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Review Article

# Psychological Burden in Behçet Disease: A Narrative Review Across Mucocutaneous, Articular, and Ocular Manifestations

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ABSTRACT

**Background:** Behçet disease is a chronic, relapsing, multisystem inflammatory vasculitis in which mucocutaneous, articular, and ocular manifestations may coexist with substantial psychological burden.
**Methods:** This narrative review synthesized English-language literature identified through structured searches of PubMed/MEDLINE, Scopus, and Google Scholar, supplemented by reference-list screening. Searches were updated through 31 January 2026 and focused on depression, anxiety, stress, fatigue, sleep disturbance, and quality-of-life outcomes in non-neuro-Behçet contexts.
**Results:** The available literature suggests that depression and anxiety are frequent in Behçet disease and are associated with disease activity, pain, fatigue, sleep disturbance, and reduced quality of life. Mucocutaneous symptoms may contribute through pain, visible lesions, embarrassment, and impaired self-image; articular involvement through pain, stiffness, fatigue, and reduced mobility; and ocular disease through visual threat, repeated treatment, and impaired visual function. Sleep disturbance, fatigue, and reduced quality of life are closely interrelated and appear to amplify overall psychosocial burden.
**Conclusions:** Psychological burden is an important dimension of Behçet disease. Although direct evidence for a rigorously defined combined mucocutaneous-articular-ocular phenotype remains limited, the current literature supports a converging burden model across these domains.

## 1. Introduction

Behçet disease is a chronic, relapsing, multisystem inflammatory vasculitis with a heterogeneous clinical spectrum that may involve the mucosa, skin, eyes, joints, blood vessels, nervous system, and gastrointestinal tract [1, 2]. Among its most clinically recognizable manifestations are recurrent oral ulcers, genital ulcers, cutaneous lesions, ocular inflammation, and articular involvement [1–3]. Mucocutaneous lesions are often among the earliest and most persistent features, whereas ocular and musculoskeletal disease contribute substantially to morbidity, functional limitation, and impaired quality of life [1–3]. Because of its relapsing course, variable severity, and potential for irreversible organ damage, Behçet disease imposes a burden that extends beyond organ-specific inflammation alone [1, 2].

From a multidisciplinary clinical perspective, mucocutaneous, articular, and ocular manifestations are particularly important because they affect pain, mobility, appearance, visual function, and social participation [1–3]. Recurrent oral and genital ulceration may be painful, stigmatizing, and disruptive to eating, speech, and intimate relationships, while visible skin lesions may adversely affect self-image and confidence [1, 3]. Articular disease, typically presenting as recurrent arthralgia or non-erosive arthritis, may further contribute to pain, stiffness, fatigue, and reduced physical function [1, 2]. Ocular involvement, especially uveitis, is of particular concern because of its recurrent and potentially sight-threatening nature and its impact on independence and daily functioning [2, 4, 5].

A growing body of literature suggests that Behçet disease is also associated with substantial psychological burden, including depressive and anxiety symptoms, fatigue, maladaptive coping, and reduced health-related quality of life [4–8]. More recent review-level syntheses have further highlighted the burden of mental

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health issues in Behçet disease and their implications for patient quality of life [9, 10]. This burden is likely multifactorial, reflecting the cumulative effects of pain, recurrent flares, visible lesions, visual threat, disability, treatment burden, and uncertainty regarding prognosis [5–8]. In addition, patients with Behçet uveitis have shown higher levels of depression and anxiety, and poorer vision-related quality of life has been associated with worse psychological outcomes [4, 5]. At the same time, psychological burden in Behçet disease should not be treated as a single uniform construct, since psychiatric symptoms, fatigue, sleep disturbance, and quality-of-life impairment represent related but distinct domains [6, 8].

Given these considerations, a focused narrative synthesis is warranted. This review aims to summarize current evidence on the psychological burden reported in Behçet disease across the mucocutaneous, articular, and ocular manifestations, with particular attention to depression, anxiety, fatigue, sleep disturbance, and reduced quality of life. The review primarily addresses the psychosocial burden in non-neuro-Behçet contexts and interprets broader psychiatric findings with caution.

## 2. Methods

This manuscript is a narrative review that summarizes and critically discusses the literature on the psychological burden of Behçet disease across its mucocutaneous, articular, and ocular manifestations. The review focused on psychological and psychosocial outcomes in non-neuro-Behçet contexts, including depression, anxiety, stress, fatigue, sleep disturbance, and quality-of-life impairment.

