Overall and subgroup prevalence of acne vulgaris among patients with hidradenitis suppurativa

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Background: Evidence establishing a link between acne vulgaris (AV) and hidradenitis suppurativa (HS) is limited, and the burden of AV in adults with HS is unknown.

Objective: To determine the prevalence of AV among adults with HS and determine the strength of this association.

Methods: Cross-sectional analysis identifying adults with AV among patients with and without HS by using electronic health record data from a population-based sample of more than 55 million patients.

Results: The prevalence of AV among adults with HS was 15.2% (7315 of 48,085) compared with 2.9% (497,360 of 16,899,470) for adults without HS ($P < .001$). The prevalence was greatest among patients with HS who were female (5870 of 35,790 [16.4%]), were 18 to 44 years old (5260 of 28,870 [18.2%]), were nonwhite (3120 of 17,825 [17.5%]), were obese (5430 of 35,135 [15.5%]), and had polycystic ovarian syndrome (685 of 2385 [28.7%]). Patients with HS had 4.51 [95% confidence interval, 4.40-4.63] times the odds of having AV than did patients without HS, with the higher likelihood of having AV persisting across all subgroups of patients with HS. The association between HS and AV was generally stronger for patients who were male, and 65 years of age or older.

Limitations: Influence of disease severity in HS, or in acne, on the strength of the association could not be assessed.

Conclusion: Patients with HS may benefit from assessment of acne status and optimization of comanagement strategies. (J Am Acad Dermatol 2019;80:1308-13.)

Key words: acne vulgaris; burden; Explorys; hidradenitis suppurativa; prevalence.

Hidradenitis suppurativa (HS) is a chronic inflammatory disease involving the follicular unit that results in painful nodules and draining abscesses and causes formation of fistulas, sinus tracts, and scarring, commonly affecting the axillae, breasts, groin, and perineum.[1] Acne vulgaris (AV) is a disease of the pilosebaceous unit that, like HS, frequently affects young adults,[2,3] has as female predominance[3,4] and may be mediated in part by androgens, as suggested by their links to polycystic ovarian syndrome (PCOS).[5,6] These conditions may also share common pathways that result in inflammation of the follicular unit.[7,8]

The prevalence of AV reported within HS cohorts ranges from 33% to 45%,[9-12] and these data support the common belief that AV is strongly linked to HS. However, the evidence linking AV to HS is substantially limited in strength. Our objective was to

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investigate the prevalence of AV among patients with HS in a population-based sample and determine the strength of association between these 2 conditions.

METHODS

This was a cross-sectional analysis using a multi—health system data analytics and research platform (Explorys) that was developed by IBM Watson Health (Cambridge, MA).[13] Clinical information from electronic medical records, laboratories, practice management systems, and claims systems was matched by using the single set of Unified Medical Language System ontologies to create de-identified longitudinal records for unique patients. The data were standardized and curated according to common controlled vocabularies and classification systems, including the International Classification of Diseases (ICD), Systemized Nomenclature of Medicine—Clinical Terms (SNOMED-CT), Logical Observation Identifiers Names and Codes (LOINC), and RxNorm.[14-17] IBM Watson Health continually monitors the data standardization process to ensure accuracy. A sample of patients is reviewed for each measure to validate that patient data are being represented accurately. At present, the database encompasses 27 participating integrated health care organizations. More than 55 million unique lives representing approximately 15% of the population across all 4 census regions of the United States are captured. Patients with all types of insurance, as well as those who are self-pay, are represented.

CAPSULE SUMMARY

- This analysis significantly augments the literature establishing a link between acne vulgaris and hidradenitis suppurativa.
- Understanding the burden of acne vulgaris among patients with hidradenitis suppurativa may support evaluation and optimization of management for both conditions.

