Original Research Article

Uveitis as a Predictor for Myocardial Infarction in Patients with Behçet's Disease, Multi Centric Cohort Study from Aseer Region, Saudi Arabia.

Abstract

Introduction:

Behçet's disease (BD) is a chronic, multisystem inflammatory disorder characterized by a diverse array of clinical manifestations, including recurrent oral and genital ulcers, ocular inflammation, skin lesions, and joint problems. Its presentation varies, requiring tailored diagnosis and management.

Methods:

Retrospective cohort study, though review of medical charts and data for patients who meet the diagnostic criteria for BD actively receiving care in rheumatology clinics. The primary objective was to investigate the correlation between uveitis and Myocardial infarction in this population.

Results:

This study included a total of 111 patients. Approximately 33% of the patients exhibited positive CRP levels. Approximately 10% (11 patients) of the subjects were diagnosed with uveitis. Notably, the majority of individuals with uveitis were males. Three patients with uveitis had arthritis, none of whom presented with gastrointestinal tract (GIT) Complaints. Remarkably, none of the patients diagnosed with uveitis had a documented history of myocardial infarction (MI).

Conclusion:

In our cohort, those with a history of MI did not have a documented history of uveitis. Larger, prospective studies are needed to evaluate the associations between MI and uveitis in a BD population.

Key Words:

Behçet's disease, Myocardial Infarction MI, Uveitis.

Introduction:

Behçet's disease (BD), also known as Behçet's syndrome, is a chronic, multisystem inflammatory disorder characterized by a diverse array of clinical manifestations. Named after the Turkish dermatologist Hulusi Behçet, who first described the condition in 1937 [1,2] BD primarily affects the blood vessels and presents with recurrent oral and genital ulcers, ocular inflammation, skin lesions, and joint involvement [3]. The disease is most

prevalent in regions along the ancient Silk Road, including the Middle East, Central Asia, and parts of Japan [4,5]. In the Arabian Peninsula, the prevalence of BD varies across different countries. Studies conducted in Saudi Arabia report a prevalence ranging from 3.3 to 7.8 cases per 100,000 individuals, underlining its regional significance. Similarly, in neighboring Gulf countries and other Arabic nations, the prevalence rates vary but generally remain elevated. Countries such as Turkey and Iran have notably high prevalence rates, as high as 20 cases per 100,000 individuals. This geographical pattern suggests a potential genetic and environmental interplay in the etiology and manifestation of BD within these populations [6,7,8].

BD affects various body systems. Key features include recurrent painful oral and genital ulcers, inflammatory eye conditions (uveitis), skin lesions, and arthritis. Neurological symptoms, gastrointestinal involvement, and vascular complications further contribute to disease complexity. BD presentation varies among individuals, necessitating tailored diagnosis and management [9,10,11]. Uveitis is a type of intraocular inflammation that is a common BD symptom. Non-invasive procedures such as eye slit lamp examination and fundoscopy are used to diagnose uveitis.

Chen Y-Y et al, reported in a retrospective cohort study of the Taiwan National Health Insurance from 1 January 2001 to 31 December 2013. The study population were 6508 patients with BD, of those (38.7%) patients had uveitis. The occurrence of acute myocardial infarction (AMI) among all participant in the study were 382 (5.9%), the uveitis group had more AMI 210 (8.3%) [12].So , we decided to investigate the potential correlation between uveitis severity in BD and myocardial infarction risk (MI) in Aseer region population.

Methods

Retrospective cohort study, though review of medical charts and data for patients who meet the diagnostic criteria for BD actively receiving care in rheumatology clinics. Specifically at Aseer region, located in the southern region of Saudi Arabia. Our cohort were, patients Fulfilled diagnostic criteria for BD. We searched medical charts between 2016 until 2023 who were actively receiving care in the rheumatology clinics at three main hospitals including Aseer Central Hospital (ACH), and Khamis Madani Hospital as well as Armed Forces Hospitals of the Southern region. The study included individuals aged 18 years and older, who fulfilled diagnostic criteria of BD by certified rheumatologists, who are living in Aseer region. We followed a meticulous data-cleaning process and excluded ineligible cases, finally selecting a sample of 111 patients. Our study gathered patient demographic data, including age, gender, presence of systemic involvement. The primary objective was to investigate the correlation between uveitis and cardiovascular disease, specifically MI. Study approval was granted by the Institutional Review Board at Aseer Central Hospital and the research committee, ensuring adherence to ethical research practices.

