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THE INFLUENCE OF GENDER AND HLA-B51 ON THE CLINICAL MANIFESTATIONS OF BEHCET DISEASE AMONG JORDANIAN PATIENTS

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ABSTRACT

Introduction: Bechet's disease (BD) is a multi-system inflammatory disorder with diverse clinical features influenced by region, ethnicity, gender, and HLA-B51. Aim: we aimed to investigate the influence of gender and HLA-B51 on the clinical manifestations of BD among Jordanian patients. Methods: We reviewed 108 BD patients' records from our rheumatology clinic who met the ICBD criteria. Age and gender were noticed for each patient. We collected clinical and laboratory data, and confirmed oral ulcer, genital ulcer, ocular, joint, vascular, and neurological involvement, and HLA-B51 status. We compared clinical features by gender and HLA-B51 using chi-square test and SPSS 24.0. We set p-value at < 0.05. Results: We examined 108 BD patients (mean age 32.6+10.1, 80% male, 4:1 M:F ratio). All had oral ulcers, 73% genital ulcers, 45% skin lesions, 28% vascular complications, and 50% HLA-B51 positive. No significant differences in major organ involvement by gender or HLA-B51 were found. Conclusion: We found different BD phenotypes in Jordanians, unaffected by gender or HLA-B51. More studies with different criteria are needed to examine these factors on BD symptoms.

KEYWORDS: Bechet's disease, HLA-B51, Gender, Clinical manifestations.

INTRODUCTION

Bechet's disease (BD), a multisystem inflammatory disorder, was first reported by a Turkish dermatologist, Dr. Hulusi Behget (1889-1948), in 1937. He identified the typical triad of recurrent hypopyon iritis and oral and genital ulcerations as the main features of the disease.[1] The ancient Greek physician Hippocrates may have been aware of this condition, as he documented the correlation between ocular inflammation and oral and genital ulcers.[2] The disease was initially prevalent in Japan and the eastern Mediterranean region, earning it the name 'Silk Road Disease'.[3] However, Behcet's disease has since been recognized globally, with varying clinical manifestations and incidence rates depending on the country and the type of medical specialty from which the data are collected. Despite its worldwide distribution, Behcet's disease is uncommon in America and Europe.[4]

The pathogenesis of BD remains elusive, but various factors, such as genetic (e.g., HLA-B51), environmental, microbiological, and immunological, have been suggested to be associated with BD (5). The clinical features of BD show geographical and ethnic variations, depending on the country, region, and race of the patients.[6] The frequency of ocular manifestations ranges from 35% to 92%, gastrointestinal manifestations from 3.3% to 37%, and central nervous system involvement from 0% to 44% among different populations.[7] In Israel, a comparison of Arab, Jewish, and Druse patients revealed that Arabs had more severe ocular disease, while Druse had less ocular and neurologic involvement.[8] Gender and genetic factors (e.g., HLA-B51) have also been implicated in modulating the clinical expression of BD.[9,10] Therefore, we hypothesize that the clinical manifestations of BD are influenced by a complex interplay of multiple factors, including race, region, country, gender, and genetics.

This study aims to explore the clinical characteristics of BD among Jordanian patients who attended the rheumatology clinic, based on demographic and genetic factors. We chose gender and HLA-B51 status as potential determinants of the clinical phenotypes, following the previous literature.

METHODS

We carried out a retrospective examination of the medical records of 108 BD patients who consulted our rheumatology clinic at King Hussein Hospital in The Jordanian Royal Medical Services during the period from January 2021 to August 2022. All of them conformed to the international criteria for BD (ICBD).[11]

We extracted the clinical and laboratory data from the medical records. The ophthalmologist confirmed the presence of ocular lesions. Joint involvement was characterized by joint swelling or pain with joint swelling or articular damage on plain radiography. Vascular manifestations comprised venous thrombophlebitis, arteritis, and superficial phlebitis that were verified by Doppler sonography or angiography. Neurologic involvement (Neuro-BD) was determined by the international consensus recommendation criteria for Neuro-BD diagnosis and encompassed the definite neuro-BD and the probable neuro-BD.[12] Gastrointestinal involvement was diagnosed by gastro-duodenoscopy or colonoscopy performed by the gastroenterologist.

