Depression As a Potential Contributing Factor in Hidradenitis Suppurativa and Associated Racial Gaps

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PRACTICE POINTS

- Hidradenitis suppurativa (HS) is known to be associated with systemic inflammation and comorbidities, including depression.
- Depression may be a potential contributing factor to HS in affected patients, and studies on HS with comorbid depression in patients with skin of color are lacking.

Hidradenitis suppurativa (HS)—a chronic, relapsing, inflammatory disorder involving terminal hair follicles in apocrine gland–rich skin—manifests as tender inflamed nodules that transform into abscesses, sinus tracts, and scarring. The etiology of HS is multifactorial, encompassing lifestyle, microbiota, hormonal status, and genetic and environmental factors. These factors activate the immune system around the terminal hair follicles and lead to hyperkeratosis of the infundibulum of the hair follicles in intertriginous regions. This progresses to follicular occlusion, stasis, and eventual rupture. Bacterial multiplication within the plugged pilosebaceous units further boosts immune activation. Resident and migrated cells of the innate and adaptive immune system then release proinflammatory cytokines such as tumor necrosis factor, IL-1β, and IL-17, which further enhance immune cell influx and inflammation. This aberrant immune response propagates the production of deep-seated inflammatory nodules and abscesses. The estimated prevalence of HS is 1% worldwide. It is more prevalent in female and Black patients (0.30%) than White patients (0.09%) and is intermediate in prevalence in the biracial population (0.22%). Hidradenitis suppurativa is thought to be associated with lower socioeconomic status (SES). In a retrospective analysis of HS patients (N=375), approximately one-third of patients...
were Black, had advanced disease, and had a notably lower SES.\textsuperscript{11} Furthermore, HS has been reported to be associated with systemic inflammation and comorbidities such as morbid obesity (38.3\%) and hypertension (39.6\%) as well as other metabolic syndrome–related disorders and depression (48.1\%).\textsuperscript{1}

Hidradenitis suppurativa may contribute to the risk for depression through its substantial impact on health-related quality of life, which culminates in social withdrawal, unemployment, and suicidal thoughts.\textsuperscript{12} The high prevalence of depression in individuals with HS\textsuperscript{1} and its association with systemic inflammation\textsuperscript{13} increases the likelihood that a common genetic predisposition also may exist between both conditions. Because depression frequently has been discovered as a concomitant diagnosis in patients with HS, we hypothesize that a shared genetic susceptibility also may exist between the 2 disorders. Our study sought to explore data on the co-occurrence of depression with HS, including its demographics and racial data.

Methods
We conducted a PubMed search of articles indexed for MEDLINE as well as Google Scholar using the terms depression and hidradenitis suppurativa to obtain all research articles published from 2000 to 2022. Articles were selected based on relevance to the topic of exploration. English-language articles that directly addressed the epidemiology, etiology, pathophysiology, and co-occurrence of both depression and HS with numerical data were included. Articles were excluded if they did not explore the information of interest on these 2 disorders or did not contain clear statistical data of patients with the 2 concurrent medical conditions.

Results
Twenty-two cross-sectional, prospective, and retrospective studies that fit the search criteria were identified and included in the analysis (eTable).\textsuperscript{1,14–34} Sixteen (72.7\%) studies were cross-sectional, 5 (22.7\%) were retrospective, and only 1 (4.5\%) was a prospective study. Only 6 of the studies provided racial data,\textsuperscript{1,14,17,26,28,32} and of them, 4 had predominately White patients,\textsuperscript{1,14,26,32} whereas the other 2 had predominantly Black patients.\textsuperscript{17,28}

Hidradenitis suppurativa was found to coexist with depression in all the studies, with a prevalence of 1.2\% to 48.1\%. There also was a higher prevalence of depression in HS patients than in the control patients without HS. Furthermore, a recent study by Wright and colleagues\textsuperscript{14} stratified the depression prevalence data by age and found a higher prevalence of depression in adults vs children with HS (30\% vs 12\%).

Comment
Major depression—a chronic and debilitating illness—is the chief cause of disability globally and in the United States alone and has a global lifetime prevalence of 17\%.\textsuperscript{35} In a study of 388 patients diagnosed with depression and 404 community-matched controls who were observed for 10 years, depressed patients had a two-thirds higher likelihood of developing a serious physical illness than controls. The depression-associated elevated risk for serious physical illness persisted after controlling for confounding variables such as alcohol abuse, smoking, and level of physical activity.\textsuperscript{36} Studies also have demonstrated that HS is more prevalent in Black individuals\textsuperscript{40} and in individuals of low SES,\textsuperscript{37} who are mostly the Black and Hispanic populations that experience the highest burden of racial microaggression\textsuperscript{38} and disparities in health access and outcomes.\textsuperscript{39,40} The severity and chronicity of major depressive disorder also is higher in Black patients compared with White patients (57\% vs 39\%).\textsuperscript{41} Because major depression and HS are most common among Black patients who experience the highest-burden negative financial and health disparities, there may be a shared genetic disposition to both medical conditions.

