

Association between hidradenitis suppurativa, depression, anxiety, and suicidality: A systematic review and meta-analysis



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Background: Previous studies found conflicting results about whether hidradenitis suppurativa (HS) is associated with depression or anxiety.

Objectives: To determine the relationship of HS with depression and anxiety.

Methods: A systematic review was performed of published observational studies in MEDLINE, PubMed, Embase, Global Resource for Eczema Trials (GREAT), Latin American and Caribbean Health Sciences Literature (LILACS), Cochrane, Scopus, and PsychInfo that analyzed depression or anxiety in HS. Two reviewers performed title/abstract review and data extraction. Meta-analysis was performed with random-effects weighting.

Results: Thirty-eight studies met inclusion criteria; 27 had sufficient data for meta-analysis. The prevalences of depression (26.5% vs 6.6%) and anxiety (18.1% vs 7.1%) were higher in persons with versus without HS. Patients with HS had higher odds of depression in 12 of 13 studies and pooled analysis (odds ratio, 2.54; 95% confidence interval, 2.15-3.01), and anxiety in 6 of 6 studies and pooled analysis (odds ratio, 2.00; 95% confidence interval, 1.66-2.42). Similar results were found in sensitivity analyses for different methods of HS diagnosis (physician diagnosed and chart review) and control groups (healthy and dermatologic control individuals). HS was associated with higher antidepressant and anxiolytic use and with suicidality, but not mean depression and anxiety scale scores.

Limitations: Individual-level data were unavailable.

Conclusions: Patients with HS have higher odds of depression, anxiety, and suicidality. (J Am Acad Dermatol 2020;83:737-44.)

Key words: acne inversa; antidepressant; anxiety; anxiolytic; comorbidity; depression; evidence; hidradenitis suppurativa; mood; suicidal ideation; suicide.

Hidradenitis suppurativa (HS) is a chronic inflammatory debilitating skin condition affecting 0.03% to 4% of the population worldwide.¹ HS is associated with multiple

comorbidities, including obesity, metabolic syndrome, smoking, depression, arthritis, autoinflammatory syndromes, and inflammatory bowel disease.² HS is highly symptomatic and is

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accompanied by pruritus, skin pain, disfiguring lesions, scarring,³ sexual disturbances,⁴ psychological distress, and impaired quality of life.⁵ However, previous studies found conflicting results about whether HS is associated with increased depression, anxiety, and/or suicidality.^{6,7} We hypothesized that HS is associated with higher prevalences of depression, anxiety, and suicidality and with increased treatment for these disorders. This systematic review sought to determine the relationship of HS with depression, anxiety, and suicidality.

METHODS

Literature search

The following databases were searched for articles from the earliest entry in the respective databases up to May 9, 2018: MEDLINE, PubMed, EMBASE, Cochrane Library, Latin American and Caribbean Health Sciences (LILACS), Scopus, PsychInfo, and Global Resource for Eczema Trials (GREAT). Search strategies were modified from previous reviews of HS,⁸ anxiety,⁹ and depression and suicidal ideation¹⁰ (Supplemental Table 1 available via Mendeley at <https://data.mendeley.com/datasets/bnj8znmdwp/1>).

Inclusion criteria included any cross-sectional or cohort study assessing the relationship between HS, depression, anxiety, and/or suicidality; with at least 20 participants with HS; published online, in print, or in press; and in any language. Editorials and review articles were excluded. Two reviewers (KRP and HHL) performed title and abstract review. Studies were excluded based on title/abstract review if there was no clear indication that the study analyzed the relationship of HS with depression, antidepressant use, anxiety, anxiolytic use, or suicidality. Two reviewers performed full-text review and data extraction. All studies were in English, and no foreign language translation was needed. If duplicate studies were encountered, only the most recent and complete study was included.

This study was exempt from institutional review board approval because data were gathered from published literature.

Data extraction and analysis

The following data were extracted: first author; publication year; funding source; study design; diagnostic approach for and severity of HS, depression, and anxiety; geographic region of the study; distribution of age and sex; frequency of

participants with and without HS and/or depression, antidepressant use, anxiety, anxiolytic use, and suicide/suicidal risk.

