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ORIGINAL ARTICLE

Qualify Of Life and Fatigue in Behcet Disease Patients and it's Relation with Disease Activity and Damage

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ABSTRACT

Background: Behcet Disease (BD) is a multisystem recurrent inflammatory disorder can range from minor mucous and skin lesions to potentially fatal lesions. As fatigue and health-related quality of life (QoL) assessment aids medical professionals in implementing clinical procedures efficiently, identifying their social, emotional, and physical requirements, and enhancing the standard of care.

Methods: This current cross-sectional observational study include 72 BD patients in Egypt, all of them subjected to assessment of disease activity, disease damage, QoL and fatigue using (The Behçet's Disease Current Activity Form (BDCAF), Behçet's Damage Index (BDI), Arabic version of BD-QOL questionnaire and Fatigue assessment scale (FAS)) respectively.

Results: This current research included 72 participants with age range from 18 to 61 years and male predominance (73.6%). About 53% had poor QoL and 73.6% had mild to severe fatigue. There is statistically significant relation between fatigue and patients' age, duration of the disease, BDCAF, BDI and neurological affection, ($P < 0.05$). There is strong statistical correlation between QOL and patients' gender females mainly, disease duration, BDCAF.

Conclusions: There was significant correlation between QOL and fatigue in BD patients and disease activity and damage.

Keywords: Behçet's disease, Fatigue Assessment Scale, Quality of life.

INTRODUCTION

Behcet Disease (BD) is a chronic, multiorgan inflammatory vascular disease of uncertain etiology. Skin lesions, uveitis, and recurring oral and vaginal ulcers are among the most prevalent clinical signs of BD [1].

BD extending from Turkey and Iran to Korea and Japan where the predominance of human leukocyte antigen-B (HLA-B*51) is relatively high, in comparison with the rest of the globe [2]. Reported prevalence has found to be as high as > 1 case per 1000 population in Turkey [3].

The disease has a high rates of morbidity and mortality, especially if it affects ocular, central nervous system (CNS) and vascular system [5]. Patients with BD patients have physical and mental symptoms and so have problems in daily life.[6].

Fatigue present in many rheumatological and non rheumatological diseases. Patients with BD may have negative effects such as, fatigue, anxiety, depression, and a decline in QOL. These symptoms may be connected to the disease's activity or the functional impairment it causes [7].

In addition to causing chronic discomfort, BD can have an impact on activity levels and bodily function. Anxiety levels are also impacted by functional limitations and a stressful existence brought on by the disease process. The immune system is suppressed by prolonged stress. Therefore, BD symptoms may affect the QOL [8].

The current study aimed to detect QOL and fatigue in patients with BD and its relation with disease activity and damage

METHODS

Ethical approval

The Institutional Review Board (IRB) at the Faculty of Medicine, Zagazig University Hospitals gave its approval to the study (ZU-IRB# 704/8) in line with the 1964 Helsinki Declaration, which is the World Medical Association's Code of Ethics for Human Research. Written informed consents were gathered from all participants.

Study Design

A cross-sectional observational study performed at the follow-up and inpatient units of the Rheumatology and Rehabilitation at Zagazig University Hospitals (ZUHs)

Study participants

All the eligible patients involved in this study were >16 years old and were meeting Behcet's Disease International Criteria (ICBD) [9]. On the other hand, participants with other autoimmune disorders, seronegative spondyloarthropathies, infections, malignancies, liver affections, renal diseases, or pregnant patients were excluded from this work.

Sampling and selection of patients

Assuming all cases met the inclusion and exclusion criteria of Behcet's Disease during the study period, 72 cases were included as a comprehensive sample. Data was collected through clinical consultations including history taking, full clinical examination, patient questioners, disease activity and damage assessment and laboratory investigations including complete blood picture (CBC), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR).

Activity of the disease was assessed by BDCAF [10], also assessment of damage in BD patients by (BDI) score [11].

All participants enrolled in the study subjected to assessment of QOL by Arabic version of BD-QOL questionnaire [12], also fatigue assessed by Arabic version of FAS [13].