Structured searches were performed in PubMed/MEDLINE, Scopus, and Google Scholar and were updated through 31 January 2026. Database-specific Boolean search strategies were used. The PubMed/MEDLINE search string was: (("Behcet Syndrome"[Mesh]) OR (Behcet*[tiab]) OR ("Behcet disease"[tiab]) OR ("Behcet syndrome"[tiab])) AND ((depress*[tiab]) OR anxi*[tiab] OR stress[tiab] OR fatigue[tiab] OR sleep[tiab] OR insomnia[tiab] OR "quality of life"[tiab] OR psychiatric[tiab] OR psychological[tiab]) AND ((mucocutaneous[tiab]) OR "oral ulcer"[tiab] OR "genital ulcer"[tiab] OR skin[tiab] OR ocular[tiab] OR uveitis[tiab] OR articular[tiab] OR arthritis[tiab]) AND english[lang]. The Scopus search string was: (TITLE-ABS-KEY("Behcet disease" OR "Behcet syndrome" OR Behcet*)) AND (TITLE-ABS-KEY(depress* OR anxi* OR stress OR fatigue OR sleep OR insomnia OR "quality of life" OR psychiatric OR psychological)) AND (TITLE-ABS-KEY(mucocutaneous OR "oral ulcer" OR "genital ulcer" OR skin OR ocular OR uveitis OR articular OR arthritis)) AND (LIMIT-TO(LANGUAGE, "English")). Google Scholar was used as a supplementary source to identify additional potentially relevant publications, and the reference lists of relevant reviews and original articles were also screened manually.

Eligible publications included original studies, cohort studies, case-control studies, cross-sectional studies, qualitative studies, and relevant narrative or systematic reviews addressing psychological, psychiatric, fatigue-related, sleep-related, or quality-of-life outcomes in patients with Behçet disease. Titles and abstracts were screened for relevance, followed by full-text assessment of potentially eligible publications. Data extracted for narrative synthesis included study design, sample characteristics, organ phenotype or clinical context, psychological outcomes, instruments used, main findings, and major limitations. Studies were included if Behçet disease was diagnosed according to accepted clinical or classification criteria used by the original authors. Most included studies used accepted Behçet disease classification criteria, particularly International Study Group (ISG) or International Criteria for Behçet's Disease (ICBD) criteria; however, some older studies were based on clinically diagnosed specialty cohorts and did not report a uniform diagnostic framework.

Studies primarily focused on neuro-Behçet or direct central nervous system involvement were excluded from the main synthesis because psychiatric, behavioral, and cognitive manifestations in neuro-Behçet may reflect primary neurological disease rather than psychosocial burden related to pain, disability, visible lesions, or visual threat. Non-English publications, conference abstracts without sufficient methodological detail, and studies lacking clear relevance to the review scope were excluded.

Because of the heterogeneity of study designs, phenotype definitions, and outcome measures, the evidence was synthesized narratively rather than quantitatively. Particular attention was given to distinguishing between psychiatric disorders, psychological symptom scales, fatigue and sleep outcomes, and generic or organ-specific quality-of-life measures. Several included studies contributed data to more than one outcome domain; therefore, repeated citation across sections should not be interpreted as fully independent confirmation across depression, fatigue, sleep, and quality-of-life outcomes.

## 3. Overview of Behçet Disease

Behçet disease is a chronic, relapsing, multisystem inflammatory vasculitis characterized by recurrent episodes of remission and exacerbation and a heterogeneous clinical spectrum [1, 2]. Current evidence supports a multifactorial pathogenesis involving genetic susceptibility, immune dysregulation, and environmental triggers, although the exact mechanisms underlying disease onset and organ-specific expression remain incompletely understood [1, 2, 11]. Clinically, Behçet disease is classically associated with recurrent oral ulcers, genital ulcers, and cutaneous lesions, but may also involve the eyes, joints, blood vessels, nervous system, and gastrointestinal tract [2, 11–13].

Among these manifestations, mucocutaneous, articular, and ocular involvement are especially relevant to the present review because they are common, recurrent, and closely linked to pain, functional limitation, and impaired quality of life [12, 14]. Mucocutaneous lesions are frequently the earliest and most persistent manifestations and remain central to both diagnosis and long-term disease burden [1, 3, 12]. Articular involvement usually presents as recurrent arthralgia or non-erosive, non-deforming arthritis, often affecting large joints and contributing to pain, stiffness, and reduced mobility [2, 13]. Ocular disease, particularly uveitis and retinal vasculitis, is among the most serious disease domains because of its recurrent nature and potential for irreversible visual impairment [2, 11, 14].