OpenMeta for Windows (version 10.10; Brown University, Providence, RI) was used to perform statistical analyses. All studies with a control group were included in pooled meta-analysis. Prevalences,

odds ratios (ORs), and 95% confidence intervals (CIs) were estimated for depression, depression symptoms, antidepressants, anxiety, anxiety symptoms, anxiolytics, and suicidality in patients with and without HS. Standardized mean differences (SMDs) and 95% CIs were estimated for depression and anxiety scales in patients with and without HS. Random-effects weight-

ing with the DerSimonian and Laird method was used to generate estimates owing to significant heterogeneity ($I^2 > 90\%$ for all analyses). Forest plots were generated, and complete case analysis was performed. A *P* value of less than .05 was considered statistically significant.

RESULTS

Literature search

Overall, 1036 nonduplicate citations were identified; 907 were excluded during title and abstract review, and 91 were excluded during full-text review. Thirty-eight observational studies met inclusion/exclusion criteria and were included in this systematic review, as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram (Fig 1)¹¹; 27 articles were included in the quantitative meta-analyses.

Study characteristics

All studies were published from 1963 through 2018. Studies examined the association between HS and depression (*n* = 37), anxiety (*n* = 14), antidepressant use (*n* = 2), anxiolytic use (*n* = 1), and/or suicide (*n* = 2). Twenty-nine (76.3%) studies were cross-sectional, 3 (7.9%) were case-control, 1 (2.7%) was longitudinal, 1 (2.7%) was a randomized controlled trial, 2 (5.2%) were chart reviews, and 2 (5.2%) were unspecified. Additional study characteristics are presented in the Supplemental Material (available via Mendeley at <https://data.mendeley.com/datasets/bnj8znmdwp/1>).

CAPSULE SUMMARY

- Hidradenitis suppurativa was found to be associated with increased odds of depression, antidepressant use, anxiety, anxiolytic use, and suicidality.
- Presence of depression, anxiety, and suicidality should be incorporated into the clinical decision making of patients with hidradenitis suppurativa.

Abbreviations used:

aOR:	adjusted odds ratio
BDI:	Beck Depression Inventory
CI:	confidence interval
HADS:	Hospital Anxiety and Depression Scale
HS:	hidradenitis suppurativa
OR:	odds ratio
SMD:	standardized mean difference

Prevalence of depression

Twenty-seven studies reported on the prevalence of depression in individuals with and without HS and had sufficient data for meta-analysis. The pooled random-effects prevalence of depression was higher in patients with versus without HS (26.5% vs 6.6%). Patients with HS had higher odds of depression overall (12 of 13 studies; pooled unadjusted OR, 2.54; 95% CI, 2.15-3.01; $P < .001$; Figure 2) and particularly in studies using self-report or physician diagnosis (5 of 5; pooled unadjusted OR, 1.82; 95% CI, 1.51-2.19) or medical record review (9 of 9; pooled unadjusted OR, 2.69; 95% CI, 2.23-3.24). The odds of depression were consistently higher across cross-sectional studies (10 of 11 studies; pooled unadjusted OR, 2.05; 95% CI, 1.79-2.36) and studies that included healthy control individuals (11 of 11; pooled unadjusted OR, 2.62; 95% CI, 2.19-3.13). Two studies compared HS with other skin conditions. One study found higher rates of depression in patients with HS compared to those with psoriasis and eczema.¹² The other study found no increased odds of depression in HS, although, the characteristics of the control patients were not described.¹³

Four studies were included in the qualitative analysis but had insufficient data for meta-analysis. A retrospective case-control study conducted in 13,016 English adults reported significantly higher age- and sex-adjusted odds of depression in patients with HS (adjusted OR [aOR], 1.69; 95% CI, 1.62-1.77).¹⁴ A retrospective case-control study conducted in 1730 US adults found higher unadjusted odds of depression in patients with versus without HS (aOR, 3.95; 95% CI, 3.02-5.17).¹⁵ A retrospective cross-sectional study adjusting for age and sex and a prospective randomized clinical trial with no mention of variable adjustments, both conducted in the United States, reported higher rates of physician-diagnosed depression with increasing Hurley stage score.^{16,17}

All studies included middle-aged adult patients; therefore, sensitivity analyses by age could not be performed. No studies stratified depression prevalence by body mass index.

