Patients' experiences with Behçet's syndrome: structured interviews among patients with different types of organ involvement

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ABSTRACT

Objective. *Behçet's syndrome (BS) is a multisystem variable-vessel vasculitis with significant life impact. The aim of this study was to explore the perspectives of patients with BS with different types of organ involvement.*

Methods. *Semi-structured qualitative interviews were conducted with 20 patients with BS with different types of organ involvement. Interviews were audio-recorded, transcribed, and translated into English. A Grounded Theory approach was employed in thematic analysis of translated interviews.*

Results. *Interviews with participants yielded four themes, including* symptoms *(skin problems, pain, vision problems, fatigue/sleep disturbances, and gastrointestinal/weight loss),* impact on function *(impact on speech and vision, mobility, energy for tasks, adaptations, and self-care),* psychological impact *(emotions and emotional management techniques), and* social impact *(ability to socialise generally and impact on familial relationships).*

Conclusion. *Patients with BS identified several domains, including physical functioning, psychological state, and social identity that are significantly modulated by the symptoms of BS. Those are inter-related with physical symptoms, reflecting the multi-system character of BS, and impair patients' function impacting on psychological and social identities. This work advances an understanding of BS, and will be useful in developing patient-oriented outcome measures for use in studying BS.*

Introduction

Behçet's syndrome (BS) is a variable-vessel vasculitis that affects multiple organ systems and is characterised by recurrent oral and genital ulcers, papulopustular and nodular lesions, uveitis, arthritis, and involvement of the vascular, neurologic, and gastrointestinal systems. Unique to BS, the underlying pathology involves vasculitis affecting both arteries and veins of all sizes. Although the pathogenesis of BS is not fully understood, the inflammatory processes of BS are currently attributed to genetic susceptibility with alterations in host-environment responses (1, 2).

BS is a rare condition ranging from 2-10 cases per 100,000 in most geographies (3). The syndrome is most common in Turkey (80-320 cases per 100,000), with the highest affected populations found between Eastern Asia and the Mediterranean (4-7). The prevalence of BS is somewhat higher in men, tends to show differences in the frequency of certain manifestations among men and women, and affect adults between 20 to 40 years of age (3, 4). Little is known about patients' experiences of living with BS (8). The specific aims of this project were to develop an initial description of the lived experiences of patients in order to better understand patients' perceptions of BS and guide the selection and development of patient-reported outcome measures for use in clinical trials of BS.

Methods

The study included patients with BS who were seen at the Cerrahpasa Medical Faculty Behçet's syndrome outpatient clinic between March and May 2016. Purposive sampling was used to select patients according to their types of organ involvement to ensure all types of patients with BS were represented. Patients with neurological involvement were included in the study if the patient had the ability to verbally express him/herself. Eligible patients were enrolled after obtaining written informed consent. The study was approved by Istanbul University-Cerrahpasa Medical School Ethical Review Board.

The interview guide was developed after a review of the literature by experts in BS and qualitative methods. The interview guide was designed as an open-ended, semi-structured discussion with patients to elicit narratives about patients' experiences living with BS, including items generating discussion of the physical symptoms experienced by patients with BS and the impact of BS on the lives of those affected. The interviews incorporated 7 conceptual components (disease onset, diagnostic experience, treatment history, disease remission, disease flare, quality of life, and mental health impact) and 41 open-ended questions. All of the interviews of patients with BS disease were conducted in person, in their native language of Turkish, by the same researcher (YO). Interviews lasted between 30 and 60 minutes. The audio files of the interviews were transcribed, translated to English by one of the investigators (MG), and the translated transcripts were checked by the senior author (GH). De-identified data were entered into NVivo 11 to facilitate thematic coding.

