

## THE INFLUENCE OF AGE OF ONSET AND PATIENT'S SEX ON THE PREVALENCE OF CLINICAL MANIFESTATIONS OF BEHCET'S DISEASE IN IRAQI PATIENTS

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Behcet's disease (BD) is a chronic relapsing disease characterized by multiple signs and symptoms such as recurrent orogenital ulceration, eye involvement, skin manifestations and other systems affection.<sup>1</sup> BD is somewhat more common among females in Japan and Korea, whereas males are frequently affected in Middle Eastern countries. The male to female ratio is reported to be 0.98:1 for Japan, 0:36 for Korea, 1:1.4 for Iran, 1:78 for Turkey and 2:93 for Iraq.<sup>2-5</sup> The age of onset of BD commonly extends from the second through the fourth decade of life. BD rarely develops before puberty or after the age of 50 years.<sup>3,6,7</sup>

Male gender is a risk factor for the severe form of the disease, and it has been reported that BD runs a more severe course in young men. It has been found that eye disease, arthritis, folliculitis and thrombophlebitis were more common among male, and erythema nodosum among female BD patients.<sup>7,8</sup>

Childhood BD is defined when the disease is fully manifested and diagnosed in children up to the age of 16 years. It is reported that children with BD have significantly less genital ulcers than adults, and have more mild gastrointestinal symptoms, as well as CNS involvement and arthralgia. Most of the early studies in juvenile-onset BD have reported a low prevalence of ocular involvement, ranging from 14%-27%.<sup>9</sup>

The effect of patient's sex and age at onset on pathergy reaction was investigated, and it was found that in male patients, the pathergy reaction were more positive than in females. The age at onset did not affect the pathergy reaction significantly.<sup>10</sup> Thus, a younger age of onset (age of onset before 24 years) seems to contribute to more severe disease. Younger males and females have higher

+1	Cells in vitreous and/or anterior chamber only
+2	Vision 50%
+3	Vision 30%
+4	Able to see few feet
+5	Blind
Skin and mucous membrane*	
Oral ulcers	
0	No ulcers
+1	1-3 minor ulcers
+2	1-3 major ulcers or more than 3 minor ulcers
+3	More than 3 major ulcers
Genital ulcers*	
0	No ulcers
+1	1-3 minor ulcers
+2	1-3 major ulcers or more than 3 minor ulcers
+3	More than 3 major ulcers
Frequency (episodes/month)	
+1	1-2 episodes/month
+2	More than 2 episodes/month
+3	Continuous (status aphthaticus)
+1	Erythema nodosum
+1	Papulopustular and acneiform
Epididymoorchitis*	
+1	Involvement of one side
+2	Involvement of both sides
Vascular*	
+1	Unilateral limb DVT and/or superficial vein thrombosis
+2	Bilateral venous thrombosis
+3	Vein thrombosis requiring bed rest
+4	Thrombosis of superior/inferior vena cava (SVC, IVC)
+5	Thrombosis of both SVC and IVC or arterial occlusion
Rheumatological*	
+1	Arthritis of each joint
+1	Arthralgia (irrespective of number of joints involved)
Neurological involvement*	
+2	Intracranial hypertension
+4	Multiple sclerosis-like syndrome
+5	Pyramidal and/or cerebellar involvement

\*The index for individual patient is the numerical sum of clinical feature<sup>6</sup> (with modification)

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Accepted for publication 15 April 2002. Received 20 August 2001.

TABLE 1. Clinical manifestation index\*.

Eye* (for each eye)	
0	Normal

TABLE 2. Age of onset, sex and disease duration.

	Early male (EM)	Early female (EF)	Late male (LM)	Late female (LF)
No. of patients	47	12	38	17
Age of onset	20±2.6	19.7±2.4	31.7±6.3	30.3±4.8
Age at initial visit	29.3±8.1	29.3±5.3	38.9±9.2	38.4±8.2
Disease duration	8.91±8	9.2±5.11	6.9±6.3	8.2±6.2

prevalence of eye disease than do older patients (age of onset 25 years or more).<sup>6</sup> While the observations in Iraqi patients are not compatible with what have been published, the aim of study was to investigate these risk factors of BD.

### Patients and Methods

A total of 114 patients who fulfilled the International Study Group (of Behcet Disease) criteria for the diagnosis of BD<sup>11</sup> were included in this prospective study. The patients were attending Behcet's disease multidisciplinary clinic at Baghdad Teaching Hospital, Iraq, from April 1999 to July 2000.

Full medical histories of the patients were taken and clinical examinations were performed. Demographic data (age at presentation, age of onset, duration of disease, male to female ratio, familial occurrence), frequencies of clinical manifestation and onset of symptoms were determined. A clinical manifestations index was calculated for each patient (Table 1)<sup>6</sup> to determine the influence of age of onset and patient's sex on the prevalence of clinical features of the disease, by analyzing the clinical manifestations throughout the course of the disease. All the studied patients received no therapy for at least three weeks prior to the study.