Antidepressant drug use

Two studies found higher odds of antidepressant drug use in patients with versus without HS (2 of 2 studies significant; 1.85; 95% CI, 1.26-2.71).^{7,18}

Mean depression scores

Three studies examined mean depression scores in patients with and without HS. There was no significant difference of depression scores in those with versus without HS overall (2 of 3 studies with significant differences; pooled SMD, 2.90; 95% CI, 0.93-4.88), although it is unknown whether the control patients had clinical depression. Likewise, there was no significant difference of depression scores in studies including healthy control individuals (1 of 3; pooled SMD, 2.63; 95% CI, 0.82-4.45) (Fig 3).

Eleven uncontrolled studies reported fairly high mean depression scores in patients with HS (pooled mean, 8.56; 95% CI, 6.68-10.46), particularly for the Hospital Anxiety and Depression Scale (HADS) (5 of 5 studies; pooled mean, 6.73; 95% CI, 5.80-7.67) and Beck Depression Inventory (BDI) (3 of 3 studies; pooled mean, 8.72; 95% CI, 4.92-12.52), although there were no control individuals without HS for comparison. For reference, a previous US population-based study¹⁹ found lower mean HADS-depression scores of 6.0 and 4.3 among adults with or without atopic dermatitis, respectively.

One study conducted across 13 European countries reported higher EQ-5D anxiety/depression domain scores in adults with versus without HS (aOR, 2.34; 95% CI, 1.34-4 vs aOR, 1.96; 95% CI, 1.7-2.3); models were adjusted for age; sex; socioeconomic status; diabetes mellitus; and cardiovascular, respiratory and rheumatologic diseases.²⁰ Another study in Italian patients with HS reported a significant difference in BDI scores compared with control individuals with nevi ($P = .006$), although it is unknown whether adjustment for any variables was performed.²¹ Similarly, a prospective cross-sectional study conducted in Ireland found significantly higher HADS depression scores in patients with HS compared to those with psoriasis ($P < .001$).²²

