HHS Public Access

Author manuscript

Curr Pain Headache Rep. Author manuscript; available in PMC 2018 November 01.

Published in final edited form as:

Curr Pain Headache Rep. ; 21(12): 49. doi:10.1007/s11916-017-0647-3.

Pain, Psychological Comorbidities, Disability and Impaired Qualify of Life in Hidradenitis Suppurativa

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Abstract

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Disclosures: Dawn C. Buse has received grant support and honoraria from Allergan, Amgen, Avanir and Eli Lilly. She is an employee of Montefiore Medical Center, which has received research support funded by Allergan, Alder, Avanir, CoLucid, Dr. Reddy's, and Labrys via grants to the National Headache Foundation and/or Montefiore Medical Center. She is on the editorial board of Current Pain and Headache Reports, the Journal of Headache and Pain, Pain Medicine News, and Pain Pathways magazine.

Disclosures: Steven R. Cohen has received grant support from Verrica and Abbvie Pharmaceuticals. He has served on the Scientific Advisory Board of Verrica.

Disclosures: Elizabeth K. Seng has received research funding from the National Institute of Neurological Disorders and Stroke (1K23 NS096107-01), the International Headache Academy, and has served as a consultant for GlaxoSmithKline.

Purpose of Review—Hidradenitis suppurativa (HS) is a chronic, painful dermatologic disease characterized by recurrent inflammatory nodules and abscesses of intertriginous areas such as the axilla and groin. People with HS suffer from greater pain and associated psychological comorbidities, including depression, anxiety, disability, and impairments in quality of life (QoL), compared to those with other dermatologic conditions. Our review focuses on the occurrence of pain and these relationships.

Recent Findings—The existing literature indicates that acute and chronic pain, depression, anxiety, and disability all contribute to poor quality of life in individuals with HS. Despite the central role of pain and distress in the presentation of HS, few studies have empirically evaluated the impact of pain and gaps remain in the existing psychosocial literature. There are no formal guidelines for treating HS-specific pain or psychological comorbidities.

Summary—The results of this review show a clear and pressing need to develop treatment recommendations and effective interventions for addressing acute and chronic pain, psychological comorbidities, disability, and impaired quality of life among people with HS. This review outlines a multidisciplinary approach to treating and managing pain and psychological comorbidities.

Keywords

Hidradenitis Suppurativa; Quality of Life; Depression; Anxiety; Pain; Disability

Introduction

Hidradenitits suppurativa (HS) is a chronic, painful inflammatory skin disease characterized by recurrent inflammatory nodules and abscesses. The disease is often under-diagnosed and misdiagnosed, and typically results in a considerable delay to diagnosis [1, 2]. While pain is a central and debilitating feature of the disease, few studies have empirically evaluated pain associated with HS [3]. People with HS have high rates of pain, psychiatric comorbidities, associated disability, and impaired quality of life (QoL). These factors are hypothesized to be highly interrelated and have multidirectional effects (Figure 1). Data on the prevalence, experience and clinical management of pain, psychiatric comorbidities, associated disability, and impaired QoL are limited. In 2015, a consensus document was written describing guidelines for the treatment of HS [4]. The document noted the substantial psychosocial impact of the disease, including depression, stigmatization, and QoL. The guidelines recommended analgesia to treat pain and the need to validate psychosocial support interventions to address psychological comorbidities in HS [4]. In this manuscript, we review the existing body of literature on pain, psychological comorbidities, associated disability, and impaired QoL in HS, review guidelines and provide clinical suggestions for optimizing management of HS considering these comorbidities and clinical consequences.

Hidradenitits Suppurativa: Epidemiology and Pathophysiology

The majority of HS lesions are found in intertriginous areas including the axilla (armpit), inframammary, and anogenital regions. Although classified as a rare or orphan disease (i.e., a disease that affects fewer than 200,000 Americans), HS is likely much more common, with a prevalence of 1–4%, predominantly in women and minorities [5–8]. The ratio of women to

men is 3:1 and HS is 2.5 times more likely in black individuals compared to white individuals [9, 10]. There is an increased incidence of obesity and tobacco smokers in HS [11••]. A substantial delay in recognizing HS is the norm, averaging seven years from onset to diagnosis [2]. This long interval typically results in an individual experiencing HS for years before treatment is initiated. The delay can also be associated with misdiagnosis, inappropriate treatment, and emotional and psychological distress, as well as extended duration of uncontrolled pain.

