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HIDRADENITIS SUPPURATIVA AND DIABETES MELLITUS: A SYSTEMATIC REVIEW

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Abstract

Objective: *Hidradenitis suppurativa (HS), also known as acne inversus is a persistent inflammatory skin disease. This condition causes lesions such as deep-seated nodules and abscesses, draining tracts, and fibrotic scars. Preliminary data indicates a possible biological connection between diabetes mellitus (DM) and HS. This study aimed to review the correlation between hidradenitis suppurative and diabetes mellitus systematically.*

Materials and methods: *A systematic search strategy was conducted across several electronic reference databases (PubMed, Cochrane Library, ProQuest) and included articles published between 2019–2023. Duplicate publications, review articles, and incomplete articles were excluded.*

Results: *Database search yielded 214 articles, which were systematically eliminated, leaving 5 relevant articles. Analyzed articles showed the association between diabetes mellitus and hidradenitis suppurativa.*

Conclusion: *Studies support a significant relationship between HS and DM. Although the prevalence was variative, the association between the two conditions was significant.*

Keyword: *alopecia areata; covid-19; hair loss*

INTRODUCTION

A persistent inflammatory skin disease known as hidradenitis suppurativa (HS), also known as acne inversus, causes lesions such as deep-seated nodules and abscesses, draining tracts, and fibrotic scars.[1] These tumors most frequently develop in the intertriginous and apocrine gland-rich regions. Women are more likely to experience this recurrent inflammatory skin disease, which has an approximate frequency of 1-4%.[2] The start age for HS is typically between 20 and 40 years of age, though reports of new-onset HS in elderly women and prepubescent children have also been made. When compared to the West, hidradenitis suppurativa (HS) in South-East Asia and East Asia exhibits unique clinical, environmental, physiological, and probably genetic variations.[3] Clinical signs can include swollen lumps, abscesses, and scarring.[4]

Previous research has suggested that dietary variables, smoking, metabolic syndrome, mechanical stress, and hormonal factors can cause or exacerbate HS.[5] Even though there is no question about the statistical support for this, at least for some risk factors like smoking and obesity, it is still unclear how these risk factors add to the pathogenesis of HS. Additionally, preliminary data indicates a possible biological connection between diabetes mellitus (DM) and HS. The few studies that have examined the connection between DM and HS have produced contradictory findings.[6] This study aimed to review the correlation between hidradenitis suppurative and diabetes mellitus systematically.

Methods

This study was a systematic review, with a systematic literature search on the PubMed, Cochrane Database of Systematic Reviews, Google Scholar, and Directory of Open Access Journals (DOAJ) databases. The search was conducted in English, using keywords related association between hidradenitis suppurativa and diabetes mellitus, including *hidradenitis suppurativa, acne inversa, and diabetes mellitus*. The search was performed with a combination of some or all of these keywords, both in the title and abstract of the article. Search is limited to publications in the period February 2019 to February 2023.

Study designs included in this study were before-and-after studies with or without controls, retrospective and prospective cohort studies, interrupted time series analysis, and randomized controlled trials. Studies on interventions in both adult and pediatric patients were included if there were complete data on pediatric patients. Literature review articles, case series, letters, notes, conference abstracts, and conference articles were excluded. Data were extracted using a standardized table that includes the name of the authors, year of publication, study design, study setting, number of subjects, the treatment used, and the key findings of each study. After searching and filtering articles based on search keywords, article analysis was done manually by considering the title's and abstract's relevance. Articles that meet the inclusion and exclusion criteria that are unclear will be analyzed further by reading the full text of the article and entering the relevant information in the data extraction table. The results obtained in the included studies will be compared with those of other systematic reviews and literature.

Result

Study Selection

A systematic search was carried out and yielded 287 articles (Fig. 1). A total of 153 articles remained, after rechecking and excluding duplicated articles. A total of 27 articles were eligible for this study. Then, after a comprehensive review of the full-text articles, the remaining 6 articles were included in this study. The database search results are described in Table 1 and Figure 1. The summary of each included study is described in Table 2.

Included Articles

Of the 5 included studies, 3 were retrospective cohort studies, and 2 were cross-sectional studies.