Statistical analysis

SPSS (Statistical Package for the Social Sciences) version 27 was used to analyze the data. The chi square test was used to compare and characterize categorical variables based on their absolute frequencies. Kolmogorov–Smirnov test was used to verify assumptions for use in parametric tests. Depending on the type of data, the means, standard deviations, median, and interquartile range were used to characterize quantitative variables. The independent sample t test (for regularly distributed data) and the Mann Whitney test (for non-normally distributed data) were employed to compare quantitative data between two groups. To find independent risk factors linked to specific health conditions, binary logistic regression was utilized. Spearman rank correlation coefficient was used to measure strength and association of correlation between two continuous not normally distributed variables. $P < 0.05$ was chosen as the threshold for statistical significance. There was a highly significant difference if $p \leq 0.001$.

RESULTS

The current research comprised 72 participants with age range from 18 to 61 years and male predominance (73.6%). About 56%, 42%, 36%, and 32% had eye affection, neurological, oral ulceration and arthritis, respectively. The duration of the disease ranged from 1.5 to 26 years. About 42% of patients had active diseases About 53% had poor QoL (BD-QoL) while 73.6% had mild to severe fatigue (Table-1). Fatigue was associated with higher patients' age, long disease duration, higher body mass index (BMI), BDCAF, BDI, CRP and neurological affection, $P < 0.05$ (Table 2). Moreover, there is a significant statistical association between quality of life and patients'

gender females mainly, disease duration, BDCAF (active patients), high CRP, oral ulcer, arthritis, gastrointestinal tract affection and retinal vasculitis in addition to patients who receiving nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids (CCS), and biological therapy, $P < 0.05$. Also, there is relationship that is statistically significant between QOL and fatigue and BDI scores (Table 3). Predictors of fatigue include BDI (AOR 1.668, $p \leq 0.001$), BMI (AOR =1.288, $p = 0.012$), while predictors of poor QOL include

active disease by BDCAF (AOR= 17.830, $p=0.049$), disease duration (AOR=0.61 , $p=0.056$), and retinal vasculitis (AOR=542.7, $p=0.047$) (Table 4). Also there is a significant positive correlation between FAS and both BDI ($r=0.763, p<0.001$) and BDCAF ($r=0.769, p<0.001$) , also there is significant positive correlation between BD-QoL and both BDI ($r=0.526, p<0.001$) and BDCAF ($r=0.371, p<0.001$) (Figure 1).

Table 1: Demographic data of the studied patients.

Variables	BD patients (n=72)
Gender	
Female (N. %)	19 (26.4%)
Male (N. %)	53 (73.6%)
Age (years)	
Mean \pm SD	35.1 \pm 9.05
Range	18 – 61
Disease duration (years)	
Median	8
Range	1.5-26
IQR	5 -11.25
BMI (kg/m2)	
Mean \pm SD	26.26 \pm 4.52
Range	18 – 40
Clinical symptoms	
Oral ulcer(N. %)	26 (36.1%)
Genital ulcer(N. %)	22 (30.6%)
Arthritis(N. %)	23 (31.9%)
Eye (N. %)	47 (56.3%)
Uveitis (N. %)	26 (36.1%)
Retinal vasculitis (N. %)	13 (18.1%)
CNS(N. %)	30 (41.7%)
GIT(N. %)	11 (15.3%)
Vascular (N. %)	17 (23.6%)
• Vascular (venous) (N. %)	17 (23.6%)
• Vascular (arterial) (N. %)	6 (8.3%)
BDCAF	
Median	2
Range	0 – 8
IQR	1-5
Active (N. %)	24 (33.3%)
BDI	
Median	6
Range	0 – 16
IQR	4-10
ESR (mm/hr)	