Taken together, Behçet disease should be understood as a multisystem inflammatory disorder whose consequences extend beyond organ-specific pathology alone. Recurrent symptoms, fluctuating disease activity, treatment burden, and the coexistence of painful, disabling, or vision-threatening manifestations may contribute to a broader illness burden that can affect psychological wellbeing and quality of life [8, 11–14].

## 4. Mucocutaneous Involvement

Mucocutaneous involvement is one of the most characteristic and often earliest domains of Behçet disease, and in many patients it remains a recurrent source of morbidity throughout the disease course [3, 12]. Recurrent oral aphthous ulcers are the most frequent manifestation and commonly represent the presenting feature. In contrast, genital ulcers, papulopustular lesions, and erythema nodosum-like lesions contribute to the typical mucocutaneous phenotype

[1, 12]. These manifestations are central not only to diagnosis but also to daily functioning. Oral ulcers may interfere with eating, swallowing, and speech, whereas genital ulcers may impair intimate relationships and contribute to embarrassment, avoidance, and social withdrawal [1, 3]. Visible cutaneous lesions may additionally affect body image, self-confidence, and interpersonal functioning, particularly in patients with recurrent or cosmetically distressing disease [3, 12].

From a psychological perspective, mucocutaneous disease is especially relevant because pain, visibility, recurrence, and unpredictability may all contribute to emotional distress and reduced quality of life [8, 12]. Reviews of the psychological burden of Behçet disease suggest that depression and anxiety are common, and this burden may be amplified in patients with active mucocutaneous disease because of stigma, discomfort, and limitations in social and occupational functioning [8]. More specifically, oral health and psychosocial wellbeing appear to be closely linked to clinical outcomes in Behçet disease, and Behçet-associated oral ulcers have been associated with poorer oral health-related quality of life and greater symptom burden [15, 16]. Recent work has also suggested that treatment response may mediate oral health-related quality of life in Behçet syndrome, further supporting the clinical importance of mucocutaneous symptoms as determinants of patient wellbeing [17]. In addition, dermatological quality of life has been shown to relate closely to disease activity, depression, and anxiety in Behçet syndrome, and qualitative work has highlighted the adverse effects of genital manifestations, painful intercourse, exhaustion, and communication difficulties on intimacy and relationships [18, 19]. Taken together, these findings indicate that mucocutaneous involvement should not be regarded as merely superficial disease, but rather as an important contributor to the broader psychosocial burden of Behçet disease [8, 15–19].

## 5. Articular Involvement

Articular involvement is one of the most frequent systemic manifestations of Behçet disease and is clinically important because it contributes directly to pain, reduced mobility, and functional limitation. Musculoskeletal symptoms usually present as recurrent arthralgia or self-limited, non-erosive, non-deforming arthritis, most often affecting large joints such as the knees, ankles, wrists, and elbows [1, 2, 13]. Although Behçet-related arthritis is generally not destructive in the same manner as other chronic inflammatory arthropathies, recurrent attacks may still impose substantial morbidity through pain, stiffness, impaired physical performance, and restriction of daily and occupational activities [2, 13].

Articular involvement is also relevant to psychological burden. Chronic or recurrent joint pain may worsen fatigue, reduce participation in work and social life, and contribute to anxiety, frustration, and depressed mood [8, 13]. In addition, musculoskeletal symptoms often coexist with mucocutaneous and ocular manifestations, creating a cumulative disease burden that may intensify illness perception and lower health-related quality of life [2, 8, 20]. Evidence from quality-of-life studies further suggests that arthritis, bodily pain, and related physical limitations are among the factors associated with worse quality-of-life scores in Behçet disease [21–26]. Taken together, these findings support the view that articular involvement should be considered not only a physical manifestation of Behçet disease, but also an important contributor to broader psychosocial burden and impaired daily functioning [8, 13, 21–26].

## 6. Ocular Involvement

Ocular involvement is one of the most serious manifestations of Behçet disease because it is recurrent, inflammatory, and potentially vision-threatening [2, 11, 14]. The most typical presentation is uveitis, which may affect the anterior or posterior segment and is often accompanied by retinal vasculitis, with repeated flares that can lead to cumulative ocular damage if inflammation is not adequately controlled [2, 14]. In many patients, ocular disease becomes a major determinant of disability and long-term quality of life, particularly when visual function is compromised [4, 5, 11, 14]. Because visual symptoms may fluctuate over time and the risk of relapse often persists even after treatment, ocular Behçet disease may generate a sustained sense of uncertainty regarding prognosis and future independence [5, 14].

