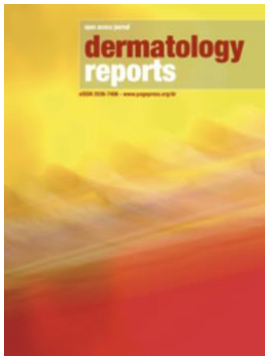

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Health-related quality of life and clinical characteristics of hidradenitis suppurativa in a paediatric population

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Abstract

Hidradenitis Suppurativa (HS) is a chronic, Skin Immune-Mediated Inflammatory Disease (sIMID), with a high impact on Quality of Life (QoL). Data on clinical management, comorbidities, psychosocial burden, and psychiatric disorders in paediatric patients with HS is scarce. The aim of our study was to compare clinical characteristics and Patient-Reported Outcome Measures (PROMs) for Health-Related Quality of Life (HRQoL) in adult and paediatric patients with HS. Data were collected on 601 patients with HS, 60 of whom (10.0%) were paediatric. The psychological and HRQoL impact was generally higher in adults than in children, but it was noteworthy also in paediatric patients. Early diagnosis and interventions based on education for the patients and their families and psychological support are the key to optimal disease management and adherence. Our study underlines the need for screening for HS-associated psychiatric disorders and for using age-specific tools to evaluate HRQoL. A multidisciplinary approach involving several specialists is needed, as well as liaison with primary care specialists to improve care, and management of comorbidities and psychological issues in patients with HS.

Introduction

Hidradenitis Suppurativa (HS) is a chronic, inflammatory disorder of the hair follicles that affects apocrine gland-bearing sites, intertriginous areas such as the axillae, inguinal and anogenital/perianal areas, mammary and inframammary regions. It usually presents in early adulthood, with painful, deep-seated, inflamed lesions. HS is a multifactorial disease which results from a combination of several features, such as dysregulated immune response, dysbiosis, genetic factors, and interactions with environmental and psychosocial factors.[1] HS typically occurs in the second and third decade of life, generally after puberty (20-24 years).[2] Few data are available in the literature on HS in paediatric age (children and adolescents, *i.e.*, from birth to 18 years), and interventional studies rarely include paediatric patients.[3] Data are extrapolated from basic science and clinical studies in adults and the clinical management is based on adult treatment guidelines.[4] Differentiation between paediatric and adult-onset HS is controversial. When compared with adults with HS, children with HS are more likely to have hormonal imbalances, making hormonal investigations integral to disease management in them. A diagnosis of HS in children may be a marker of precocious puberty.[5] Retrospective studies suggest that in about 35% of all HS patients, the first symptoms appear between 11 and 20 years of age, and only 2% of HS patients report that first symptoms appeared before the age of 11.[6] Only one study showed onset before 10 years old.[7] Early-onset HS (before 16 years of age) is associated with more widespread disease, positive family history, obesity, and disease severity.[8-9] Clinical presentation in paediatrics is usually more severe often presenting with complications such as infection, lymphedema, and fistulization.[2] The prevalence of HS in children and adolescents has been estimated at 0.06%, while in adults, studies have shown a prevalence ranging from 0.03% to 4.1%. An incidence of 6 per 100,000 people/year has been estimated overall. In the zero to 19-year-old age group, the incidence has been estimated as 2.7 per 100,000, 4.4 times higher in females than in males.[10] These figures are, however, based on registered cases and may therefore be affected by diagnostic delay (time interval from first symptoms to diagnosis). A study[10] has shown an average

diagnostic delay of 7.2±8.7 years in HS patients, which would suggest that a part of the paediatric population is diagnosed at a non-paediatric age. HS is a distressing condition with a high impact on quality of life.[11] Several factors, such as HS severity, medical comorbidities, and psychiatric and somatic disorders make this impact even more severe.[12-15] Data on quality of life in HS paediatric patients are scarce as well as on psychosocial burden and psychiatric disorders.[16] The aim of our study was to compare clinical characteristics and Health-Related Quality of Life (HRQoL) in paediatric and adult patients with HS.

