# HLA-B27 Prevalence in Arab Populations and Among Patients with Ankylosing Spondylitis

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ABSTRACT. Objective. To investigate prevalence of HLA-B27 among general Arab populations and among patients with ankylosing spondylitis (AS), and to review published data.

*Methods.* The prevalence of HLA-B27 was studied among 2579 unrelated healthy Jordanians, almost equally divided among Palestinian refugees and natives of Jordan, reflecting the general population of Jordan. The prevalence of HLA-B27 was also studied among 129 patients with AS, 70 from Jordan, and the remaining 59 from Qatar. HLA typing was performed by standard 2-stage micro-lymphocytotoxicity method. We also reviewed published English language studies of HLA-B27 in Arab patients with AS and general populations retrieved through Medline and cross-reference search.

*Results.* We observed that the general prevalence of HLA-B27 among Jordanians is 2.4%; while the reported prevalence ranges between 2% and 5% among major Arab populations. The prevalence of HLA-B27 among patients with AS is 71% in Jordan and 73% in Qatar, while the reported prevalence from pooled published data from various Arab populations is 64%.

*Conclusion.* From these data one can conclude that HLA-B27 is present in about 2% to 5% among major Arab populations and that its prevalence in Arab patients with AS is closer to 70%. (First Release July 1 2012; J Rheumatol 2012;39:1675–7; doi:10.3899/jrheum.120403)

Key Indexing Terms:HLA-B27ANKYLOSING SPONDYLITISPREVALENCEMIDDLE EASTNORTH AFRICA

There is a remarkably strong association between ankylosing spondylitis (AS) and HLA-B27<sup>1,2</sup>. The world-wide prevalence of HLA-B27 and the strength of its association with AS vary markedly. Generally speaking, there is a close correlation between prevalence of HLA-B27 and prevalence of AS in a given population. Thus, AS is virtually absent in populations that lack HLA-B27, such as the Australian Aborigines and African Bantu populations of unmixed ancestry<sup>2,3,4</sup>. A few studies from the Arab world have looked into the prevalence of HLA-B27 in the general population and among patients with AS; these studies have involved a relatively small number of subjects.

We present data on the prevalence of HLA-B27 from Jordan and Qatar, based on a larger number of subjects, and

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summarize studies of Arab populations published in English.

# MATERIALS AND METHODS

Prevalence of HLA-B27 was studied among 2579 unrelated healthy Jordanians who were HLA typed as potential organ transplant donors; they comprised an almost equal number of Palestinians and native Jordanians, reflecting the general population of Jordan. We also studied 134 patients with AS, all of whom satisfied the modified New York criteria<sup>5</sup>; 70 of these patients were identified at the University Hospital in Amman, Jordan, and the remaining 64 at Hamad Medical Corporation in Doha, Qatar.

HLA typing was done by the standard 2-stage micro-lymphocytotoxicity technique with commercial kits.

We also reviewed previous studies of Arab populations that have been published in English by searching Medline and cross-reference between published data from different parts of the Arab world.

#### RESULTS

We observed that HLA-B27 was present in 2.4% of 2579 healthy unrelated individuals among the general population in Jordan. A total of 70 patients with AS were identified at the University Hospital in Amman, Jordan, between 1996 and 2010. Their male to female ratio was 10:1; mean age at onset of symptoms (inflammatory back pain or peripheral arthritis) was 22.7  $\pm$  5 years and median age was 22 years (range 12–40 yrs). HLA-B27 typing was done in 49 of these 70 patients, and 71% of them were found to possess this gene. Grade 4 sacroiliitis was seen in 83%, while 17% had grade 2–3 sacroiliitis. Complete fusion of the lumbar spine

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was seen in 76% of patients, while the rest had either early changes or partial fusion. Cervical spine was involved in 86% of patients. Hip and peripheral arthritis were seen in about half the patients for each. Anterior uveitis was seen in 26%.

In Doha, Qatar, a total of 59 Arab patients with AS (15 Qatari, 26 Jordanians/Palestinians, and 18 Egyptians) were typed for HLA-B27, and 73% (43/59) were found to possess this gene [the percentages were 80% (12/15) among Qatari, 69% (18/26) among Jordanians/Palestinians, and 72% (13/18) among Egyptian patients].