Populations of Included Articles

A total of 4548 patients were involved in the 5 included studies. The age of the research subjects varied from zero years to more than eighty years. All studies were single-center studies.

Figure 1. Systematic Search

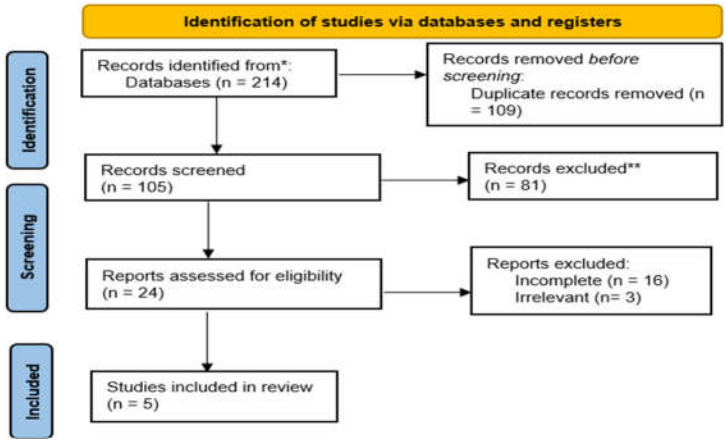

Table 1. Study Characteristics and Finding

Author	Design	Country	Subjects	Age	Findings
Jorgensen et al, 2021[7]	Retrospective cohort	Denmark	302	39.4 (13.3)	There were 2.1 conditions on average for each subject. With indications of significant underdiagnosis and undertreatment, 76.5% of people had one or more cardiovascular (CV) conditions, including 36.7% of people with obesity, 9.3% of people with diabetes, 48.4% of people with hypertension, and 57.7% of people with dyslipidemia. Significant indicators of the start of diabetes were P 0.001.
Yuksel et al, 2020[8]	Retrospective cohort	Turkey	208	10-60	Diabetes was one of the associated systemic illnesses in 2.4% subjects.
Reddy et al, 2019[9]	Cross-sectional	US	3818	43.7 (14.6)	Chronic pulmonary disease (1540 [40.3%]; diabetes with chronic complications (365 [9.6%]; diabetes without chronic complications (927 [24.3%]); and moderate liver disease (455 [11.9%]) were the most prevalent comorbidities among individuals with HS.
Kluger et al, 2020[10]	Retrospective cohort	Finland	166	38.4 (13.8)	The current cohort's T2DM incidence was 15.7% (n=26). At the time that HS was diagnosed, sixteen individuals had T2DM. It is unknown how T2DM and HS are related causally. According to Hurley stages, patients with T2DM appeared to have a more serious condition.
Garg et al, 2019[11]	Cross-sectional	US	Female	54	Patients with HS had a frequency of DM overall of 24.8%, compared to patients without HS who had a prevalence of 15.6%. The prevalence was highest in elderly, male, non-white, obese, smokers, hypertensive, and hyperlipidemic HS patients.

Discussion

Hidradenitis suppurativa (HS) is a persistent skin condition that significantly impacts quality of life due to its mental, physical, and psychological effects. Prevalence estimates vary from 1% to 4%.[2] The disease typically first manifests between adolescence and age 40, most frequently between the ages of 21 and 29. About three to one, women are more likely than males to be impacted. The available data cannot demonstrate a trend of racial or cultural preference.[1,4]

The precise cause of HS is still unknown. It is thought that hidradenitis suppurativa appears to be influenced by factors in the surroundings, society, and behavior.[4,5] A first-degree cousin with hidradenitis suppurativa is reported by 33–40% of those with the condition, which raises the possibility of an underlying genetic factor with an autosomal dominant transmission pattern. Researchers have discovered a mutation of the gamma-secretase, notch signaling pathway in a tiny subgroup of afflicted families.[12] Additionally, behavioral and environmental variables play a role. People with HS are more likely to be overweight or obese. Since metabolic syndrome is more prevalent in fat people, it is also more frequent in HS. Occlusion and following inflammation of the hair follicle are the main pathophysiologic defects in HS; these conditions, along with both innate and adaptive immune dysfunction, are required to start the development of clinical HS.[13] Infection and colonization by bacteria are regarded as additional pathogenic components that can exacerbate HS. The follicular contents leak into the adjacent dermis due to follicular occlusion, which causes dilation and then burst. This causes a strong chemotactic reaction from neutrophils and lymphocytes. The pilosebaceous unit and ultimately other nearby adnexal structures are destroyed when an abscess forms as a result of the inflammatory cellular invasion.[4,14]