Materials and Methods

This cross-sectional study was conducted on patients with HS who are part of the IDI-IRCCS HS Registry, which is a regular contributor to the Italian National HS Registry.[17] Consecutive individuals with a diagnosis of HS, on their first access to the HS outpatient clinic, were recruited between November 2015 and December 2021 at the dermatological hospital IDI-IRCCS, in Rome, Italy. The study was approved by the Local Ethical Committee of IDI-IRCCS (459/1, 2015) and all the participants signed a written informed consent. Socio-demographic, anthropometric, and clinical data were collected at enrolment. Clinical data on HS included age at onset, duration of the disease, family history in first-degree relatives, number of affected regions, nodules, fistulas, abscesses, scars, and Visual Analogue Scale (VAS) pain (from 0 “no pain” to 10 “worst imaginable pain”). Clinical severity of HS was assessed with the International Hidradenitis Suppurativa Severity Score System (IHS4), Sartorius Hidradenitis Suppurativa Score, and Hurley classification.[18] Patient-Reported Outcome Measures (PROMs) used to evaluate HRQoL in our study were: the Dermatology Life Quality Index (DLQI), to assess the dermatology-related quality of life in adults (16 years or higher) and the Children-DLQI (CDLQI) in paediatric patients (until 15 years and 11 months).[19-20] They both include 10 items with possible scores from 0 to 3 (not at all, a little, a lot, very much). The DLQI is to be interpreted with the following cut-off values for the effects on patients’ HRQoL: 0-1 = no effect

at all; 2-5 = small effect; 6-10 = moderate effect; 11-20 = very large effect; 21-30 = extremely large effect. The 12-item General Health Questionnaire (GHQ-12) was administered to patients aged from 14 years. It is constituted of 12 items with possible answers on a four-point scale. When scored with the continuous Likert scoring (range from 0 to 36) it measures psychological distress, while with the dichotomous scoring, 0-0-1-1 (possible scores from 0 to 12) patients scoring 4 or more are operationally defined as having possible non-psychotic and minor psychiatric disorders. Patients with a score of 7 or more were defined as probable "GHQ cases" of depressive disorder. This cut-off has been shown to have good sensitivity and specificity to identify cases of Major Depressive Disorder (MDD) in patients with skin conditions.[21] The 36-item Short Form Health Survey (SF-36) measures the general quality of life in two subscales, the Physical Component Summary (PCS) and the Mental Component Summary (MCS). It was validated also in primary care from 16 years.[22] In the GHQ-12 and the DLQI higher scores indicate a higher psychological impact and a worse HRQoL, while higher SF-36 scores indicate a better health status. The ratio of GHQ-Likert to IHS4, and of DLQI score to IHS4 were calculated in order to adjust the psychological scores for clinical severity. The scores represent the GHQ and the DLQI scores for each point of IHS4. Categorical variables were described as numbers and percentages, and continuous variables as mean and Standard Deviation (SD) and median and Interquartile Range (IQR). Paediatric (*i.e.*, aged less than 18 years) and adult HS patients were compared in subgroups according to sex, family history, presence of comorbidities, obesity, Hurley stage, IHS4 score classification, categories of number of body sites involved, number of body sites involved, presence of possible non-psychotic and minor psychiatric disorders (GHQ-12≥4), presence of depression (GHQ-12 ≥7), using the Fisher's exact test. Mean values of year of diagnostic delay, weight, Sartorius score, VAS pain, number of body sites involved, number of nodules, fistulas, abscesses, and scars, GHQ-Likert, the ratio of GHQ-Likert to IHS4, DLQI score, the ratio of DLQI score to IHS4, and of the SF-36 PCS and MCS scales were compared between paediatric and adult individuals using the Mann-Whitney U test.

