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FREQUENCY OF HLA-B*51 IN PATIENTS WITH BEHÇET'S DISEASE AND ITS RELATIONSHIP WITH THE CLINICAL FINDINGS IN KURDISH POPULATION IN IRAQ

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Abstract

Background and Objective: Behçet's disease (BD) is a relapsing multisystem vasculitis with marked geographic variation and a strong genetic association with HLA-B*51. Data from Kurdish patients in Kurdistan/Iraq remain limited. The aim of the study was to determine the frequency of HLA-B*51 positivity in Kurdish BD patients and to evaluate its relationship with the demographic and the clinical manifestations.
Materials and Methods: In this case–control study, 53 Kurdish patients with active BD attending rheumatology clinics in Duhok and Hawler from May 2024 to May 2025, and 25 age- and sex-matched healthy controls were enrolled. HLA-B*51 was detected by PCR. The associations between HLA-B*51 positivity and the gender, age, and clinical features were analyzed using the Chi-square test or Fisher's exact test for categorical variables, the unpaired t-test for comparison of means, and the Kruskal-Wallis and Mann-Whitney tests for severity score comparisons, as appropriate.
Results: All patients had oral ulcers (100%), followed by genital lesions (81.1%), arthritis (73.6%), skin lesions (71.7%), eye lesions (52.8%), vascular problems (43.4%), neurological problems (34.0%), and abdominal pain (32.1%). The prevalence of HLA-B*51 positivity was 63.6% among males and 51.6% among females ($p = 0.384$). Among age groups, 72.7% of patients aged 14–29 years had positive HLA-B*51, compared with 51.9% and 53.3% among those aged 30–45 years and ≥46 years, respectively, but the difference was not significant ($p = 0.478$). No significant association was detected between HLA-B*51 positivity and the clinical features. The prevalence of HLA-B*51 positivity was 62.5% among patients with mild disease, 57.5% among those with moderate disease, and 40.0% among those with severe disease, with no significant difference ($p = 0.799$).
Conclusion: HLA-B*51 is highly prevalent among Kurdish BD patients in Kurdistan/Iraq. HLA-B*51 testing may support clinical assessment, but in this study it was not associated with specific clinical manifestations or disease severity.

Keywords: Behçet's disease; HLA-B*51; Ocular involvement; Genetic involvement, Skin involvement.

INTRODUCTION

Behçet's disease (BD) is a relapsing systemic inflammatory disorder and is regarded as one of the most complex forms of systemic vasculitis.[1-3] Its geographic distribution shows marked variation, with the highest prevalence reported in countries located along the ancient Silk Road, extending from East Asia through the Middle East to the Mediterranean region.[4,5] Differences in prevalence among countries suggest contributions from both genetic and environmental factors.[1,5] Male predominance has been reported in several Arab populations, whereas female predominance has been described in China, Japan, United States, and Korea.[5-7] The disease most commonly affects adults in the 31–40-year age group.[5]

Because there is no pathognomonic laboratory test for BD, diagnosis is based on the clinical criteria. Clinical manifestations range from mild mucocutaneous involvement to severe systemic complications. Recurrent oral ulceration is common, is often the earliest manifestation, and is observed in most patients.[8] Other frequent clinical manifestations include genital ulcers, skin lesions, uveitis, neurological involvement, arthritis, and vascular thrombosis. Disease severity differs substantially among patients and populations, reflecting heterogeneity in the underlying pathogenic mechanisms.[9]

HLA-B*51 is the genetic factor most strongly associated with BD. In combination with other genetic contributors, HLA-B*51 has been linked to an exaggerated immune response, including heightened neutrophil activity, which is thought to play an important role in the early stages of BD inflammation.[10] Across different

ethnic groups, many studies have demonstrated a significantly higher frequency of HLA-B*51 positivity in patients with BD than in healthy controls.[11]
This study was designed to characterize the clinical manifestations of Kurdish patients with BD who were referred to the rheumatology departments in Duhok and Hawler, and to investigate the relationship between HLA-B*51 positivity and the demographic and clinical findings of these patients.