All patients underwent HLA-B51 testing. The involvement of the eyes, nervous system, gastrointestinal tract or vessels constituted major organ involvement. The chi-square test was employed to compare the clinical manifestations by gender and HLA-B51 status. SPSS version 24.0 (SPSS Inc., Chicago, IL, USA) was used for statistical calculations. A p-value of < 0.05 was deemed statistically significant.

RESULTS

As delineated in Table (1), the investigation encompassed a cohort of 108 BD patients, exhibiting a mean age of 32.6+10.1 years. The demographic distribution was predominantly male, constituting 80% of the sample, resulting in a male-to-female ratio of approximately (4:1). Oral ulceration was a universal manifestation among the participants. Additionally, the prevalence of other clinical symptoms included genital ulcers in 73% of the cases, cutaneous lesions in 45%, and vascular complications in 28%. Notably, 50% of the patients demonstrated seropositivity for HLA-B51 antigen.

Clinical manifestations according to gender

The distribution of HLA-B51 status was observed to be nearly equivalent across both genders. Furthermore, the disparities in the incidence of major organ involvement between the sexes did not reach statistical significance, as indicated in Table (2).

Clinical manifestations according to the status of HLA-B51

Variations in the frequencies of major organ involvements across different HLA-B51 statuses did not exhibit statistical significance, as presented in Table (3).

Tables

Table (1): Demographics, clinical characteristics, and HLA-B51 status of patients with Behcet's disease (n=108).

N=108	Frequency	Percent
Gender		
Male	86	80
Female	22	20
Oral ulcer		
No	0	0
Yes	108	100
Genital ulcer		
No	29	27
Yes	79	73
Skin lesion		
No	59	55
Yes	49	45
Eye involvement		
No	82	76
Yes	26	24
HLA B51		
Negative	54	50
Positive	54	50
Vascular involvement		
No	78	72
Yes	30	28
Arthropathy		
0	92	85
1	16	15
CNS involvement		
No	95	88
Yes	13	12
Age		
Mean	32.6	
Std. Deviation	10.1	

Table (2): Gender-Specific Clinical Characteristics of Bechet's Disease.

Characteristic	N=108		Gender		p-value
			Male	Female	
Oral ulcer	No	Count	0	0	
		% within Gender	0%	0%	
	Yes	Count	86	22	
		% within Gender	100.0%	100.0%	
Genital ulcer	No	Count	24	5	0.63
		% within Gender	27.9%	22.7%	
	Yes	Count	62	17	
		% within Gender	72.1%	77.3%	
Skin lesion	No	Count	48	11	0.63
		% within Gender	55.8%	50.0%	
	Yes	Count	38	11	

		% within Gender	44.2%	50.0%	
Eye involvement	No	Count	65	17	0.87
		% within Gender	75.6%	77.3%	
	Yes	Count	21	5	
		% within Gender	24.4%	22.7%	
HLA B51	Negative	Count	44	10	0.63
		% within Gender	51.2%	45.5%	
	Positive	Count	42	12	
		% within Gender	48.8%	54.5%	
Vascular involvement	No	Count	62	16	0.95
		% within Gender	72.1%	72.7%	
	Yes	Count	24	6	
		% within Gender	27.9%	27.9%	
Arthropathy	No	Count	71	21	0.13
		% within Gender	82.6%	95.5%	
	Yes	Count	15	1	
		% within Gender	17.4%	4.5%	
CNS involvement	No	Count	76	19	0.80
		% within Gender	88.4%	86.4%	
	Yes	Count	10	3	
		% within Gender	11.6%	13.6%	

Table (3): HLA B51 Specific Clinical Characteristics of Bechet's Disease.