Moreover, the common detrimental lifestyle choices associated with patients with depression and HS also suggest the possibility of a collective genetic susceptibility. Patients with depression also report increased consumption of alcohol, tobacco, and illicit substances; sedentary lifestyle leading to obesity; and poor compliance with prescribed medical treatment.\textsuperscript{42} Smoking and obesity are known contributors to the pathogenesis of HS, and their modification also is known to positively impact the disease course. In a retrospective single-cohort study, 50\% of obese HS patients (n = 35) reported a substantial decrease in disease severity after a reduction of more than 15\% in body mass index over 2 years following bariatric surgery (n = 35).\textsuperscript{43} Patients with HS also have reported disease remission following extensive weight loss.\textsuperscript{44} In addition, evidence has supported smoking cessation in improving the disease course of HS.\textsuperscript{43} Because these detrimental lifestyle choices are prevalent in both patients with HS and those with depression, a co-genetic susceptibility also may exist.

Furthermore, depression is characterized by a persistent inflammatory state,\textsuperscript{13,45} similar to HS.\textsuperscript{46} Elevated levels of a variety of inflammatory markers, such as C-reactive protein (CRP), IL-6, and soluble intercellular adhesion molecule 1, have been reported in patients with depression compared with healthy controls.\textsuperscript{13,45} Further analysis found a positive correlation and a strong association between depression and these inflammatory markers.\textsuperscript{47} Moreover, adipokines regulate inflammatory responses, and adipokines play a role in the pathogenesis of HS. Adipokine levels such as elevated omentin-1 (a recently identified adipokine) were found to be altered in patients with HS compared with controls.\textsuperscript{48} Results from clinical studies and meta-analyses of patients with depression also have demonstrated that adipokines are dysregulated in this population,\textsuperscript{49,50} which may be another potential genetic link between depression and HS.
In addition, genetic susceptibility to depression and HS may be shared because the inflammatory markers that have a strong association with depression also have been found to play an important role in HS treatment and disease severity prediction. In a retrospective cohort study of 404 patients, CRP or IL-6 levels were found to be reliable predictors of HS disease severity, which may explain why anti-tumor necrosis factor antibody regimens such as adalimumab and infliximab have clinically ameliorated disease activity in several cases of HS. In a study evaluating these drugs, high baseline levels of high-sensitivity CRP and IL-6 were predictive of patient response to infliximab. In a meta-analysis evaluating 20,791 participants, an association was found between concurrent depression and CRP. Furthermore, inflammation measured by high levels of CRP or IL-6 was observed to predict future depression. If the same inflammatory markers—CRP and IL-6—both play a major role in the disease activity of depression and HS, then a concurrent genetic predisposition may exist.

**Conclusion**

Understanding the comorbidities, etiologies, and risk factors for the development and progression of HS is an important step toward improved disease management. Available studies on comorbid depression in HS largely involve White patients, and more studies are needed in patients with skin of color, particularly the Black population, who have the highest prevalence of HS. Given the evidence for an association between depression and HS, we suggest a large-scale investigation of this patient population that includes a complete medical history, onset of HS in comparison to the onset of depression, and specific measures of disease progress and lifetime management of depression, which may help to increase knowledge about the role of depression in HS and encourage more research in this area. If shared genetic susceptibility is established, aggressive management of depression in patients at risk for HS may reduce disease incidence and severity as well as the psychological burden on patients.

**REFERENCES**


49. Taylor VJ, Macqueen GM. The role of adipokines in understanding the associations between obesity and depression. J Obes. 2010;2010:748048.


## Studies on Depression and Hidradenitis Suppurativa

<table>
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<tr>
<th>Reference (year)</th>
<th>Type of study</th>
<th>Mean age of patients, y</th>
<th>No. of HS patients</th>
<th>No. of female patients (%)</th>
<th>No. of patients with depression (%)</th>
<th>No. of White patients (%)</th>
<th>No. of Black patients (%)</th>
<th>No. of Hispanic patients (%)</th>
<th>No. of patients of other races/unspecified (%)</th>
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<td>Wright et al(^{14}) (2022)</td>
<td>C</td>
<td>Adults, 43.8; pediatrics, 15.2</td>
<td>Adults, 38,140; pediatrics, 1162</td>
<td>Adults, 29,399 (77); pediatrics, 941 (81)</td>
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Abbreviations: C, cross-sectional; HS, hidradenitis suppurativa; P, prospective; R, retrospective.

*No mean reported; only a range.