METHODS

This case–control study included 53 Kurdish patients with active BD diagnosed according to the International Criteria for Behçet's Disease (ICBD).[8] The patients were recruited from the outpatient rheumatology clinics in the Duhok and Hawler centers for rheumatic diseases and medical rehabilitation between May 2024 and May 2025. A total of 25 age- and gender-matched healthy Kurdish participants served as the control group.
The inclusion criteria comprised all participants aged 14 years or older. Gender, age, clinical features, and severity were recorded according to HLA-B*51 status. Exclusion criteria included oral ulceration due to causes other than BD, such as traumatic ulcers, pemphigus vulgaris, mucous membrane pemphigoid, lichen planus, lupus erythematosus, erythema multiforme, infectious ulcers, or malignant lesions. Participants with other autoimmune diseases were also excluded.
DNA was extracted from whole blood using the AddPrep Genomic DNA Extraction Kit (AddBio, Korea) according to the manufacturer's instructions. DNA quality was assessed by 0.8% agarose gel electrophoresis, followed by RedSafe staining and visualization under ultraviolet light.
The HLA-B*51 gene was analyzed using a conventional thermal cycler (AlphaMAX, UK) and a specific primer pair for amplification of HLA-B*51. The primer oligonucleotide sequence was obtained from accession number S999230.1. The forward primer sequence was 5′-GTATTTCTACACCGCCATGTCC-3′ and the reverse primer sequence was 5′-CGACCTATAGGAGATGGGGA-3′. PCR was performed with an initial denaturation step at 95°C for five minutes, followed by 35 cycles of denaturation at 95°C for 40 seconds, annealing at 59°C for 40 seconds, and extension at 72°C for 60 seconds, with a final extension at 72°C for five minutes. PCR products were separated on 2% agarose gel electrophoresis, and an 818-bp band indicated successful amplification of the HLA-B*51 target sequence
The study was approved by the Scientific Research Ethical Committee of the College of Dentistry, Hawler Medical University(Reference No.HMUD-2425132). Written informed consent was obtained from all enrolled participants. Statistical analysis was performed using SPSS version 27. The Chi-square test or Fisher's exact test was used for categorical variables, the unpaired t-test was used for comparison of means, and Kruskal-Wallis and Mann-Whitney tests were used for the severity score comparisons, as appropriate. P - value less than or equal to 0.05 was considered statistically significant.

RESULTS

Fifty-three patients with BD and 25 healthy controls were included in the study. Among BD patients, 20.8% were aged 14–29 years, 50.9% were aged 30–45 years, and 28.3% were aged ≥46 years. Statistical analysis showed a non-significant difference in age distribution between the BD patients and control group (p = 0.353). Regarding gender distribution, 58.5% of BD cases were female compared with 60.0% of the controls, and 41.5% were male compared with 40.0% of the controls, with a non-significant difference (p = 0.899). More details are presented in Table- 1.

Table -1. Age and gender distribution.

	Group						
	Case		**Control**		**Total**		
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**p-value**
Age (years)							0.353*
14-29	11	(20.8)	9	(36.0)	20	(25.6)	
30-45	27	(50.9)	10	(40.0)	37	(47.5)	
≥ 46	15	(28.3)	6	(24.0)	21	(26.9)	
Mean (SD)	38.7	(12.5)	35.8	(12.2)			0.331**
Gender							0.899*
Male	22	(41.5)	10	(40.0)	32	(41.0)	
Female	31	(58.5)	15	(60.0)	46	(59.0)	
Total	53	(100.0)	25	(100.0)	78	(100.0)	

*Calculated by Chi-square test. **Calculated by unpaired t-test.

All BD patients had oral ulcers (100.0%), while skin lesions were present in 71.7%, eye lesions in 52.8%, genital lesions in 81.1%, arthritis in 73.6%, abdominal pain in 32.1%, vascular problems in 43.4%, and

neurological problems in 34.0%. All differences in symptom prevalence between males and females were not significant ($p > 0.05$). More details are presented in Table- 2.

Table -2. Clinical characteristics of Behçet's disease patients by gender.