A further analysis was conducted including as adults a subset of patients matched to paediatric by sex and quartiles of the duration of disease according to paediatric distribution, to control the strong confounding effect of these two variables. Single items of the DLQI and the CDLQI were compared, when possible, between paediatrics and adults. All the positive answers (*i.e.*, a little, a lot, very much) were pooled to obtain a dichotomous score.

Results

Data were collected on 601 patients with HS: 280 (46.7%) had an onset before 18 years, 60 of whom (10.0% of the total, 21.4% of those with "paediatric onset") were still of paediatric age when they entered the study. The demographic and clinical characteristics of the study population, as well as HS clinical severity, are reported in Table 1. The percentage of females was significantly higher in paediatric patients than in adults (80.0% *vs* 59.5%). Mean age at onset and diagnostic delay were significantly higher in adults compared to the paediatric population. Adults had more comorbidities and a higher severity according to Hurley stage. No differences were observed in clinical severity measured with the other scales, nor in pain. Characteristics of the lesions (Table 2) were not significantly different in paediatric patients compared to adults, except for the suprapubic localization which was more frequent in the former group. The psychological impact (Table 3) was generally higher in adults than in paediatric patients. In fact, the percentage of patients with depression (*i.e.*, GHQ≥7) was (almost) significantly higher in adults, as well as the impact on mental health measured with the mental scale of the SF-36. Dermatology-related quality of life (measured with the DLQI) was worse in adults, and in particular, scores between 21 and 30 were observed in 17.2% of adults and never in paediatric patients. The SF-36 PCS mean score was not different between the two groups. There were no differences in the GHQ/IHS4 mean scores, while the DLQI/IHS4 mean score was higher in adults. Positive answers to all the DLQI/CDLQI items (Figure 1), except for work/study and treatment, were significantly more frequent in adults than in paediatric patients. The analysis of

the subset of adults matched to paediatric patients by sex and quartiles of the duration of disease confirmed most results. However, there was no longer a difference in diagnostic delay, in the localization in the suprapubic area, and the DLQI score (results not shown).

Discussion

In this study, we observed that the psychological impact of HS was higher and HRQoL was worse among adults than in the paediatric population. However, the impact was noteworthy also in paediatric patients. In fact, their mean DLQI score indicated a moderate effect on HRQoL, the prevalence of possible non-psychotic and minor psychiatric disorders was 44%, and that of probable depression was 18%, both significantly higher than in the general population. It is well known that HS has a profound effect on patients' quality of life, because of symptoms such as pain and malodorous discharge, which deeply affect social and work life.[23-24] Those aspects have been thoroughly studied in adults, while in the paediatric population data are scarce. In a cross-sectional study on 25 patients aged from 12 to 17 years data from the Skindex-teen questionnaires showed a high impact of HS on HRQoL and the rate of positive screening results for depression was 32%, significantly higher than that of a general adolescent population (12%).[25] In a retrospective study on 73 paediatric HS patients, the authors observed a significantly increased rate of several comorbidities compared to the general US paediatric population.[16] Concerning psychiatric conditions, 22% were diagnosed with anxiety, 19% with depression, 8% with Attention-Deficit Hyperactivity Disorder (ADHD), and 7% reported suicidal ideation, and there was a case of bipolar disorder. An association between HS and bipolar disorder was observed in previous studies.[26]

In our study, there were no differences between adults and the paediatric population in clinical severity measured with both IHS4 and Sartorius scores, nor in VAS pain. The different impacts on HRQoL and psychological problems cannot thus be attributed to a different degree of severity.