The psychological relevance of ocular Behçet disease is therefore substantial. Fear of visual loss, uncertainty regarding relapse, repeated ophthalmic assessments and treatment, and reduced visual functioning may all contribute to emotional distress [4, 5]. Studies in patients with Behçet uveitis have shown higher levels of depression and anxiety, and poorer vision-related quality of life has been associated with worse psychological outcomes [4]. Longitudinal evidence also suggests that psychological status in Behçet disease is not explained by inflammatory activity alone, indicating that persistent psychosocial and illness-related factors contribute to the overall burden [5]. More recent quality-of-life data have also linked ocular involvement to poorer patient-reported outcomes in broader Behçet cohorts [27]. Taken together, these findings support the view that ocular involvement is not only an organ-threatening manifestation of Behçet disease, but also an important contributor to psychological burden and reduced quality of life [5, 14, 27].

## 7. Integrative Burden of Concurrent Mucocutaneous, Articular, and Ocular Manifestations

In Behçet disease, mucocutaneous, articular, and ocular manifestations are typically described as separate clinical domains; however, their burden may be cumulative when they coexist in the same patient. These manifestations affect distinct but interrelated aspects of daily life, including pain, mobility, appearance, visual function, social participation, and independence [1, 12–14]. Accordingly, the overall illness burden in such patients is unlikely to be explained by single-organ involvement alone, but rather by the interplay among recurrent symptoms, fluctuating disease activity, functional limitations, and uncertainty regarding prognosis [2, 5, 8].

Mucocutaneous disease may contribute through pain, visible lesions, embarrassment, and impaired self-image, whereas articular involvement adds recurrent pain, stiffness, fatigue, and reduced physical function [8, 12, 13]. Ocular disease may further intensify this burden by introducing fear of visual loss, repeated monitoring and treatment, and compromised visual functioning, all of which may adversely affect autonomy and quality of life [4, 5, 14]. In parallel, studies addressing oral health-related quality of life and psychosocial wellbeing suggest that symptom burden in one clinical domain may extend beyond local manifestations and influence broader psychological adjustment [15–17]. Illness perception may further mediate the relationship between symptom severity and perceived health status, indicating that psychological burden is shaped not only by manifestations themselves but also by how patients cognitively and emotionally interpret the illness [20]. Quality-of-life studies likewise indicate that pain, fatigue, physical limitation, employment status, and lifestyle factors are important correlates of reduced wellbeing in Behçet disease [8, 22, 23, 25, 26].

Importantly, the available literature more often supports this relationship indirectly than through studies of a rigorously defined combined mucocutaneous-articular-ocular phenotype. Therefore, it is more appropriate to interpret the evidence as suggesting a converging rather than definitively quantified burden. Nevertheless, the current data support the view that concurrent involvement across these domains may increase vulnerability to depression, anxiety, fatigue, sleep disturbance, and impaired quality of life. At the same time, recent patient-centered work also underscores the contribution of fatigue, pain, psychological distress, and treatment-related challenges to unmet needs in Behçet disease [5, 8, 22, 26, 28].

## 8. Psychological Manifestations

### 8.1. Depression and anxiety

Depression and anxiety are among the most consistently reported psychological manifestations in Behçet disease and have been described across different clinical presentations, including patients without overt neurological involvement [7, 8, 29]. Available studies suggest that these symptoms are related not only to the burden of chronic multisystem disease itself, but also to disease activity, pain, fatigue, sleep disturbance, uncertainty regarding prognosis, and the cumulative effects of recurrent mucocutaneous, articular, and ocular flares [8, 29, 30]. In one study, Behçet disease activity correlated positively with depressive symptoms and poor sleep quality, supporting a close relationship between inflammatory burden and psychological distress [29]. Reviews likewise conclude that depression and anxiety are prevalent in Behçet disease and substantially contribute to poorer functioning and lower quality of life [8, 10]. In patients with ocular disease, poorer vision-related quality of life has also been associated with higher levels of depression and anxiety, highlighting the emotional burden of potentially sight-threatening involvement [4, 5].