	Male (n = 22)		Female (n = 31)		Total (n = 53)		
	No.	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**p-value**
Oral ulcers	22	(100.0)	31	(100.0)	53	(100.0)	N/A†
Skin lesion	14	(63.6)	24	(77.4)	38	(71.7)	0.272*
Eye lesion	9	(40.9)	19	(61.3)	28	(52.8)	0.143*
Genital lesion	17	(77.3)	26	(83.9)	43	(81.1)	0.724**
Arthritis	15	(68.2)	24	(77.4)	39	(73.6)	0.452*
Abdominal pain	6	(27.3)	11	(35.5)	17	(32.1)	0.528*
Vascular problems	11	(50.0)	12	(38.7)	23	(43.4)	0.414*
Neurological problems	5	(22.7)	13	(41.9)	18	(34.0)	0.146*

*Calculated by Chi-square test. **Calculated by Fisher's exact test. †N/A: Not applicable (both percentages were 100%). Note: A patient may have one or more lesions.

The majority (75.48%) of the patients had moderate disease, 15.09% had mild disease, and 9.43% had severe disease. None of the patients aged 14-29 years had a severe disease. The rate of severe disease was 14.8% and 6.6% among those aged 30-45 and ≥ 46, respectively ($p = 0.215$). None of the males had severe disease, compared with 16.1% among females ($p = 0.073$). More details are presented in Table -3.

Table -3. Disease severity level by age and gender.

	Disease severity				
	Mild	**Moderate**	**Severe**	**Total**	
	No. (%)	**No. (%)**	**No. (%)**	**No. (%)**	**p-value***
Age					0.215
14-29	4 (36.4)	7 (63.6)	0 (0.0)	11 (100.0)	
30-45	3 (11.1)	20 (74.1)	4 (14.8)	27 (100.0)	
≥ 46	1 (6.7)	13 (86.7)	1 (6.6)	15 (100.0)	
Gender					0.073
Male	5 (22.7)	17 (77.3)	0 (0.0)	22 (100.0)	
Female	3 (9.7)	23 (74.2)	5 (16.1)	31 (100.0)	
Total	8 (15.09)	40 (75.48)	5 (9.43)	53 (100.0)	

*Calculated by Fisher's exact test.

It is evident in Table -4 that the mean, median, and mean rank of severity score of those aged 14-29 years were less than those of the other age groups, but the difference was not significant ($p = 0.095$). The mean and mean rank of the severity score of males were less than those of females, but the difference was not significant ($p = 0.073$). More details are shown in Table- 4.

Table -4. Severity score by age and gender.

	Severity score			
	Mean	**Median**	**Mean Rank**	**p-value**
Age (years)				
14-29	4.18	4.00	18.36	
30-45	5.07	5.00	29.31	0.095*
≥ 46	5.07	5.00	29.17	
Gender				
Male	4.50	5.00	22.66	0.073**
Female	5.16	5.00	30.08	

*Calculated by the Kruskal-Wallis test. **Calculated by the Mann-Whitney test.

More than half (56.6%) of the cases had positive HLA-B*51, compared with 20% of the controls with a significant difference ($p = 0.002$) as seen in Figure- 2.

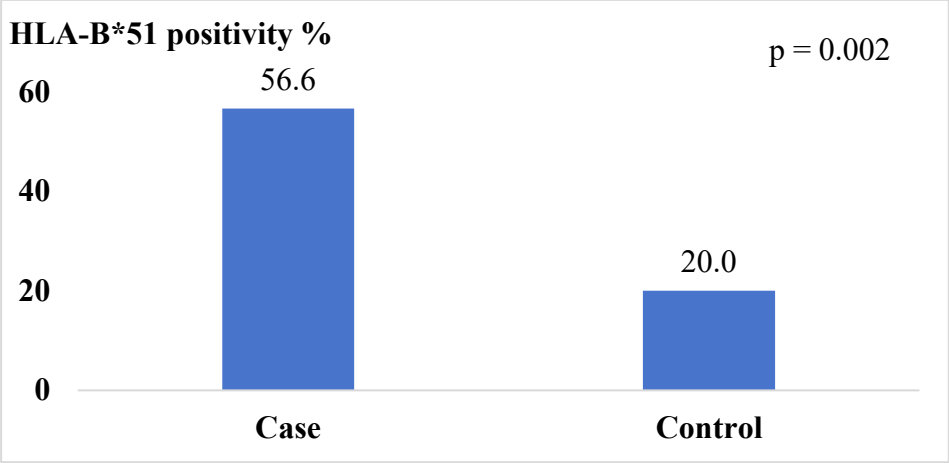

Figure -2. HLA-B*51 positivity among BD patients and control group.