Variables	BD patients (n=72)
Median	21
Range	3 – 66
IQR	12.25- 35
CRP (mg/L)	
Median	5.75
Range	0.5 – 33
IQR	3.7-12
Medications	
Analgesia (N. %)	18(25%)
NSAIDs(N. %)	20(27.8%)
CCS(N. %)	57(79.2%)
Azathioprine (N. %)	44(61.1%)
Cyclophosphamide (N. %)	10(13.9%)
Colchicine (N. %)	49(68.1%)
Biological therapy(N. %)	32(44.4%)
BDQoL	
Median	17
Range	3 – 29
IQR	11-23
<17 (Good) (N. %)	34(47.2%)
≥17 (poor) (N. %)	38(52.8%)
FAS	
Median	25.5
Range	11 – 45
IQR	21.25-31.75
Fatigue (N. %)	53(73.6%)

IQR interquartile range **CCS** corticosteroids, **CRP** C - reactive protein **NSAIDs** nonsteroidal anti-inflammatory drugs.

Table 2: Association of fatigue of studied patients and different patients' characteristics.

	BD without fatigue n=19	BD with Fatigue n=53	Test	p
Gender				
Female(N. %)	5 (26.3%)	14 (73.7%)	0 ^{\$}	0.993
Male (N. %)	14 (26.4%)	39 (73.6%)		
Age (year)[mean ± SD]	30.42 ± 7.88	36.77 ± 8.92	-2.742 [∞]	0.008*
BMI [mean ± SD]	24.0 ± 3.96	27.08 ± 4.47	-2.649 [∞]	0.01*
Disease duration (year) [median(IQR)]	4(2.5 – 9)	8(6.5 – 12.5)	-3.036 [¥]	0.002*
BDCAF[median(IQR)]	1(1 – 2)	3(1 – 5)	-3.123 [¥]	0.002*
Active (N. %)	2 (8%)	23 (92%)	6.667 ^{\$}	0.01*
BDI [median(IQR)]	4(3 – 5)	9(5 – 11.5)	-4.448 [¥]	<0.001**
ESR [median(IQR)]	23(14 – 27)	20(11.5 – 38)	-0.07 [¥]	0.944
CRP [median(IQR)]	6(3.1 – 11)	5.5(4 – 13.5)	-2.999 [¥]	0.003*
Clinical symptoms				
Oral ulcer(N. %)	7 (24.1%)	22 (75.9%)	0.127 ^{\$}	0.722
Genital ulcer (N. %)	5 (33.3%)	10 (66.7%)	0.47 ^{\$}	0.493
Arthritis(N. %)	3 (15%)	17 (85%)	1.849 ^{\$}	0.174
Eye (N. %)	14 (22.6%)	48 (77.4%)	3.333 ^{\$}	0.068
• Uveitis(N. %)	4 (33.3%)	8 (66.7%)	0.357 ^{\$}	0.55

	BD without fatigue n=19	BD with Fatigue n=53	Test	p
• Retinal vasculitis (N. %)	6 (40%)	9 (60%)	1.087 [§]	0.179
CNS(N. %)	4 (12.1%)	29 (87.9%)	6.384 [§]	0.012*
Vascular (N. %)	3 (17.6%)	14 (82.4%)	0.876 [§]	0.349
GIT(N. %)	4 (36.4%)	7 (63.6%)	0.665 [§]	0.415
Medications				
Analgesia	4 (22.2%)	14 (77.8%)	Fisher [§]	0.764
NSAIDs	5 (25%)	15 (75%)	0.027 [§]	0.868
CCS	14 (24.6%)	43 (75.4%)	0.47 [§]	0.493
Azathioprine	13 (29.5%)	31 (70.5%)	0.58 [§]	0.446
Cyclophosphamide	3 (30%)	7 (70%)	Fisher [§]	0.717
Colchicine	14 (28.6%)	35 (71.4%)	0.376 [§]	0.54
Biological therapy	10 (31.2%)	22 (68.8%)	0.701 [§]	0.403

IQR interquartile range [§]Chi square test [¥]Mann Whitney test [∞]independent sample t test *p<0.05 is statistically significant

Table 3: Association of quality of life of studied patients and different patients' characteristics.