The study team utilised a grounded theory approach to develop themes, patterns, and ultimately a conceptual model driving outcomes (9-11). Grounded theory methodologies represent a discovery-based approach used to construct conceptual models and inductive theories arising directly from the data used to explain stakeholder perspectives without pre-conceived bias. Grounded approaches involve an iterative and in-depth review of open-ended responses, identification of emergent themes and higher level constructs arising from the data, and refining codes (*i.e.* themes). The codes were used to categorise the data and ultimately inform the construction of the theory explaining stakeholder perspectives regarding the phenomena under study, in this study the patient experiences of BS. The codebook of the salient themes that emerged from the interviews was developed and reviewed by study team members to define higher-order categories across identified themes. During inter-rater agreement meetings, two reviewers established strong post-inter-rater reliability (κ=0.99) with four (20%) of the interviews. The remaining interviews were coded independently.

Table I. Characteristics of patients with Behçet's syndrome participating in the study.

Number of patients	20
Median age [range]	36 years [29-46]
Sex	Female: 5/Male: 15
Education (%)	≤ High School: 16 (80) > High School: 4 (20)
Marital status (%)	Single: 7 (35) Married: 13 (65)
Employment status (%)	Employed: 10 (50) Unemployed due to disability: 5 (25) Homemaker: 5 (25)
Type of organ involvement (%)	Isolated mucocutaneous: 2 (10) Eye: 10 (50) Vascular: 8 (40) Joint: 6 (30) Neurologic 5 (25) Gastrointestinal: 3 (15)
Median disease duration [range]	11 years [9-18]

Results

A total of 20 respondents, 15 men and 5 women, were sampled. The median age was 36 years (IQR: 29-46) and the median disease duration was 11 years (IQR: 9-18). Five (25%) of the patients were unemployed due to the severity of their BS. Table I describes the characteristics of the respondents. Table II demonstrates that saturation was reached in all key domains. One sub-domain theme appeared later in the interviews, but saturation was reached for this sub-domain through one additional interview that confirmed the finding. The primary results identified in analyses were described using the following domains: *symptoms*, *impact on function*, *psychological impact,* and *social impact*. Table III summarises the main- and sub-themes and patients' quotes.

Symptoms

The most frequently symptoms shared by patients were sorted into five categories: skin problems, pain, vision problems, fatigue and sleep disturbances, and gastrointestinal concerns and weight loss.

Skin problems were shared by 19 patients with BS and included descriptions of genital or oral ulcers, pustules, nodular lesions or leg ulcers. Oral or genital ulcers often existed prior to the establishment of the diagnosis of BS and were thus unrecognised by patients and/or their doctors as symptoms of BS.

Pain was frequently discussed as an indicator of a flare, and patients experienced pain associated with their mucocutaneous lesions. Seventeen patients described pain with ulcers, general pain in the body, pain in the joints, leg, abdominal pain, or a headache.

Eleven patients described eye symptoms that affected sight, particularly blindness, blurry vision, eye swelling, or visual disturbances due to the disease. For some, eye symptoms represented the key symptoms that lead to their BS diagnosis; even if these participants presented with other symptoms previously, these symptoms were not attributed to BS.

Fatigue and disturbances with sleep were discussed by 9 patients. Patients described sleep deprivation and fatigue as a separate symptom or as a side-effect of a flare. Four participants noted that sleep deprivation and fatigue could later exacerbate their symptoms.

Four patients discussed gastrointestinal issues that affected their appetite and weight, especially if they experienced a flare of gastrointestinal involvement.

Table II. Saturation of a-priori themes.