Our review of published data showed the prevalence of HLA-B27 to be 0.3% in Oman<sup>6</sup>, 0.5% and 0.8% in Emarati Arabs in the United Arab Emirate (UAE)<sup>7,8</sup>, 1.3% in Saudi Arabia<sup>9</sup>, 4% in Kuwait<sup>10</sup>, 1.4% in Syria<sup>11</sup>, 1.4% in Lebanon<sup>12,13,14</sup>, 2.1% in Iraq<sup>15</sup>, 4.7% in Egypt<sup>16</sup>, 4% in Algeria<sup>17</sup>, 2.8% in Sudan<sup>18</sup>, 1.9% to 6% in Tunisia<sup>19,20,21,22</sup>, and 2.7% to 6.4% in Morocco<sup>23,24,25</sup>.

Table 1 lists the reported frequency of HLA-B27 in patients with AS from the various Arab countries. It includes 2 previous reports from Jordan containing a small number of patients that had reported 75% and 81% prevalence of HLA-B27 in patients with  $AS^{26,27}$ , not much higher than that observed (71%) in our study.

# DISCUSSION

The world-wide prevalence of HLA-B27 as well as the strength of its association with AS varies markedly. Whereas approximately 90% of northern European patients with primary AS (unassociated with psoriasis or inflammatory bowel disease) possess HLA-B27, this association drops appreciably in countries surrounding the Mediterranean Sea. Among the non-Arab countries in and near the Middle East,

Table 1. HLA-B27	in Arab patients with AS.	Data are percentages.
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Country	HLA-B27 Prevalence in Patients with AS
Jnited Arab Emirates	$56 (n = 16)^{35}$
audi Arabia	$67 (n = 12)^{36}$
yria	$60 (n = 50)^{11}$
ebanon	$26.3 (n = 19)^{13}$
aq	$84 (n = 25)^{15}$
uwait	25.7 $(n = 35)^{10}$
	$78 (n = 9)^{37}$
ordan	71 $(n = 59)^{\text{Current study}}$
	75 (n = 20) <sup>25,30</sup>
	$81 (n = 52)^{26,31}$
atar	73 (n = $64$ ) <sup>Current study</sup>
unisia	55.85 $(n = 34)^{19}$
	42.9 $(n = 14)^{20}$
	$69 \ (n = 50)^{38}$
	$62 (n = 100)^{21}$
Iorocco	$67 (n = 49)^{39}$
	$63 (n = 32)^{40}$
	58.6 (n = 46) <sup>24</sup>
lgeria	$63 (n = 129)^{17}$
otal	64 (n = 800)

HLA-B27 is present in 70% to 91% in Turkish patients with AS<sup>28,29</sup>, 80.5% in Greek patients<sup>30</sup>, and in 68% to 73% in Iranian patients<sup>31,32</sup>. The frequency of HLA-B27 in the general population was found to be 2.6% to 6.8% in Turkey<sup>33,34</sup> and 3.95% in Iran.

A few studies from the Arab world have reported the prevalence of HLA-B27 in the general population and among patients with AS. Published data indicate that HLA-B27 is present in about 2% to 5% among the major Arab populations. We found HLA-B27 prevalence to be 2.4% in Jordan among a much larger number of subjects. We failed to find any published data on HLA-B27 prevalence in the general population or among patients with AS from Yemen, Libya, and Mauritania.

The prevalence of HLA-B27 is 64% if derived from pooled data of 805 Arab patients with AS (Table 1), but many reports are based on small numbers of patients. The reason for such small numbers could possibly be low disease ascertainment or a true low prevalence of AS in some parts of the Arab world that may be associated with low prevalence of HLA-B27 in that specific population. If one restricts analysis to larger studies, about 70% of Arab patients with AS possess HLA-B27. Lastly, it is important to point out that there are no reports of proper epidemiologic studies from Arab countries to determine the prevalence of AS in the general population.