	BDQOL ≥17 Good {n=34(%)}	BDQOL <17 Poor {n=38(%)}	Test	p
Gender				
Female	13 (68.4%)	6 (31.6%)	4.654 [§]	0.031*
Male	21 (39.6%)	32 (60.4%)		
Age (year)[mean ± SD]	33.15 ± 9.25	36.84 ± 8.62	-1.754 [∞]	0.084
BMI [mean ± SD]	25.44 ± 3.93	27.0 ± 4.93	-1.472 [∞]	0.145
Disease duration (year) [median(IQR)]	7(4 – 10)	9(7 – 12.75)	-1.986 [¥]	0.047*
BDCAF[median(IQR)]	2(1 – 5)	2(1 – 5)	-4.95 [¥]	<0.001**
Active	4 (16.7%)	20 (83.3%)	13.486 [§]	<0.001**
BDI [median(IQR)]	5(3 – 7.25)	10(5 – 13)	-4.574 [¥]	<0.001**
FAS [median(IQR)]	22(18.75 – 25.25)	30.5(24 – 35.25)	-5.004 [¥]	<0.001**
Absent	14 (73.7%)	5 (26.3%)	7.252 [§]	0.007*
Present	20 (37.7%)	33 (62.3%)		
ESR [median(IQR)]	16.5(10 – 28.25)	22(15 – 39.5)	-1.846 [¥]	0.065
CRP [median(IQR)]	4(1.8 – 4.63)	12(7.6 – 19.75)	-6.802 [¥]	<0.001**
Clinical symptoms				
Oral ulcer	7 (24.1%)	22 (75.9%)	10.382 [§]	<0.001**
Genital ulcer	6 (40%)	9 (60%)	0.397 [§]	0.529
Arthritis	3 (15%)	17 (85%)	11.536 [§]	<0.001**
Eye	28 (45.2%)	34 (54.8%)	0.761 [§]	0.383
• Uveitis	3 (25%)	9 (75%)	2.853 [§]	0.091
• Retinal vasculitis	3 (20%)	12 (80%)	5.634 [§]	0.018*
CNS	12 (36.4%)	21 (63.6%)	2.882 [§]	0.09
Vascular	5 (29.4%)	12 (70.6%)	2.833 [§]	0.092
GIT	9 (81.8%)	2 (18.2%)	6.235 [§]	0.012*
Medications				
Analgesia	11 (61.1%)	7 (38.9%)	1.858 [§]	0.137
NSAIDs	5 (25%)	15 (75%)	5.487 [§]	0.019*

	BDQOL ≥ 17 Good {n=34(%)} Good {n=34(%)}	BDQOL < 17 Poor {n=38(%)} Poor {n=38(%)}	Test	p
CCS	22 (38.6%)	35 (61.4%)	8.168 [§]	0.004*
Azathioprine	21 (47.7%)	23 (52.3%)	0.012 [§]	0.914
Cyclophosphamide	4 (40%)	6 (60%)	Fisher [§]	0.74
Colchicine	21 (42.9%)	28 (57.1%)	1.173 [§]	0.279
Biological therapy	10 (31.2%)	22 (68.8%)	5.896 [§]	0.015*

IQR interquartile range [§]Chi square test [¶]Mann Whitney test [∞]independent sample t test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

Table 4: Multivariate regression analysis of predictors of fatigue and poor quality of life

	Predictors	B	p	AOR	95% C.I.	
					Lower	Upper
Fatigue	BDI	0.512	0.001**	1.668	1.244	2.238
	BMI	0.253	0.012*	1.288	1.057	1.559
Poor QOL	BDCAF(active)	2.881	0.049	17.830	1.007	315.819
	Disease duration	-.494	0.056	0.610	.367	1.013
	BDI	1.778	0.033	5.920	1.153	30.405
	CRP	1.333	0.041	3.792	1.059	13.581
	Retinal vasculitis	6.297	0.047	542.706	1.084	271777.514

AOR adjusted odds ratio CI Confidence interval **p≤0.001 is statistically highly significant