While generally considered a disease process of the hair follicle and apocrine gland, the specific pathogenic mechanisms underlying HS remain unknown. The diagnosis is based on clinical characteristics, including morphology, configuration, and distribution of skin lesions with a pattern of chronicity and recurrence [12]. Hurley staging (I–III) is commonly used to classify disease severity, with mild disease limited to recurrent, acutely painful inflammatory cystic nodules (stage I), that may be connected by isolated tunnels/sinuses (stage II), or form a network of bridging tunnels/sinuses (stage III) associated with odiferous, purulent drainage (Figure 2) [13]. As no cure for HS exists, the few available and effective treatment options focus on management of the chronic recurrent HS symptoms. Hidradenitis suppurativa lesions are acute, painful, deep-seated inflammatory nodules and abscesses, often accompanied by throbbing. Acute pain is not relieved until nodules and abscesses rupture. Furthermore, ongoing inflammation can lead to persistent drainage of a malodourous purulent effluent from chronic painful dermal nodules and sinuses, and significant, debilitating scarring [12].

Pain in HS

Pain is one of the most debilitating symptoms of HS; however, few studies have empirically evaluated pain in individuals with HS. A large cross-sectional study found that participants with HS (n = 211) had higher pain scores on a Numeric Rating Scale (NRS) than those with psoriasis, skin tumors, eczema, acne, and other skin diseases (n = 233) [14•]. A cross-sectional self-report study of Danish study subjects with HS (n = 46) found that pain was considered one of the most unbearable aspects of the disease [15• •]. In a large European multicenter study comparing participants with skin disease (n = 4010) to healthy controls (n = 1359), participants with HS (n = 48) had the highest risk of pain and discomfort on a measure of health-related quality of life (HRQoL) [16].

Hidradenitis suppurativa lesions are painful, deep-seated inflammatory nodules and cysts [17•]. A recent review of pain management in HS characterized two separate types of HS-related pain: acute and chronic [18• •]. Acute, sharp pain arises from inflammatory cysts, nodules, and abscesses that quickly evolve, and often requires urgent medical treatment for management. This presents as neuropathic pain characterized by burning, stinging, shooting, and stabbing [18• •]. Chronic pain is associated with more advanced inflammatory HS. This is a stimulus-dependent, nociceptive pain, characterized by gnawing, aching, tenderness, and throbbing [18• •]. Research is continuing to evaluate the pathophysiologic mechanisms of acute and chronic pain in HS.

The following descriptions of pain and associated disability were collected from patients with HS. These patients were enrolled in an ongoing observational study that has been approved by the Albert Einstein College of Medicine Institutional Review Board (#2016-6425):

> "You feel the whole thing instead of anesthesia making it numb. Basically, it feels like being stabbed, anywhere you have lesions … The wounds were open for a year and a half. I would feel the pain all the time. I could not move my arms at all; I could not lift them up and my mom had to dress me. I had no movement." (Patient A)

> "It feels like you are being stabbed or like you just got a cut. And then it's very sore, to the point where [if] you even move; it is going to hurt even worse. I would be in my room crying and rocking back and forth because the pain was so bad … The pain started coming and I did not know how to deal with it. I had this for a very long time, but I kept it quiet. I was scared and nervous to even find out what it was." (Patient B)

Current Management of Pain Associated with HS

Management of pain in dermatologic conditions is important. Guidelines for pain management in dermatology recommend the monitored use of nonopioid analgesics such as NSAIDs, topical agents, and alternative therapies for mild to moderate dermatologic pain [19•]. The European guidelines for the treatment of HS include recommendations for nonsteroidal anti-inflammatory drugs (NSAIDs) [4]. A number of small studies reference analgesic use among HS individuals for pain reduction. For example, a cross-sectional study of 50 participants with HS hospitalized in Denmark found that 77% had used analgesics for pain relief (most commonly tramadol and paracetamol) [20]. The Danish self-report study found that those with HS receiving care also used naturopathic methods and a range of home remedies to alleviate pain, including cold baths (33%), cold wraps (22%), and the application of ice cubes (15%) [15• •].