Additional studies strengthen this association. Fatigue-centered work in Behçet syndrome has shown that depression and anxiety are closely linked with disability, disease activity, and poorer quality of life, suggesting that mood symptoms are embedded within a broader network of physical and psychosocial impairment [30]. Case-control data have also demonstrated higher anxiety levels, worse biopsychosocial status, poorer sleep quality, and impaired quality of life in patients with Behçet disease compared with controls [31]. Cross-sectional evidence has further shown that depression in Behçet disease is associated with major organ involvement, higher disease activity, fatigue, and poorer quality of life. At the same time, dermatological quality of life has also been closely related to disease activity, depression, and anxiety [18, 32]. Taken together, these findings indicate that depression and anxiety in Behçet disease should not be viewed merely as secondary emotional reactions, but rather as clinically meaningful dimensions of the disease experience that may affect coping, adherence, and long-term well-being [8, 10, 18, 30–32].

### 8.2. Stress and broader psychiatric burden

Psychological stress appears to be both a consequence of Behçet disease and a potential amplifier of symptom burden. The relapsing and unpredictable nature of the disease, combined with pain, visible lesions, functional limitation, and fear of organ damage, may promote chronic stress and maladaptive coping [8, 33, 34]. A recent correlational study found that perceived stress levels were associated with disease activity and sleep quality in Behçet disease, reinforcing the view that stress is embedded within the overall burden of illness [34]. Earlier work also demonstrated that stressful life events, anxiety, depression, and coping mechanisms are closely interrelated in Behçet disease, suggesting that stress may influence both symptom perception and psychological adaptation [33]. In addition, illness perception appears to mediate the relationship between symptom severity and perceived health status, providing a plausible cognitive pathway through which multisystem burden may translate into poorer psychological adjustment [20].

Beyond depression and anxiety, the psychiatric profile of Behçet disease may be broader and more heterogeneous. Cohort-based studies have reported a high frequency of psychiatric disorders, particularly mood symptoms and insomnia, with associations to disease activity rather than to a single specific organ pattern [35]. Some broader assessments have also described psychopathological symptoms and cognitive complaints in mixed Behçet cohorts; however, such findings should be interpreted cautiously in the context of the present review, because primary neuropsychiatric manifestations related to direct central nervous system involvement were excluded from the main synthesis [36]. More recent clinical data further support this broader burden, showing reduced sleep quality, elevated anxiety and depression scores, and lower quality of life in patients with Behçet disease, with disease activity exerting a measurable negative effect on these domains [37]. Overall, the available data suggest that psychological burden in Behçet disease extends beyond isolated symptoms of depression or anxiety and may include stress-related dysfunction, maladaptive coping, insomnia, and global psychosocial impairment [8, 10, 20, 33–37].

### 8.3. Fatigue

Fatigue is one of the most disabling non-organ manifestations of Behçet disease and represents an important link between physical inflammation and psychological burden [8, 30, 31]. It may persist even when overt organ activity appears limited and has been associated with disease activity, pain, disability, anxiety, depression, and poorer quality of life [8, 30]. In a dedicated study of patients with Behçet syndrome, fatigue was significantly related to depression, anxiety, disability. It reduced quality of life, emphasizing that it should be recognized as a clinically meaningful component of disease burden rather than a nonspecific complaint [30]. More recent work has reinforced this view, demonstrating impaired fatigue scores together with worse biopsychosocial status and lower quality of life in patients with Behçet disease, regardless of whether major or minor organ involvement was present [31]. Patient-centered burden studies likewise identify fatigue as one of the most troublesome symptoms affecting daily life [28]. These findings suggest that fatigue is not merely secondary to active inflammation, but a multidimensional manifestation shaped by physical symptoms, emotional distress, sleep disturbance, and functional limitation [8, 28, 30, 31].

### 8.4. Sleep disturbance

Sleep disturbance is increasingly recognized as an important component of the overall burden of Behçet disease and appears to be closely linked to both physical and psychological morbidity [29, 34, 37, 38]. Multiple studies have shown that sleep quality is poorer in patients with Behçet disease than in healthy controls and is associated with disease activity, pain, depression, anxiety, fatigue, and reduced quality of life [29, 34, 37]. In one study, poorer sleep quality correlated with higher disease activity and greater depressive symptoms, supporting a close relationship between inflammatory burden and psychological well-being [29]. Other studies have similarly shown that sleep impairment is associated with anxiety, depression, genital ulcers, and arthritis, suggesting that both physical symptoms and emotional distress contribute to disturbed sleep [31, 34, 37]. Cross-sectional evidence has also shown that sleep quality is independently associated with lower self-rated