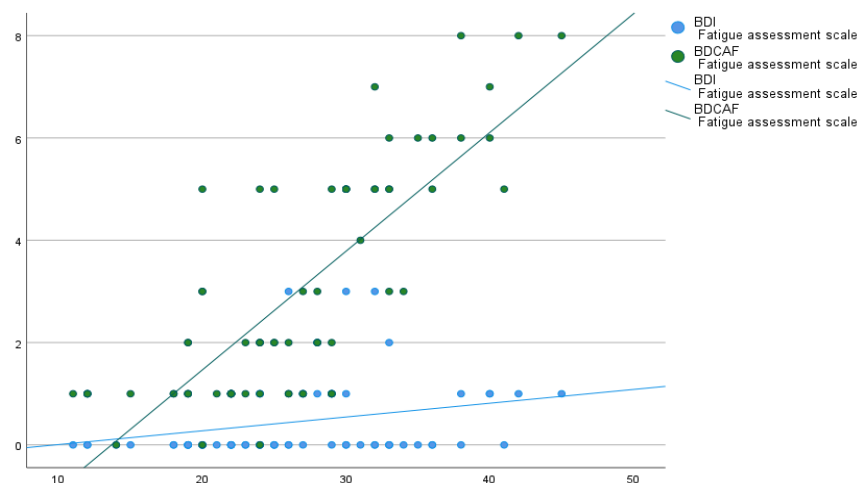


Figure (1-a) Scatter dot plot showing substantial positive correlation between fatigue assessment scale and both BDI ($r=0.763, p<0.001$) and BDCAF ($r=0.769, p<0.001$)

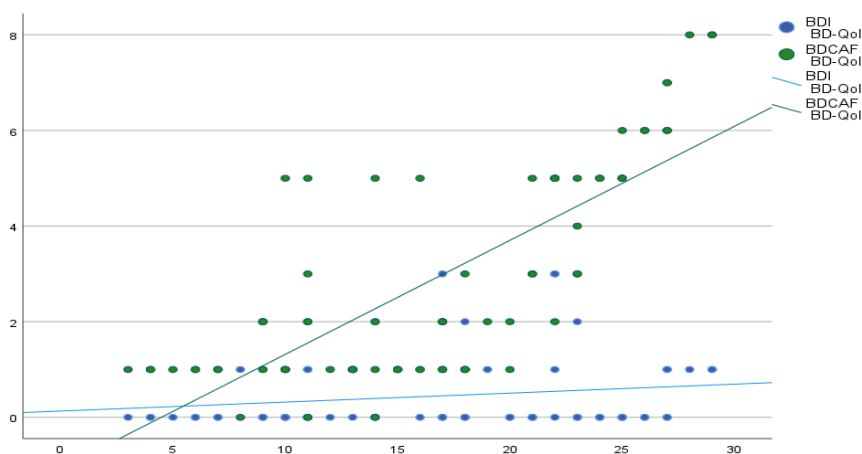


Figure (1-b) Scatter dot plot showing significant positive correlation between BD-QoL and both BDI ($r=0.526, p<0.001$) and BDCAF ($r=0.371, p<0.001$)

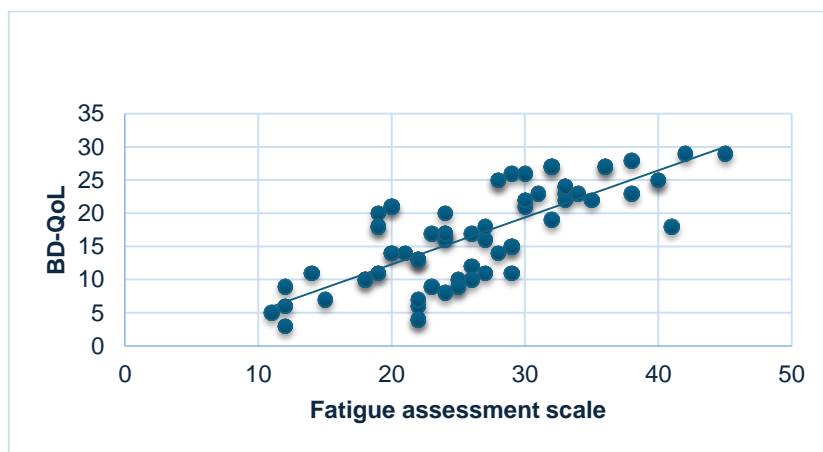


Figure (1-c) Scatter dot plot showing significant positive correlation between BD-QoL and fatigue assessment scale ($r=0.777, p<0.001$)

