The prevalence of Behçet's disease in the north of Jordan: a hospital-based epidemiological survey

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ABSTRACT

Objective. *To estimate the prevalence of Behçet's disease (BD) in Jordan, with the additional aim of comparing this prevalence among hospital workers in other geographical areas.*

Methods. *In the first stage of our survey, 2,569 employees from 6 hospitals in north Jordan were interviewed using a screening questionnaire to identify individuals with recurrent oral ulcers (ROU), a previous diagnosis of BD (PDBD) and/or any major symptom related to BD. In the second stage, all individuals with ROU or PDBD identified at stage 1, were examined by 2 rheumatologists for the presence/confirmation of BD according to the International Study Group (ISG) criteria. Pathergy test was performed according to recommendations.*

Results. *ROU were present in 210 (8.2%) individuals. BD was confirmed in 10 employees with PDBD. Seven more BD patients were found. Mean age of 17 BD patients was 38.6±10.7 (range 26–65 y). M: F was 2.4:1. Pathergy test was positive in 8/17. A family history of ROU or BD was noted in 9 (52%) and 3 (25.0%), respectively, compared to 227 (8.9%) and 62 (2.6%) in the whole group, excluding the BD patients (p<0.001 and 0.008, respectively).*
The prevalence rate of BD in the north of Jordan was estimated as 66:10.000 (95% CI 34.8 to 97.5:10000).

Conclusion. *The results of this first ever survey indicated that the prevalence of BD in the north of Jordan is among the highest in the world. This prevalence can now be compared to hospital workers in other geographical areas.*

Introduction

BD is a multisystem disorder of unknown aetiology characterised by vasculitis (1). It has a worldwide distribution, but most of the cases cluster along the ancient Silk Road, which extends from eastern Asia to the Mediterranean basin (2).

The prevalence of BD shows considerable geographical variation. Epidemiological studies had shown that the prevalence/100000 populations was: in Japan 7-8.5 (3), in Iran 16.7 (4), in Iraq 17 (5), in Saudi Arabia 20 (6), in Egypt 7.6 (7) and in Yorkshire, UK 0.6 (8), while Turkey had the highest prevalence of 80–421/100000 population (9-11), indicating that there may be regional differences in the same country. Lately, a decrease in the prevalence and a tendency towards a less severe disease were reported by different groups from different ethnic origins (12).

The relative contribution of genetic and environmental causes have not been well described, while the genetic tendency is supported by the higher frequency of the HLA B51 allele in the Mediterranean countries and Japan, in contrast to the north of Europe where the disease is less prevalent (13, 14).

Large epidemiological surveys are lacking, prevalence rates are based on case registries and hospital records.

Jordan is located in the east Mediterranean, Petra the ancient city, which is located in the south of Jordan, was a meeting place for merchants' caravans travelling the trade routes to and from Europe, India and China.

Although Jordan is a Middle Eastern country and BD has been reported in Jordanians, epidemiological studies are lacking. Here we report the first epidemiological study of BD in Jordan. For this purpose we used a different epidemiological approach, reasoning that comparative epidemiological data could be obtained by using hospital employees at different geographical areas, assuming that potential biases would be similar. We also reasoned that some validation of the hospital data could be

achieved if a survey for a disease with a known general population frequency was included in this hospital survey.

The aim of this study was to estimate the prevalence of BD in Jordan by using Jordanian hospital workers in the north of the country, with the further aim of comparing this prevalence among hospital workers in other geographical areas.

Subjects and methods

In the first stage of our survey, 2569 hospital works from 6 government hospitals in the north of Jordan, including one university hospital, were interviewed by trained resident physicians, using a screening questionnaire to identify individuals with recurrent oral ulcers (ROU), PDBD, any symptom of major BD manifestations. A previous diagnosis of rheumatoid arthritis (RA) was also sought for validation purposes. In the second stage all individuals with ROU or PDBD identified at stage one, who agreed for further analysis were examined by two rheumatologists for the presence or confirmation of BD, according to the ISG classification/diagnostic criteria for BD (14).