### REFERENCES

- Khan MA. Ankylosing spondylitis. New York: Oxford University Press; 2009:1-147.
- Khan MA. HLA-B27 and its pathogenic role. J Clin Rheumatol 2008;14:50-2.
- Mijiyawa M, Oniankitan O, Khan MA. Spondyloarthropathies in sub-Saharan Africa. Curr Opin Rheumatol 2000;12:281-6.
- Akkoc N, Khan MA. Epidemiology of ankylosing spondylitis and related spondyloarthropathies. In: Weisman MH, Reveille JD, van der Heijde DM, editors. Ankylosing spondylitis and the spondyloarthropathies. London: Mosby; 2005:117–31.
- van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. Arthritis Rheum 1984;27:361–8.
- White AG, Leheny W, Kuchipudi P, Varghese M, Al Riyami H, Al Hashmi S, et al. Histocompatibility antigens in Omanis: Comparison with other Gulf populations and implications for disease association. Ann Saudi Med 1999;19:193-6.
- Al-Attia HM, al-Amiri N. HLA-B27 in healthy adults in UAE. An extremely low prevalence in Emirian Arabs. Scand J Rheumatol 1995;4:225-7.
- Valluei V, Mustafa M, Santhosh A, Middleton D, Alvares M, El Haj E, et al. Frequencies of HLA-A, HLA-B, HLA-DR, and HLA-DQ phenotypes in the United Arab Emirates population. Tissue Antigens 2005;66:107-13.
- Sheth KV, Edward JA, Godwin JT. Study of the HLA gene and antigen frequency from a Saudi Arabian hospital. Tissue Antigens 1985;25:156-62.
- Alharbi SA, Mahmoud FF, Al Awadi A, Al Jumma RA, Khodakhast F, Alsulaiman SM. Association of MHC class I with spondyloarthropathies in Kuwait. Eur J Immunogenet 1996; 23:67-70.

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- 11. Harfouch EI, Al-Cheikh SA. HLA-B27 and its subtypes in Syrian patients with ankylosing spondylitis. Saudi Med J 2011;32:364-8.
- Mansour I, Klaymé S, Naman R, Loiselet J, Hallé L, Kaplan C. HLA phenotype polymorphism in the Lebanese population. Transfus Clin Biol 1996;3:289-95.
- Awadia H, Baddoura R, Naman R, Klayme S, Mansour I, Tamouza R, et al. Weak association between HLA-B27 and the spondylarthropathies in Lebanon. Arthritis Rheum 1997;40:388-9.
- Serre JL, Lefranc G, Loiselet J, Jacquard A. HLA markers in six Lebanese religious subpopulations. Tissue Antigens 1979;14:251-5.
- Al-Rawi ZS, Al-Shakarchi HA, Hasan F, Thewaini AJ. Ankylosing spondylitis and its association with the histocompatibility antigen HL-A B27: An epidemiological and clinical study. Rheumatol Rehabil 1978;17:72-5.
- 16. Hafez M, El-Shennawy FA. HLA antigens in the Egyptian population. Forensic Sci Int 1986;31:241-6.
- Amroun H, Djoudi H, Busson M, Allat R, El Sherbini SM, Sloma I, et al. Early-onset ankylosing spondylitis is associated with a functional MICA polymorphism. Hum Immunol 2005;66:1057-61.
- Dafalla AM, McCloskey DJ, Alemam AA, Ibrahim AA, Babikir AM, Gasmelseed N, et al. HLA polymorphism in Sudanese renal donors. Saudi J Kidney Dis Transpl 2011;22:834-40.
- Makni H, Lahiani-Mahfoudh N, Baklouti S, Bahloul Z, Ayadi H. Study of the HLA-B27/ankylosing spondylitis association about 34 cases [abstract]. Immunol Lett 1997;56:167.
- Sakly N, Boumiza R, Zrour-Hassen S, Hamzaoui A, Ben Yahia S, Amara H, et al. HLA-B27 and HLA-B51 determination in Tunisian healthy subjects and patients with suspected ankylosing spondylitis and Behçet's disease. Ann NY Acad Sci 2009;173:564-9.
- Kchir MM, Hamdi W, Laadhar L, Kochbati S, Kaffel D, Saadellaoui K, et al. HLA-B, DR and DQ antigens polymorphism in Tunisian patients with ankylosing spondylitis (a case-control study). Rheumatol Int 2010;30:933-9.
- Ayed, K, Ayed-Jendoubi S, Sfar I, Labonne MP, Gebuhrer L. HLA class-I and HLA class-II phenotypic, gene and haplotypic frequencies in Tunisians by using molecular typing data. Tissue Antigens 2004;64:520–32.
- Brick C, Bennani N, Atouf O, Essakalli M. HLA-A, -B, -DR and -DQ allele and haplotype frequencies in the Moroccan population: A general population study. Transfus Clin Biol 2006;13:346-52.
- Choukri F, Chakib A, Himmich H, Raissi H, Caillat-Zucman S. HLA class I polymorphism in a Moroccan population from Casablanca. Eur J Immunogenet 2002;29:205-11.
- 25. Atouf O, Benbouazza K, Brick C, Saoud B, Benseffaj N, Amine B, et al. Distribution of HLA class I and II genes in ankylosing spondylitis patients from Morocco. Pathol Biol 2012 Feb 21. [Epub ahead of print]

