

# Comorbidities of hidradenitis suppurativa

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## ■ Abstract

Hidradenitis suppurativa (HS) is an inflammatory skin disorder with many associated comorbidities, including obesity, metabolic syndrome, smoking, depression, arthritis, autoinflammatory syndromes, inflammatory bowel disease, and genetic syndromes. In addition, HS patients can suffer from a variety of diseases related to the chronic inflammatory nature of their HS such as cardiovascular disease and anemia. An understanding of these comorbidities and associations is essential for the management of HS, and routine screening for these entities should be considered in all HS patients.

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**H**idradenitis suppurativa (HS) is associated with multiple comorbidities, including metabolic syndrome, smoking, depression, the follicular occlusion tetrad, genetic syndromes, malignancy, and autoimmune diseases (ie, inflammatory bowel disease (IBD), arthritis, and spondyloarthropathy). Additionally, due to the persistent inflammation and chronic nature of the disease, patients may experience a variety of other conditions that may be a result of the disease process itself (ie, depression, anxiety, anemia, and cardiovascular disease). Knowledge and management of these comorbidities and associations can be relevant in the treatment of HS and may also be beneficial for the overall health of HS patients.

## Obesity and metabolic syndrome

Obesity is a well known comorbidity of HS. One study found that abdominal obesity, independent of body mass index (BMI), was associated with HS;<sup>1</sup> but a more recent study of HS patients noted more peripheral distribution of adiposity as compared to controls.<sup>2</sup> Both groups of authors speculated that increased friction and maceration from overlapping skin folds may worsen inflammatory HS lesions in these obese patients. Multiple studies also observed that overweight and obese HS patients have more severe disease and fewer remissions than nonobese HS patients.<sup>3,4</sup>

Three studies have documented a higher prevalence of metabolic

syndrome, a condition that is defined as the presence of 3 of the following 5 metabolic alterations in HS patients as compared to controls: (1) elevated fasting blood glucose, (2) hypertriglyceridemia, (3) hypertension, (4) low high-density lipoprotein (HDL) cholesterol level, and (5) obesity. Not surprisingly, patients with metabolic syndrome are at increased risk for diabetes, heart disease, and stroke. However, unlike obesity, studies to date have not correlated the presence of metabolic syndrome to severity of HS disease.<sup>1,5,6</sup>

## Smoking

An association between smoking and HS is well documented in the literature.<sup>5-7</sup> Smoking rates in HS patients are greater than controls with reported rates ranging from 30% to 92% or higher,<sup>4,6,7</sup> and the severity of HS is greater in smokers.<sup>5,7</sup> One survey of HS patients with long-standing disease found statistically significant, lower rates of self-reported remission in active smokers versus non-smokers (29% vs 40%).<sup>4</sup> Another retrospective cohort study found that nonsmokers and former smokers were more than 2 times more likely to have a positive response to first-line HS therapy than smokers.<sup>8</sup>

## Inflammatory bowel disease

Studies looking at HS and IBD have found both that HS is more common in IBD patients and that IBD is more common in HS patients. A population-based study of patients with IBD found that the cumulative probability of developing HS was 2%-3% over 30 years from IBD diagnosis.<sup>9</sup> A recent multicenter, cross-sectional study conducted in the Netherlands and Belgium reported the prevalence of IBD in HS patients at 3.3% in 1076 total patients surveyed, which was 4 to 8 times greater than the estimated prevalence of IBD in Northern Europe. These patients did not have a distinct HS phenotype but were less likely to be obese. They also tended to develop HS before IBD.<sup>10</sup> Of HS patients with IBD, HS is more commonly associated with Crohn's disease (CD) than ulcerative colitis (UC).<sup>10,11</sup> A small, retrospective study of 15 patients with both CD and HS identified a particular pattern of CD in HS patients, describing only colonic or ileocolonic disease but no isolated cases of ileal or upper gastrointestinal involvement of CD. These patients tended to have more severe HS with perianal involvement and a diagnosis of CD that preceded their HS diagnosis by years.<sup>12</sup>

## Arthritis and spondyloarthropathy

In addition to IBD, arthropathies are more prevalent in the HS population and typically precede the diagnosis of HS.<sup>6,13</sup> Patients may have peripheral and/or axial arthritis.<sup>14</sup> A prospective survey of 100 patients with HS with Hurley stage 2 or 3 in the groin or buttocks region found very high rates of back pain (71%). Further