		Participant number (1 = theme appears, 0 = theme does not appear)																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Impact	Level of physical function	1	1	0	0	1	1	1	1	1	1	1	1	1	0	0	0	0	0	1	0
	Personal mobility	0	1	1	0	1	1	1	0	1	1	1	0	1	1	1	0	1	0	0	0
	scope for travel	0	0	0	0	0	1	1	0	1	0	0	1	0	0	0	0	1	0	0	0
	Household tasks	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0
	Treatment consumes time/ focus	0	1	0	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0
	Adaptation	1	0	0	1	0	0	0	1	1	0	0	0	1	0	1	1	0	1	1	1
	Hobbies and interests	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
	Use of everyday transport	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0
	Eating and drinking	1	0	0	0	0	0	1	0	1	0	0	1	0	1	0	1	0	1	1	1
	Everyday technology	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Washing self	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Dressing and undressing	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	Speech	1	0	0	0	0	0	0	0	1	0	0	1	0	1	0	1	0	0	0	0
	Vision	0	0	1	1	1	0	1	0	1	1	0	0	0	0	0	1	0	1	0	0
Symptoms	Fatigue	1	1	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0
	Cognition and poor concentration	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Issues related to body weight	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Sleep symptoms	1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	0	1
	Temperature instability	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0
	Skin and nail problems	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1
	Earache and hearing difficulties	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Upper respiratory tract	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Eye symptoms and affected sight	0	1	1	0	1	1	1	1	1	1	0	0	0	0	0	1	0	1	0	1
	Cardiorespiratory symptoms	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Gastrointestinal symptoms	1	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0
	Muscle symptoms	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Numbness and nerve symptoms	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	Joint symptoms	1	0	0	1	0	0	1	1	1	0	0	1	0	1	1	0	0	1	0	0
	Kidney and urinary tract	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Appetite	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
	Sense of taste	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Feeling unsteady or faint	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Pain	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Psychological	Uncertainty/concerns about future	0	0	0	0	1	1	1	1	1	1	0	0	0	0	1	0	0	1	0	1
	Fear anxiety stress	1	0	1	1	1	0	1	1	1	0	1	0	0	0	1	0	1	0	0	1
	AAV dominates	0	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	0
	Self-efficacy	1	0	0	1	1	0	0	0	1	1	0	0	0	0	0	1	1	0	0	0
	Information and knowledge	1	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	1
	Support	1	0	1	0	1	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0
	Depression low mood	1	1	1	0	1	1	0	1	0	1	0	0	0	0	0	1	0	0	1	0
	Anger and irritation	1	1	0	0	0	0	1	1	0	1	0	1	0	1	0	0	0	0	0	0
Social perceptions	Visibility of condition or side effects	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Empathy and emotional connections	1	0	1	1	1	0	0	1	0	0	0	0	1	0	1	1	1	0	0	0
	Source of other people's worry	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	1	1	0	0
Social contact	Impact on social life	1	1	0	0	1	1	0	1	1	1	1	1	0	1	1	1	0	1	0	0
	Social activities and participation	0	0	0	0	0	1	0	0	1	1	0	1	0	0	0	1	0	1	0	0
	Adaptations to facilitate social life	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Quality of communication	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	1	0
	Sex and intimate relationships	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Social role	Occupation or finances	0	1	1	1	1	1	1	0	0	1	0	0	0	0	1	1	1	0	0	0
	Family and family planning	1	0	0	0	1	1	0	1	1	1	0	1	0	0	1	1	1	1	0	0
	Dependency on others	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	Role identity and status	1	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0

Table III. Main- and sub-themes and representative examples of patients' quotes retrieved from the qualitative interviews.

