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Frequent Cases of Spondylarthritis and Hereditary Propensity (HLA-B27) in the Same Family Name Relatives from the Keda Region of Ajara, Georgia

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ABSTRACT

Background: Typical clinical characteristics of spondyloarthropathies (SpA) include inflammatory back pain (caused by sacroiliitis and peripheral oligoarthritis), enteropathy, anterior uveitis, and an association with HLA-B27. The disease begins in the second or third decade of life and affects more men than women. The prevalence of SpA among first-degree relatives of the affected patients was found to be 12%. Ankylosing spondylitis (AS) is the most common subgroup of SpA, with a crucial role for HLA-B27 in the pathogenesis. HLA-B27 presents in 88–90% of AS patients, compared to 4–8% among the general population.

Objectives: In this study, we explored the relationship and hereditary propensity of the same family name relatives from the Keda region of Ajara, Georgia, where we frequently encountered cases of ankylosing spondylitis.

Methods: The study was conducted at the Clinic "SoloMed" and "Merlab" Laboratory Services from 05.01–10.03, 2023, using real-time polymerase chain reaction (PCR).

Results: Among the 105 evaluated participants included in this study (average age of 40.5 [15–60] years), 53.33% (n=56) were females, and 46.67% (n=49) were males. The highly HLA-B27-positive individuals were six males aged ≥56 years and two women between the ages of 26 and 35. In the relatives with the same family names, 14.29% (n=15) were HLA-B27 positive.

Conclusions: The same family name relatives from the Keda region of Ajara, Georgia, showed a considerably higher risk of the distribution of ankylosing spondylitis (14.29).

Keywords: Ankylosing spondylitis; HLA-B27; relatives.

BACKGROUND

The term "spondyloarthropathy" (SpA) refers to a class of inflammatory rheumatic diseases that includes ankylosing spondylitis (AS), the prototypical spondyloarthropathies, reactive arthritis (ReA), psoriatic arthritis (PsA), arthritis associated with inflammatory bowel disease (AIBD), and undifferentiated SpA (USpA), a recently recognized subset.[1]

Over 100 diseases are associated with classical HLA class I and II genes.[2]

A deeper awareness of the disease began with identifying a strong link between SpA and HLA-B27 in 1973. It was discovered that the ratio of affected male patients to affected female patients, which was previously believed to be 10 to 1, was significantly lower. Additionally, it has gradually come to be known that symptoms often persist for years before a disease is identified.[3-5]

The disease occurs in the second or third decade of life and affects men more frequently than women (ranging from 2.6:1 to 5:1).[4,6] SpA was shown to be 12% more common among first-degree relatives of the affected patients.[5,7]

In the pathogenesis of the disease, HLA-B27 plays an important role. 88 to 90% of AS patients have the HLA-B27 gene, compared to 4–8% of the general population.[5,8,9]

By now, 238 subtypes of HLA-B*27 have been reported (The IPD-IMGT/HLA Database, Release 3.43.0, 2021). The IPD-IMGT/HLA Database, Release 3.43.0, 2021, states that there are currently 238 HLA-B*27 subtypes known. The following subtypes of AS have been linked to AS: HLAB*2702, HLAB*2703, HLAB*2704, HLAB*2705, HLAB*2706, HLAB*2707, HLAB*2708, HLAB*2710, HLAB*2714, HLAB*2715, and HLAB*2719.7,810–12 Most frequently, HLA-B*2705, HLA-B*2702, and HLA-B*2704 have been found to have significant associations with AS in different populations. Distinct ethnic groups and geographical regions have other distributions of HLA-B*27 subtypes.[10,13]

Regarding allelic frequencies, HLA-B*2702 and HLA-B*2705 are the most common subtypes in Caucasians; HLA-B*2702 exhibits a higher frequency in the Jewish population and Caucasians from North Africa and is also found in Asians.

