Late-onset hidradenitis suppurativa: A cluster analysis of the National Italian Registry IRHIS

To the Editor: Although hidradenitis suppurativa (HS) has a mean age of onset at about 22 years, late-onset HS can occur.[1,2] We analyzed data from 1100 consecutive, newly diagnosed patients with HS from 17 Italian outpatient clinics participating in the Italian Registry of HS (IRHIS).[1] Our aim was to assess the existence of clusters in the HS distribution in terms of age at onset and to evaluate differences between clusters with respect to demographics, clinical characteristics, and HS phenotypes. A detailed description of the methods used is reported in the Supplementary Materials (available via Mendeley at https://data.mendeley.com/datasets/hstfswp5nv/1). In this analysis, we relied on both k-means and Gaussian mixture model (GMM) clustering algorithms. Both methods indicated that a two-cluster model was best fitted to our data (Fig 1, Supplemental Table I) with early-onset HS peaking in the late teen years (mean = 17.0 years) and late-onset HS peaking at around the age of 40 years (mean = 38.4 years), with an optimal separation threshold at 28 years. Both univariate and age-adjusted and sex-adjusted multivariable logistic regression analyses were performed (Table I).

Patients were found to be similarly overweight in both early-onset and late-onset groups, with no sex differences found after adjusting for confounding variables. A significantly lower proportion of patients in the late-onset group were smokers (odds ratio [OR], 0.61; 95% confidence interval [CI], 0.40-0.93) and had a reported history of HS in first-degree relatives (OR, 0.31; 95% CI, 0.18-0.56). In addition, a shorter mean diagnostic delay and illness duration since the onset were observed in late-onset patients. Moreover, a less severe disease (according to the Sartorius score) was documented in the late-onset group compared with the early-onset group (OR, 0.42; 95% CI, 0.25-0.69). The frequency of involvement of the axillary-groin-buttocks and anogenital areas was similar between the 2 groups, whereas the neck and mammary locations were significantly and more frequently reported in the early-onset group ($P < .05$). Similarly, follicular lesions, such as pilonidal cysts, were more frequently associated with early-onset HS (OR, 0.40; 95% CI, 0.20-0.77). Among additional HS-related features and comorbidities, atopic, seborrheic, and perioral dermatitis were all significantly associated with late-onset HS (OR, 5.46; 95% CI, 1.15-25.81).

Limitations of our analyses are the inclusion of tertiary care outpatient HS cases, the potential recall bias of self-reported age at onset, the absence of a formal validation on an independent dataset in order to test cluster stability, and the possibility of having residual confounding variables concerning the effect of age on the observed associations. Nevertheless, our analyses relied on a robust method for stratifying patients, and we were able to confirm the possibility of a late-onset HS variety in Italian patients in agreement with observations from another single study from North America.[2,3] The correlation

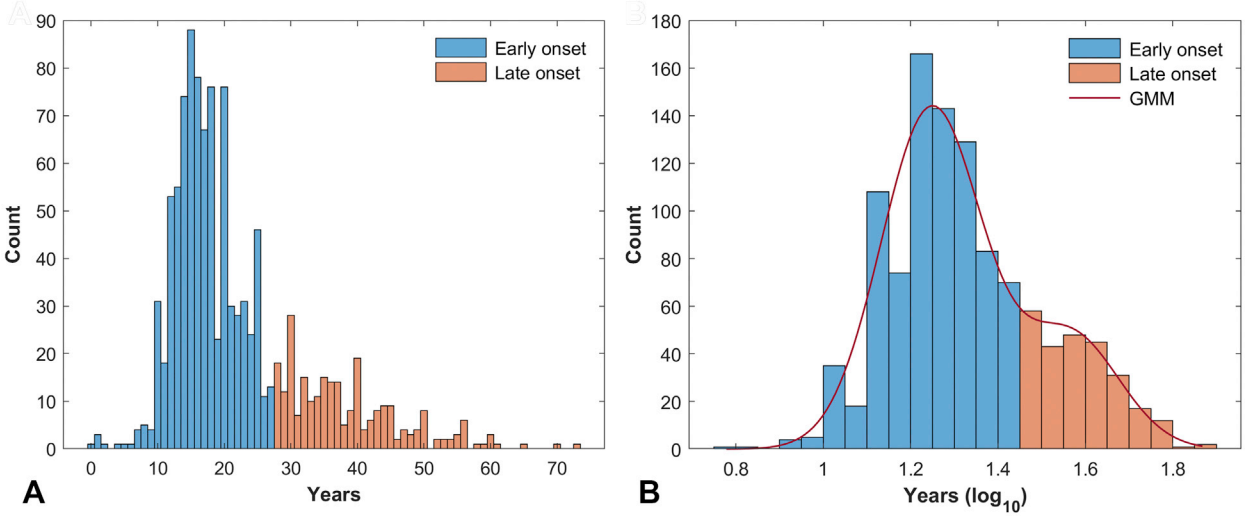

Fig 1. The distribution of age at hidradenitis suppurativa onset based on standard (**A**) and logarithmic scale (**B**) and with separation by identified clusters. The estimated distribution based on the two-component GMM is shown in (**B**). *GMM*, Gaussian mixture model.