**Table 1:** Selected key studies evaluating psychological burden and quality-of-life outcomes in Behçet disease

| Study | Design | Sample size | Clinical context | Outcomes assessed | Main findings |
|---|---|---|---|---|---|
| Koca et al., 2015 [29] | Case-control | 40 BD / 30 controls | General adult Behçet cohort | Depression, sleep quality, disease activity | Disease activity correlated positively with depressive symptoms and poorer sleep quality. |
| Senusi et al., 2017 [26] | Postal survey / cross-sectional | 315 BS | UK adult Behçet cohort | HRQoL, symptom burden, oral health/lifestyle, employment | Symptoms, smoking, oral-health behaviors, employment status, and benefits status significantly influenced EQ-5D. |
| Ilhan et al., 2018 [30] | Cross-sectional case-control | 123 BS / 71 controls | General adult Behçet syndrome cohort | Fatigue, anxiety, depression, disability, QoL | Fatigue was strongly associated with anxiety, depression, disability, disease activity, and poorer quality of life. |
| Yankouskaya et al., 2019 [20] | Cross-sectional survey | 273 BD | General adult Behçet cohort | Illness perception, symptom severity, perceived health status | Illness perception mediated the relationship between symptom severity and perceived health status. |
| Sandikci et al., 2019 [7] | Cross-sectional case-control | 155 BD / 107 controls | General adult Behçet cohort | Depression, anxiety, fatigue, disease activity | Anxiety and fatigue were more frequent in active disease and were related to disease activity. |
| Gorial and Jabbar, 2020 [23] | Cross-sectional | NR | General adult Behçet cohort | Disease activity, HRQoL | Higher disease activity was associated with worse health-related quality of life. |
| Zulfiqar et al., 2020 [5] | Longitudinal cohort | 102 BD | Behçet cohort with substantial ocular involvement | Disease activity, psychological status, QoL | Higher disease activity was associated with worse psychological status and lower quality of life over time. |
| Masoumi et al., 2020 [24] | Cross-sectional | 52 BD | General adult Behçet cohort | Sleep quality, mood status, wellness/health status | Poor sleep quality was the strongest independent predictor of lower self-rated wellness and health status. |
| Eser-Öztürk et al., 2021 [4] | Cross-sectional | 105 Behçet uveitis | Adult Behçet uveitis cohort | Depression, anxiety, vision-related QoL | Poorer vision-related quality of life was associated with higher depression and anxiety scores. |
| Fawzy et al., 2021 [32] | Case-control | 35 BD / 35 controls | General adult Behçet cohort | Depression, fatigue, disease activity, QoL | Depression was common and was associated with major organ involvement, fatigue, higher disease activity, and poorer quality of life. |
| Senusi et al., 2022 [25] | Survey-based longitudinal comparison | 371 BD (full-data participants) | Behçet cohort assessed over 10 years | HRQoL, symptom burden, lifestyle and work-related factors | Arthropathy and neurological symptoms remained major drivers of reduced QoL; employment and lifestyle factors were also relevant. |
| Kabul et al., 2023 [31] | Single-center cohort / cross-sectional | 50 BD | Adult Behçet cohort; major vs minor organ involvement | Biopsychosocial status, fatigue, sleep quality, alexithymia, cognition, QoL | Behçet disease adversely affected biopsychosocial status, fatigue, sleep quality, and quality of life regardless of major vs minor organ involvement. |
| Shaddad et al., 2023 [37] | Case-control | 30 BD / 30 controls | Adult Behçet cohort | Sleep, anxiety, depression, QoL | Behçet disease was associated with significantly worse sleep quality, anxiety, depression, and SF-36 domains than controls. |
| Karacan et al., 2025 [18] | Cross-sectional | 263 BS | Behçet syndrome with dermatologic assessment | Dermatological QoL, disease activity, depression, anxiety | Dermatological quality of life was closely related to disease activity, depression, and anxiety. |
| Teixeira et al., 2025 [10] | Narrative review | Not applicable | Review of published Behçet literature | Mental health burden, depression/anxiety, QoL | Recent review-level synthesis highlighted the burden of mental health issues in Behçet disease and their implications for quality of life. |
| Ben Hassine et al., 2025 [27] | Cross-sectional | 35 BD (QoL analysis set) | Tunisian adult Behçet cohort | QoL, sexual health | Quality of life was substantially impaired; sexual dysfunction and disease activity were important correlates of burden. |
| Tharwat et al., 2026 [28] | Cross-sectional patient-centric cohort | 528 BD | Large adult Behçet cohort | Patient-reported burden, treatment challenges, unmet needs | Fatigue, pain, mood disturbance, and treatment-related challenges contributed substantially to unmet needs and overall burden. |

