

## CASE STUDY

# Role of Drugs in the Presence of HLA-B\*51 and HLA-B\*51 Subtypes in Iraqi Behcet's Disease Patients

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## ABSTRACT

**Background:** Behcet's disease (BD) is a chronic, progressive disease with an unknown cause that affects numerous organs and systems. Several alleles of HLA-B\*51 (HLA-B\*5101, HLA-B\*5108, HLA-B\*5105 and HLA-B\*5104) are found to be associated with Behcet's disease.

**Objective:** Detection of the most common HLA-B\*51 subtypes in Iraqi Behcet's disease patients.

**Patients and methods:** This study compared 60 patients with BD to 30 healthy people as a control group from December 2020 to the end of May 2021. Their blood samples were taken in order to test for the presence of HLA-B\*51 and HLA-B\*51 subtypes using real-time PCR (rtPCR) and the sequence-specific primers technique (PCR-SSP).

**Results:** HLA-B\*51 frequency was highly significant among patient group 49 (81.70%) in comparison to the control group, and the most frequent subtype was HLA-B\*5105 22 (36.67%) in Iraqi patients.

**Conclusion:** In Iraq, there may be a link between HLA-B\*51 frequency and Behcet's illness patients. HLA-B\*5105 was the most common subtype in Iraqi patients.

**Keywords:** BD, HLA-B\*51, HLA-B\*51 subtype.

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## INTRODUCTION

Behcet's disease (BD) is a chronic, progressive disease with an unknown cause that affects many organs and systems.<sup>1</sup> The etiology of Behcet's disease is unknown, but a number of variables, including genetics, viral and bacterial infections, and abnormalities in humoral and/or cellular immunity, are thought to play a role.<sup>2</sup> Male sex and a younger age of disease beginning (less than 40 years) were linked to a higher incidence of ocular affliction and a more severe type of disease.<sup>3,4</sup> Behcet's disease is more prevalent in countries along the ancient 'Silk Road,' which connects Japan to the Mediterranean region.<sup>5-7</sup> This particular geographical distribution. The significant prevalence of human leukocyte antigen (HLA-B\*51) positive in a wide range of affected individuals and ethnic cultures demonstrates the significance of a unique genetic background; even though it is not used as a diagnostic criterion, HLA-B\*51 positive increases the risk of Behcet's disease by almost six times.<sup>8,9</sup> Several alleles of HLA-B\*51 (HLA-B\*5101, HLA-B\*5108, HLA-B\*5105, and HLA-B\*5104) are found in BD.<sup>10</sup>

## PATIENTS AND METHODS

The following groups were studied between December 2020 and May 2021.

A rheumatologist diagnosed 60 individuals with Behcet's disease who were visiting the Baghdad Medical City Teaching Hospital, Department of Medicine, Rheumatology Unit.

About 30 people who look to be in good health, with the same age and gender as the controls. Prior to enrolling in this study. The scientific ethical committee of the University of Baghdad, College of Medicine, received ethics approval, and each subject supplied informed consent.

A venous blood sample was taken, and tested for HLA-B\*51 subtypes using EDTA. HLA-B\*51 (HLA-B\*51:01, HLA-B\*51:02, HLA-B\*51:03 and HLA-B\*51:09) by real-time PCR, human leukocyte antigen-B\*51 allele in human genomic DNA (HLA-B\*51) single nucleotide polymorphisms (SNP) (Biotechnology, Ankara/Turkey). Catalog number (503R-10-01). Extracted DNA quantitation (QuantiFluor®dsDNA System) Promega, USA (Catalogue NO.E2670).

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**Statistical Analysis**

The mean and standard deviation are utilized to represent quantitative data. Count and percentage are used to represent qualitative data with a significant difference at (p <0.05).

**RESULTS**

The study included 60 Behçet’s disease patients. About 40 (66.7%) were male, while 20 (33.3%) were female. The mean age of the patients was (6.95 ± 30.13) range (18–42 years). A total of 30 matched age and sex-healthy volunteers were considered control groups: 15 (50.0%) were male and 15 (50.0%) were female. General characteristics of the studied groups are shown in (Table 1). Table 1 shows that BD patients mainly presented between the ages of 26 and 35 (45.0%).

The most often found HLA-B\*51 in the patient group HLA-B\*51 was found in 49 (81.70%) of the control groups but only in 6 (20.00%) (p0.001). Table 2 shows that the most common subtype among BD Iraqi patients was HLA-B\*5105 (22.67%), while the most common among the control group was HLA-B\*5102 (30.00%).

Other subtypes detected in BD patients as HLA-B5103 (23.30%), HLA-B\*5102 (18.3%), HLA-B\*5104 (18.3%), HLA-B\*5109 (15.00%) and HLA-B\*51018 (15.00%), respectively.