DISCUSSION

Behcet's disease is an autoinflammatory disease with vasculitis the main pathological manifestation. BD characterized mainly by mucocutaneous, ocular and vascular lesions and arthritis [14]

The current study assessed the relation of QOL and fatigue in BD patients with disease activity and damage.

Most of previous studies reported that the QOL in patients with BD was negatively affected by the activity [15].

Our study viewed significant relationship between QOL in BD patients and disease activity. There is significant association between QOL and gender, mainly the females, disease duration, oral ulcers, arthritis,

gastrointestinal affection, increased CRP, retinal vasculitis and patients who received biologics, systemic corticosteroids and NSAIDS.

In agreement with us, a study showed that the QOL is affected in BD and this impairment related to disease activity and severity [16].

Khabbazi et al, viewed that the quality of life in patients with BD was low and it is associated with disease severity, arthritis, eye and vascular involvement [17]. A similar study reported that BD patients had a poor physical impact, mainly due to joints, eye and other organ involvement and also affects their psychology. It showed that the low QOL correlated with increased disease activity and severity [18].

Regarding to patients sex, there was study found that females have more disease activity, despite males have more impaired QOL than female. Other finding in this study, which not consistent with our findings, reported that mycophenolate mofetil use was correlated with lower QoL among BD patients [19].

Canpolate et al, concluded that BD patients has low QoL and it is associated with gender, age, work status, education status as well as oral and genital ulcers, arthritis, skin lesions and bodily pain [20].

In agreement with us Ertam et al, showed that vascular, eye affection and arthritis associated with low QOL in BD patients [21].

Sahin et al, proved that BD was associated with low QoL in children patients and and also disease duration was an influencing factors [22].

A systematic review by Mastrolia et al, reported that among 47 different tools that were used to evaluate QoL in patients, the only tool specifically for BD was BD-QoL, that we used its Arabic version in our study [23].

Organ damage as a result of the disease or the drugs used in its treatment was influencing QoL. Long use of steroid was associated with organ damage and low of QoL, while usage of immunosuppressive drugs protect against of damage [24]

Another study viewed that low QoL in BD patients was correlated with high disease activity and damage [19].

Also in agreement with us Dhrif AS reported that the presence of neurological affection and organ damage are associated with low QOL in BD and there was correlation between vascular damage index and mental health and vitality domain of short form(SF-36) questionnaire [30].

Also similar to our results, Floris discovered that impairment of several components of HR-QoL, particularly those linked to mental health, was correlated with the accumulation of organ damage rather than its severity

Our study reported significant relation between fatigue and age, BMI, disease duration, damage

index, CRP, neurological affection and disease activity (BDCAF).

There was a study reporting increase fatigue and fibromyalgia in patients with BD [25].

Ilhan et al, reported that fatigue is common in BD patients with active disease and it is significantly correlated with depression ,anxiety and physical dysfunction. In contrast to our study, fatigue not associated with sex or major organ involvement [26]

Tascilar et al, reported that BD patients had high rates of fatigue, poor QoL and sleep disorder [27].

Unlike our findings, Saliva et al, showed that patients with active behcet disease had no higher levels of fatigue [28].

Another study showed that fatigue is common problem in BD patient and it was correlated with disease activity. It also observed correlation between QoL and fatigue BD patients [29].

The discrepancy between our findings and other studies may be attributed to differences in studied patients.

The main limitation in our study was the small sample size.

CONCLUSION

Quality of life is impaired and fatigue is common in BD patients and they are related to disease activity and damage.

Authors' contributions: All authors had made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content. The final manuscript has been read and approved by all authors.

Authorship:

All authors had made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content.

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