Data analysis

Following data extraction, we revised, coded, and entered data into statistical software. Statistical analyses employed two-tailed tests, considering a p-value below 0.05 as statistical significance. We utilized a univariate analysis to examine the association between various variables and gender. We presented continuous variables, due to their abnormal distribution (as determined by the Shapiro-Wilk test), as median and interquartile range and analyzed them using the Mann-Whitney U test. We expressed categorical variables as absolute numbers and case proportions and compared them using the chi-squared or Fisher's exact test. All statistical analyses were performed using the R software.

Results:

In our study, we had a total of 111 patients, evenly distributed between male and female participants. The majority of patients fell within the 20-40 age range. Other baseline characteristics are illustrated in (Table 1).

In our cohort, approximately 10% of Behçet's disease patients (11 patients) were diagnosed with uveitis. Notably, the majority of uveitis cases were observed in males, constituting around three-quarters of the affected individuals. Furthermore, half of the uveitis patients exhibited elevated inflammatory markers, specifically ESR or CRP. Remarkably, none of the patients diagnosed with uveitis had a documented history of myocardial infarction (Tables 2,3).

Discussion

BD involves inflammation in both the arteries and veins, often presenting as venous thrombosis, but its impact is more severe in arteries. Coronary artery involvement is uncommon but can be a serious complication during acute MI. Various studies have found a higher incidence of MI in the uveitis group, although the exact mechanism remains uncertain. Encouragingly, none of the individuals with uveitis in our study experienced MI [23,24,25,26].

This study examined Behçet's disease, emphasizing its clinical presentation, particularly uveitis, and investigating its defining characteristics. We also explored the correlation between uveitis severity in BD and MI risk.

In our cohort, approximately 10% of BD cases were associated with uveitis. Notably, the majority of uveitis cases were observed in males, constituting about 75% of those affected. This aligns with findings from a local study that displayed a similar amount of uveitis cases. However, ocular symptoms were noted in approximately 67% of the previous cohort. This trend is also observed in Egypt and Kuwait. Interestingly, there is a significantly lower prevalence in Southeast Asian countries and China (35%), possibly attributed to specific genetic or environmental factors within those populations [20,21,22].

One of the biggest limitations we had in conducting this study is sample size. Our study wasn't powered enough to detect any significant difference in the two groups, future studies are needed to evaluate the significance of the association between Myocardial infarction and uveitis in this population.

Conclusion

In our cohort, those with a history of MI did not have a documented history of uveitis. Larger, prospective studies are needed to evaluate the associations between MI and uveitis in a BD population.

