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REVIEW

Incidence, Risk Factors, and Prognosis of Hidradenitis Suppurativa Across the Globe: Insights from the Literature

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Abstract: Hidradenitis suppurativa, a chronic inflammatory disease of the skin, affects a patient's quality of life to a greater extent. While the disease burden, including its incidence and prevalence, has been extensively studied in the western population, there is a paucity of data from developing countries on the epidemiology of Hidradenitis suppurativa. Therefore, a general literature review was conducted to shed light on the epidemiology of Hidradenitis suppurativa across the globe. We reviewed the most recently available information on epidemiology, including incidence, prevalence, risk factors, prognosis and quality of life, complications, and associated comorbid among patients with Hidradenitis suppurativa. The estimated global prevalence of Hidradenitis suppurativa is found to be 0.00033–4.1%, with a relatively higher prevalence of 0.7–1.2% in European and US populations. Both genetic and environmental factors are associated with Hidradenitis suppurativa. Patients with Hidradenitis suppurativa have associated comorbid such as cardiovascular disease, type II diabetes mellitus, mental health issues, and sleep and sexual dysfunctions. These patients spend poor quality of life and tend to be less productive. Future studies are needed to assess the burden of Hidradenitis suppurativa in developing countries. Since the disease tends to be underdiagnosed, future studies should rely on clinical diagnosis rather than self-reporting to avoid the potential of recall bias. Attention needs to be diverted to developing countries with less amount of data on Hidradenitis suppurativa.

Keywords: Hidradenitis suppurativa, epidemiology, globe, literature review

Introduction

Hidradenitis suppurativa (HS) is a chronic inflammatory disease of the skin characterized by several painful lesions that mostly affect intertriginous areas such as the axilla, inguinal region, perianal, and gluteal regions.[1,2] HS is manifested by the occlusion of hair follicles characterized by inflammation, healing, and scarring in a cyclical manner.[2] HS typically starts in adulthood; however, it is unclear whether its remission occurs during menopause.[3] It is considered an orphan disease with substantial diagnostic delays, and it has been a challenge for clinicians to estimate the true burden of Hidradenitis suppurativa.[4] Because HS is under recognized, the true prevalence of this disease is underestimated. Based on the existing evidence, the prevalence of HS shows wide variations between 0.00033% and 4.1%.[5–7] The gender ratio of HS varies across the regions.[8] For example, females are three times more likely to be affected by HS than males in North America and Europe.[8] On the contrary, males are two times more likely to be affected by HS than females in South Korea.[8] This implies that the epidemiology of Hidradenitis suppurativa may not be similar and, therefore, cannot be generalized from one population to the other.[5,6] However, the variations in the epidemiology could be because of heterogeneity in measurement methods and differences in populations being studied.[5,6]

Overall, the prevalence of HS remains uncertain. However, utilization of large databases may help epidemiologists with the precision of existing estimates.[9] While the epidemiology of HS may be well established in Western countries such as the United States of America (USA) and Europe, Hidradenitis suppurativa needs to be explored in other countries

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of the world, especially non-western populations. For example, existing evidence on HS is mostly from countries such as the USA, the United Kingdom (UK), Spain, Denmark, France and Mali.[8] For instance, recently, a systematic review was published on the prevalence of Hidradenitis suppurativa.[10] However, the authors only included studies from the USA, Australia, Scandinavian countries, and Western Europe.[10] This suggests a dearth of literature from other parts of the world, mainly non-western countries.

Consequently, researchers and clinicians are not aware of the burden of HS, its risk factors, incidence or prevalence, and its prognosis in developing countries. Since HS is associated with substantial physical, emotional, and psychological burdens, it is important to shed light on its epidemiology from both developed and developing countries as well.[11–14] Given the lack of literature on the epidemiology of HS from developing countries, we undertook a review of different domains of epidemiology such as prevalence, incidence, risk factors, outcomes, prognostic factors, and distribution across the globe.

Epidemiology of the Hidradenitis Suppurativa

Prevalence or Incidence of Hidradenitis Suppurativa

According to various studies conducted across the globe, the prevalence of HS varies across different countries, depending upon the type of population, methods to collect data, and data sources used.[15] More precisely, studies using registry-based sources report a low prevalence of <0.1%. In contrast, studies based on self-reporting report a high prevalence of 1 to 2%.[15] However, the most recent data from western countries, such as USA and Norway, reveal a surge in the incidence of the disease compared to the past years.[16–18] The prevalence and incidence in Germany was reported to be 0.03%.[19] Women and 30–40 years old individuals were found to have a higher prevalence rate of HS.[19] This discrepancy may be due to under-reporting of mild disease or misclassification or underdiagnosis of the disease. In addition, the variations in ethnicities cannot be ruled out as the burden of the disease is even lower in countries such as japan (0.03–0.40%) and Korea (0.06%).[20,21] Similarly, the data from the USA reveal that HS is relatively more common in African Americans (0.3%) than white population (0.09%).[22] However, the prevalence in biracial individuals is 0.22%, at an intermediate level.[22] Generally, the prevalence of HS is higher in western countries such as the USA, UK, Denmark, and Norway than in non-western countries such as Japan, Korea, and Taiwan, as shown in Table 1.

