armenians. A relatively low prevalence of HLA-B27 in the general population and its 25 - 65% prevalence among seronegative spondyloarthropathies patients can show the relation between this marker and each type of diseases [12].

In the present study prevalence of HLA-B27 among patients with seronegative spondyloarthropathies was mostly observed in ankylosing splodytis so that about 70% of them had positive HLA-B7, while after, prevalence was observed in patients with psoriatic arthritis, entropathic arthropathy and undifferentiated spondiloarthropathy. In two studies of De Keyser et al. and Reveille, prevalence of HLA-B27 in ankylosing spondylitis patients was along with the present study results and reported about 90 to 95% which was more than the present results [13, 14].

De Keyser et al. studied patients with reactive arthritis after ankylosing spondylitis in which HLA-B27 was positive for about 80% of them [13]. Reveille has also reported prevalence of HLA-B7 for reactive arthritis as the second rank and about 70 - 90% which is five times more than that of the antigen in the present study [14]. De Keyser et al. have discussed HLA-B27 prevalence in psoriatic arthritis patients after reactive arthritis and ankylosing spondylitis. They have reported it about 40% which is a little more than the present study. About 13% of the studied patients had a positive family background of seronegative spondiloarthropathy [13]. HLA-B27 was 70% prevalent in these patients while HLA-B27 prevalence was about 20% in patients with no family background of seronegative spondiloarthropathy diseases [13]. This difference which shows more prevalence of HLA-B27 in positive family background was statistically significant.

In Buschiazzo et al. study a positive family background was observed in 16.8% of the patients with seronegative spondiloarthropathy, so this study results are similar and a little more than present study [10]. According to the results it seems that HLA-B27 prevalence in patients with spondiloarthropathy in Kashan was low and it may not be used as a strong significant experimental criterion. As there is a high relationship between HLA-B27 in patients with family background, relation between positive family background and HLA-B27 can be used as a trustful reliable criterion to diagnose diseases and patients. Complementary studies are recommended as comparisons between patient and control groups to reach clearer results.

Acknowledgements

The present study was stemmed from research plan No. 8715 in 2008 with financial support of Research Assistant Department of Medical Science University of Kashan, hereby is acknowledged.

Authors' Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

References

1. Firestein GS, Budd RC, Gabriel SE. *Kelly's text book of rheumatology.* 9 edPhiladelphia: W.B.Saunders; 2005.
2. Murphy NM, Pouton CW, Irving HR. Human leukocyte antigen haplotype phasing by allele-specific enrichment with peptide nucleic acid probes. *Mol Genet Genomic Med.* 2014;**2**(3):245–53.
3. Ballestar E. Epigenetic alterations in autoimmune rheumatic diseases. *Nat Rev Rheumatol.* 2011;**7**(5):263–71.
4. Sonkar GK, Usha. Role of HLA B27 in diagnosis of seronegative spondyloarthropathies. *Indian J Pathol Microbiol.* 2007;**50**(4):908–13.
5. Kanga U, Mehra NK, Larrea CL, Lardy NM, Kumar A, Feltkamp TE. Seronegative spondyloarthropathies and HLA-B27 subtyes: a study in Asian Indians. *Clin Rheumatol.* 1996;**15 Suppl 1**:13–8.
6. Malaviya AN, Sawhney S, Mehra NK, Kanga U. Seronegative arthritis in South Asia: an up-to-date review. *Curr Rheumatol Rep.* 2014;**16**(4):413.
7. Reveille JD, Hirsch R, Dillon CF, Carroll MD, Weisman MH. The prevalence of HLA-B27 in the US: data from the US National Health and Nutrition Examination Survey, 2009. *Arthritis Rheum.* 2012;**64**(5):1407–11.
8. Baron M, Zendel I. HLA-B27 testing in ankylosing spondylitis: an analysis of the pretesting assumptions. *J Rheumatol.* 1989;**16**(5):631–4.
9. Wu ZB, Zhu P, Wang HK, Zheng ZH, Jia Y, Ding J, et al. Prevalence of seronegative spondyloarthritis in the army force of China. *Zhonghua Liu Xing Bing Xue Za Zhi.* 2004;**25**(9):753–5. [In Chinese]
10. Buschiazzo E, Maldonado-Cocco JA, Arturi P, Citera G, Berman A, Nitsche A, et al. Epidemiology of spondyloarthritis in Argentina. *Am J Med Sci.* 2011;**341**(4):289–92.
11. Mijiyawa M, Oniankitan O, Khan MA. Spondyloarthropathies in sub-Saharan Africa. *Curr Opin Rheumatol.* 2000;**12**(4):281–6.
12. Adib M, Salehi M, Fooladi S , Ostadi V. HLA-B2 frequency by flow cytometry in blood donors in Isfahan: 2006. *J Isfahan Med School.* 2007;**24**(80-81):12–8.
13. De Keyser F, Elewaut D, De Vos M, De Vlam K, Cuvelier C, Mielants H, et al. Bowel inflammation and the spondyloarthropathies. *Rheum Dis Clin North Am.* 1998;**24**(4):785–813.
14. Reveille JD. HLA-B27 and the seronegative spondyloarthropathies. *Am J Med Sci.* 1998;**316**(4):239–49.