Both guidelines for HS management discuss the cautious use of opioids for severe dermatological pain [4, 21•]. Due to the national opioid crisis and the concern of addiction, dependence, misuse and diversion, the use of opioids for pain management must be considered judiciously. In select cases of severe pain, the use of individualized and carefully prescribed opioid analgesics may need to be assessed [21•]. This should be done in partnership with a pain management specialist physicians and psychologists when possible.

In clinical trials of HS treatment response, pain has been considered a secondary end point. Treating HS with TNF inhibitors can significantly reduce pain severity as measured by a visual analog scale (VAS) [22–24]. A multicenter, Phase 2 trial of a TNF inhibitor (adalimumab) for moderate to severe HS evaluated baseline pain using a VAS ranging from 0 mm (no pain) to 100 mm (maximum pain) [22]. The mean baseline VAS for 154 study subjects with HS was 52.0 mm to 57.8 mm. Clinically relevant reduction in pain was defined as a 30% reduction and a 10 mm reduction. In this study, 36.2% and 47.9% in the treatment groups (every other week and weekly respectively) and 27.1% of the placebo group met the

criteria [22]. In a similar trial to evaluate another TNF inhibitor (infliximab), the mean VAS at baseline for 38 participants ranged from 48.8 mm to 53.3 mm (on a scale of 100) and decreased by 74.7% in the treatment group and 1% in the placebo group [23]. Pain-related, patient-centered outcomes can be part of future HS clinical trials.

HS & Depression

Depression is a well-established and common comorbidity among people with chronic pain or painful health conditions and is generally associated with worse clinical outcomes [25]. According to The National Comorbidity Survey, a large US population-based survey study, chronic pain was associated with a significantly higher prevalence of depression (20.2%) compared to the general population (9.3%) [26].

Population-based studies report that approximately 43% of participants with HS have comorbid depression [27]. The prevalence of depression is higher among people with HS compared to those with other dermatological conditions [14•, 28–30]. In the Danish self-report study, 48% of the ambulatory cohort with HS reported current or former depression diagnosed by a psychiatrist [15• •]. A cross-sectional study was conducted with 54 Polish adults with HS and found that increased disease severity (according to Hurley stage rating) was associated with the higher scores on the Beck Depression Inventory and the Evers' "6-Item Scale" to assess stigmatization levels [31]. In a qualitative study of focus groups and semi-structured interviews (n=12), study subjects with HS described feeling depressed and unworthy [32•].

Along with depression, suicidal ideation is also prevalent among people with chronic pain [33]. In a European multicenter study of 250 dermatology outpatients, 12.7% reported suicidal ideation compared to 8.3% of controls [34]. Previous findings of depression and suicidal ideation in individuals with acne and psoriasis led researchers to emphasize the importance of recognizing psychiatric comorbidities [35, 36]. A qualitative study (n = 12) found that that several participants with HS described suicidal ideation [32•]. A recent population-based study found that participants with HS have a higher than two-fold risk of completed suicide compared to people without HS [37]. The authors point to the potential need for an interdisciplinary approach to risk management and suicide prevention in this disease population [37].

Pain and other HS symptoms may contribute to the onset of depressive symptoms or may aggravate existing symptoms of reactive or endogenous depression [38]. It seems likely that the unpredictable flares of painful, malodorous abscesses lead to feelings of helplessness, hopelessness and low self-esteem. Individuals with HS avoid social interactions to cope with the disease and reduce embarrassment; which, in turn, may contribute to depressive symptoms [29• •, 32•]. A qualitative study (n = 12) found that participants with HS expressed fear of revealing their scars and experiencing stigmatization [32•]. Pro-inflammatory cytokines in HS may mediate depression [38]. A case-control study of 45 German study subjects with HS found that the presence of inflammatory markers (C-reactive protein) were associated with higher depression scores on the Hospital Anxiety and

Depression Scale [28•]. The authors concluded that inflammation in HS could lead to depression onset [28•].