Interleukin (IL)-10, IL-17, IL-1b, and tumour necrosis factor (TNF)-a levels in HS tissue were found to be elevated through biomolecular analysis, supporting a widespread inflammatory etiology. The link between HS and cardiovascular risk factors like smoking, obesity, hyperlipidemia, and metabolic syndrome is also supported by accumulating research.[15,16]

Kluger et al found that T2DM prevalence of 15.7% is consistent with the literature's 4.5 to 25% values. It is unknown how T2DM and HS are related causally. Through chronic inflammation with increased TNF-alpha, HS may contribute to T2DM, or insulin intolerance may make HS more likely. Although 61% of the patients had T2DM prior to receiving an HS diagnosis, our findings do not support a causal link between T2DM and HS.[10] When we received our prognosis, we had no T2DM. In addition, individuals may have had HS for a prolonged time before even developing T2DM, and diagnosis delays can be significant. According to Hurley stages, patients with T2DM also appeared to have a more serious form of the illness.[8]

Garg et al also found that prevalence of DM in patient with HS was higher than general population. Patients with HS had a frequency of DM overall of 24.8%, compared to patients without HS who had a prevalence of 15.6%. The prevalence of DM was highest in elderly, male, non-white, obese, smokers, hypertensive, and hyperlipidemic HS patients.[17] The results are consistent with previous meta-analysis data that showed HS was linked to a 1.69-fold higher risk of diabetes than non-HS patients. The total risk difference, however, was incredibly tiny (16.1% vs. 15.7%).[18]

The relationship between HS and DM has been the subject of numerous potential explanations in earlier research. First, a hyperandrogenic condition with increased androgenic hormone aromatization in peripheral adipose tissue is believed to be the precursor to HS. Additionally, there is clinical proof linking polycystic ovary syndrome, another hyperandrogenic condition, and HS. The finding that patients with HS are more likely to become obese is believed to be explained by this mechanism.[19–21] Patients with HS who are obese have a higher chance of getting diabetes because obesity is a significant

risk factor for the disease. However, Phan et al multivariate's adjusted analysis revealed that HS still accurately predicted DM even after controlling for weight as a mitigating variable.[18]

It has been established that inflammatory pathways play a key role in the etiology of HS. According to biomolecular research, HS is associated with significant increases in a number of cytokines and indicators, especially TNF-a. TNF-a dysregulation could prevent insulin signaling, including the activation of insulin receptor substrate 1 in its downstream pathways. A possible process linking HS to DM is altered regulation of this pathway, which has been associated with the emergence of insulin resistance and diabetes.[19,20] In addition, HS has been found to have considerably greater levels of inflammatory indicators than other dermatological conditions like psoriasis, including C-reactive protein and leucocyte counts. Additionally, it has been noted that HS has lower levels of precursor endothelial cells in circulation, which are known to increase pancreas b-cell viability.[11,18,22]

According to a previous comprehensive review and meta-analysis by Phan et al, there are numerous clinical consequences for the link between HS and DM.[18] First, regardless of the patient's cardiovascular risk factors, treating physicians should be cautious of possible blood glucose elevations given the increased and separate risk of DM in HS.[23,24] As a result, even if a patient does not have conventional cardiovascular or metabolic risk factors, their HS disease process still puts them at risk of getting DM. Another consequence is that traditional hypoglycemic therapies for DM may also be useful for treating and managing HS. For instance, metformin treatment for HS patients has been linked to a better quality of life.[25]

Conclusion

Hidradenitis suppurative (HS) is a persistent skin condition that significantly impacts the quality of life due to its mental, physical, and psychological effects. Prevalence estimates vary from 1% to 4%. Studies support a significant relationship between HS and DM. Although the prevalence was variative, the association between the two conditions was significant. Clinicians working with patients with HS need to be mindful of this possible link.

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