Pathergy test was performed at 4 sites according to recommendations.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences, SPSS 17.0 for windows. The differences between groups were compared by means and proportions. *P*-values of ≤0.05 were considered to be statistically significant. The 95% CI was also calculated.

The study protocol was approved by the ethics committees at Jordan University of Science and Technology, Irbid, Jordan, and the Jordanian Ministry of Health.

Results

2569 employees were interviewed, representing 60% of the total number of hospital workers.

All were Arabs, except for one individual of Sherkasian ethnicity. Demographic data of interviewed Jordanian hospital workers are shown in Table I.

ROU were present in 210 (8.2%) and family history of ROU in 236 (9.2%) individuals.

A PDBD was recorded in 10, family history of BD was reported in 65 (2.5%).

Among individuals with ROU, 9 gave no data on frequency, 54 had the frequency <3 times/year, 4 had inflammatory bowel disease and 1 coeliac disease, for a total of 68; these were excluded and not examined further.

The remaining 142 individuals with ROU and PDBD were invited to be examined further and to perform the pathergy test.

Only 60 individuals agreed (42.2%), and 82 (57.7%) either refused or were not available.

Pathergy test was applied to the skin of forearm at 4 different sites and it was evaluated by 2 rheumatologists after 24–48 hours, and a papulo-erythema larger than 2 mm at any of the sites was considered positive.

A positive test was found in 12 people and negative in 48. Among the 12 employees with positive results, 4 had a PDBD, 3 others, in addition to oral ulcers and positive pathergy test, were found to have skin lesions in the form of folliculitis and acne-form le-

Table I. Demographic data of 2569 interviewed Jordanian hospital workers.

Variable	Absolute	%
Mean age	34.4±8.4(18-73)	-------
Males	1245	48.5
Females	1324	51.5
M:F	0.94:1	--------
Consanguinity		
Parents first degree cousins	639	24.9
Parents further relatives	469	18.3
Not relatives	1447	56.3
Level of education:		
Illiterate	12	0.5
High school or less	259	10.1
More than high school	2287	89.4
Smoking	793	30.9

Table II. Demographic and clinical characteristics of newly diagnosed patients with BD.

Number	Sex	Age	Pathergy test	Symptoms
1	F	27y	Positive	ROU and skin lesions.
2	M	29y	Positive	ROU and skin lesions.
3	M	23y	Positive	ROU and skin lesions.
4	F	32y	Positive	ROU, and genital ulcers.
5	M	39y	Negative	ROU, genital and skin lesions.
6	M	48y	Negative	ROU, genital and skin lesions.
7	F	40y	Negative	ROU, uveitis and skin lesions.

Table III. Demographic and clinical characteristics of 10 patients with PDBD.

Number	Sex	Age	Pathergy	Clinical manifestations
1	M	42	Not done	ROU, genital ulcers, skin lesions and arthritis.
2	M	39	Positive	ROU, genital ulcers, uveitis, central nervous system and pulmonary involvement.
3	M	39	Negative	ROU, genital ulcers, skin, arthritis, and central nervous system involvement.
4	M	33	Not done	ROU, genital ulcers and skin lesions
5	M	26	Not done	ROU, uveitis and skin lesions.
6	M	36	Positive	ROU, uveitis and skin lesions
7	M	65	Not done	ROU, genital and uveitis.
8	M	35	Positive	ROU, genital ulcers, skin lesions, uveitis and arthritis,
9	F	48	Not done	ROU, genital ulcers, skin lesions and arthritis.
10	F	33	Positive	ROU, genital ulcers and arthritis.

Table IV. Demographic data of 17 patients with diagnosis of BD compared to the whole group of interviewed individuals.