HLA-B*2704 is the most common subtype in Asian populations.[10,11,14]

In seronegative spondylarthritis (SSpA) patients, the association of HLA-B27 ranges from 19 to 94%, while it is 1.4 to 8% in the general Indian population.[4,15,16] Seronegative spondylarthritis is characterized by the rheumatoid factor (RF), anti-cyclic citrullinated peptide (Anti-CCP), HLA-B27, or sacroiliitis on a scan in a patient with rheumatoid arthritis-like clinical symptoms. In the South Indian population, B*27:05 and B*27:04 subtypes of SpA are the most often seen.[4,17,18]

Due to numerous genetic and environmental factors that affect the disease, there may be variations in the clinical features of AS in different populations, along with variations in the frequency of HLA-B27. It has been suggested that in countries with lower incomes, AS may manifest earlier in life and with more frequent involvement of peripheral joints.[19,20]

Ankylosing spondylitis was identified in 1.3% of HLA-B27-positive people in the general population and 21% of HLA-B27-positive relatives of B27-positive patients with spondylitis in a study of the European population. This results in a 16-fold higher risk of ankylosing spondylitis in HLA-B27-positive relatives compared to B27-positive people in the general population.[21,23] Caucasians who are HLA-B27+ are 20 times more likely to develop any spondyloarthropathy, especially ankylosing spondylitis and undifferentiated spondylarthritis.[21,22]

Although HLA-B27-positive AS patients and those without this gene share a lot in common, they also differ from each other clinically in the following ways:[24-28]

- younger age at onset and diagnosis;
- greater familial occurrence;
- frequent association with acute anterior uveitis;
- more favorable clinical response to tumor necrosis factor (TNF) inhibitors;
- less frequent association with Crohn's disease, ulcerative colitis, and psoriasis.

Although there is a substantial correlation between HLA-B27 and ankylosing spondylitis, only about 2% of those with HLA-B27 positivity will ever develop the disease. This demonstrates that the inherited feature of diseases with HLA links is not the disease itself but rather the propensity to develop it.[24]

Our study investigated hereditary propensity (HLA-B27) in the same family name relatives in the Keda Region of Ajara, Georgia, where it was found that ankylosing spondylitis was relatively common. The initial aspect that attracted our attention was that ten of the 32 patients with ankylosing spondylitis who underwent biological medication treatment were from the same family and lived in the same area.

METHODS

We investigated 105 individuals who were relatives with the same family names using the laboratory technique of real-time PCR (DNA typing of HLA-B27 by polymerase chain reaction) to detect HLA-B27. In addition, the Inflammatory Back Pain (The Ultimate Guide, 2023) questionnaire was completed by each person.24,29 The research was conducted at the "Solomed Clinic" and "Merlab" Laboratory Services from May 1 to March 3, 2023.

RESULTS

53.33% (n = 56) of the 105 people that were investigated for this study, who had an average age of 40.5 years (15–60), were females, and 46.67% (n=49) were males. In our investigation, patients 56 years of age and older (n=6) were found to have a high level of HLA-B27 positivity; however, among females between the ages of 26 and 35 (n=2 cases), this positivity level was found to be 1.9%. The same family name relatives comprised 14.29% (n=15) of the total HLA-B27 positive individuals, with men accounting for 9.52% (n=10) and women accounting for 4.76% (n=5) of that group (Tab.1).

TABLE 1. Distribution of HLA-B27 by age and gender

Age	HLA-B27 positive				HLA-B27 negative			
	Male		Female		Male		Female	
	n	%	n	%	n	%	n	%
5-15	0	0	0	0	2	1.9	6	5.7
16-25	1	0.95	1	0.95	10	9.5	9	8.6
26-35	1	0.95	2	1.9	6	5.7	10	9.5
36-45	0	0	1	0.95	10	9.5	2	1.9
46-55	2	1.9	1	0.95	7	6.7	8	7.6
≥56	6	5.7	0	0	4	3.8	16	15.2
Total	10	9.5	5	4.8	39	37.1	51	48.6

Among the 105 individuals who underwent examination, 38.10% (n=40) had more than three of the disease's previously mentioned signs and symptoms, 25,71% (n=27) had fewer signs/symptoms, and 36.19% (n=38) had none at all. At the age of ≥56, most disease features become apparent. In 15 HLA-B27-positive individuals who underwent examination, positive illness characteristics were found in 9 (n=9) and 6 (n=6) of them (Tab.2).

TABLE 2. Distribution of disease features by ages

Age	Features of disease					
	0		<3		>3	
5-15	5	4.76%	1	0.95%	2	1.9%
16-25	13	12.38%	4	3.81%	3	2.86%
26-35	6	5.71%	5	4.76%	6	5.71%
36-45	6	5.71%	3	2.86%	4	3.81%
46-55	6	5.71%	3	2.86%	9	8.57%
56-<	2	1.9%	11	10.48%	16	15.24%
Total	38	36.19%	27	25.71%	40	38.10%

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DISCUSSION

The results of our study suggest that 105 relatives (49 men and 56 women) with the same family names have a high level of HLA-B27 positivity. In contrast to the findings of other authors, the male-to-female HLA-B27 positivity ratio was more elevated and equal to 2:1.[6,9]

In our study, HLA-B27 shows a higher male prevalence than females (ranging from 2:1), in contrast to 2.6:1–5:1.[6] Men aged 56 and older, and females aged 26 to 35 showed significant levels of HLA-B27 positivity. In addition, all 15 of the HLA-B27-positive individuals displayed disease-related features.