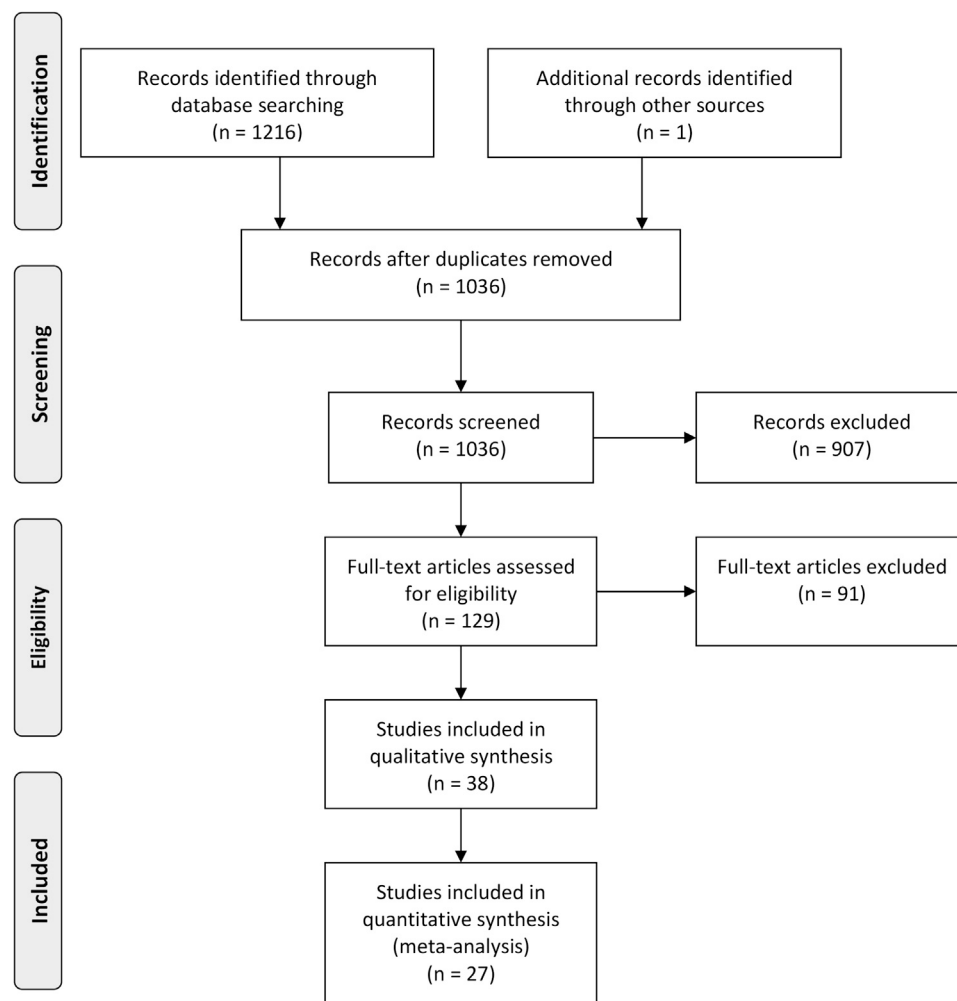
Prevalence of anxiety

Nine studies reported on the prevalence of anxiety in HS and had sufficient data for meta-analysis. The pooled random-effects prevalence of anxiety was higher in patients with versus without HS (18.1% vs 7.1%, respectively). Patients with HS had higher odds of anxiety overall (6 of 6 studies; pooled unadjusted OR, 2.00; 95% CI, 1.66-2.42; $P < .001$), and particularly in studies using

Table I. Summary of associations between HS, depression, and anxiety

Mental health comorbidity	Overall association with HS	Sensitivity analysis								
		Diagnosis type			Control type		Study origin			
		Self-reported	Physician diagnosed	Medical record	Healthy	Dermatologic	United States	Europe	Asia	Africa
Depression	↑	↑	↑	↑	↑	-	NA	NA	NA	NA
Antidepressant use	↑	NA	NA	NA	NA	NA	NA	NA	NA	NA
Anxiety	↑	↑	↑	↑	↑	↑	↑	↑	NA	NA
Anxiolytic use	-	NA	NA	NA	NA	NA	NA	NA	NA	NA
Suicide	↑	NA	NA	NA	NA	NA	NA	NA	NA	NA

↑, Positively significant association; -, no significant association; HS, hidradenitis suppurativa; NA, not assessed due to inadequate studies.

**Fig 1.** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

self-report or physician diagnosis (2 of 2; pooled unadjusted OR, 1.67; 95% CI, 1.37-2.05) and medical record review (4 of 4; pooled unadjusted OR, 2.13; 95% CI, 1.70-2.66) (Fig 4). The odds of having anxiety was higher in studies that included healthy control individuals (4 of 4; pooled unadjusted OR, 2.03; 95% CI, 1.59-2.60) or those with other

dermatologic disorders as control patients (2 of 2; pooled unadjusted OR, 2.05; 95% CI, 1.88-2.22). Increased odds of anxiety were observed in both European (4 of 4; pooled unadjusted OR, 2.04; 95% CI, 1.69-2.46) and US (2 of 2; pooled unadjusted OR, 1.97; 95% CI, 1.41-2.74) studies. No studies stratified anxiety prevalence by body mass index.