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retrospective evaluation of 46 of these patients who underwent pelvic MRIs as part of a preoperative evaluation found evidence of spondyloarthropathy in over half of these patients. No association between back pain and weight, height, HS disease severity or onset, or smoking was found.<sup>15</sup> Also, unlike other seronegative spondyloarthropathies, there does not appear to be an increased incidence of HLA-B27 in HS patients.<sup>14</sup>

Arthritis in HS may also present as part of an autoinflammatory syndrome. Autoinflammatory syndromes represent dysregulation of the innate immune system; however, no autoantibodies or auto-reactive T cells are identified. Historically, synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome and pyogenic arthritis, pyoderma gangrenosum, and acne (PAPA) syndrome were both linked to HS.<sup>13,16</sup> More recently, many new autoinflammatory syndromes associated with HS and pyoderma gangrenosum (PG), both neutrophilic dermatoses, have been described in the literature as follows:

- PG, Acne, and Suppurative Hidradenitis (PASH) syndrome<sup>17</sup>
- Pyogenic Arthritis, PG, Acne, and Suppurative Hidradenitis (PAPASH) syndrome<sup>18</sup>
- Psoriatic arthritis, PG, acne, and Suppurative Hidradenitis (PsA-PASH) syndrome<sup>19</sup>
- PG, acne conglobata, suppurative hidradenitis, and seronegative spondyloarthritis (PASS) syndrome<sup>20,21</sup>

### Follicular occlusion tetrad

The follicular occlusion tetrad includes acne conglobata, dissecting cellulitis of the scalp, hidradenitis suppurativa, and pilonidal cyst. Reported rates of pilonidal disease in HS patients range from 6% to 30%.<sup>7,22,23</sup> Acne vulgaris is likely not associated with HS although it is frequently reported in HS patients. Recent studies show no increased prevalence of acne in HS patients compared to controls and no correlation between acne severity and HS severity.<sup>7,24</sup>

### Genetic syndromes

HS has been described in the context of several genetic syndromes, most of which share a disruption in pathways of follicular keratinization or follicular obstruction. For example, HS has been described in patients with Dowling-Degos Disease, Jackson-Lawler type pachyonychia congenita, Keratitis-Ichthyosis-Deafness (KID) syndrome, and Fox-Fordyce disease, suggesting a common pathophysiology of the underlying defect and the presentation of HS.<sup>16</sup>

### Depression and mental health disorders

HS patients are more likely to have comorbid mental health disorders, including anxiety, depression, substance abuse, and alcohol dependence.<sup>6,25</sup> No studies have specifically identified causal roles of HS in the development of depression or anxiety in patients, but the profound psychosocial impact and stigma of HS is well documented and may worsen these mental health disorders. HS patients describe social isolation,<sup>26</sup> abstention from intimate activity,<sup>16</sup> unemployment,<sup>27</sup> and impoverishment<sup>28</sup> resulting from their disease. A study comparing Dermatology Life Quality Index Questionnaire scores in HS to other dermatologic diseases found HS to have the greatest disease burden on patients' quality of life.<sup>29</sup>

### Cardiovascular disease

An increased risk of cardiovascular disease is described in many

chronic inflammatory diseases, and a recent cohort study of over 5000 Danish patients with HS and 29000 controls found an increased risk of myocardial infarction (MI), ischemic stroke, cardiovascular-associated death, major adverse cardiovascular events, and all-cause mortality in HS patients after adjusting for confounding factors. Even compared to psoriasis, another common inflammatory skin disease, HS patients were at significantly higher risk of cardiovascular-associated death.<sup>30</sup>

### Conclusion

HS patients are at increased risk of obesity, inflammatory bowel disease, autoinflammatory syndromes, smoking, depression or other mental health disorders, arthritis, and cardiovascular disease. Knowledge and treatment of these comorbidities and detrimental health habits or statuses in addition to treatment of HS itself may ultimately improve patients' HS disease or response to treatment. Additionally, HS patients should be screened regularly for signs or symptoms of inflammatory bowel disease, cardiovascular disease, depression, and substance abuse.

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