In BD patients, the prevalence of HLA-B*51 positivity was 63.6% among males and 51.6% among females, with a non-significant difference (p = 0.384). In the (14–29)year age group, 72.7% of BD patients had positive HLA-B*51, compared with 51.9% and 53.3% among those aged (30–45) years and(≥46) years, respectively, but the difference was not significant (p = 0.478), as shown in Table- 5.

Table -5. Gene polymorphism (HLA-B*51 positivity) by age and gender among patients with Behçet's disease.

	HLA-B*51			
	Positive	**Negative**	**Total**	**p-value†**
	No. (%)	**No. (%)**	**No. (%)**	
Age (years)				
14-29	8 (72.7)	3 (27.3)	11 (100.0)	
30-45	14 (51.9)	13 (48.1)	27 (100.0)	
≥ 46	8 (53.3)	7 (46.7)	15 (100.0)	0.478
Gender				
Male	14 (63.6)	8 (36.4)	22 (100.0)	
Female	16 (51.6)	15 (48.4)	31 (100.0)	0.384
Total	30 (56.6)	23 (43.4)	53 (100.0)	

†Calculated by the Chi-square test.

In the control group, the picture is different, where the prevalence of HLA-B*51 positivity was 11.1% among those aged 14-29 years, 0% among those aged 30-45, and 66.7% among those aged ≥ 46 with a significant difference (p = 0.005). The mentioned prevalence was 20% among males and females (p = 1.000). More details are presented in Table- 6.

Table- 6. Gene polymorphism (HLA-B*51 positivity) by age and gender among control group.

	HLA-B*51			
	Positive	**Negative**	**Total**	**p-value†**
	No. (%)	**No. (%)**	**No. (%)**	
Age (years)				
14-29	1 (11.1)	8 (88.9)	9 (100.0)	
30-45	0 (0.0)	10 (100.0)	10 (100.0)	
≥ 46	4 (66.7)	2 (33.3)	6 (100.0)	0.005
Gender				
Male	2 (20.0)	8 (80.0)	10 (100.0)	
Female	3 (20.0)	12 (80.0)	15 (100.0)	1.000
Total	5 (20.0)	20 (80.0)	25 (100.0)	

†Calculated by Fisher's exact test.

A non significant association was detected between HLA-B*51 positivity and the following signs and symptoms: skin lesion (p = 0.754), eye lesion (p = 0.933), genital lesion (p = 1.000), arthritis (p = 0.962), abdominal pain (p = 0.413), vascular problems (p = 0.583), and neurological problems (p = 0.912). More details are presented in Table- 7.

Table- 7. Gene polymorphism (HLA-B*51 positivity) by signs and symptoms.

	HLA-B*51			
Signs and symptoms	**Positive**	**Negative**	**Total**	**p-value**
	No. (%)	**No. (%)**	**No. (%)**	
Oral ulcer				
Yes	30 (56.6)	23 (43.4)	53 (100.0)	N/A
Skin lesion				
Yes	21 (55.3)	17 (44.7)	38 (100.0)	
No	9 (60.0)	6 (40.0)	15 (100.0)	0.754†
Eye lesion				
Yes	16 (57.1)	12 (42.9)	28 (100.0)	
No	14 (56.0)	11 (44.0)	25 (100.0)	0.933†
Genital lesion				
Yes	24 (55.8)	19 (44.2)	43 (100.0)	
No	6 (60.0)	4 (40.0)	10 (100.0)	1.000††
Arthritis				
Yes	22 (56.4)	17 (43.6)	39 (100.0)	
No	8 (57.1)	6 (42.9)	14 (100.0)	0.962†
Abdominal pain				
Yes	11 (64.7)	6 (35.3)	17 (100.0)	
No	19 (52.8)	17 (47.2)	36 (100.0)	0.413†
Vascular problems				
Yes	14 (60.9)	9 (39.1)	23 (100.0)	
No	16 (53.3)	14 (46.7)	30 (100.0)	0.583†
Neurological problems				
Yes	10 (55.6)	8 (44.4)	18 (100.0)	
No	20 (57.1)	15 (42.9)	35 (100.0)	0.912†
Total	30 (56.6)	23 (43.4)	53 (100.0)	