In our investigation, only 36.2% of the individuals were found to have no features, whereas 38.1% exhibited more than three signs of disease. Therefore, it is reasonable to pay attention to the fact that, even though 14.3% of tested individuals were positive for HLA B-27, only 38.1% of them had more than three symptoms of ankylosing spondylitis.

CONCLUSIONS

Our research in the Keda Region of Ajara, Georgia, demonstrates a high degree of genetic susceptibility to ankylosing spondylitis in the same family name relatives. To prevent the long-term consequences of this disease and the potential development of limitations, rheumatologists should be able to focus primarily on the accurate diagnosis and prompt, adequate treatment of ankylosing spondylitis.

AUTHOR AFFILIATION

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REFERENCES

1. Braun J, Bollow M, Remlinger G, Eggens U, Rudwaleit M, Distler A, Sieper J Prevalence of spondyloarthropathies in HLA-B27 positive and negative blood donors Arthritis Rheum Vol 41. No 1, January 1998, pp 58-67 0 1998, AineriLan College of Rheumatology
2. Mascaretti L, Bevilacqua E Review Article the Role of HLA Typing in Rheumatic Diseases DOI: 10.33602/mebm.3.1.1Molecular and Experimental Biology in Medicine, 2020, 3(1): 1-8
3. Trowsdale J. The MHC, disease and selection. Immunol Lett. 2011;137(1-2):1-8.
4. Jayaprakash T., Lokesh Muthamilan Om, Leela K.V., Panchapakesa Rajendran C., Arul Raja Murugan and Sujith Ravi Association of Genetic Marker HLA-B27 with Spondylarthritis In A Tertiary Care Centre In South India Jayaprakash et al. | J Pure Appl Microbiol | 16(2):901-908 | June 2022 Article 7561 | https://doi.org/10.22207/JPAM.16.2.10 Published Online April 25, 2022 Print ISSN: 0973-7510; E-ISSN: 2581-690X Journal of Pure and Applied Microbiology 901 www.microbiologyjournal.org
5. Chavan H, Samant R, Deshpande A, Mankeshwar R. Correlation of HLA B27 subtypes with clinical features of ankylosing spondylitis. Int J Rheum Dis. 2011;14(4):369-374. doi: 10.1111/j.1756-185X.2011.01635.x
6. Chatzikyriakidou A, Voulgari PV, Drosos AA. What is the role of HLA-B27 in spondyloarthropathies? Auto-Immun Rev. 2011;10(8):464-468. doi: 10.1016/j. autrev.2011.01.011
7. Prasad P, Niraj MK. Association of HLA-B27 with Ankylosing Spondylitis in Jharkhand. IOSR-JDMS.2017;16(7):05-07. doi: 10.9790/0853-1607060507
8. Singh S, Sonkar GK, Singh U. Association of various inflammatory diseases with human leukocyte antigens B27, B7, Bw4 and Bw6 in patients with SSA. Rheumatol Int. 2009;29(9):1013-1016. doi: 10.1007/s00296-009-0902-y
9. Seager K, Bashir HV, Geczy AF, Edmonds J, De Vere-Tyndall A. Evidence for a specific B27associated cell surface marker on lymphocytes of patients with Ankylosing spondylitis. Nature. 1979;277(5691):68-70.doi: 10.1038/277068a0
10. Lu J J, Yang J, Dong W X, Tang B J, Cao L Y, Lin Y H, Huang B Y, Fu X G Predominant frequency of HLA-B*27 in patients with ankylosing spondylitis in southeastern China Immunity, Inflammation and Disease Volume9, Issue 4 December 2021 Pages 1696-1701
11. Huang C, Ying H, Yang X, et al. The clinical characteristics of other HLA-B types in Chinese ankylosing spondylitis patients. Front Med. 2021;7:1-10.
12. Yang T, Duan Z, Wu S, et al. Association of HLA-B27 genetic polymorphisms with ankylosing spondylitis susceptibility worldwide: a meta-analysis. Modern Rheumatology. 2014; 24(1):150-161.
13. Díaz-Peña R, Castro-Santos P, Durán J, Santiago C, Lucia A. The genetics of spondylarthritis. J Pers Med. 2020;10(4):E151.
14. Gonzalez-Roces S, Alvarez MV, Gonzalez S, et al. HLA-B27 polymorphism and worldwide susceptibility to ankylosing spondylitis. Tissue Antigens. 2010;49(2):116-123.
15. Shankarkumar U, Ghosh K, Colah RB, Gorakshakar AC, Gupte SC, Mohanty D. HLA antigen distribution in selected caste groups from Mumbai, Maharastra, India. Journal of Human Ecology. 2002;13(3):209-215. doi: 10.1080/09709274.2002.11905535
16. Parasannanavar DJ, Rajadhyaksha A, Ghosh K. Application of a simple in-house PCR-SSP technique for HLA-B* 27 typing in spondylarthritis patients. Arthritis. 2013;2013:504109. doi: 10.1155/2013/504109
17. Howe HS, Zhao L, Song YW, Springer L, Edmonds J, Gu J, Yu DT. Seronegative spondyloarthropathy-studies from the Asia Pacific region. Ann Acad Med Singap. 2007;36(2):135.
18. Haridas V, Shetty P, Kumar MN, et al. Human leukocyte Antigen-B* 27 allele subtype prevalence and disease association of ankylosing spondylitis among south Indian population. Indian J Rheumatol. 2018;1;13(1):38-43. doi: 10.4103/injr.injr_95_17
19. Fırat S N, Yazıcı A, Yılmazer B, Coşan 2, Savlı H, Cefle A Low frequency of HLA-B27 in ankylosing spondylitis and its relationship with clinical findings in patients from Turkey Eur J Rheumatol 2017; 4: 268-271 DOI: 10.5152/eurjrheum.2017.17015
20. Van der Linden SJ, van der Heijde D. Spondyloarthropathies: ankylosing spondylitis. In: Ruddy S, Harris ED, Sledge CB, eds. Kelley's Textbook of Rheumatology, 6th ed. Philadelphia: WB Saunders, 2000: 1039-53.
21. John D. Reveille, MD and Michael H. Weisman, MD. The Epidemiology of Back Pain, Axial Spondylarthritis and HLA-B27 in the United States NIH Public Access Am J Med Sci. Author manuscript; available in PMC 2014 August 05. Published in final edited form as: Am J Med Sci. 2013 June; 345(6): 431–436.
22. van der Linden S, Valkenburg H, Cats A. The risk of developing ankylosing spondylitis in HLAB27 positive individuals: a family and population study. Br J Rheumatol. 1983; 22(4 Suppl 2):18–19. [PubMed: 6606472]
23. Dougados M, van der Linden S, Juhlin R, et al. The European Spondyloarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. Arthritis Rheum. 1991; 34(10): 1218–27. [PubMed: 1930310]
24. Khan M A, Yong S B, Wei J C C Ankylosing spondylitis: History, epidemiology, and HLA-B27 International Journal of Rheumatic Disease 01 March 2023