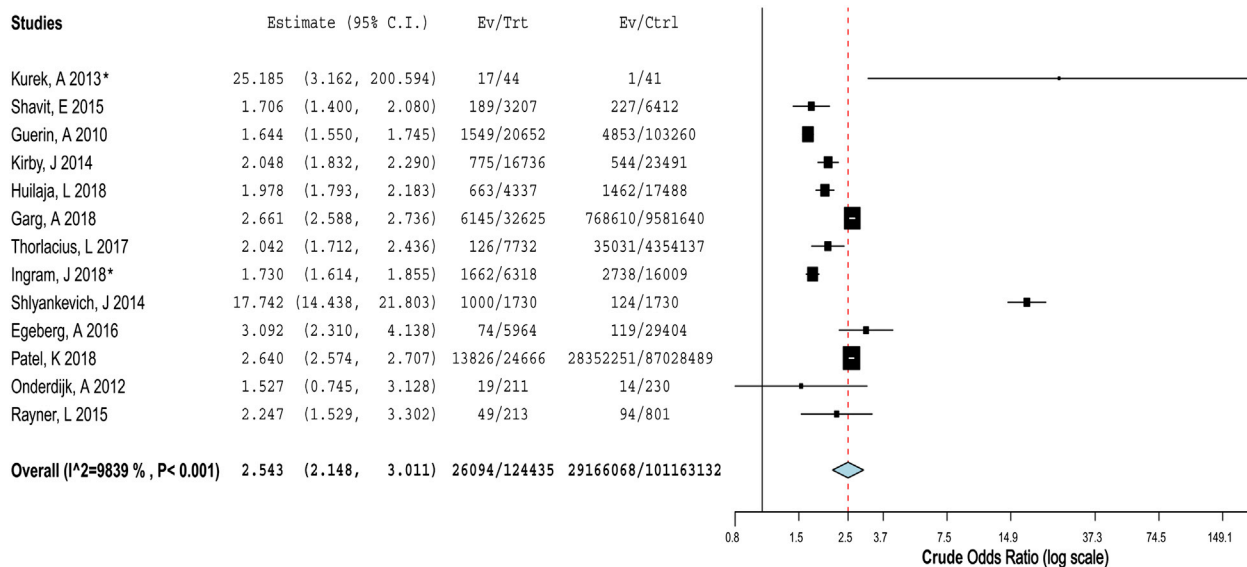


Fig 2. Forest plot of the proportion of depression in persons with versus without hidradenitis suppurativa. Unadjusted proportion of clinical depression or depression symptoms, 95% confidence intervals (squares), and pooled proportion (diamond) are presented.

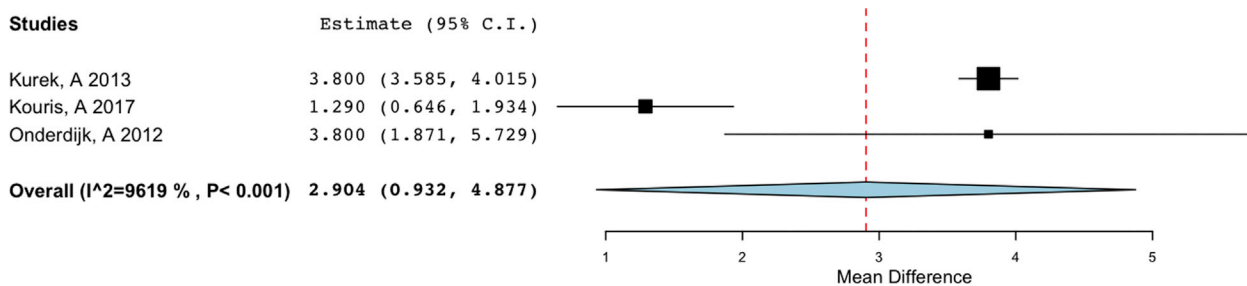


Fig 3. Forest plot of the standardized mean differences of depression scales in persons with versus without hidradenitis suppurativa. Unadjusted standardized mean differences of depression scales, 95% confidence intervals (squares), pooled standardized mean difference (diamond) are presented.

Mean anxiety scores

One study examined mean anxiety scores in patients with and without HS. There was no significant difference in anxiety scores in those with versus without HS (1.41; 95% CI, 0.89-1.94), and it was unknown whether the control patients had clinically diagnosed anxiety. However, 3 articles reported mean HADS anxiety scores in patients with HS alone (pooled mean, 7.35; 95% CI, 5.58-9.12). A prospective cross-sectional study investigated anxiety scores among 94 patients with HS and found a mean \pm standard deviation score of 6.4 ± 3.3 .²³ A study of 50 Danish adults with HS reported a mean anxiety score of 9.25 (95% CI, 8.49-10.01), with a HADS anxiety score greater than 7, signifying a borderline or abnormal response.²⁴ A study of 94