†Calculated by the Chi-square test. ††Calculated by Fisher's exact test.

The prevalence of HLA-B*51 positivity was 62.5% among patients with mild disease, it decreased to 57.5% among those with moderate disease, and to 40% among those with severe disease, but the difference was not significant (p = 0.799) as seen in Table- 8.

Table -8. Gene polymorphism (HLA-B*51 positivity) by Behçet's disease severity.

	HLA-B*51			
Severity	**Positive**	**Negative**	**Total**	**p-value**
	No. (%)	**No. (%)**	**No. (%)**	
Mild	5 (62.5)	3 (37.5)	8 (100.0)	
Moderate	23 (57.5)	17 (42.5)	40 (100.0)	
Severe	2 (40.0)	3 (60.0)	5 (100.0)	0.799**
Total	30 (56.6)	23 (43.4)	53 (100.0)	

**Calculated by Fisher's exact test.

DISCUSSION

This study provides updated local data on the frequency of HLA-B*51 in Kurdish patients with BD in Kurdistan/Iraq and examines its relationship with demographic variables, clinical manifestations, and the disease severity. The main finding was a significantly higher frequency of HLA-B*51 positivity in BD patients than in healthy controls (56.6% versus 20.0%, p = 0.002), which supports the well-established role of HLA-B*51 as the strongest genetic susceptibility marker for BD across populations living along or near the historical Silk Road. Recent reviews continue to identify HLA-B*51 as the principal genetic factor in BD, although its contribution appears to be one component of a broader polygenic and immunologically heterogeneous disease process.[8-10]

The clinical profile of our cohort was dominated by mucocutaneous and musculoskeletal manifestations. Oral ulcerations were present in all patients, ocular involvement were observed in 52.8% of patients, while the genital lesions, arthritis, and skin lesions were also frequent, but the vascular, neurologic, and abdominal manifestations were less common. This overall distribution is broadly consistent with recent observational studies from nearby and Silk Road populations, where oral ulcers remain nearly universal and genital, skin, articular, and ocular manifestations are among the most prevalent features.[10,12] However, the exact frequencies

vary substantially by ethnicity, referral setting, and case definition, highlighting the importance of regional datasets such as the present study.

Females represented a slightly higher proportion of the BD cohort in the present study. However, among patients with BD, HLA-B*51 positivity did not differ significantly between males and females, despite a numerically higher proportion in males. This agrees with several contemporary reports showing that the association between HLA-B*51 and BD is not always sex-specific, even when the clinical phenotype may differ by sex.[9,13,14] Some recent cohorts have shown greater major-organ involvement in males, but our study did not demonstrate significant sex-based differences in individual manifestations or severity class, although severe disease was observed only among females and approached statistical significance.

Most patients in the present study were aged 30–45 years, which is consistent with the age range reported in other studies.[2,5] Although HLA-B*51 positivity was numerically highest in the 14–29-year age group, the association between age category and HLA-B*51 status was not statistically significant. Likewise, disease severity category and severity score tended to be lower in younger patients, but these differences were also not significant. These findings suggest that, in our cohort, age may influence the descriptive pattern of disease presentation, but it was not a robust determinant of HLA-B*51 carriage or disease burden.