Risk Factors or Determinants of Hidradenitis Suppurativa

The existing literature provides a wide evidence base to advance our understanding of the risk factors associated with HS. Both genetics and environment play a vital role in the disease pathogenesis. For example, the evidence shows that 34% of the first-degree relatives had HS, suggesting a link with genetics.[23] The evidence suggests that one type of HS may be transmitted in an autosomal dominant fashion.[23,24] In addition, both genders (males and females) are affected through vertical transmission across several generations, indicating the autosomal dominant inheritance of the disease.[23–25] Genetic research in a large study (four generations of Chinese family) suggested that the locus for the disease is found on chromosome 1p21.1–1q25.3; however, a specific gene could not be identified.[26] The majority of variants implicated in HS involve one of the four γ-secretase complex (GSC) genes but predominantly NCSTN.[27]

Besides a link to genetics, environmental factors also contribute to HS. For example, a retrospective study (n=45) demonstrated that ten patients had reported mechanical irritation before the disease started.[28] The mechanism by which inflammatory skin disease forms localized patterns of lesions is poorly understood. Hidradenitis suppurativa is usually located to intertriginous areas. These areas are exposed to significant mechanical stress (friction, pressure and shear forces).[29] Additionally, it is believed that HS is worsened by the usage of antiperspirants.[30] The literature suggests that antiperspirants can aggravate HS by forming a film on the skin in the axilla.[31] However, the studies are limited by recall bias.[31] Mechanical stimuli have also been shown to promote keratinocyte differentiation and proliferation, thus contributing to epidermal thickening and retention of hair follicle debris. In addition to these physical effects, friction has also been shown to contribute to the inflammatory cascade in HS through immunologic means. Mechanical stress increases matrix metalloproteinase 9 levels in keratinocytes, and several genes related to wound healing (connexin 43,

Table 1 Epidemiology of Hidradenitis Suppurativa: Insights from Literature Review

Study	Year	Setting	Data Source	Sample Size	Study Design	Gender Distribution	Prevalence/Incidence	Risk Factors	Comorbid Associated with HS	Conclusion
Revuz et al[36]	2008	France	Population-based survey	10,000	Case-control study	M: 26.0% F: 73%	The prevalence was 1% in French population	Current smoking: (OR: 4.16 and 95% CI: 2.99 to 8.69) Body mass index (OR: 1.12 and 95% CI: 1.08 to 1.15)	Not the scope of the study	The disease is associated with smoking and being overweight
Vinding et al[68]	2013	Denmark	Danish General Suburban Population Study	16,404	Cross-sectional population-based study	M: 34.3% F: 65.7%	The prevalence was 2.10% (95% CI: 1.88–2.32) with 1.58% prevalence among men (95% CI: 1.29–1.86%) and 2.56% among women (95% CI: 2.21–2.86%)	Not the scope of the study	Not the scope of the study	The findings suggest a higher prevalence than it used to be in the past. However, findings need to be interpreted cautiously because the data heavily relied on patient recall.
Kromann et al[69]	2014	Netherlands	Postal follow-up survey and medical records	212	cross-sectional study	M: 12.3% F: 87.7%	Not the scope of the study	Smoking and obesity were not associated with remission of HS	Not the scope of the study	39% of the patients had remission of HS, and 31.5% reported improvement in the disease. 8.7% of the patients reported worsening of the disease.
Carg et al[22]	2017	USA	Electronic medical records, claim systems, practice management systems, and laboratories	4769	Population-based analysis	M: 26.2% F: 73.8%	The Point prevalence was 0.10 (98/100,000 persons), with the highest prevalence among women (137/100,000) and those aged 30–39 years (172/100,000) and African American (296/100,000) and biracial (218/100,000 persons)	Not the scope of the study	Not the scope of the study	HS is neither an uncommon nor rare disease in the USA that affects females, youngsters, and African American populations
Lee et al[70]	2018	Korea	National Health Insurance database	28,516	Nationwide population-based cross-sectional study	M: 61.3% F: 38.7%	Period prevalence rate: 0.06% 55.8 patients per 1,000,000 persons (95% CI: 55.1 to 56.4) The standardized prevalence rate was 59.6 per 100,000 persons Males: 68.3 patients per 100,000 persons Females: 43.2 patients per 100,000 persons	Not the scope of the study	Rheumatoid Arthritis type I diabetes Ankylosing Spondylitis Ulcerative Colitis Type 2 Diabetes Hypertension Acne Conglobata Psoriasis alopecia areata Vitiligo	Prevalence was lower in Korea compared to western countries Males had a higher prevalence than females

(*Continued*)

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Table 1 (Continued).