ISSN (Online): 2720-8796 ISSN (Print): 2720-7994

25. Khan MA, Akkoc N. Ankylosing Spondylitis –Axial Spondylarthritis, 2nd ed. Professional Communications Inc.; 2021, pp. 1–436. (www.pcboo ks.com).
26. Bittar M, Yong WC, Magrey M, Khan MA. Worldwide differences in clinical phenotype of axial Spondylarthritis. Curr Rheumatol Rep.2023;23:76. doi:10.1007/s11926-021-01043-5
27. Khan MA, Kushner I, Braun WE. Comparison of clinical features of HLAB27 positive and negative patients with ankylosing spondylitis. Arthritis Rheum. 1977;20:909-912.
28. Akkoc N, Yarkan H, Kenar G, Khan MA. Ankylosing spondylitis: HLA-B*27-positiveversus HLA-B*27-negativedisease. CurrRheumatol Rep. 2017;19(5):26. doi:10.1007/s11926-017-0654-8
29. Joel D. Taurog, M.D., Avneesh Chhabra, M.D., and Robert A. Colbert, M.D., Ph.D. Ankylosing Spondylitis and Axial Spondyloarthritis The new england journal of medicine. This article was updated on September 8, 2016, at NEJM.org. N Engl J Med 2016;374:2563-74. DOI: 10.1056/NEJMra1406182 Copyright © 2016 Massachusetts Medical Society.