HS & Anxiety

A smaller body of literature also suggests that anxiety may be comorbid with HS. Anxiety in HS has been attributed to the fear of disease flare-ups and revealing scars to others, malodourous discharge, and financial distress [38, 39• •]. Anxiety disorders are more prevalent among people with chronic pain in general (35.1%) compared to the general population (18.1%) [26]. Relatively few studies have evaluated the association between anxiety and HS. A recent cross-sectional study found that individuals with HS (n = 94) reported significantly higher anxiety scores on the Hospital Anxiety and Depression Scale (anxiety score = 6.41 ± 3.31) than healthy controls (n = 94; anxiety score = 5.00 ± 1.59) [39• •]. Further, higher disease severity (Hurley stage III) was also linked to higher anxiety levels (10 ± 3.34) [39• •]. A registry-based study of 3,207 study subjects with HS found that an anxiety disorder was diagnosed in 3.9% of those with HS compared to 2.4% of those without HS [38]. Anxiety disorders were highest among participants with HS between the ages of 41–60 [38].

HS & Quality of Life

Quality of life is a patient-centered approach to evaluating the impact of the patient's disease on how they live their life. The main factors that impact QoL will differ for each patient, but commonly include limitation of daily activities by elements such as pain, stigma, depression, anxiety, and disease severity. HS has a profound negative influence on QoL, often surpassing the impaired QoL measured in other dermatologic conditions [14•, 31, 40•, 41]. The reduced QoL in HS is attributable to many factors, including chronic pain, disfigurement, malodorous discharge, scarring, and impaired sexual health [39• •, 42, 43]. In a large European multicenter study, participants with HS had one of the lowest self-reported health state on a measure of health-related QoL compared to healthy controls and other dermatology conditions [16]. Participants with HS scored in a similar range on the measure of health-related QoL compared to participants with rheumatoid arthritis pain, cardiovascular disease, cancer, liver disease, and chronic obstructive pulmonary disease [16].

In a qualitative study (n=12), respondents with HS indicated that pain was a significant component of impaired daily functioning and poor QoL [32•]. There have been several cross-sectional studies evaluating the contributing factors to impaired QoL in HS. A survey study of 211 study subjects with HS found that pain was among the most important contributors to poor QoL as measured by the Dermatology Life Quality Index (DLQI) [14•]. Similarly, a study of 114 participants with HS found that lower QoL as measured by the DLQI was significantly associated with a higher number of painful lesions, suggesting those with a higher pain burden report a greater impaired QoL [44]. The most frequent problem in study of 68 participants with HS was lesion soreness (97%), followed by suppuration (37%), appearance (31%), and smell (10%) [6]. An additional study (n=61), found that individuals with HS reported greater bodily pain, and associated difficulty with emotion, symptom, and functional parameters compared to those with neurofibromatosis 1 (n = 128) [40•].

Overall, these studies suggest that HS has a profound impact on QoL. However, there are many gaps in the literature. Future studies should evaluate the extent to which depression or anxiety impacts QoL among people with HS. Existing QoL measures used in dermatology may be insufficient for assessing the wide-ranging impact of HS [45]. A new HS-specific QoL assessment [46• •] is currently under development, and includes more explicit measures of pain, limitation in physical activity, and sexual functioning associated with HS. This measure aims to capture the multifaceted HS experience.

HS & Disability

The painful symptoms of HS can cause significant disability, including interference with work, social and leisure activities, and sleep. Disability as it relates to chronic pain has been defined as the interference of daily activities [47]. A qualitative study (n=12) reported that limitations in activities of daily living (such as dressing and moving around) interfered with work and led to many secondary problems, such as missed appointments, social isolation, feelings of helplessness, dependency, and a sense that HS has taken control of the participants' lives [32•]. The previously cited European multicenter study found that participants with HS showed a high risk for interference with mobility, self-care, and impairment of usual activity [16].

The incidence of HS disproportionally impacts adults 18 to 29 years of age [1]. Thus, HS onset and diagnosis occurs during the most potentially productive years of life [29• •]. Findings are mixed on the overall impact of annual missed workdays each year for participants with HS, with estimates ranging from 2.7 to 33.6 workdays [6, 29• •, 31]. Limited data suggest that HS also interferes with sleep as there is an association between pruritus (itching) and pain intensity, and sleep abnormalities as measured by the Athens Insomnia Scale [48].