			HLA B51		p-value
			Negative	Positive	
Oral ulcer	No	Count	0	0	
		% within HLA B51	0%	0%	
	Yes	Count	54	54	
		% within HLA B51	100.0%	100.0%	
Genital ulcer	No	Count	17	12	0.28
		% within HLA B51	31.5%	22.2%	
	Yes	Count	37	42	
		% within HLA B51	68.5%	77.8%	
Skin lesion	No	Count	27	32	0.33
		% within HLA B51	50.0%	59.3%	
	Yes	Count	27	22	
		% within HLA B51	50.0%	40.7%	
Eye involvement	No	Count	45	37	0.07
		% within HLA B51	83.3%	68.5%	
	Yes	Count	9	17	
		% within HLA B51	16.7%	31.5%	
Vascular involvemen	No	Count	36	42	0.20
		% within HLA B51	66.7%	77.8%	
	Yes	Count	18	12	
		% within HLA B51	33.3%	22.2%	
Arthropathy	No	Count	46	46	1.00
		% within HLA B51	85.2%	85.2%	
	Yes	Count	8	8	
		% within HLA B51	14.8%	14.8%	
CNS involvement	No	Count	48	47	0.77
		% within HLA B51	88.9%	87.0%	
	Yes	Count	6	7	
		% within HLA B51	11.1%	13.0%	

DISCUSSION

Current literature provides a limited dataset regarding the impact of gender, age at onset, and HLA-B51 on the clinical manifestations of BD. These factors have been reported with variability across different countries and regions.[13] The observed discrepancies may be ascribed to the heterogeneous diagnostic criteria employed for Bechet's Disease, in conjunction with racial and

ethnological variations.[14] Oral ulceration is an essential diagnostic criterion for Behçet's Disease according to the International Study Group (ISG), which may preclude the diagnosis in patients lacking this manifestation.[15] The diagnostic criteria established by the Research Committee of Japan (RCJ) significantly prioritize ocular manifestations. However, these criteria may encompass individuals presenting with ocular lesions that are concomitant with disparate conditions, including but not limited to spondyloarthritis.[16] The criteria for BD have been evaluated for their diagnostic accuracy, yielding a sensitivity of 79.8% and specificity of 98.3% according to the ISG standards. Concurrently, the RCJ criteria demonstrated a sensitivity of 85.3% and specificity of 97.1%, while O'Duffy's criteria reported a sensitivity of 70.7% and specificity of 97.6%.[17] A novel method, ICBD, was introduced and demonstrated enhanced performance in terms of sensitivity and accuracy, achieving 20.1% and 11.8% improvements, respectively, relative to the ISG criteria.[18]

We conducted a study on the patients with BD who attended the rheumatology clinic and fulfilled the ISG criteria. In contrast to the majority of previous studies that focused on a single specific parameter, we examined the combined influences of various factors, such as gender and HLA-B51, on the clinical manifestations of BD. During the course of our extensive literature review, we meticulously scrutinized scholarly articles pertinent to our research inquiry, specifically focusing on resources from PubMed and Medline Plus. Unfortunately, despite our rigorous investigation, we discovered a notable dearth of published works directly aligned with the subject matter of our study, particularly within the context of Jordan. This absence of relevant literature highlights the imperative for additional investigation and original research in this domain. Our investigation revealed that neither gender nor HLA-B51 significantly influences the clinical phenotype of BD. In light of these findings, we recommend further studies employing alternative classification criteria to explore the impact of these variables on the BD clinical phenotype specifically within the context of Jordanian patients.

CONCLUSION

Our study findings indicate distinct clinical phenotypes of BD among Jordanian patients. Notably, neither gender nor HLA-B51 significantly impacts these phenotypes. However, we recommend conducting further investigations using alternative classification criteria to thoroughly explore the influence of these variables on the clinical manifestations of BD within this specific population.

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