Factors associated with disease-specific life impact in patients with hidradenitis suppurativa: results from the Global VOICE project

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20 **Data availability:** The data underlying this article will be shared on reasonable request to the

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23 **Ethics statement:** This study was approved by the human subjects research committee at the
24 Feinstein Institutes for Medical research at Northwell Health.
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1   Dear Editor, Among dermatologic conditions, hidradenitis suppurativa (HS) may be associated

2   with the largest impact on health and quality of life (QOL).[1] Impact and QOL in HS has largely been

3   assessed by measures developed for general skin disease or physical and mental health. Information from

4   HS patients on factors related to disease-specific life impact may support patient-centered strategies to

5   optimize outcomes. The purpose of this study was to measure association between HS-specific QOL with

6   demographic and clinical characteristics.

7   We performed a cross-sectional survey of HS patients at 27 institutions, mainly HS referral

8   centers, in 14 different countries from October, 2017 through July, 2018 (Global Survey Of Impact and

9   Healthcare Needs (Global VOICE).[1] Life impact questions comprised the 17 items from the hidradenitis

10 suppurativa quality of life (HiSQOL) measure, a validated disease-specific patient reported outcome that

11 assesses symptoms, psychosocial impact, and activity restrictions. Response to each question is scored on

12 a 5-point scale (0-4), with higher scores corresponding to worse QOL. Individual scores for each item are

13 summed to create a total score ranging from 0 to 68.[2]

14   Univariable linear regression models were used to measure the bivariate relationship between

15 each demographic and clinical variable and HiSQOL total score. Multivariable linear regression was used

16 to assess the relationship between each variable and the HiSQOL total score while adjusting for all other

17 covariates. Group differences and associations with QOL were expected to lessen when adjusting for flare

18 frequency, since flare itself is a measure of disease activity and as such it is part of the process by which

19 QOL is impaired. Accordingly, adjusting for flare frequency would reduce estimated differences in QOL

20 between groups that differ in flare frequency. Multiple imputation by chained equations with 30

21 imputations was used to account for missing data.

22   Among 1,927 participants completing the survey in clinic, 1,828 reported being diagnosed with

23 HS by dermatologists, general practitioners, or other physicians and were eligible for analysis.

24 Demographic and clinical characteristics of participants have been described previously.[1,3] Briefly, most

25 patients were aged 18-40 years (62%), female (85%), either overweight or obese (79%), and nearly half

26 were active smokers (44%).

6

1   Mean HiSQOL total score was 29.3 (SD 16.7), which corresponds to a moderate to very large

2   effect in terms of established DLQI score bands.[2] Median total score was 28.5 (IQR 16-42). In bivariable

3   analysis, factors associated with worse HS-related QOL included younger age, BMI >40.0, active

4   smoking status, increasing flare frequency, depression and anxiety, higher number of comorbidities, high

5   school education level or less, inability to work, and difficult or very difficult access to a dermatologist.

6   **(Table I)**

7   In the multivariable adjusted linear regression model, differences in HiSQOL according to

8   demographic and other factors were attenuated. **(Table I)** For example, adjusted mean HiSQOL

9   difference between patients with BMI > 40 and BMI < 25.0 was reduced from 7.9 (95% CI 5.0, 10.8) to

10 1.5 (95% CI -1.2, 4.1). Factors which remained strongly associated with HS-related QOL included

11 disability (β=4.8 vs. employed, 95% CI 2.7, 7.0), increasing number of comorbidities (β=1.5, 95% CI 0.8,

12 2.2 per comorbidity) and very difficult access to a dermatologist (β=7.4 vs. very easy, 95% CI 4.4, 10.4).

13 Increasing flare frequency was strongly associated with lower HS-related QOL and showed a graded

14 relationship. In subgroup analysis of American and Canadian patients, Black race was associated with

15 similar HS-related QOL [β=0.5, 95% CI -3.7, 4.8] before adjustment for covariates, and worse HS-related

16 QOL β=5.9, 95% CI 2.0-9.7] after covariate adjustment, compared to white race. **(Table I)**

17   Limitations include enrolment of participants from HS referral clinics, which may overrepresent

18 experiences of patients with more severe disease. Response denominator could not be calculated.

19 Thresholds for minimal clinically important differences in QOL by score are not yet established for

20 HiSQOL.

21   In this Global VOICE analysis, patients with HS experienced high life impact related to their

22 disease. Younger age, high BMI, active smoking, flares, depression, high comorbidity burden, disability,

23 and difficult access to a dermatologist were associated with disease-related life impact in HS in

24 unadjusted analysis. Age and access to a dermatologist had a graded relationship with life impact in

25 unadjusted analysis. Attenuation of regression coefficients after adjusting for flare frequency suggests that

26 increased flare frequency partially explains poorer disease-related QOL in certain groups. Black patients

with HS may experience worse disease-specific life impact compared to whites, and this topic warrants further study. In the absence of highly satisfactory treatments,[3] attention to factors, particularly modifiable ones, that correlate with poor QOL in HS patients may reduce overall impact of disease.

References

1. Garg A, Neuren E, Cha D, Kirby JS, Ingram JR, Jemec GBE, et al. Evaluating patients' unmet needs in hidradenitis suppurativa: results from the Global Survey of Impact and Healthcare Needs (VOICE) project. *J Am Acad Dermatol*. 2020;82(2):366-376.