References

1. rursachte Geschwüre am Mund, am Auge, und an den Genitalien . Dermatol Wochenzchr. 1937, 105:1152.
2. Yazici H, Seyahi E, Hatemi G, Yazici Y: Behçet syndrome: a contemporary view . Nat Rev Rheumatol. 2018, 14:107-19. 10.1038/nrrheum.2017.208
3. Kural-Seyahi E, Fresko I, Seyahi N, et al.: The long-term mortality and morbidity of Behçet syndrome: a 2-decade outcome survey of 387 patients followed at a dedicated center. Medicine. 2003, 82:60-76. 10.1097/00005792-200301000-00006
4. Azizlerli G, Köse AA, Sarica R, et al.: Prevalence of Behçet's disease in Istanbul, Turkey . Int J Dermatol. 2003, 42:803-6. 10.1046/j.1365-4362.2003.01893.x
5. Al-Rawi Z, Al-Rawi ZS, Neda AH: Prevalence of Behçet's disease among Iraqis . Adv Exp Med Biol. 2003, 528:37-41. 10.1007/0-306-48382-3_6
6. Kirino Y, Nakajima H: Clinical and genetic aspects of Behçet's disease in Japan . Intern Med. 2019, 58:1199-1207.10.2169/internalmedicine.2035-18
7. Fernández-Ávila DG, Rincón-Riaño DN, Bernal-Macías S, Dávila JM, Rosselli D: Prevalence and demographic characteristics of Behcet disease in Colombia: data from the national health registry 2012-2016. Rheumatol Int. 2020, 40:17-20. 10.1007/s00296-019-04466-7
8. Alharthy F, Almaqati A S, Alsulami S, et al.: (February 11, 2023) Behçet's Disease in Saudi Arabia: Clinical and Demographic Characteristics. Cureus. 15:34867. 10.7759/cureus.34867
9. Al-Araji A, Kidd DP: Neuro-Behc¸ et's disease: epidemiology, clinical characteristics, and management . Lancet Neurol. 2009, 8:192-204. 10.1016/S1474-4422(09)70015-8
10. Gotkine M, Vaknin-Dembinsky A: Central nervous system vasculitis. Curr Treat Options Neurol. 2013, 15:367-74. 10.1007/s11940-013-0227-8
11. Saadoun D, Bodaghi B, Bienvenu B, et al.: Biotherapies in inflammatory ocular disorders: interferons, immunoglobulins, monoclonal antibodies. Autoimmun Rev. 2013, 12:774-83. 10.1016/j.autrev.2013.02.002
12. Chen YY, Lai YJ, Yen YF, Chen HH, Chou P. Uveitis as a potential predictor of acute myocardial infarction in patients with Behcet's disease: A population-based cohort study. BMJ Open. 2021;11(1):1-9. doi:10.1136/bmjopen-2020-042201
13. Davatchi F, Shahram F, Chams-Davatchi C, et al.: Behcet's disease: from East to West . Clin Rheumatol. 2010,
29:823-33. 10.1007/s10067-010-1430-6
14. Gorial F, Jabbar M: Demographic and clinical characteristics of Behçet's disease in Iraqi patients . Archives of Medical Science-Aging. 20211, 4:1-5. 10.5114/amsa.2021.106113
15. Kidd DP: Neurological complications of Behçet's syndrome . J Neurol. 2017, 264:2178-2183. 10.1007/s00415-017-8436-9
16. El Menyawi MM, Raslam HM, Edrees A: Clinical features of Behçet's disease in Egypt . Rheumatol Int. 2009, 29:641-646. 10.1007/s00296-008-0741-2
17. Valentincic NV, de Groot-Mijnes JDF, Kraut A, et al.: Intraocular and serum cytokine profiles in patients with intermediate uveitis. Mol Vis. 201117, 2003:10.
18. Nizamuddin SH, Bawazeer AM: Causes of uveitis in a tertiary center in Western . Saudi Arabia. Saudi Med J. 2013, 34:379-87.
19. C. H. C. Zouboulis, D. Djawari, and W. Kirch: "Adamantiades-Behc¸et's disease in Germany," in Behc¸et's Disease, P. Godeau and B. Wechsler, Eds., pp. 193-196, Elsevier Science, Amsterdam, The Netherlands. 1:1993.
20. Al Zahrani FM, Alsultan B, Alahmari H, et al.: Behçet's disease presentations and care outcomes in a tertiary hospital in south-western Saudi Arabia. Int J Rheum Dis. 2019, 22:1466-1473. 10.1111/1756-185X.13598
21. El-Garf A, Abdo M, Alkemary A, Mohamed S. Behçet's disease patterns and subsets in a cohort of Egyptian patients. Egypt Rheumatol. 2019, 41:135-138.
22. El-Najjar AR, Abou El-Soud AM: Amar HA, Al Sayed Diab M. Clinical characteristics and disease activity of Behçet's disease patients in Zagazig, Egypt. Egypt Rheumatol. 2015, 37:191-196.
23. Ahn HS, Lee D, Lee SY: Increased cardiovascular risk and all-cause death in patients with Behçet disease: a