BD, Behçet's Disease; BS, Behçet's Syndrome; HRQoL, Health-Related Quality of Life; NR, Not Reported; QoL, Quality of Life.

wellness and health status among patients with Behçet disease [24]. A recent systematic review further concluded that sleep impairment is a recurrent and clinically relevant feature of Behçet disease and likely interacts bidirectionally with fatigue and psychosocial distress [38]. Taken together, these findings support the view that sleep disturbance is an integral part of the overall disease burden and an important contributor to reduced well-being in Behçet disease [24, 34, 37, 38].

### 8.5. Reduced quality of life

Reduced quality of life is one of the most important patient-centered consequences of Behçet disease because the disorder affects physical, psychological, and social domains simultaneously [8, 22, 39]. Unlike single-organ conditions, Behçet disease may combine painful mucocutaneous lesions, recurrent articular symptoms, ocular inflammation, fatigue, sleep disturbance, and emotional distress, all of which can impair daily functioning and well-being [8, 31, 37, 39]. Systematic review-level evidence indicates that quality of life is consistently reduced in Behçet disease, with disease activity, organ involvement, fatigue, depression, anxiety, and sleep problems among the main determinants [10, 39]. Cross-sectional and longitudinal cohort data likewise show that disease activity, symptom burden, employment status, oral health, lifestyle factors, and treatment context can all influence patient-reported quality of life [23, 25, 26, 28].

This impairment develops through several overlapping pathways. Painful oral and genital ulcers may interfere with eating, speaking, sexual wellbeing, and interpersonal relationships, while visible skin lesions may negatively affect body image and social confidence [3, 12, 19]. Articular involvement may further reduce mobility, physical function, and work capacity through recurrent arthralgia and arthritis [2, 13]. Ocular disease adds a particularly important dimension because recurrent uveitis and impaired visual function may threaten independence, increase fear of blindness, and intensify emotional distress [4, 5]. In patients with Behçet uveitis, poorer vision-related quality of life has been associated with higher depression and anxiety scores [4]. Pediatric evidence further suggests that Behçet disease may adversely affect quality of life in both affected children and their parents, indicating that burden may extend beyond the individual patient and vary across age groups [40].

Quality of life is also closely linked to fatigue and sleep disturbance. Poor sleep quality in Behçet disease has been associated with higher disease activity, greater depressive symptoms, and lower quality-of-life scores [29, 34, 37, 38]. Fatigue has likewise been linked to depression, anxiety, disability, and impaired quality of life [30, 31]. Recent studies have additionally emphasized the influence of dermatological quality of life, sexual health, treatment burden, and unmet needs on broader patient-reported wellbeing [9, 18, 27, 28]. Taken together, these findings suggest that reduced quality of life in Behçet disease is not merely a secondary outcome, but a central expression of cumulative disease burden. Although direct evidence for a rigorously defined combined mucocutaneous-articular-ocular phenotype remains limited, the available literature supports the view that concurrent involvement across these domains may amplify overall psychosocial burden [4, 8, 39].

## 9. Clinical Pathways Linking Mucocutaneous, Articular, and Ocular Manifestations to Psychological Burden

The relationship between Behçet disease and psychological burden is likely multifactorial, reflecting the interaction of inflammatory activity, recurrent symptoms, functional limitation, illness perception, and psychosocial stress rather than a single isolated mechanism [5, 8, 20, 39]. When mucocutaneous, articular, and ocular manifestations coexist, their effects may be cumulative, affecting pain, mobility, appearance, visual function, social participation, and independence [2, 4, 5, 8, 12–14]. Although the available literature more often supports this relationship indirectly than through studies of a rigorously defined combined phenotype, the evidence suggests that concurrent involvement across these domains may increase vulnerability to depression, anxiety, fatigue, sleep disturbance, and impaired quality of life [4, 5, 8, 22, 39].

Mucocutaneous disease may contribute through pain, visible lesions, embarrassment, impaired self-image, and relationship strain. Recurrent oral and genital ulcers can interfere with eating, speech, intimacy, and social confidence, while visible skin lesions may adversely affect body image and interpersonal functioning [3, 12, 19]. This interpretation is supported by studies showing that oral health and psychosocial wellbeing are closely linked to clinical outcomes in Behçet disease, and that Behçet-associated oral ulcers are associated with poorer oral health-related quality of life and greater symptom burden [15–17]. Stress-related pathways may also be relevant, as perceived stress and stressful life events have been associated with disease activity, sleep quality, and coping in Behçet disease [33, 34].