2. Kirby JS, Thorlacius L, Villumsen B, Ingram JR, Garg A, Christensen KB, et al. The Hidradenitis Suppurativa Quality of Life (HiSQOL) score: development and validation of a measure for clinical trials. *Br J Dermatol*. 2020;183(2):340-348.

3. Midgette B, Strunk A, Akilov O, et al. Factors associated with treatment satisfaction in patients with hidradenitis suppurativa: results from the Global VOICE project [published online ahead of print, 2022 Jul 30]. Br J Dermatol. 2022;10.1111/bjd.21798. doi:10.1111/bjd.21798

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1   **Table 1. Mean difference in HiSQOL score according to patient characteristics**

Variable	Unadjusted mean HiSQOL difference[a] (95% CI)	p-value	Adjusted mean HiSQOL difference[a,b] (95% CI)	p-value
Delay in diagnosis (per 1-yr.)	-0.02 (-0.11, 0.08)	.67	-0.04 (-0.14, 0.05)	.36
Comorbidity count (per 1-unit increase)	2.4 (1.6, 3.1)	<.001	1.5 (0.8, 2.2)	<.001
Age (yrs.)				
18-30	Ref.	Ref.	Ref.	Ref.
31-40	-0.2 (-2.4, 2.0)	.87	-0.3 (-2.2, 1.7)	.80
41-50	-1.8 (-4.1, 0.4)	.11	-0.9 (-3.1, 1.3)	.42
51-60	-6.2 (-9.0, -3.3)	<.001	-4.2 (-7.1, -1.4)	.004
61 +	-7.6 (-13.3, -1.9)	.009	-3.9 (-9.0, 1.2)	.13
Sex, male vs. female (ref.)	-3.7 (-6.0, -1.3)	.003	-1.0 (-3.2, 1.1)	.34
BMI category				
Underweight/Normal weight (BMI < 25)	Ref.	Ref.	Ref.	Ref.
Overweight (BMI 25.0-29.99)	3.0 (0.4, 5.7)	.03	1.6 (-0.7, 4.0)	.17
Obese 1 (BMI 30.0-34.99)	2.2 (-0.6, 5.0)	.12	-0.2 (-2.6, 2.2)	.87
Obese 2 (BMI 35.0-39.99)	3.6 (0.6, 6.6)	.02	0.2 (-2.4, 2.9)	.85
Obese 3 (BMI $\geq$ 40)	7.9 (5.0, 10.8)	<.001	1.5 (-1.2, 4.1)	.28
Smoking status (Ref. = Never)				
Former smoker	2.1 (-0.1, 4.3)	.06	1.1 (-0.9, 3.0)	.30
Active smoker	4.9 (2.8, 6.9)	<.001	1.7 (-0.2, 3.6)	.08
Education				
College/university degree	Ref.	Ref.	Ref.	Ref.
Graduate school degree	-1.2 (-3.7, 1.3)	.34	-0.7 (-2.9, 1.5)	.55
High school	5.8 (3.9, 7.7)	<.001	2.1 (0.4, 3.8)	.02
Less than high school	4.4 (0.7, 8.1)	.02	3.5 (0.1, 6.8)	.04
Married/in relationship, Ref = No	-0.7 (-2.6, 1.1)	.42	-0.5 (-2.1, 1.1)	.52
Employment (Ref. = Employed)				
Not looking for work or Retired	1.6 (-0.9, 4.1)	.21	0.9 (-1.4, 3.1)	.45
Unemployed	2.8 (-0.1, 5.6)	.06	0.5 (-2.0, 3.1)	.67
Disabled	9.5 (7.2, 11.8)	<.001	4.8 (2.7, 7.0)	<.001
Main physician for HS is a dermatologist, Yes vs. No (ref.)	-2.0 (-3.7, -0.3)	.02	0.4 (-1.2, 2.0)	.62
Access to a dermatologist				
Very easy	Ref.	Ref.	Ref.	Ref.
Easy	0.8 (-1.9, 3.5)	.57	0.7 (-1.7, 3.2)	.56
Neutral	2.2 (-0.5, 5.0)	.11	2.1 (-0.4, 4.6)	.10
Difficult	5.4 (2.7, 8.2)	<.001	4.7 (2.2, 7.2)	<.001
Very difficult	11.8 (8.6, 15.0)	<.001	7.4 (4.4, 10.4)	<.001
Depression diagnosis, Ref = No	7.8 (6.1, 9.5)	<.001	3.1 (1.2, 4.9)	<.001
Anxiety diagnosis, Ref = No	6.6 (4.8, 8.3)	<.001	1.5 (-0.3, 3.4)	.10
Flare frequency				
Every 6 months	Ref.	Ref.	Ref.	Ref.
Every 3 months	4.5 (0.7, 8.4)	.02	3.6 (-0.2, 7.3)	.06
Monthly	11.7 (8.5, 14.9)	<.001	10.2 (7.1, 13.3)	<.001
Weekly	18.8 (15.5, 22.1)	<.001	15.5 (12.3, 18.7)	<.001
Daily	24.6 (21.3, 27.9)	<.001	20.6 (17.3, 23.9)	<.001

1   a – Mean difference in HiSQOL total score compared to the reference group. Higher HiSQOL scores

2   correspond to worse QOL impairment. Accordingly, negative mean differences imply better QOL

3   compared to the reference group, and positive mean differences imply worse QOL compared to the

4   reference group.

5   b – Derived from a multiple linear regression model including all variables in the table as predictors. No

6   variable selection procedure was performed.

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