An important finding of this study is that no significant association was detected between HLA-B*51 positivity and the different individual clinical manifestations. This contrasts with some reports that linked HLA-B*51, particularly certain subtypes, with ocular involvement, while other studies have suggested that neurological and ocular phenotypes may reflect broader genetic effects within the HLA region rather than HLA-B*51 alone.[9,15,21] At the same time, our findings are in line with reports indicating that HLA-B*51 is more consistently associated with overall susceptibility to BD than with a single reproducible clinical phenotype.[10,11,23,24] Therefore, our negative association findings should not be interpreted as evidence against a biological contribution of HLA-B*51, but rather as support for the view that BD phenotype is shaped by multiple interacting genetic and environmental factors.

The absence of a significant relationship between HLA-B*51 and disease severity in our BD patients was also noteworthy. HLA-B*51 positivity was observed in 62.5% of patients with mild disease, 57.5% of those with moderate disease, and 40.0% of those with severe disease, with a non significant difference. Other study from Pakistan similarly found a strong association of HLA-B*51 with BD diagnosis but no association with severity subgroups, which supporting our results.[11] Taken together, these observations indicate that HLA-B*51 may be more useful as a susceptibility marker than as a prognostic marker of severity in routine clinical practice.

From a mechanistic perspective, current research supports the biological plausibility of the observed association between HLA-B*51 and BD susceptibility. HLA-B*51 is thought to influence antigen presentation and HLA-I peptidome composition, with downstream effects on cytotoxic T-cell responses, neutrophil activation, and related inflammatory pathways.[9-11] At the same time, other studies emphasize that ERAP1 interactions, IL-10 and IL23R/IL12RB2 pathways, innate immune dysregulation, and endothelial inflammation all contribute to disease expression.[9-13] This broader framework may explain why HLA-B*51-positive and HLA-B*51-negative patients in our cohort showed largely overlapping clinical features. In other words, HLA-B*51 may increase the probability of developing BD, but the eventual organ pattern likely depends on additional host and environmental determinants.[3,9,11]

Clinically, our findings suggest that HLA-B*51 positivity may be helpful as a supportive marker in Kurdish patients with suspected BD, especially when the diagnosis is uncertain, because positivity was significantly more common among cases than controls. However, the presence of HLA-B*51 in 20% of healthy controls and the lack of association with specific manifestations or severity indicate that the test should not be used in isolation to confirm diagnosis, estimate organ involvement, or predict prognosis. Careful clinical assessment based on accepted classification criteria remains essential, and multidisciplinary follow-up is particularly important for patients with ocular, vascular, or neurological disease regardless of HLA status.[3,6]

Overall, the present study adds clinically relevant evidence on the relationship between HLA-B*51 and Behçet's disease in Kurdish patients from Iraq. The use of standardized diagnostic criteria, molecular detection of HLA-B*51, and a matched control group strengthens the reliability of the findings. In addition, the study contributes valuable regional data from an underrepresented population and helps clarify that, in this cohort, HLA-B*51 is more strongly linked to disease susceptibility than to specific clinical manifestations or severity. These findings may support future regional studies and provide a useful basis for broader comparative research across neighboring populations.

CONCLUSIONS

This study showed that HLA-B*51 positivity is significantly more frequent in Kurdish patients with Behçet's disease than in healthy controls, supporting its role as an important susceptibility marker in this population. However, HLA-B*51 was not significantly associated with sex, age group, individual clinical manifestations, or disease severity in our cohort. These findings suggest that HLA-B*51 may be useful as a supportive genetic marker in the diagnostic context, but it has limited value for predicting phenotype or severity. Larger

prospective studies from Iraq and neighboring populations are warranted to further clarify its clinical and prognostic significance.

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DECLARATION OF COMPETING INTEREST
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