The SNOMED-CT term *hidradenitis*, which has 1-to-1 mapping with the ninth revision of the ICD (ICD-9) code for hidradenitis (705.83), was used to identify patients with HS. In validating the case cohort, we observed a positive predictive value (PPV) of 79.3% and an accuracy of 90% for diagnosis of HS with use of a single ICD-9 code for HS.[18] This case identification method was previously validated by an independent group, and it was shown to have a PPV of 77%.[19] The SNOMED-CT term *acne,* which is associated with ICD-9 code 706, was used to identify the AV cohort; this method has been validated previously.[20]

Statistical analysis

The study population included patients 18 years or older with an active status in the database within the past 5 years (October 2012 to October 2017) who had available race, sex, and age information, as well as at least 1 measurement of body mass index (BMI) within the study period. The primary outcome of interest was diagnosis of AV. Sex (male vs female) and race (white vs nonwhite) were recorded as categoric variables. Age in years was recorded as a categoric variable within 1 of 3 groups: 18 to 44, 45 to 64, and 65 or older. Information on BMI was derived from height and weight measurements taken during the course of care. Patients with a BMI of 30.0 kg/m^2 or more were classified as obese, whereas those with BMI less than 30.0 kg/m^2 were considered nonobese. The SNOMED-CT terms *tobacco user* (ICD-9 code 305.1) and *nicotine dependence* (ICD-10 code F17.2) were used to identify the cohort of active tobacco smokers. Individuals with no record of either of these terms were considered nonsmokers. The SNOMED-CT term *polycystic ovarian syndrome*, corresponding to the ICD-9 code 256.4, was used to identify patients with PCOS. The use of this code to identify PCOS has 90% PPV for definite and probable PCOS.[21]

We obtained population level counts for the numbers of patients with and without a diagnosis of AV for each combination of categoric predictor variables (HS status, age, sex, obesity, smoking status, and PCOS status). Descriptive statistics were produced to characterize the cohorts with and without HS. We calculated the crude prevalence of AV among patients with HS and without HS, as well as group-specific prevalences for demographic subgroups within these 2 cohorts. The prevalence of acne among patients with and without HS was compared by using an adjusted odds ratio (OR) from a logistic regression model, controlling for HS status, age, sex, race, obesity, smoking status, and PCOS status. Potential differences in the relationship between HS and AV across subgroups were tested by including an interaction term for HS and the subgroup variable of interest in separate logistic regression models. All analyses were performed with use of SAS software (version 9.4, SAS Institute Inc, Cary, NC). This investigation was approved by the human subjects committee of the Feinstein Institute for Medical Research at the Northwell Health.

Abbreviations used:

AV:	acne vulgaris
BMI:	body mass index
CI:	confidence interval
HS:	hidradenitis suppurativa
ICD:	International Classification of Diseases
ICD-9:	International Classification of Diseases, Ninth Revision
OR:	odds ratio
PCOS:	polycystic ovarian syndrome
PPV:	positive predictive value
SNOMED-CT:	Systemized Nomenclature of Medicine—Clinical Terms

RESULTS

We identified 48,085 adult patients with HS; their characteristics are described in Table I. The overall prevalences of AV were 15.2% (7315 of 48,085) and 2.9% (497,360 of 16,899,470) among patients with and without HS, respectively ($P < .0001$). In the univariable model, patients with HS had 5.92 (95% confidence interval [CI], 5.77-6.07) times the odds of having AV than did patients without HS. After adjustment for age, sex, obesity smoking status, and PCOS status, the likelihood of patients with HS having AV remained substantially increased (OR, 4.51; 95% CI, 4.40-4.63).