Patients were divided into four sex-age groups, depending on the age of onset; patients who were 24 years old or younger at age of onset were classified as the early onset group, and those 25 years or older as the late onset group. Pathergy test was performed on 83 patients using a 20-gauge-needle.<sup>12</sup>

Statistical analysis was performed using means and standard deviations. *T*-test and *Z*-test were applied to investigate possible difference between the groups.

### Results

The number of patients in each age-sex group, the mean age at the onset of the symptoms and the initial clinic visit, and the duration of the disease are given in Table 2. The early onset males (EM) and females (EF) were of similar age ( $P>0.05$ ). The late-onset males (LM), on the other hand, were slightly older than late-onset females (LF), but this was statistically not significant ( $P>0.05$ ). The disease duration before presentation was slightly shorter in LM than the other groups ( $P>0.05$ ).

The earliest age of onset was 17 years (3 males and 1 female) and the latest was 49 years (1 male patient). The difference in prevalence of clinical manifestations was

statistically not significant in the early - and late-onset age groups. When sex was taken into consideration, it was found that there was a statistically significant difference in eye involvement between the different age-sex groups

TABLE 3. Frequency of main manifestations according to the age of onset and sex.

	Aphthae	Genital ulcer	Eye disease	Arthritis	Vascular	Erythema nodosum	Folliculitis	Neurological
EM (n=47)	47(100)	44(93.6)	22(46.8)	13(27.65)	11(23.4)	16(34.04)	21(44.68)	8(17.02)

(Table 3). The results showed that clinical manifestation (in percentage terms), early-onset males (EM) were more likely to develop eye involvement than late-onset males (LM), even though the difference was not statistically significant when pure eye indices were considered. When early-onset females (EF) were compared with late-onset females (LF), no statistically significant difference was found in eye involvement when clinical manifestation was expressed in percentage terms or by using the scoring index.

When both sexes were compared to each other, there was no statistically significant difference between them when eye involvement was considered in percentage terms, but when pure eye indices were considered, the difference was statistically more significant in males of both age groups.

When age was considered, there was statistically more eye involvement in the early age group in percentage terms, but no statistically significant difference between these age group when pure eye indices were considered.

### Discussion

In all the studied patients, the disease manifestations before presentation to the clinic was determined from the patient's history and clinical examination at initial visit to the Behcet's disease clinic. In this study, the percentage of ocular involvement was higher in the early-onset male group than the late-onset male group, and the difference was statistically significant, and the percentage of eye involvement was higher in the early-onset patients (both sexes) than late-onset patients, with a statistically significant difference. Regarding pure eye indices (those with only eye involvement), pure eye index was statistically higher in the early-onset males than the early onset females, and also higher in late-onset males than late onset females. But there was not statistically significant difference between eye indices in early and late age-group patients. Thus, both sex and age of onset seem to affect the severity of eye involvement in patients with BD. This result is in agreement with studies from other countries which reported that eye involvement is the chief indicator of disease severity in those with early onset BD,<sup>3,6,9</sup> and that it was more frequent among males than females and among early-onset than late onset patients.<sup>6</sup>

It was reported in studies from other countries that arthritis and folliculitis were more common among the late onset male group. Erythema nodosum was the only manifestation of BD that was more common in females; thrombophlebitis was more common in males and did not show any trend with age.<sup>6,9</sup>

EF (n=12)	12(100)	10(83.3)	7(58.3)	5(41.6)	3(25)	5(41.6)	7(58.3)	4(33.3)
LM (n=38)	38(100)	34(89.3)	11(28.9)	14(36.84)	8(21)	17(44.73)	19(50)	3(7.89)
LF (n=17)	17(100)	14(82.3)	7(41.17)	10(58.8)	2(11.7)	4(23.5)	6(35.3)	3(17.6)
EMVsEF	ND	1.14:NS	0.71:NS	0.94:NS	0.11NS	0.49:NS	0.84:NS	1.25NS
LMVsLF	ND	0.73:NS	0.89:NS	1.51:NS	0.82NS	1.49:NS	1.01:NS	1.07NS
EMVsLM	ND	0.69:NS	1.67*sign P<0.05	0.15:NS	0.25NS	1.00:NS	0.48:NS	1.24NS
EFVsLF	ND	6.88:NS	0.91:NS	0.91:NS	0.92NS	1.03:NS	1.22:NS	0.97NS

ND=not done; NS=not significant; \*significant.

Although we found that arthritis was more common in females than males in the present study, erythema nodosum was more prevalent in late-onset males, and epididymoorchitis was more common in early-onset males than in late-onset males, but this difference did not reach statistical significance.

With regards to total clinical manifestation indices, these were reported to be higher among patients with early onset of either sex than in late-onset patients.<sup>9,12</sup> In the present study, there was no statistically significant difference between the means of total clinical manifestation indices among different age-sex groups. We can thus conclude that the age of onset and the patient's sex do not significantly influence the disease expression in Iraqi BD patients, in contrast to results of other studies, but eye disease was more common in early-onset males. The age at onset and patient's sex did not affect the result of pathergy test in our study.

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