Possible reasons for such difference may be that, as expected, diagnostic delay is necessarily shorter in the youngest patients, as well as the disease duration. Localizations of the lesions, too, were similar in paediatric patients compared to adults, except for the suprapubic localization which was more frequent in the youngest ones. In a study of paediatric patients with HS, the most commonly affected location was the groin, followed by the axillae and anogenital area, and the most common dermatologic presentation was painful nodules, followed by ulcers and fibrosing scars.[3] HS is more common in women than in men by a ratio of 2:1, and it is also predominant in girls in the paediatric population although the prevalence is unknown.[7] In our study, the percentage of females was particularly high (80%) in paediatric patients, significantly higher than in adults, with a female/male ratio of 4:1. It is also known that HS onset in the paediatric age is associated with positive family history and in fact, in our population the proportion of paediatric patients with family history was higher than in adults, even though such difference was not statistically significant.[7] Obesity and metabolic syndrome are factors associated with HS. The prevalence in morbidly obese patients is increased about 20-fold, while conversely, weight reduction is associated with a decrease in severity. Obesity is considered an important independent factor in HS development and is associated with a higher prevalence of HS in children and adolescents.[9] A large study on 248,775 children identified an approximately six-fold increase in HS among obese children.[27] Although not significantly, in our study the percentage of obese was higher in paediatric patients than in adults. This study suggests the need for increased education and counseling on weight control and nutrition for paediatric HS patients.[28]

To our knowledge, this is the first study which compared detailed information on HRQoL and psychological issues in paediatric patients with HS and adults. For this aim, we used PROMs that are increasingly recognized as providing valuable and essential information for health and quality of care (not “cure”). A limitation of our study is that we compared HRQoL scores obtained by two different instruments, the DLQI and the CDLQI. The comparison between the scores of two different

questionnaires may be arbitrary, however, it has been shown that DLQI and CDLQI scores strongly correlate. In a study by Van Geel *et al.* (2016) the two instruments were administered to a group of adolescents with psoriasis aged 16-17 years and they showed a strong correlation ($r=0.90$, $p<0,001$).[29] However, since children and adolescents are not a homogeneous group, specific HRQoL dermatological measures should be used in adolescents, and to our knowledge such instruments are not available in Italian.

Conclusions

Our finding that as disease progresses so does the negative impact on HRQoL underlines the importance of early diagnosis and treatment of HS to potentially prevent disease progression and limit the negative impact on HRQoL. Psychiatric disorders associated with HS are underdiagnosed and underrepresented in dermatologic literature, and dermatologists should increase awareness of these conditions and boost screening for psychiatric comorbidity in paediatric HS patients. The absence of resources dedicated to paediatric HS may hide the true burden of this disease and miss opportunities to improve the health of young adults. Prospective studies are needed to better understand the barriers that adolescents face during the transitioning of care for chronic skin disorders and the efficacy of proposed solutions, such as visit guides, to improve patient well-being, improve "primary care" and "early prevention" based on "Patient-Centred Care" and "Family Centred Care". Education of patients and their families regarding the diagnosis, the chronic nature of HS, therapeutic modalities, and psychological support is key to optimal disease management and adherence to medical recommendations. In summary, the management principles of HS include early intervention and long-term monitoring, with the correction whenever possible of the metabolic/endocrine disturbance, the promotion of overall health, including weight control, symptoms management, medical treatment, and psychological support. For these aims, multidisciplinary teams (dermatologists,

psychodermatologists, paediatric dermatologists, paediatric psychologists, nurses, dietitians, endocrinologists and other stakeholders) and liaison with primary care specialists are needed.