In subgroup analysis, the prevalence of AV was greater among women with HS (16.4%, vs 11.8% in men [$P < .0001$]) and women without HS (3.6% vs 2.1% in men [$P < .0001$]). Among males, patients with HS had 6.01 (95% CI, 5.68-6.36)] times the odds of having AV than did patients without HS. Among females, patients with HS had 4.22 (95% CI, 4.10-4.34) times the odds of having AV than did patients without HS (interaction P value $< .0001$) (Table II). The prevalence of AV was higher among patients with HS who were 18 to 44 years old (18.2%) and 45 to 64 years old (12.3%) than among patients with HS who were age 65 years or older (5.8%). Within each age group, patients with HS had a higher prevalence of AV than did patients without HS, with the largest relative difference observed among those age 65 years or older (OR, 10.14; 95% CI, 8.97-11.46). The strength of association among patients age 65 years or older is due in part to the low prevalence (0.7%) of AV among patients without HS in this age group. Nonwhite patients with HS had a higher prevalence of AV (17.5%) than did whites with HS (13.9% [$P < .0001$]). The association between AV and HS was similar among nonwhites and whites. The prevalence of AV was similar among obese and nonobese patients, as was the strength of association for the 2 conditions in both groups. Patients with HS who were smokers and nonsmokers had similar prevalences of AV; the difference in strength of the association between the 2 conditions was insignificant. Among patients with HS, the prevalence of AV was nearly twice as high in women with PCOS (28.7%) as among women without PCOS (15.5% [$P < .0001$]). HS was associated with increased prevalence of AV in female patients with PCOS (OR, 3.14; 95% CI, 2.86-3.44) and in female patients without PCOS (OR, 4.24; 95% CI, 4.11-4.37) (Table II).

Table I. Characteristics of the study population

Characteristic	Patients with HS (n = 48,085)	Patients without HS (n = 16,899,470)
Sex		
Female	35,790 (74.4%)	9,542,430 (56.5%)
Male	12,295 (25.6%)	7,357,040 (43.5%)
Age, y		
18-44	28,870 (60.0%)	6,695,730 (39.6%)
45-64	14,495 (30.1%)	5,577,030 (33.0%)
≥65	4720 (9.8%)	4,626,710 (27.4%)
Race		
White	30,260 (62.9%)	13,271,050 (78.5%)
Nonwhite	17,825 (37.1%)	3,628,420 (21.5%)
Obese (BMI ≥ 30.0 kg/m^2)	35,135 (73.1%)	7,624,750 (45.1%)
Tobacco smoker	28,150 (58.5%)	5,475,225 (32.4%)
Polycystic ovarian syndrome	2385 (6.7%)*	129,610 (1.4%)*

BMI, Body mass index; *HS*, hidradenitis suppurativa.
*Percentage of female patients.

DISCUSSION

In this study, we have observed an overall AV prevalence of 15.2% among adult patients with HS. Adults with HS were 4.5 times more likely to have AV than were patients without HS, and the association between AV and HS was present across all demographic subgroups. The prevalence was highest among patients with HS who were female, were 18 to 44 years of age, and had PCOS. When patients with and without HS were compared, however, the largest relative difference in AV prevalence was observed between males and older patients.

To our knowledge, there has been no prior controlled population-based analysis evaluating the burden of AV among patients with HS. The prevalence of AV among 268 patients with incident HS in Olmstead County, Minnesota, from 1968 to 2008 was 36.2%.[9] The cohort on which the prevalence of AV was based included children and adolescents, and this may account for the higher

Table II. Prevalence of acne vulgaris in subgroups of patients with HS

Subgroup	Acne prevalence		Group-specific odds ratios* (95% CI)	Interaction *P* value
	Patients with HS (n = 48,085)	Patients without HS (n = 16,899,470)		
Overall	7315 (15.2%)	497,360 (2.9%)	4.51 (4.40-4.63)	
Sex				<.0001
Female	16.4% (5870/35,790)	3.6% (344,920/9,542,430)	4.22 (4.10-4.34)	
Male	11.8% (1445/12,295)	2.1% (152,440/7,357,040)	6.01 (5.68-6.36)	
Age				<.0001
18-44	18.2% (5260/28,870)	5,6% (377,420/6,695,730)	3.67 (3.56-3.78)	
45-64	12.3% (1780/14,495)	1.6% (89,750/5,577,030)	8.52 (8.11-8.97)	
≥65	5.8% (275/4720)	0.7% (30,190/4,626,710)	10.14 (8.97-11.46)	
Race				<.0001
White	13.9% (4195/30,260)	2.9% (389,110/13,271,050)	4.03 (3.90-4.17)	
Nonwhite	17.5% (3120/17,825)	3.0% (108,250/3,628,420)	5.36 (5.15-5.58)	
Obese (BMI ≥30.0 kg/m^2)				<.0001
Yes	15.5% (5430/35,135)	2.3% (176,600/7,624,750)	4.81 (4.67-4.96)	
No	14.6% (1885/12,950)	3.5% (320,760/9,274,720)	3.82 (3.63-4.02)	
Tobacco smoker				.83
Yes	14.7% (4150/28,150)	2.8% (155,725/5,475,225)	4.50 (4.35-4.66)	
No	15.9% (3165/19,935)	3.0% (341,635/11,424,245)	4.53 (4.35-4.71)	
Polycystic ovarian syndrome				<.0001
Yes	28.7% (685/2385)†	11.6% (15,050/129,610)†	3.14 (2.86-3.44)‡	
No	15.5% (5185/33,405)†	3.5% (329,870/9,412,820)†	4.24 (4.11-4.37)‡	