Variable	BD patients		Whole group		
	Absolute	Percentage	Absolute	Percentage	*p*-value
Age: mean	37.12±10.1		34.5±8.4		0.734
Range	(23:65)		(18:73)		
Gender					
Male	12	70.60%	1233	48.30%	0.088
Female	5	29.40%	1319	51.70%	0.045
M:F	2.4:1		0.94:1		
Family history of BD	3	17.60%	62	2.4%	0.008
Family history of ROU	9	52.90%	227	8.90%	<0.001
Level of education					
Illiterate	0	0%	12	0.50%	1.00
High school or less	6	35.30%	253	9.90%	0.029
More than high School	11	64.70%	2276	89.20%	0.035
Consanguinity					
First degree cousins	7	41.20%	632	24.80%	0.119
Parents further relatives	2	11.80%	467	18.30%	0.753
Not relatives	8	47.10%	1439	56.40%	0.442
Smoking	9	52.90%	784	30.70%	0.067

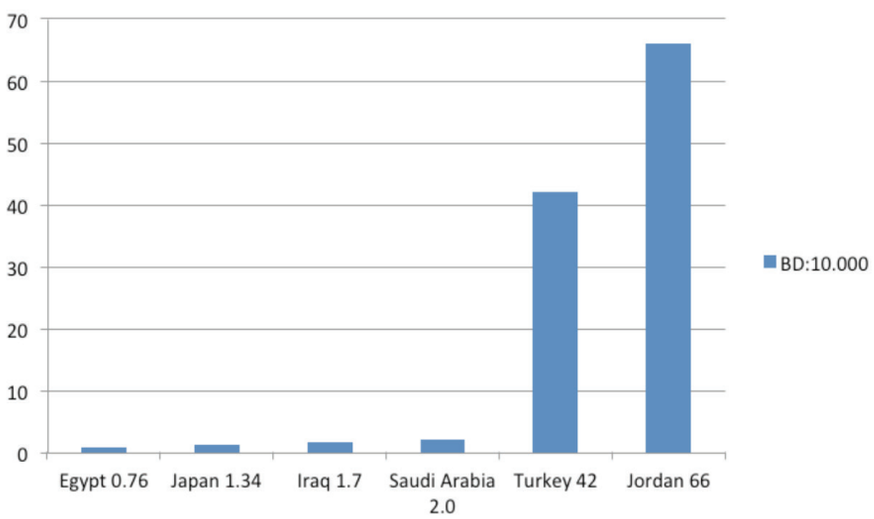

Fig. 1. The prevalence of BD (per 10,000) among different countries in comparison to Jordan.

sions, and 1 had genital ulcers, and were considered as new cases of BD. The remaining 4 did not have any other symptoms related to BD and did not meet the ISG criteria.

On the other hand, in 3 individuals were pathergy test negative, 2 had genital ulcers and skin lesions and one had anterior uveitis and skin lesions fulfilling the ISG criteria and were also considered as new cases of BD. Table II, shows characteristics of newly identified BD patients.

The diagnosis of BD in subjects with PDBD was confirmed after examination by 2 rheumatologists: all patients had ROU, 8 had genital ulcers, 4 had uveitis, and 7 had skin lesions, 5 had history of arthritis, 2 had neuro-Behcet's manifestations and one had pulmonary involvement. Among the patients tested for pathergy, 4 were positive and one negative, Table III shows the characteristics of patients with PDBD.

The estimated prevalence of BD was found to be 17/2560, 0.0066, approximately 66:10.000 inhabitants with 95% confidence interval 34.8 to 97.5:10000. Table IV shows demographic data of 17 patients with BD compared to the whole group of interviewed individuals.

Previous diagnosis of rheumatoid arthritis (RA) was reported by 8 individuals and all fulfilled the 1987 ACR criteria for RA (15), one other female individual had pain and stiffness in both hands suggesting RA, but on further questioning and examination she was found to have uncontrolled diabetes mellitus and tendinitis of both hands.

Mean age of RA patients was 43.38±7.52 (35-56) and F:M was 3:1. The estimated prevalence of RA was 8/2569=0.00311, 31.1:10.000 with 95% confidence interval 9.6 to 52.7: 10000.

Discussion

This is the first study on the prevalence of BD in Jordan. Jordan is a Middle Eastern country that lies within the ancient Silk Road, and 97% of its population are Arabs.