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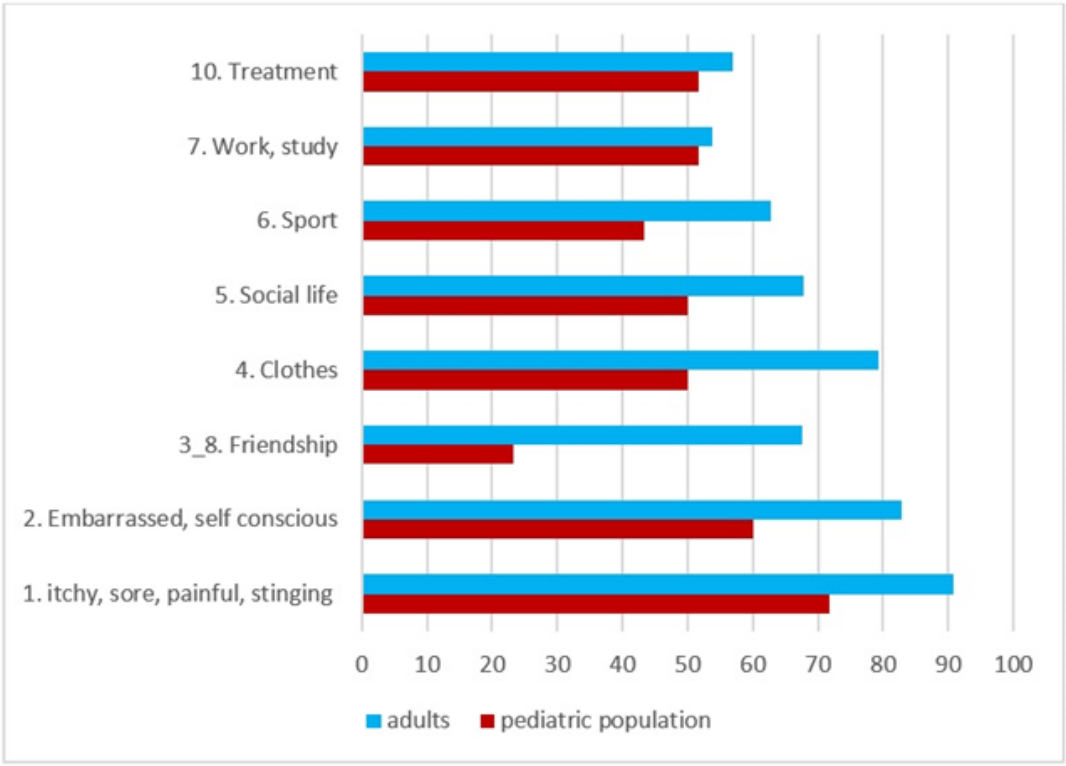

Figure 1. Frequency of the positive answers to the single items of the Dermatology Life Quality Index (DLQI) and the Children-DLQI (CDLQI) in pediatric patients and adults. All differences between pediatric patients and adults are significant (Fisher's exact test), except for items 7 and 10.

Table 1. Clinical characteristics and severity in patients included in the IDI-IRCCS HS Registry, Rome, Italy, 2015-2021.

	Pediatric HS	Adult HS	p-value[a]
N[b] (%)	60 (10.0)	541 (90.0)	
Age, years			
Mean (SD)	15.5 (2.0)	33.3 (11.9)	
Median (IQR)	15.8 (14.7-17.2)	30.4 (23.0-41.6)	
Age at onset, years			
Mean (SD)	12.4 (2.8)	22.4 (10.8)	
Median (IQR)	13 (11-15)	19 (16-27)	
Female sex (%)	48 (80.0)	322 (59.5)	0.002
Diagnostic delay (years)			
Mean (SD)	1.9 (2.2)	7.2 (8.3)	0.0001[c]
Median (IQR)	1 (0-3)	5 (1-10)	
Family history (%)			
No	39 (69.6)	396 (79.2)	
Yes	17 (30.4)	104 (20.8)	0.123
Presence of HS comorbidities[d]			
No	48 (80.0)	329 (60.8)	
Yes	12 (20.0)	212 (39.2)	0.003
Obesity (BMI≥30 kg/m^2)	20 (34.5)	130 (24.8)	0.115
Weight, kg			
Mean (SD)	74.5 (18.9)	79.0 (19.0)	
Median (IQR)	73 (60-87)	77 (67-88)	0.141[c]
Hurley stage (%)			
I	60(100.0)	487 (90.4)	
II-III	0 (-)	52 (9.6)	0.006
IHS4 score (%)			
mild (≤3)	13 (21.7)	93 (17.2)	

moderate (4-10)	20 (33.3)	176 (32.7)	
severe (≥11)	27 (45.0)	270 (50.1)	0.607
Sartorius score			
Mean (SD)	37.1 (23.5)	50.8 (48.0)	
Median (IQR)	32.0 (18.0-55.5)	37.0 (22.0-64.0)	0.060[c]
Pain (VAS)			
Mean (SD)	4.1 (3.3)	4.6 (3.4)	
Median (IQR)	4 (0-7)	4 (2-8)	0.223[c]