REFERENCES
1. Leccese P, Alpsoy E. Behçet's disease: an overview of etiopathogenesis. Front Immunol. 2019;10:1067.
2. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. N Engl J Med. 1999;341(17):1284-91.
3. Saadoun D, Bodaghi B, Cacoub P. Behçet's syndrome. N Engl J Med. 2024;390:640-651.
4. Hatemi G, Christensen R, Bang D, et al. Update of the EULAR recommendations for the management of Behçet's syndrome. Ann Rheum Dis. 2018;77(6):808-818.
5. Davatchi F, Shahram F, Chams-Davatchi C, et al. Behçet's disease: from East to West. Clin Rheumatol. 2010;29(8):823-833.
6. Al-Dalaan AN, Al Balaa SR, El Ramahi K, et al. Behçet's disease in Saudi Arabia. J Rheumatol. 1994;21(4):658-661.
7. Leccese P, Yazici Y, Olivieri I. Behcet's syndrome in nonendemic regions. Curr Opin Rheumatol. 2017;29(1):12-16.
8. Davatchi F, Assaad-Khalil S, Calamia KT, et al. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol. 2014;28(3):338-347.
9. Takeuchi M, Kastner DL, Remmers EF. The immunogenetics of Behçet's disease: a comprehensive review. J Autoimmun. 2015;64:137-148.
10. Takeno M. The association of Behçet's syndrome with HLA-B51 as understood in 2021. Curr Opin Rheumatol. 2022;34(1):4-9.
11. Khoshbakht S, Başkurt D, Vural A, Vural S. Behçet's Disease: A Comprehensive Review on the Role of HLA-B*51, Antigen Presentation, and Inflammatory Cascade. Int J Mol Sci. 2023;24(22):16382.
12. Mizuki N, Meguro A, Ota M, et al. Genome-wide association studies identify IL23R-IL12RB2 and IL10 as Behçet's disease susceptibility loci. Nat Genet. 2010;42(8):703-706.
13. Riahi P, Kazemnejad A, Mostafaei S, et al. ERAP1 polymorphisms interactions and their association with Behçet's disease susceptibly: application of model-based multifactor dimension reduction algorithm (MB-MDR). PLoS One. 2020;15(2):e0227997.
14. Gao W, Jin X, Zhou P, et al. The correlation of endoplasmic reticulum aminopeptidase 1 polymorphisms with Behçet's disease: a meta-analysis. Clin Exp Rheumatol. 2023;41(10):2027-2038.
15. Hatemi G, Seyahi E, Fresko I, et al. Behçet's syndrome: one year in review 2025. Clin Exp Rheumatol. 2025;43(10):1699-1708.
16. Hatemi G, Seyahi E, Fresko I, et al. Behçet's syndrome: one year in review. Clin Exp Rheumatol. 2024;42:1999-2007.
17. Yurdakul S, Hamuryudan V, et al. Behçet syndrome. Curr Opin Rheumatol. 2004;16(1):38-42.
18. Gueudry J, Leclercq M, Saadoun D, Bodaghi B. Old and New Challenges in Uveitis Associated with Behçet's Disease. J Clin Med. 2021;10(11):2318.
19. Tinti MG, Vaira F, Inglese M, et al. Ocular involvement in Behçet's disease: relevance of new diagnostic tools. Rheumatol Adv Pract. 2020;4(2):rkaa038.
20. Balta S, Balta I, Ozturk C, et al. Behçet's disease and risk of vascular events. Curr Opin Cardiol. 2016;31(4):451-457.
21. Houman MH, Bellakhal S, Ben Salem T, et al. Characteristics of neurological manifestations of Behçet's disease: a retrospective monocentric study in Tunisia. Clin Neurol Neurosurg. 2013;115(10):2015-2018.
22. Leccese P, Padula MC, Lascaro N, et al. Clinical phenotypes of Behçet's syndrome in a large cohort of Italian patients: focus on gender differences. Scand J Rheumatol. 2021;50(6):475-478.
23. Pamukcu M, Izci Duran T, Demirag MD. HLA-B51 impact on clinical symptoms in Behcet's disease. J Coll Physicians Surg Pak. 2022;32(7):904-908.
24. Sultanoğlu TE, Eröz R, Ataoğlu S. Evaluation of HLA-B51 frequency and its relationship with clinical findings in patients with Behçet's disease: 4-year analysis in a single center. Egypt Rheumatol Rehabil. 2023;50:15.

25. Alam M, Khalid UB, Ahmad D, et al. Association of HLA-B51/5 in patients of Behcet's disease referred to a tertiary care hospital in Pakistan. J Coll Physicians Surg Pak. 2025;35(2):247-250