Study	Year	Setting	Data Source	Sample Size	Study Design	Gender Distribution	Prevalence/Incidence	Risk Factors	Comorbid Associated with HS	Conclusion
Ingram et al[71]	2018	UK	Clinical Practice Research Datalink linked to hospital episode statistics data	68,890	A population-based observational and case-control study	Not reported	Point prevalence was 0.77%, with a 95% CI of 0.76–0.78%	Smoking (OR: 3.61 and 95% CI: 3.44–3.79) and Obesity (OR: 3.29: 95% CI: 3.14–3.45) were found to be risk factors for the HS Women tend to have more prevalence in their fourth or fifth decades	Type 2 DM, Chron's disease, depression, hyperlipidemia, and acne	Contrary to the previous studies, HS was found to be common in UK with an increase to prevalence from 0.77% to 1.19% after including the probable cases
Kirsten et al[19]	2019	Germany	Hospital discharge data, health insurance data	2.3 million	Population-based study	M: 40.0% F: 60.0%	The Incidence and prevalence of HS were 0.03% Age and sex-adjusted prevalence is 0.04%	Women were at a higher risk (0.03) than men (0.02) and the age group of 30–40 years had a higher risk	Not the scope of the study	The prevalence in Germany was lower than the expected prevalence. This could be due to the underdiagnosis of the disease.
Hayama et al[72]	2020	Japan	Nationwide questionnaire-based study	300	Survey	M: 73.0% F: 27.0%	There is a higher incidence of Hurley stages II (36.3%) and III (40.3%). The mean duration of the disease was 92.3 months.	Male was at higher risk than females. Diabetes was associated with more severity of the disease	Not the scope of the study	Patients with HS in Japan have different backgrounds than patients in the western world, with male predominance and higher Incidence of stages II and III.
Liang et al[73]	2021	Taiwan	National Health Insurance database	23 million	Retrospective population-based cohort study	Not reported	The 14-Year period prevalence rate was 185.6 per 100,000 (95% CI: 177.3–194.3) with an annual percentage change of 2.96% (95% CI: 1.73–4.17). Mean annual adjusted incidence rate was 11.8 per 100,000 with an annual percentage change of 4.65% (95% CI: 3.32–5.95) The female: Male ratio for prevalence was 0.92 and 0.94 for incident cases	Male was at higher risk than females. Age group of 15 to 24 years was at higher risk	Not the scope of the study	Lower Incidence and prevalence were reported compared to western countries. Male predominance was reported in Taiwan

laminin α5, interleukin α, endothelin 1, keratinocyte growth factor) which are downregulated in response to mechanical stress.[32]

Another mechanism could be by causing chemical irritation leading to the closure of pores or causing alteration in the normal flora of the axillary region. Another study suggested that usage of razors may increase the vulnerability of HS by enhancing access to bacteria through follicular infundibulum transection. However, a matched case–control study did not show any significant differences in shaving, application of deodorants, and talcum powder application in both inguinal and axillary regions, as suggested by the previous studies.[33]

The role of bacteria in HS is matter of debate. An impaired immunity, especially the upregulation of the Th17 pathway, is likely to be an important factor in the pathogenesis of HS. It is possible that bacteria play a role in maintaining the chronic inflammatory response.[34]

Bacterial growth in HS patients has shown a high level of resistance to antibiotics, including rifampicin, clindamycin and tetracyclines, mentioned as an empirical choice in HS therapeutic guidelines. A targeted and specific antibiotics, determined by microbiological evaluations with prolonged culture periods, seems more appropriate.[35]

Lifestyle factors such as smoking and obesity are linked to Hidradenitis suppurativa.[36,37] The literature suggests that 70–89% of the patients with Hidradenitis suppurativa are smokers, indicating that tobacco is a triggering factor for HS[37,38] For example, a study conducted in France illustrated a strong association between smoking and HS.[36] These findings can be explained by that smoking tends to alter neutrophilic granulocytes and function of sweat glands.[39] Similar to smoking, obesity appears to be associated with HS. For example, around 52% of the subjects with HS were obese, and 21.5% were markedly obese in one study.[40] Recently, a study found a significant association between obesity and HS.[36] The association between obesity and HS can be explained by many ways. For instance, obesity can cause sweat retention and abnormal metabolism of hormones. Skin-to-skin contact leads to shearing that may trigger follicular plugging.[41,42] In addition, the skin to skin contact can also promote keratin hydration within sweat glands, resulting in a reduction of the diameter of the follicular orifice and occlusion of pores.[41,42] Furthermore, obesity also alters hormonal metabolism, resulting in excess of androgens. Androgens excess release may lead to coarsening of the hair shaft, thereby follicular plugging.[41,42]