Korean nationwide population-based dynamic cohort. study. 2020, 47:903-8. 10.3899/jrheum.190408
24. Yavne Y, Tiosano S, Watad A, et al.: Investigating the link between ischemic heart disease and Behcet′s disease: a cross-sectional analysis. Int J Cardiol. 2017, 241:41-5. 10.1016/j.ijcard.2017.02.135
25. Chen Y-Y, Lai Y-J, Yen Y-F, et al.: Uveitis as a potential predictor of acute myocardialinfarction in patients with Behcet′s disease: a population-based cohort study. BMJ Open. 2021, 11:042201. 10.1136/bmjopen-2020-042201
26. Moreira DM, da Silva RL, Vieira JL, et al.: Role of vascular inflammation in coronary artery disease: potential of anti-inflammatory drugs in the prevention of atherothrombosis.Inflammation and anti-inflammatory drugs in coronary artery disease.Am. J Cardiovasc Drugs. 2015, 15:1-11. 10.1007/s40256-014-0094-z

Table 1: Baseline Demographics and clinical characteristics of BD patients.

Mean(SD)

**Table 1: Baseline Demographics and clinical characteristics of BD patients. **

Variable	N	Female N = 56[1]	Male N = 55[1]	p-value[2]
Age	111			0.3
<21		1 (1.8%)	1 (1.8%)	
>60		8 (14%)	6 (11%)	
21–40		22 (39%)	31 (56%)	
41–60		25 (45%)	17 (31%)	
ESR	70	34 (26)	22 (26)	0.007
CRP	65			0.8
−VE		22 (65%)	21 (68%)	
+VE		12 (35%)	10 (32%)	
Organs_involvement	111			0.2
Mild		19 (34%)	16 (29%)	
Moderate		21 (38%)	28 (51%)	
No organ involvement		1 (1.8%)	3 (5.5%)	
Severe		15 (27%)	8 (15%)	
Muco_cutaneous	111			0.6
No		21 (38%)	26 (47%)	
Oral and genital ulcers		13 (23%)	10 (18%)	
Oral ulcers		22 (39%)	19 (35%)	
Cutaneous	111			>0.9
Both		2 (3.6%)	2 (3.6%)	
Erythema		9 (16%)	7 (13%)	
No		44 (79%)	45 (82%)	
Skin pustules		1 (1.8%)	1 (1.8%)	
Musculoskeletal	111			0.2
Arthritis (mono, oligo, spondylarthritis)		13 (23%)	8 (15%)	
No		43 (77%)	47 (85%)	
Eye_complications	111			0.4
Cataracts		0 (0%)	1 (1.8%)	
Conjunctivitis		1 (1.8%)	2 (3.6%)	

No		34 (61%)	30 (55%)	
Normal		18 (32%)	14 (25%)	
Uveitis		3 (5.4%)	8 (15%)	
Neurological_involvement	111			0.7
Gait disturbance		1 (1.8%)	2 (3.6%)	
Headache		15 (27%)	13 (24%)	
No		39 (70%)	38 (69%)	
Optic neuritis		1 (1.8%)	0 (0%)	
Seizure		0 (0%)	2 (3.6%)	
Gastrointestinal	111			0.5
Abdominal pain		1 (1.8%)	3 (5.5%)	
Abdominal pain, Rectal bleeding		0 (0%)	1 (1.8%)	
Diarrhea		0 (0%)	1 (1.8%)	
Gastroenteritis		5 (8.9%)	3 (5.5%)	
No		49 (88%)	46 (84%)	
Peptic ulcer		1 (1.8%)	0 (0%)	
Rectal bleeding		0 (0%)	1 (1.8%)	
Pulmonary	111			0.2
Chest pain		6 (11%)	1 (1.8%)	
Chest pain, Shortness of breath		3 (5.4%)	3 (5.5%)	
No		44 (79%)	50 (91%)	
Shortness of breath		3 (5.4%)	1 (1.8%)	

[1] n (%); Mean (SD)

[2] Fisher's exact test; Wilcoxon rank sum test; Pearson's Chi-squared test

Table 2: Uveitis patients, clinical characteristics compared to no uveitis in Behçet's Disease.