Symptoms	
Mucocutaneous symptoms	• *After my oral ulcers started, I went to a lot of doctors. I went from doctor to doctor for one or two years. Some told me that I was sleeping with my mouth open and my mouth got infected, some told me some other things etcetera, and then I went to every hospital around [CITY]. I had only not gone to [CITY] and such big hospitals and finally a friend told me to go to [DISTRICT of CITY] and I was diagnosed there.* (Patient 07)
Pain	• *I remember. I can tell approximately (pause). It started when I was about 25 years old. Now I'm 48. There was swelling in my legs and pain. That's how it started, lots of swelling in my leg, pain and a feeling of fatigue. It started this way.* (Patient 02) • *Well when it does flare small red patches appear and cause me a lot of pain. Two days ago this place got really red (points at leg) and now it's going away. For three days it makes me unable to concentrate, it gives me a lot of pain but then it passes away… Well these pains, these aches, these ulcers, they made everything a lot more difficult.* (Patient 06) • *Physically, I couldn't eat because of my oral ulcers, I had multiple oral ulcers, about 10 or 15, so you can't talk you can't eat and it coincided with my high school, so it affected my school as well, regarding attendance. Plus, I mean there were also the pains associated with it.* (Patient 16)
Eye symptoms	• *As a year, it started in 1973, when I was fifteen, first in my oral and genital regions. Then it struck my eye in a severe fashion, and then I went to a hospital and the rest continued with the treatment… Physically it was severe. As for my body, it was quite severe. In my eye it started as blindness, severe genital ulcers appeared, and later these appeared on my other side.* (Patient 03) • *It started in early 2000's with an episode in my eye. At least that was how I noticed it, maybe it did have some other things. I did have oral ulcers before, but very rarely, especially as I was completing my military service. But I noticed it after it hit my eye. My first doctor advised me to go to [UNIVERSITY NAME] so I came here and my file was opened.* (Patient 18) • *Eye episodes. I did have oral ulcers, and everyone has oral ulcers, I still see them in other people, these small spots. But they go away in like three to five days and return after 3 to 5 months. It was like that for me too. I had oral ulcers but I never thought about it. Then I had an episode in my eye, I lost my vision and I went to an ophthalmologist. […]. I came here and learned that I had uveitis and Behçet's. I was given medications and still continue using them.* (Patient 18)
Fatigue and sleep disturbances	• *There was swelling in my legs and pain. That's how it started, lots of swelling in my leg, pain and a feeling of fatigue. It started this way.* (Patient 02) • *Psychologically it affects me a lot. Most of the time, when I have oral ulcers, I feel lethargic, I can't do anything. I can't take care of my children and my husband. It affects me a lot. I often wake up at nights because of this pain. It also causes headache.* (Patient 12)
Gastrointestinal symptoms	• *When I get flares, I experience fevers, abdominal pain, CRP elevations, lack of appetite, nausea, umm, I mean diarrhea at times, sometimes I need to defecate 7 or 8 times per day.* (Patient 19)
Impact on function	
Impact on speech	• *My oral ulcers affected me a lot. They caused me a lot of pain, I couldn't talk, I couldn't eat, there was a lot of pain. The ones in my genital region were similar too, they were painful, so I was extremely restless at the time.* (Patient 14) • *In that regard I didn't have any problems. As I said, at times, I wonder if I bore people too much with my disease, and I learned to not say that. They could understand when I was worse, since you can't speak that fluently when you have oral ulcers. Your voice changes, you have to produce weird noises when you try to enunciate words…In my harder times, I try to not see or speak to anyone as much as I can, because it hurts when I speak.* (Patient 01)
Impact on vision	• *When I first came here my left eye was like striped, and a week after it closed off completely. As I was dealing with postponing my military service it hit my right eye too, my right eye became blind. And then I said immediately refer me somewhere else and that was how I came here. With treatment, it started to clear and now it's clear. (Patient 10)* • *I got a doctor's report because of my eye, I'm retired and I wish this didn't happen and I could work all my life. I mean, for bad effects, my favorite pastime was driving my car.* (Patient 18)
Impact on mobility	• *When it flared, I used to be unable to walk. That was the most severe complaint…I experienced that state in which I was unable to walk about once per year. But my leg constantly swelled up and got huge.* (Patient 02) • *Of course I mean [the symptoms] impaired my walking, my working, it impaired me in every regard.* (Patient 06)
Impact on daily activities and working	• *I take [my family] out but wherever I go I just have to sit around. So if we go to a mall, I have to sit down immediately and tell my family to wander around (without me), that I'll remain here. I can't fit their tempo. (Patient 06)* • *It does prevent me from living my daily life normally because I can't do most of my daily work, like 50%. I mean I can't work… The reason I can't work is because of the problems in my feet, I mean I can't work, I was given a 90% disabled report…So it affects my daily life by about 50%.* (Patient 09) • *It causes fever. You get fatigued because of the fever and because it leaves you so tired. You can't work. (Patient 08)* • *Yes. When I get sick, I have to lay [the house chores] off a little.* (Patient 12) • *It did affect the decisions I make. I didn't go on with private sector, I switched to governmental job. I established a calm, orderly life at an early age by marrying and having kids. I started to lead a more calm, slow, uneventful life. (Patient 20)*