Prognosis and Complications

Hidradenitis suppurativa can lead to substantial complications such as squamous cell carcinoma, with a higher ratio in males than females.[43] The literature suggests that about 61% of patients with HS may have scc in the perineum or buttocks and 48% of these patients died within the duration of two years after being diagnosed with squamous cell carcinoma.[44] The probable factor in the development of squamous cell carcinoma could be human papillomavirus.[45] Additionally, HS can lead to anemia, anal and urethral strictures and fistulas, lumbosacral epidural abscess, and sacral bacterial osteomyelitis.[46,47] The findings of a retrospective study (n=200) demonstrated that patients with Hidradenitis suppurativa had a 50% more risk of the incidence of malignancy.[48] Also, these patients were 4.6 times more likely to develop cutaneous squamous cell carcinoma.[48]

Comorbidities Associated with Hidradenitis Suppurativa

HS is associated with a myriad of comorbidities. The most intuitive comorbidity is probably the follicular occlusion triad, comprised of HS, acne conglobata, and dissecting cellulitis affecting the scalp.[49] This triad can become follicular occlusion tetrad if it occurs in conjunction with pilonidal sinus.[49] The associated comorbidities of HS are mostly autoimmune diseases such as ulcerative colitis, Crohn's disease, and seronegative spondyloarthropathies.[50] In addition, endocrine disorders such as acromegaly, diabetes, and Cushing disease are also associated with HS. Further, some genetic disorders such as down syndrome and keratitis-ichthyosis-deafness syndrome have also been recognized.[51] Further, HS has also found to be associated with metabolic syndrome and risk factors for cardiovascular disease.[52] For instance, findings from a systematic review and meta-analysis revealed that adults with HS are two times more likely to develop metabolic syndrome than adults without HS.[53] In addition, the findings from the meta-analysis suggest that type-II diabetes and polycystic ovarian syndrome are more commonly found among patients with HS than without.[54] Similarly, mental health issues, such as substance use disorders, including alcohol use, cannabis, opioid use, and suicide, are

common in these patients.[55,56] The prevalence of substance use is 4% among patients with HS than without HS.[57] While the data on the association between HS and other comorbid is obtained from large data sets, one should not overlook the potential for recall bias and lack of clinical information.[58] Also, population-based cohort studies have people with unique demographics, so the findings may not be generalizable to other populations.[59]

Quality of Life Among Patients with Hidradenitis Suppurativa

HS negatively influences the quality of life in multiple ways.[60] Patients with HS suffer from pain, low self-esteem, itching, sexual dysfunctions, and deteriorated mental health. Symptoms such as pain (neuropathic and nociceptive) and itching may interfere with daily functions and quality of sleep, impair duration and amount of sleep, thereby resulting in a less productive life and dysfunction during day timings.[61,62] In addition, the associated comorbidities such as anxiety, depression, and loneliness may affect the quality of life in these patients.[63,64] Another crucial aspect of quality of life is sexual health, which is affected badly in patients with HS.[65] Studies also reveal that patients with HS report a lack of intimacy with their partners and report sexual assault as well.[66]

Regarding effect of HS on patients' work, Matusiak et al studied the impact of HS on quality of life and professional activity including work among 54 Polish patients with HS aged 16–65 years. The disease caused the work absence of 58.1% of patients among the 30 employed and professionally active HS patients. Annually, the absence from work caused by HS occurred from one to 10 times with average 34 days absence from work annually. During follow-up, three employees (10%) were dismissed from work because of the frequent absences and inability to perform their work duties properly. Moreover, seven individuals (23.3%) reported that they were unable to be promoted or affected by disease-related difficulties to promotion or improvement.[67]

Conclusion

This general literature review provides a comprehensive overview of the epidemiology of Hidradenitis suppurativa, including prevalence, incidence, risk factors, complications, associated comorbid, prognosis, and quality of life. It seems that most of the evidence on epidemiology is from high-income countries, and there is a paucity of literature from developing countries. Since the disease tends to be under recognized, future studies should rely on clinical diagnosis rather than self-reporting to avoid the potential of recall bias. Attention needs to be diverted to developing countries with less amount of data on Hidradenitis suppurativa.

Disclosure

The author reports no conflicts of interest in this work.

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