BMI, Body mass index; *CI*, confidence interval; *HS*, Hidradenitis suppurativa.
*Odds ratio for acne vulgaris, comparing patients with HS with patients without HS, adjusted for all other covariates.
†Percentage of female patients.
‡Adjusted odds ratio was calculated on the basis of the sample of female patients age 18 to 64 years. Patients 65 years or older were excluded to avoid separation in the logistic regression model.

acne burden observed in this population.[2,22] Importantly however, there was no comparison with the prevalence of AV in patients without HS, nor was there any analysis of the strength of the association. The Olmstead County study noted that AV was not associated with HS severity. In a British cohort, the prevalence of past or present AV among 42 women with HS was 45%. However, this was a small sample from a single institution, and male patients with HS were not included in the analysis.[10] Several case reports and uncontrolled smaller series have also documented the presence of AV among patients with HS.[11,12,23] In contrast, 1 prospective study of 70 women with HS and 100 control patients reported no difference between cohorts in terms of the prevalence of AV.[24] Males were excluded from this analysis.

AV and HS are 2 components of the follicular occlusion tetrad that classically also includes dissecting cellulitis of the scalp and pilonidal cyst or abscess.[25] Although AV and HS both result from inflammatory pathology of the follicular unit, there are nonetheless important clinical distinctions that have been raised. Whereas follicular occlusion occurs in the terminal hair follicles in HS, follicles as part of the pilosebaceous unit are involved in AV, which may explain the differential in sites of involvement for the 2 conditions. Indeed the presence of excess sebum is a fundamental feature in acne, whereas sebum production is normal in HS. Moreover, whereas acne commonly presents with open or closed comedones, HS features only open comedones.[7,26]

Follicular obstruction, dilatation, and rupture are central features in the pathogenesis of both AV[27,28] and HS.[29,30] Inflammation in these conditions may result from shared pathways, which may partially explain their frequent coexistence. Toll-like receptor 2 is overexpressed in lesional AV and HS.[31,32] When activated, Toll-like receptors trigger downstream inflammation mediated by various cytokines.[7,27] Interleukin 1β, the levels of which are elevated in lesional HS skin and inflammatory acne, is a driver for tissue neutrophilia and promotes the type 17 helper T cell response.[33-35] Interleukin 17, which is also overexpressed in lesional AV[36] and HS,[37] is thought to play a role in pathogenesis by mobilizing neutrophils to peripheral tissues, increasing their local survival, and promoting Th17-mediated keratinocyte activation.

There are limits that warrant consideration when interpreting the results of this study. We could not capture patients who did not seek care in health systems included in the database. The extent to which our cohort underestimates AV frequency for this reason is unknown. Our analysis does not establish a temporal relationship or causal link between AV and HS. We could not assess the influence of disease severity in HS, or in acne, on the strength of the association in this claims-based analysis, nor could we establish a phenotype for patients with AV and HS. Despite these limitations, the present study reports important data describing the association between AV and HS. The prevalence and strength of association reported in this study are based on the largest and most ethnically diversified cohort of patients with HS drawn from various health care settings across all US census regions.

In conclusion, patients with HS have an increased prevalence of AV. Clinicians treating patients with HS should be aware of this burden and its potential implications, including a further impact on quality of life. Management strategies should include consideration of both conditions, either with treatments that have overlapping efficacy or with concomitant therapies.

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