Mean(SD)

Table 2: Uveitis patients, clinical characteristics compared to no uveitis in Behçet's Disease

Variable	N	No N = 100[1]	Yes N = 11[1]	p-value[2]
Age	111			0.2
<21		1 (1.0%)	1 (9.1%)	
>60		13 (13%)	1 (9.1%)	
21–40		46 (46%)	7 (64%)	
41–60		40 (40%)	2 (18%)	
Gender	111			0.11
Female		53 (53%)	3 (27%)	
male		47 (47%)	8 (73%)	
ESR	70	29 (26)	26 (29)	0.4
CRP	65			0.5
−VE		38 (68%)	5 (56%)	
+VE		18 (32%)	4 (44%)	
Organs_involvement	111			0.3
Mild		34 (34%)	1 (9.1%)	
Moderate		42 (42%)	7 (64%)	
No organ involvement		4 (4.0%)	0 (0%)	
Severe		20 (20%)	3 (27%)	
Muco_cutaneous	111			0.8
No		43 (43%)	4 (36%)	
Oral and genital ulcers		20 (20%)	3 (27%)	
Oral ulcers		37 (37%)	4 (36%)	
Cutaneous	111			0.1
Both		3 (3.0%)	1 (9.1%)	
Erythema		14 (14%)	2 (18%)	
No		82 (82%)	7 (64%)	

Skin pustules		1 (1.0%)	1 (9.1%)	
Musculoskeletal	111			0.4
Arthritis (mono, oligo, spondylarthritis)		18 (18%)	3 (27%)	
No		82 (82%)	8 (73%)	
Eye_complications	111			<0.001
Cataracts		1 (1.0%)	0 (0%)	
Conjunctivitis		3 (3.0%)	0 (0%)	
No		64 (64%)	0 (0%)	
Normal		32 (32%)	0 (0%)	
Uveitis		0 (0%)	11 (100%)	
Neurological_involvement	111			0.1
Gait disturbance		1 (1.0%)	2 (18%)	
Headache		26 (26%)	2 (18%)	
No		70 (70%)	7 (64%)	
Optic neuritis		1 (1.0%)	0 (0%)	
Seizure		2 (2.0%)	0 (0%)	
Gastrointestinal	111			0.7
Abdominal pain		3 (3.0%)	1 (9.1%)	
Abdominal pain, Rectal bleeding		1 (1.0%)	0 (0%)	
Diarrhea		1 (1.0%)	0 (0%)	
Gastroenteritis		8 (8.0%)	0 (0%)	
No		85 (85%)	10 (91%)	
Peptic ulcer		1 (1.0%)	0 (0%)	
Rectal bleeding		1 (1.0%)	0 (0%)	
Pulmonary	111			0.7
Chest pain		7 (7.0%)	0 (0%)	
Chest pain, Shortness of breath		5 (5.0%)	1 (9.1%)	
No		84 (84%)	10 (91%)	
Shortness of breath		4 (4.0%)	0 (0%)	

[1] n (%); Mean (SD)

[2] Fisher's exact test; Pearson's Chi-squared test; Wilcoxon rank sum test

Table 3: Association between Uveitis and MI in in Behçet's Disease Patients.

Table 3: Association between Uveitis and MI in in Behçet's Disease Patients

Variable	N	No N = 100[1]	Yes N = 11[1]	p-value[2]
MI	111	2 (2.0%)	0 (0%)	>0.9

[1] n (%)

[2] Fisher's exact test