Greek patients with HS reported a mean anxiety score of 6.41 (95% CI, 5.74-7.08).²⁵ For reference, a US population-based study previously found mean HADS-anxiety scores of 5.6 and 7.7 among adults with or without AD, respectively.¹⁹

Two studies were included in the qualitative analysis but had insufficient data for meta-analysis. One Italian study of 38 patients with HS found significantly increased age- and sex-adjusted General Health Questionnaire-28 anxiety symptoms scores compared with patients with nevi ($P = .002$).²¹ Another prospective study in Ireland found no significant difference in HADS-anxiety scores between patients with HS and those with psoriasis ($P > .05$), although it is unknown whether adjustment for any variables was performed.²²

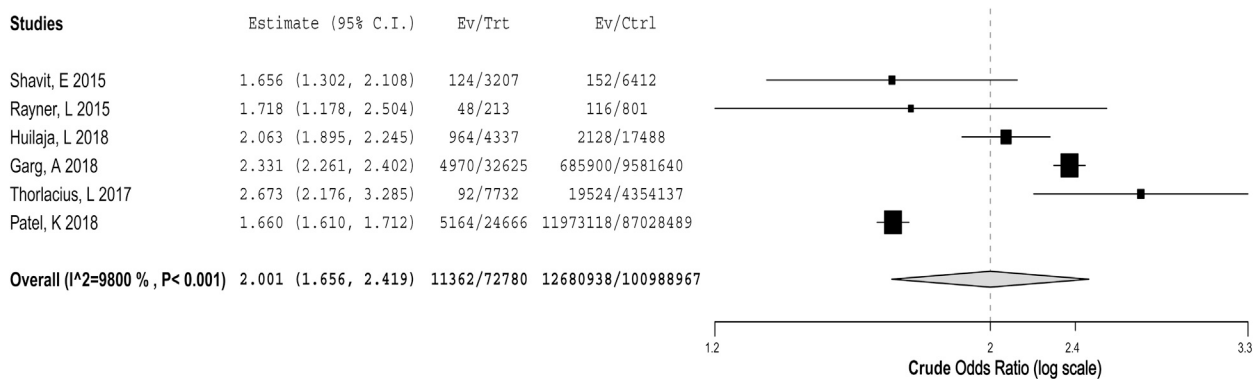


Fig 4. Forest plot of the proportion of anxiety in persons with versus without hidradenitis suppurativa. Unadjusted proportion of clinical depression or depression symptoms, 95% confidence intervals (squares), pooled proportion (diamond) are presented.

Anxiolytic use

One retrospective cross-sectional study adjusting for age, sex, socioeconomic status, tobacco, and alcohol use found that anxiolytic use was higher in patients with HS versus the general population overall (29.7% vs 18.0%); however, the differences were not significant in proportional hazards regression models ($P = .55$).⁶

Suicidality

Prevalence of suicide in HS was reported in 1 study. In 1 US population-based study adjusting for age, sex, and race, the prevalence of suicide was significantly higher in patients with versus without HS (0.8% vs 0.3%, respectively).⁷ A Danish study adjusting for age, sex, socioeconomic status, tobacco, and alcohol use found a dramatically and statistically significantly higher prevalence of suicidality in adults with versus without HS (10.4% vs 0.1%, respectively).²⁶

No studies examined the relationship of parental depression or anxiety and childhood HS.

Effects of HS treatment on depression and anxiety

One longitudinal study of 23 patients with Hurley stage III HS showed a significant improvement of Patient Health Questionnaire-9 ($P = .001$) and Generalized Anxiety Disorder-7 scores ($P = .046$) immediately after skin-tissue-saving excision with electrosurgical peeling.²⁷

DISCUSSION

This systematic review and meta-analysis found that approximately 1 in 4 adults with HS had depression and that 1 in 5 had anxiety (summarized in Table I). Specifically, adults with HS had significantly higher odds of depression and anxiety, regardless of the study design, control population,

and disease classification. Patients with HS had higher rates of antidepressant and anxiolytic medication use. HS was associated with increased depression and/or anxiety scores in some studies in the qualitative analysis but not in pooled meta-analysis. Finally, HS was associated with higher rates of suicidality. Importantly, 1 study found that surgical treatment of HS decreased depressive and anxiety symptoms, indicating that these may be modifiable symptoms of HS.