**Table 1:** General characteristics of the studied groups

	Patient	Control	p-value
Number	60	30	-
Age(y)Range	30.13 ± 6.95 (18-42)	28.97 ± 6.54 (16-40)	0.548 <sup>NS</sup>
	21–25 years		
Age groups No.(%)	17 (28.3%)	10 (33.3%)	0.762 <sup>NS</sup>
	26–35 years		
	27 (45.0%)	14 (46.7%)	
	36–45 years		
	16 (26.7%)	6 (20.0%)	0.126 <sup>NS</sup>
Sex,No, (%)	Male 40 (66.7%)	15 (50.0%)	
	Female 20 (33.3%)	15 (50.0%)	

No. = number, % = percentage, NS = non -significant

**Table 2:** HLA-B\*51 subtype frequency in BD patients and healthy controls

HLA-B*51 Subtypes	p-value					
	Patient		Control			
	Number	%	Number	%		
HLA-B*51	Present	49	81.70	6	20.00	<0.001**
	Absent	11	18.30	24	80.00	-
HLA-B*5101	Present	0	0.00	0	0.00	1.000NS
	Absent	60	100.00	30	100.00	-

HLA-B*5102	Present	11	18.30	3	10.00	0.002*
	Absent	49	81.70	27	90.00	-
HLA-B*5103	Present	14	23.30	1	3.30	<0.001**
	Absent	46	76.70	29	96.70	-
HLA-B*5104	Present	11	18.30	1	3.30	0.002*
	Absent	49	81.70	29	96.70	-
HLA-B*5105	Present	22	36.67	2	6.67	<0.001**
	Absent	38	63.33	28	93.33	-
HLA-B*5106	Present	3	5.00	0	0.00	0.548NS
	Absent	57	95.00	30	100.00	-
HLA-B*5109	Present	9	15.00	0	0.00	<0.001**
	Absent	51	85.00	30	100.00	-
HLA-B*51018	Present	9	15.00	0	0.00	<0.001**
	Absent	51	85.00	30	100.00	-

\* = significant ,\*\* = highly significant,% = percentage

**DISCUSSION**

Patients with BD often present between the ages of (26–35) years. This finding is comparable to that of Reham *et al.*<sup>11-15</sup> According to Moschella *et al.* (2008), Behçet’s disease is most prevalent in young individuals aged 20 to 40. Although it can happen at any age, children and those over the age of 50 are more prone to get it.<sup>16</sup> The current age of BD patients was primarily less than 40 years (mean age = 34 years).<sup>17</sup> Uslu *et al.* discovered that the average age of onset of symptoms was 27.1 years, but Karıncaoglu *et al.* discovered that it was between (16–25) years.<sup>18-21</sup> The male:female ratio in the BD patient group was (2.0:1) in the current study. This is backed by other studies.<sup>16,18,19,22,23</sup> Other studies have revealed that the sickness is most common in women and that men have a more severe form of the disease.<sup>24</sup>

The gender distribution of BD patients differs substantially depending on ethnicity and country of residence. It indicates that both genetic and environmental factors can influence Behçet’s disease expression.<sup>25</sup>

This study showed a significant connection between HLA-B\*51 and Behçet’s disease in the patient’s group versus the control groups (p <0.001). These findings agreed with Kilmartin *et al.*, who proposed that the HLA-B\*51 link existed globally and has been proven in many different ethnic groups, primarily from the far East and Mediterranean countries.<sup>3,26,27</sup> Chang *et al.* showed that HLA-B\*51 is not higher in patients of BD than the control group.<sup>28</sup> However; the present data showed the non-significant presence of HLA-B\*5101 subtypes in BD patient’s group.

In other studies, HLA-B\*5101 has been positively reported to be (62–98%) in various populations.<sup>2,29-32</sup> The present study showed that HLA-B\*5105 was the most frequent subtype in patients with BD as a result, it disagreed with numerous

studies.<sup>33-35</sup> The present study detected HLA-B\*5103 in (23.30%) of BD patients. This result agreed with another study.<sup>2</sup> In the present study detected HLA-B\*5104 in (18.30%) of the patient group and this was the first study of this subtype, and there is no other similar study.

Other subtypes detected of (18.30%) for HLA-B\*5102 and (15.00%) for HLA-B\*5109. this result agrees with many studies.<sup>2,30,33,36-38</sup>

In the present study detected HLA-B\*51018 in (15.00%) of the patient group and this was the first study of this subtype, and there is no other similar study.

## CONCLUSION

In Iraq, there may be a link between HLA-B\*51 frequency and Behçet's illness patients. HLA-B5105 was the most common subtype in Iraqi patients.

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