Psychological impact	
Emotions	• *I feel very tired, as if I've not slept at all. You feel burdened, you don't want to do anything and even if you want to, you feel very tired. And it causes a lot of anger. One of the main effects of this disease on me was that I got excessively angry. (Patient 01)* • *It affected it greatly, I mean in a negative way. Back then it was. But now since I don't have as much problems as before, it no longer has a great impact that makes life more difficult. But now even small (and unrelated) wounds in my legs can affect me and demoralize me… You are a sick individual, you get grumpy and you reflect that to your surroundings.* (Patient 02) • *Yeah, let me put it this way, at first when my eye became, umm blind I had hysteric episodes of sobbing and crying.* (Patient 03) • *May God help Behçet's sufferers. I don't have anything else. I also wonder what awaits me next. Which body part will be affected next. Will I get blind or lame, I wonder (laughs). (Patient 10)* • *Psychologically… I get angry, I become angry. I think whether I'll be able to see again, if I'll never be able to see again, or will I never be able walk again.. I come in here and see people in worse conditions than I am. And it affects your mind, your thinking quite a bit. I'm afraid, I'm afraid that I'll not be able to see anymore. (Patient 07)* • *Emotionally it did give me some despair but later on I said to myself that this will be a disease that will live with me until I die so we must be friends. Then I tried to shake it off but it wasn't all that successful. Not much. (Patient 06)* • *When I get mad or stressed out, nothing happens during that day. But the day later, it starts to become manifest. My knee starts to develop an ache, I experience difficulty in walking, these things. Yes, after those I see that the usual symptoms start appearing on my legs.* (Patient 15)
Emotional management techniques	• *Psychologically it didn't affect me that much. At first, I was constantly thinking about the future and about my eye but I started to live with this, I accepted it. Right now there are no psychological effects, I'm in peace with my disease and I've come this far in my life. (Patient 18)* • *No, no, they went away. After that, I accepted my fate. I was going to live like that, I would take my medications. I accepted it and after I accepted it the rest just went on from there. I opened up, and after realizing that I would live like that, I started to make fun of myself, like I accepted it and that people surrounding me should also accept it as it is, this is who I am, that's what I said. That's still what I say. (Patient 05)*
Social impact	
Ability to socialize	• *I can't get out of the house. I don't have any social life anymore, it's over. The headache. I also feel like 70-year-old grandpa. (Patient 10)* • *2 years ago, when I could travel and walk normally, I was doing great with everyone, but after a certain stage of my disease had passed, I saw some people turn their backs on me, and this made me sad. Because this makes me sad, I don't want to say anything about it.* (Patient 09) • *As I told, the support groups, the trainings… They made it easier… The things that made it more difficult were the other people being ignorant (regarding this condition), them looking at you as a sick individual rather than an individual, them asking me suffocating questions (detailed in the social life section). I had some problems with some doctors. If the doctor doesn't know much about the disease, you don't either and you have a more difficult time in coming to terms with your disease. These things made life more difficult.* (Patient 05)
Impact on familial relationship	• *My husband did not accept my disease, I had lots of problems with my husband, our children were very young, there were three of them. When I think about this, this period comes to my mind. These were the things I had difficulty with, it was horrible. (Patient 05)* • *I get very angry. Excessively angry. Yesterday my child was taking a video of himself saying 'I'm a very fun person but I'm also as angry as my mother'. So I didn't enjoy hearing that to be honest. Seeing that's how I'm seen in his eyes, it made me sad, that's a bad thing. I need to eliminate this, I need to curb it but it's not up to me.* (Patient 01) • *I mean as for bad aspects, there have been many times when I was unable to be adequate for my family. There were many times when I wanted someone to be near me, when I needed their help. These are things everyone can experience. You can want someone to be near you even when you have a flu.* (Patient 01)
Impact on work	• *The things that made things worse were, I mean, since I'm a doctor, I can't just decide not to go to work on any given day because the patients come first. So even then, even during flares, I got to go to work and deal with my patients. This makes things difficult. The fever, the abdominal pain.* (Patient 19) • *It affected my work life as well. I can't work as much, I have to get doctor's notices, I experience problems with my bosses. I fear about getting fired. After all, this is a disease. (Patient 07)* • *My original profession is teaching. So, I'll put it this way, I graduated from a faculty of literature, and at the time I graduated with good grades in order to stay at school, so I was talented in that regard, but when my disease interfered with that profession, I left it.* (Patient 03)