Articular involvement may increase psychological burden due to chronic pain, stiffness, fatigue, and reduced mobility. Although Behçet arthritis is usually non-erosive, recurrent attacks may still impair work capacity, physical independence, and participation in daily life [2, 13]. Fatigue appears especially important in this pathway, as it has been associated with depression, anxiety, disability, and lower quality of life [30, 31]. Ocular involvement adds a further layer of vulnerability because recurrent uveitis and impaired visual function may increase fear of visual loss, dependency, and uncertainty regarding future disease control [4, 5, 14]. In Behçet uveitis, poorer vision-related quality of life has been associated with higher depression and anxiety scores [4]. Taken together, the available evidence supports a converging burden model in which mucocutaneous, articular, and ocular manifestations contribute to psychological distress through overlapping pathways of pain, fatigue, visual threat, stress, illness perception, and reduced social and functional wellbeing [4, 5, 8, 20, 30, 31, 33, 34, 39].

## 10. Clinical Implications and Directions for Future Research

The available evidence suggests that Behçet disease should be approached as a multisystem disorder with important psychological as well as physical consequences [5, 8, 39]. In clinical practice, patients with recurrent mucocutaneous symptoms, chronic articular pain, ocular involvement, fatigue, sleep disturbance, reduced quality of life, or pronounced illness concerns may warrant broader psychosocial assessment in addition to organ-specific evaluation. However, the current literature remains limited by heterogeneous outcome measures, variable definitions of phenotype, and a relative lack of longitudinal data [8, 35, 36, 38–40]. Future research should prioritize prospective and multicenter studies that use clearer diagnostic and phenotypic characterization, standardized psychiatric and quality-of-life measures, and a more explicit separation between psychosocial burden and primary neuropsychiatric disease. Key studies evaluating psychological burden in Behçet disease are summarized in **(Table 1)**.

## 11. Limitations of the Evidence Base

This review has several limitations. First, as a narrative review, it does not provide pooled quantitative estimates and remains susceptible to

selection bias despite the structured search approach. Second, the synthesis was limited to English-language publications and therefore may not fully represent all relevant literature. Third, the included studies were heterogeneous in design, sample size, disease activity measures, organ phenotypes, and outcome instruments, limiting direct comparability across studies. Fourth, several publications evaluated overlapping domains such as depression, fatigue, sleep quality, and quality of life within the same cohorts, which may give an impression of broader evidentiary convergence than is actually present. In addition, many available studies could not clearly separate disease-related psychosocial burden from treatment-related burden, including the effects of corticosteroids, immunosuppressive therapy, repeated ophthalmic procedures, and overall treatment intensity. Finally, direct evidence for a rigorously defined combined mucocutaneous-articular-ocular phenotype remains limited, and some broader psychiatric findings require cautious interpretation due to possible overlap with primary neuropsychiatric disease or treatment-related effects.

## 12. Conclusion

Behçet disease is a multisystem inflammatory disorder with important psychological as well as physical consequences. The available literature suggests that depression, anxiety, stress, fatigue, sleep disturbance, and impaired quality of life are frequent and clinically relevant features of the disease. Mucocutaneous, articular, and ocular manifestations may contribute to this burden through pain, functional limitation, social stigma, visual threat, relationship strain, and uncertainty regarding disease course. Although direct evidence for a rigorously defined combined phenotype remains limited, the current data support a converging burden model in which involvement across these domains may adversely affect wellbeing. Greater attention to psychological burden may support more comprehensive and multidisciplinary care. Further prospective studies using standardized psychiatric and quality-of-life measures are needed to clarify mechanisms, identify higher-risk clinical patterns, and improve interpretation of psychological outcomes in Behçet disease.

## Conflicts of Interest

The authors declare no conflicts of interest.

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## Institutional Review Board (IRB)

None.

## Large Language Model

The authors declare that generative artificial intelligence (AI) tools were used only for language refinement and grammar support during manuscript preparation. These tools were not used for literature searching, study screening, study selection, data extraction, data analysis, or interpretation of findings. All content was reviewed and verified by the authors, who take full responsibility for the accuracy and integrity of the manuscript.

## Author Contributions

All authors contributed to the study conception and design, literature review, manuscript drafting, critical revision, and approval of the final version.

## Data Availability

None.

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