This study identified previous studies that found higher odds of suicidality and/or completed suicide in HS patients. Chronic disease, such as heart disease, systemic lupus erythematosus, and HIV, has been shown to be associated with increased suicidality secondary to feelings of helplessness and depression.²⁸ However, suicidal patients often do not report depression symptoms or meet depression criteria.²⁹ It is unknown if increased suicidality in HS is mediated by increased depression symptoms or whether suicidality is associated with increased HS severity. Regardless, these results suggest that patients with HS warrant increased screening for depression, anxiety, and suicidality. Symptoms of depression, anxiety, and suicidality may reflect overall HS severity and should be included into therapeutic decision making and monitoring in HS.

Previous studies showed the coexistence of depression and anxiety symptoms/disorders in patients with chronic inflammatory skin diseases. A cross-sectional study of 208 Chinese adults with psoriasis vulgaris found high prevalences of both depression and anxiety (13.9% and 10.6%, respectively) and that moderate to severe psoriasis was a positive predictor for the presence of both depression and anxiety symptoms.³⁰ Meta-analyses found high prevalences of depression and anxiety in adults with psoriasis (20.0% and 27.0%, respectively)³¹ and depression in atopic dermatitis

(20.0%).³² This study found relatively similar or higher prevalences of depression and anxiety in patients with HS. Thus, symptoms of depression and anxiety may occur across the gamut of symptomatic inflammatory skin diseases.

The exact mechanism(s) of association between HS, depression, anxiety, and/or suicidality remain unknown, although it is likely multifactorial. A systematic review and meta-analysis reported that patients tended to experience their chronic disease, such as heart disease, diabetes, and chronic obstructive pulmonary disease, as interrelated with their depression and/or anxiety.³³ That is, chronic disease exacerbated mental health symptoms, and mental health symptoms aggravated the chronic disease.³³ Similarly, HS may lead to depression and/or anxiety and/or be worsened by underlying mental health comorbidities. Chronic pain, in particular, has been associated with depression in mature patients.³⁴ Pain is a commonly reported symptom in HS³⁵ and may play an important role in the development of mental health symptoms in HS.³⁶ Previous studies showed that depression may be in part attributed to elevated proinflammatory cytokines in psoriasis rather than to the psychosocial impact of the disease.^{37,38} Likewise, depression and anxiety symptoms may be caused by immune dysregulation and neuroinflammation in HS. As such, some anti-inflammatory treatments may directly reduce mental health symptoms in patients with HS. However, surgical intervention was also found to reduce depression and anxiety symptoms.²⁷ Thus, it is likely that the association of HS with mental health symptoms is multifactorial.

We found inconsistent results regarding different depression and anxiety scores across studies. One explanation for this is that patients with HS without mental health symptoms dilute overall depression and anxiety mean scores. Nonetheless, HS was associated with increased HADS and BDI scores. HADS is the most frequently used observer-rated depression and anxiety scale and has been shown to be reliable and valid in psychiatric and primary care setting and in the general population.³⁷ BDI, a self-reported depression scale, exhibits adequate reliability and validity.³⁸ These scales are time efficient, do not require trained personnel for use, and are likely feasible for use in the clinical setting. However, the validity and reliability of depression and anxiety scales have not been studied in HS and, therefore, further evaluation is warranted.

Strengths of this study include comprehensive search strategies across multiple databases, inclusion of international articles, and multiple sensitivity analyses by HS classification and study design.

Limitations include a dearth of longitudinal studies and individual-level data, as well as the inability to adjust for HS severity or confounders across studies.

In conclusion, patients with HS have higher odds of depression, anxiety, and suicidality. These findings underscore the mental health comorbidity of HS, including depression, anxiety, and suicidality. Future longitudinal studies are needed to determine and assess the relationship of HS with depression, anxiety, and suicidality to develop optimal strategies for their prevention and treatment.

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