Impact on function

Patients discussed broad impacts on function subsequent to their BS. The impacts were grouped into the following categories: impact on speech and vision, mobility, energy for tasks, adaptations, and self-care.

Five patients described that they could not talk because of painful oral ulcers. When BS involved the eye, 8 individuals described the loss of vision impacting their ability to work and one participant's ability to drive.

Loss of mobility is a symptom burden described by 15 patients with BS.

Based on patients' accounts, loss of mobility usually meant the inability to walk often due to leg swelling, knee joint pain, genital ulcers, or ulcers on the feet. This loss of mobility impacted patients' daily activities, including limitations working or limited ability to travel with friends and family.

Additionally, 13 patients discussed a reduced energy for their daily tasks. The patients said that the disease or being sick left them "tired", but also described resting as a treatment for their BS.

Due to the impact on their symptoms, 13 patients discussed a need to adapt. Individuals largely described an adaptation as 'doing less', including not driving, avoiding places or certain times of day because of visual problems, modifying their diet because of oral ulcers, performing less work, or changing careers.

Ten patients described the impact of oral ulcers on self-care, mostly because the oral ulcers affected individuals' ability to eat or drink.

Psychological impact

Psychological impact was described in two main categories: emotions and emotional management techniques. The emotions discussed are fear, anxiety, stress, depression, and anger. Overall, patients expressed a desire for more psychological support from their medical teams.

The emotional impact of the side-effects of BS was described by eighteen patients. Individuals discussed that the side-effects make them sad or angry, particularly the loss of mobility, the fatigue, low energy, or the treatments for BS.

Eleven patients expressed fear or worry about how the symptoms of BS would progress, if the symptoms would be more severe, or if individuals would have a complete lack of functioning. These patients described a "helplessness" regarding their inability to control the disease. Participants were sad or angry about their uncertain future, their disease progression, or if they would lose more functioning.

Eleven patients also indicated a relationship between stress and their disease, described stress exacerbating their disease, and cited stress reduction as a treatment technique for BS.

Psychological methods for disease management suggested by patients included psychological support for patients with BS to accept their chronic disease. Participants that described improvements or changes in their depression or anger also described an attitude of disease acceptance.

Eight patients desired more information from their medical team about their disease, and suggested more information about the disease at the time of diagnosis could help patients accept their disease sooner or help manage the psychological impact of BS.

Social impact

Social impact included two main categories: ability to socialise generally and impact on familial relationships. Fourteen patients described a decreased ability to socialise due to their symptoms. Oral ulcers negatively affected 5 patients' ability to talk and communicate with others.

Nine patients described being ostracised by others without the disease or uneducated medical staff, so it was helpful for some patients to talk to others with BS or utilise support groups.