Guidelines and Recommendations for Managing Pain in HS

The 2015 European guidelines for the treatment of HS emphasize the need to manage and alleviate pain [4]. The biopsychosocial model is widely regarded as the most comprehensive and effective way to conceptualize the experience of chronic pain. This model views the individual with chronic pain in terms of the dynamic and complex interactions among biological, psychological, and social factors. These dynamic interactions may cause, perpetuate, and exacerbate the condition and associated features, such as disability and comorbidities. Every person experiences pain in a unique way based upon these variables and their interaction. Therefore treatment must be tailored to each individual based upon a detailed assessment.

In many cases a coordinated, multidisciplinary approach to the management of chronic painful conditions is most effective. A multidisciplinary approach may include a range of treatments from various providers often including specialist physicians, pain management physicians, psychologists, psychiatrists, social workers, physical therapists, occupational therapists, and other healthcare professionals. The efficacy of a multidisciplinary approach is well established in the treatment of other conditions characterized by chronic pain [49].

Both the assessment and management of pain should be core elements of a comprehensive approach to treatment. Pain in HS can be addressed both in multidisciplinary HS treatment center settings, as well as in primary care or specialty care medical settings. Pain-related, patient-centered outcomes (such as pain severity and pain interference) should be considered among secondary outcomes in trials evaluating therapeutic options for HS [50]. Regular assessment of pain is necessary to obtain a baseline of symptom severity, and to track progress of pain management. As pain is such a significant component of HS, decreasing pain could even be considered as a primary outcome in clinical treatment trials.

Guidelines and Recommendations for Managing Psychological Comorbidities

It is vital to assess depression and anxiety among individuals with HS [14•, 28•]. Psychiatric comorbidities may be negatively associated with adherence and motivation in treatment [38]. As depression and anxiety are well-recognized comorbidities of chronic pain, routine assessment and intervention protocols for the treatment of depression and anxiety in this population may also help to improve pain management and QoL. Since depression and anxiety are associated with QoL, disability, adherence, and outcomes in HS, additional studies are needed to assess the extent and prevalence of these conditions in the HS population and to develop effective screening and treatment strategies.

There are currently no available recommendations for specific psychosocial interventions in the treatment of patients with HS. We recommend a multidisciplinary approach to create formal practices for management of psychological comorbidities, associated disability, and impairment in QoL. Treatments should include a patient-centered, optimized selection of empirically supported pharmacologic and behavioral treatments. A benefit of a multidisciplinary approach that includes psychosocial assessment and intervention is the ability to include other lifestyle changes important for HS. For example, psychosocial interventions for HS may address pain and QoL, but may also address smoking cessation and weight loss, which are also important lifestyle components of HS management [51, 52].

Conclusions

Acute and chronic HS-related pain, psychiatric comorbidities, and disability all contribute to poor QoL among people with HS. Pain is a central component to the experience of living with HS and may contribute to the onset or worsening of comorbid depression, anxiety, and disability. Despite an increase in the study of factors related to impaired QoL in HS, there remain gaps in our understanding of acute and chronic HS-related pain, psychiatric comorbities, and disability in the HS population. Studies to date have not differentiated between acute and chronic pain in HS. Acute and chronic HS-related pain requires different treatment approaches, and should be evaluated separately. Depression is a well-established comorbidity of HS and additional research is required to fully understand the relationship between HS and anxiety. There is growing body of research examining the impact of HS on disability related to disrupted work, social and leisure activities, and sleep. Further studies should ascertain the extent to which depression, anxiety, and disability impact QoL in HS. Greater research evaluating the ways in which HS interferes with daily activities, including

work, social and leisure activities, will help clinicians, researchers and policymakers better understand the burden of HS. A validated HS-specific QoL measure that includes explicit measures of pain, physical activity limitation, psychosocial factors, and sexual functioning will most certainly improve research in this area. There is a need for tailored treatment of HS that incorporates a multidisciplinary approach. We recommend the creation of formal patient-centered practices for acute and chronic pain management, psychological comorbidities, associated disability, and impairment in QoL based on empirically supported pharmacologic and behavioral treatments for this population.