- 26. Askari A, Al-Bdour MD, Saadeh A, Sawalha AH. Ankylosing spondylitis in north Jordan: Descriptive and analytical study. Ann Rheum Dis 2000;59:571-3.
- 27. Al-Amayreh IA, Zaidat BO. Ankylosing spondylitis in Northern Jordan. Saudi Med J 2000;21:950-2.
- Gunal EK, Sarvan FO, Kamali S, Gul A, Inanc M, Carin M, et al. Low frequency of HLA-B27 in ankylosing spondylitis patients from Turkey. Joint Bone Spine 2008;75:299–302.
- Bodur H, Ataman S, Akbulut L, Evcik D, Kavuncu V, Kaya T, et al. Characteristics and medical management of patients with rheumatoid arthritis and ankylosing spondylitis. Clin Rheumatol 2008;27:1119-25.
- Alamanos Y, Papadopoulos NG, Voulgari PV, Karakatsanis A, Siozos C, Drosos AA. Epidemiology of ankylosing spondylitis in Northwest Greece, 1983-2002. Rheumatology 2004;43:615-8.
- Fouladi S, Adib M, Salehi M, Karimzadeh H, Bakhshiani Z, Ostadi V. Distribution of HLA-B\*27 alleles in patients with ankylosing spondylitis in Iran. Iran J Immunol 2009;6:49-54.
- Nazarinia MA, Ghaffarpasand F, Heiran HR, Habibagahi Z. Pattern of ankylosing spondylitis in an Iranian population of 98 patients. Mod Rheumatol 2009;19:309-15.
- Oguz FS, Ocal L, Diler AS, Ozkul H, Asicioglu F, Kasapoglu E, et al. HLA B-27 subtypes in Turkish patients with spondyloarthropathy and healthy controls. Dis Markers 2004;20:309-12.
- Gül A, Uyar FA, Inanç M, Ocal L, Barrett JH, Aral O, et al. A weak association of HLA-B\*2702 with Behçet's disease. Genes Immun 2002;3:368-72.
- Al-Attia HM, Sherif AM, Hossain MM, Ahmed YH. The demographic and clinical spectrum of Arab versus Asian patients with ankylosing spondylitis in the UAE. Rheumatol Int 1998;17:193-6.
- Al-Arfaj A. Profile of ankylosing spondylitis in Saudi Arabia. Clin Rheumatol 1996;15:287–9.
- 37. Uppal SS, Abraham M, Chowdhury RI, Kumari R, Pathan EM, Al Rashed A. Ankylosing spondylitis and undifferentiated spondyloarthritis in Kuwait: A comparison between Arabs and South Asians. Clin Rheumatol 2006;25:219-24.
- Younes M, Jalled A, Aydi Z, Zrour S, Korbaa W, Ben Salah Z, et al. Socioeconomic impact of ankylosing spondylitis in Tunisia. Joint Bone Spine 2010;77:41-6.
- Younsi R, Azrib S, Aitouazar M, Harifi G, El Hassani SL. Evaluation de l'incidence du gène HLA-B27 chez le patient atteint de spondylarthrite ankylosante au Maroc. Rev Rhum 2007;74:976–1037.
- Rkain H, Allali F, Bentalha A, Lazrak N, Abouqal R, Hajjaj-Hassouni N. Socioeconomic impact of ankylosing spondylitis in Morocco. Clin Rheumatol 2007;26:2081-8.

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