Sixteen patients described that the disease had a large, negative impact on their familial relationships. Two patients cited the disease as a factor for deciding not to have children because of uncertainty about future progression of their disease.

Eleven patients discussed feeling "inadequate" because they cannot fulfill their duties, complete their daily tasks as needed, or are a burden to their caretakers.

Fifteen patients discussed the negative impact of BS on social duties, particularly family life and work. Patients expressed fear about being fired or a need to change career paths to accommodate for their disease.

Discussion

The results of this study indicate that the primary domains patients with BS experience include *symptoms*, *impact on function*, *psychological impact,* and *social impact*. The identified domains were inter-related with noted symptoms driving impacts in function which in turn impacted patients' psychological and social identities.

The described physical symptoms map well onto the clinical understanding of BS as a condition affecting multiple organ systems and noted for recurrent oral and genital ulcerations, and other skin lesions. The expanded understanding of how the physical symptoms of BS impact other patient-centered domains of health is critical to understanding patients' experiences of their disease, but also the ability to measure improvements in the lives of those affected by this disease through the identification or development of appropriate patient-reported outcome (PRO) measures.

There was a previous study exploring the impact of living with BS among 8 patients from New Zealand (12). This study reported several findings similar to the current study findings, including patients' experiences with physical symptoms, and the social and physiological impact of the disease. Symptoms such as pain, fatigue and visual impairment, social difficulties and lack of support were commonly in both groups, On the other hand, the rarity of BS in New Zealand revealed a difficulty in diagnosis and patients had concerns regarding receiving an incorrect diagnosis and inability to access appropriate care, and a lack of knowledge about the disease. Only 8 patients with BS were included and representation of patients with severe organ involvement such as vascular and neurologic involvement was minimal.

Another recent work exploring patients' experiences in BS was a focus-group interview study (13). Thirty-five patients with BS were included, however patients' characteristics, especially the type of organ involvement, were not clearly reported. Some of the themes such as symptoms and impact of symptoms on patients' life that were described were similar to the current study. However some important themes such as physiological and social impact did not clearly emerge in that study. Due to the nature of focus-groups, some topics may not be disclosed due to reluctance to discuss in group settings.

Limitations to consider when assessing the results of the current study include sampling biases and avoiding suggestions of causality as the qualitative methods used here were for hypothesis generation. Limitations to our sampling in a single geographic location include the consideration of how the range and emphasis of noted symptoms and functional impact may vary due to the cultural norms and variations present, thus potentially limiting generalisability. However, a notable strength in sampling from the country with the highest rates of BS enabled the inclusion of patients with all possible types of Behçet's lesions. Self-reported data may include biases from social desirability.

Although several generic measures such as SF-36, EQ-5D, MDHAQ and Beck depression scale were used to evaluate the quality of life and psychological, cognitive, or sexual effect of BS (14-18), there was only one BS-specific health related quality of life measure. The Behçet's Disease Quality of Life (BDQoL) measure has been used in clinical trials to address impact of disease on activities of daily living. This study showed that several items, such as work disability, difficulty in eating and drinking, difficulty in concentrating, suicidal ideation, anxiety, feeling judged or pitied by others, and sleep problems that were emphasised by the patients are not among the items assessed in BDQoL, indicating that different or additional PRO tools are needed to more comprehensively capture patients' experiences.

Future research should inform the development of PRO measures validated in the population of patients with BS. Advancement of PRO development would include sampling of patients with BS from other countries to explore the variation across geographies and cultures. PRO development would also include the development of items reflecting the primary symptoms and domains of impact with cognitive interviewing of items and validation across populations of patients with BS. Additional work could examine variations in the impact of BS and other forms of vasculitis.

This study has substantially expanded the understanding of patients' experiences with BS and helps lay the foundation for selection and/or development of PROs for the study of BS, including the conduct of clinical trials.

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