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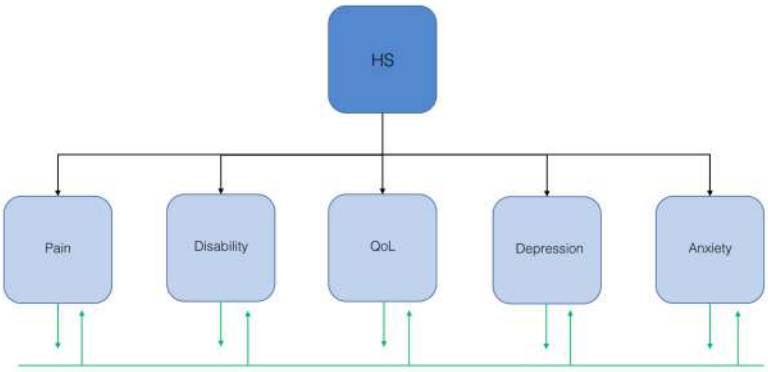

Figure 1.
Relationships between HS, pain, disability, quality of life, depression, and anxiety

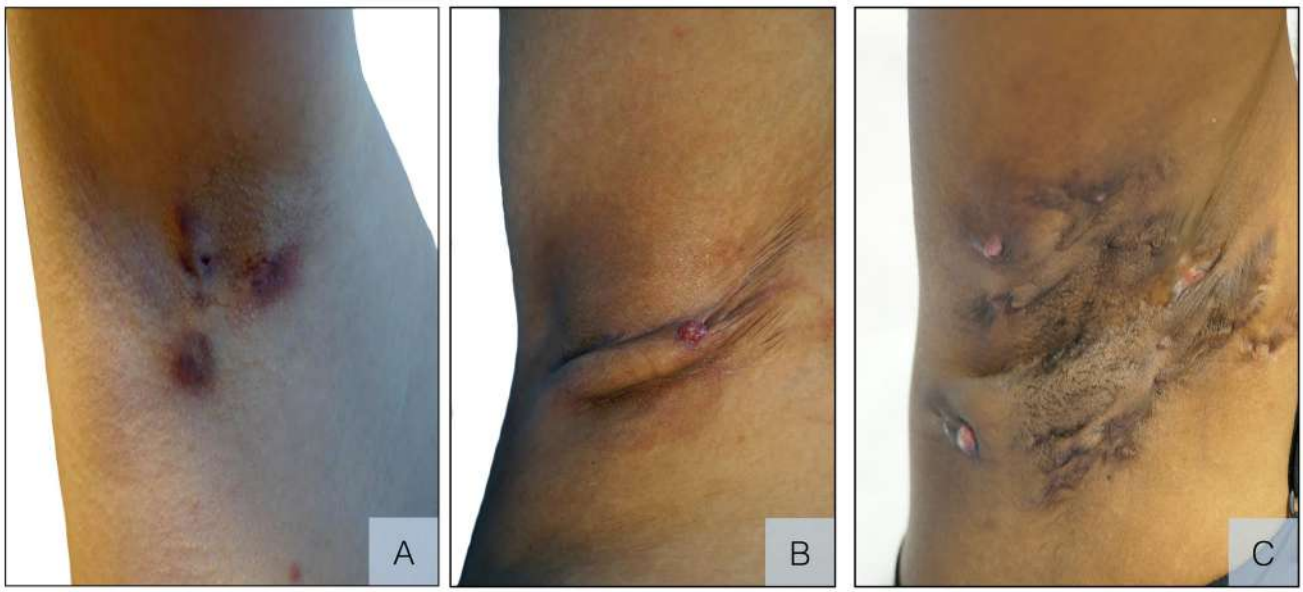

Figure 2. Hurley Stages of Hidradenitis Lesions

Above are examples of HS lesions in the axilla. Stage I is characterized by mild disease limited to recurrent, acutely inflammatory cystic nodules (Panel A), that may be connected by isolated sinuses in Stage II (Panel B), or form a network of bridging sinuses in Stage III (Panel C) associated with odiferous, purulent drainage.