Table I. Demographics and clinical characteristics of 1100 patients included in the study according to hidradenitis suppurativa onset

	Early-onset HS		Late-onset HS			Multivariable analysis[‡]		
Variable	**n[*] = 843**	**%**	**n[*] = 257**	**%**	***P* value[†]**	**N[*]**	**OR (95% CI)**	***P* value**
Sex								
Male	320	38.0%	110	42.8%	.16	430	1	.41
Female	523	62.0%	147	57.2%		670	0.86 (0.61-1.23)	
Age (years)								
Mean, SD	28.4	10.5	45.3	9.7	<.001	1100	1.14 (1.12-1.16)[§]	<.001
BMI (kg/m^2)								
Mean, SD	26.5	5.7	28.7	6.5	<.001	1080	1.02 (0.99-1.05)[§]	.10
Education								
Elementary/lower secondary	223	26.5%	87	33.9%	.02	310	1	
Upper secondary	466	55.3%	118	45.9%		584	0.76 (0.50-1.15)	.20
University	154	18.3%	52	20.2%		206	0.74 (0.45-1.23)	.25
Smoker								
No	286	33.9%	64	24.9%	<.001	350	1	
Yes	517	61.3%	155	60.3%		672	0.61 (0.40-0.93)	.02
Ex	40	4.7%	38	14.8%		78	1.54 (0.79-3.01)	.20
HS in first-degree relatives								
No	573	77.0%	191	89.7%	<.001	764	1	
Yes	171	23.0%	22	10.3%		193	0.31 (0.18-0.56)	<.001
Age at HS onset (years)								
Mean, SD	17.0	4.6	38.4	8.7	-	-	-	-
HS duration since onset (years)								
Mean, SD	11.4	9.8	7.0	6.7	<.001	1100	0.48 (0.37-0.62)[‖¶]	<.001
Diagnostic delay (years)								
Mean, SD	7.6	8.4	4.2	4.9	<.001	1100	0.21 (0.16-0.28)[‖]	<.001
Hurley								
I	303	35.9%	87	33.9%	.08	390	1	
II	399	47.3%	111	43.2%		510	1.05 (0.71-1.56)	.81
III	141	16.7%	59	23.0%		200	0.70 (0.43-1.16)	.17
Sartorius score								
Mean, SD	55.1	50.1	60.4	61.6	.80	1035	0.42 (0.25-0.69)[‖]	.001
DLQI								
Mean, SD	12.9	7.8	14.3	8.4	.04	739	1.01 (0.99-1.04)	.30
Localization[#]								
Neck	50	5.9%	6	2.3%	.02	1100	0.27 (0.10-0.74)	.01
Mammary	189	22.4%	41	16.0%	.03		0.51 (0.31-0.82)	.006
Axillae	536	63.6%	145	56.4%	.04		0.79 (0.55-1.13)	.20
Buttocks	258	30.6%	87	33.9%	.33		0.85 (0.58-1.24)	.40
Groin	591	70.1%	178	69.3%	.80		0.79 (0.54-1.16)	.22

Anogenital area	76	9.0%	37	14.4%	.01		0.76 (0.45-1.28)	.31
Other	151	17.9%	42	16.3%	.56		1.04 (0.65-1.64)	.88
HS-related characteristics and comorbidities[#]								
Acne conglobata	89	10.6%	23	8.9%	.45	1100	0.63 (0.34-1.18)	.15
Pilonidal cyst	109	12.9%	13	5.1%	<.001		0.40 (0.20-0.77)	.007
Folliculitis decalvans	9	1.1%	2	0.8%	1		0.62 (0.10-3.69)	.60
Other forms of acne	37	4.4%	6	2.3%	.14		0.80 (0.28-2.31)	.68
Dermatitis[**]	6	0.7%	5	1.9%	.14		5.46 (1.15-25.81)	.03
Psoriasis	11	1.3%	9	3.5%	.03		2.45 (0.85-7.09)	.10
Diabetes	2	0.2%	3	1.2%	.09		0.72 (0.09-5.92)	.76
Thyroid disease	11	1.3%	4	1.6%	.76		1.23 (0.30-5.05)	.77
Crohn disease	8	0.9%	3	1.2%	.72		0.47 (0.10-2.14)	.33

BMI, Body mass index; *CI*, confidence interval; *DLQI*, dermatology life quality index; *HS*, hidradenitis suppurativa; *n*, number of patients in each group; *N*, total number of patients included in multivariable analysis; *OR*, odds ratio; *SD*, standard deviation.

*Numbers may not add up to the total due to missing data.

†Pearson's X^2 test (or Fisher's exact test where required) and Mann-Whitney U tests were used in univariate analysis to compare nominal and continuous variables, respectively.

‡Results from logistic regression models including age and sex as covariates.

§OR per unit increase.

‖OR of $\log_{10}$ transformed data, representing OR per 10 units increase.

¶Adjusted for sex only.

#Multiple localizations/comorbidities were possible.

**Including atopic, seborrheic, and perioral dermatitis.

between early-onset HS and a stronger familial history was previously reported in another retrospective study.[4] Distinct late-onset phenotypes have been reported in Crohn's disease, a chronic inflammatory condition sharing clinical and pathogenetic characteristics with HS. An age of onset of Crohn's disease after 60-65 years has been associated with stenosing disease, increased comorbidities, and medication burden.[5] The natural history and disease course in older adults with HS are unknown. Fixed-age cut-offs for the definition of early-onset and late-onset disease may prove challenging for clinical studies because of the skewed age distributions found in patients with HS. Cluster analysis may prove to be a useful strategy for addressing this issue and better defining the trajectories of comorbid conditions in HS. Future investigations assessing the significance of our phenotypes and outcomes in late-onset HS in terms of disease characteristics, prognostic factors, and treatments are recommended.

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Conflicts of interest

None disclosed.

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