According to a population census in 2012, the total population of Jordan was 6.388.000 and the percentage of population between ages 15–64 was 59.4% (3.794.472).

The interviewed individuals are within this group and probably represent the target population needed for the estimation of the prevalence of BD in the country, as BD is rare in children and the elderly.

Our results show that the estimated prevalence of BD in Jordan is 66:10.000 inhabitants, which is higher than the reported frequency in other neighboring Arab countries (5-7) and even to that reported in some parts of Turkey (10, 11), as shown in Figure 1.

In 1997 Bang *et al*. (16) reported that about 52% of individuals with ROU would have developed BD, while in a Turkish study (10) 101 out of 700 individuals with ROU had BD (144:1000); in our study 17 out of 210 with ROU had BD (80.9:1000), and taking into consideration that in 57% of the interviewed individuals who had ROU, pathergy was not performed, we had expected that more patients could have been identified and thus the prevalence rate might be higher.

The difference in these results, which showed almost similar results in Turkish and Jordanian populations in contrast to the Korean, might be due to regional or ethnic differences.

Table V. Prevalence of BD and RA in Jordan compared to neighbouring countries.

	Jordan	Turkey	Saudi Arabia
Behcet's disease	66:10.000	42:10.000	2:10.000
Rheumatoid arthritis	0.31%	0.38%	0.22%

Genetic factors play an important role in the aetiology of BD in Jordan, and this is supported by several findings; the significant high frequency of family history of ROU and BD in patients compared to the whole group, and the high frequency of consanguineous marriages; in 24.8% of the whole group, parents were first cousin relatives, while in the BD group it was encountered in 41.2%. It seems that this is a common tradition among Jordanians, first cousin marriages were reported in 32.03% in the Jordanain population (17).

In our opinion this fact may have strongly contributed to the high prevalence of BD in Jordanians.

Furthermore, a previous study on the frequency of HLA B 51 in Jordanian patients with BD showed that it was positive in 66% *vs*. 15% in controls thus supporting genetic susceptibility to the disease (18).

BD in Jordan shows male predominance, M:F was 2.4.1 in agreement with other studies from the region, in contrast to European and Japanese patients, where female predominance is observed (3, 8). 35.3% of patients with BD had a lower level of education (high school or less) compared to 9.9% of the whole group, reflecting a lower socioeconomic status and supporting environmental factors in the aetiology of BD.

A limitation of our survey was that only 60/142 (42%) of the individuals with ROU agreed to be investigated further, even after being contacted several times. This was probably due to the fact that Jordan is a small country and people are not keen to exchange their medical conditions with others. It is quite possible that the prevalence for BD we found in this survey would have increased even more, had these individuals agreed to be examined further.

The estimated prevalence of RA was 8/2569=0.00311, 31.1:10000 with higher mean age of patients 43.38±7.52y when compared to the whole group and the group with BD. Female predominance was also noted F:M was 3:1, in agreement with other studies.

The questionnaire used in the study also included questions on the presence of other rheumatic diseases, including RA, for mainly 2 reasons: a) to find the prevalence and b) to test the credibility of our results.

The data were then compared with that from Saudi Arabia and some parts of Turkey (Table V). In contrast with the high frequency of BD in Jordan compared to other geographical areas, the frequency of RA was found to be comparable to that reported from Saudi Arabia 0.22% (19) and some parts of Turkey (20), where the prevalence of RA in Antalya was 0.38% and in contrast to that reported from Northern European countries, where the prevalence is reported to be around 1% (21). We like to think that these data give reasonable support to our findings in this survey.

Conclusions

In this first survey of BD in Jordan, our results indicated that the prevalence of BD in the north of Jordan is among the highest around the world, at 66:10.000, similar to that reported from some parts in Turkey. Genetic factors probably play an important role in the development of BD in Jordan.

Finally, further work from other hospitals at different geographical areas and a conventional epidemiological study from North Jordan, will better judge the validity of our novel approach for comparative epidemiology.

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