HS, Hidradenitis Suppurativa; SD, Standard Deviation; IQR, Interquartile Range; BMI, Body Mass Index; IHS4, International Hidradenitis Suppurativa Severity Score System; VAS, Visual Analogue Scale

[a]Fisher's exact test

[b]Totals may vary because of missing values

[c]Mann-Whitney U test

[d]Folliculitis decalvans, gangrenous pyoderma, cyst of the pilonidal sinus, psoriasis, sacred coccygeal fistula, psoriatic arthritis, acne and acne conglobata, sapho syndrome (synovitis; acne; pustulosis; hyperostosis; osteitis)

Table 2. Number and locations involved, nodules, fistolas, abscesses and scars.

	Pediatric HS	Adult HS	p-value[a]
Number of body sites involved			
Mean (SD)	2.1 (1.1)	2.5 (1.2)	
Median (IQR)	2 (1-3)	2 (2-3)	0.059
Number of body-sites involved N[b] (%)			
1-2	38 (63.3)	312 (57.8)	
≥3	22 (36.7)	228 (42.2)	0.490[c]
Body-sites more frequently involved, N[b] (%)			
Groin	38 (63.3)	347 (69.3)	0.379[c]
Axilla	36 (60.0)	345 (63.9)	0.573[c]
Gluteal	17 (28.3)	190 (35.2)	0.319[c]
Mammary region	15 (25.0)	115 (21.3)	0.510[c]
Supra-pubic region	16 (26.7)	84 (15.6)	0.043[c]
Neck	1 (1.7)	35 (6.5)	0.244[c]
Nodules			
Mean (SD)	6.5 (6.6)	7.6 (7.8)	
Median (IQR)	5 (2-8)	5 (2-10)	0.390
Fistulas			
Mean (SD)	1.0 (1.3)	1.9 (3.6)	
Median (IQR)	0 (0-2)	0 (0-2)	0.408
Abscesses			
Mean (SD)	0.8 (1.2)	1.4 (3.5)	
Median (IQR)	0 (0-1)	0 (0-2)	0.980
Scars			
Mean (SD)	4.6 (5.5)	7.5 (13.2)	
Median (IQR)	3 (0-6)	3 (0-9)	0.593

HS, Hidradenitis Suppurativa; SD, Standard Deviation; IQR, Interquartile Range.

[a]Mann-Whitney U test

[b]Totals may vary because of missing values

[c]Fisher's exact test

Table 3. Psychological distress, health-related quality of life, health status in Hidradenitis Suppurativa (HS) patients.

	Pediatric HS	Adult HS	p-value[a]
GHQ-Likert			
Mean (SD)	13.3 (6.0)	15.4 (6.9)	
Median (IQR)	12.5 (8.0-18.0)	14.0 (10.0-20.0)	0.055
Presence of distress (GHQ-12≥4), N[b] (%)	22 (44.0)	255 (50.6)	0.459
Presence of depression (GHQ-12≥7), N[b] (%)	9 (18.0)	158 (31.4)	0.053
GHQ-Likert/IHS4[c]			
Mean (SD)	2.1 (2.4)	2.6 (3.9)	
Median (IQR)	1.2 (0.6-2.8)	1.2 (0.6-2.8)	0.802
DLQI			
Mean (SD)	8.0 (6.2)	11.9 (7.6)	
Median (IQR)	7 (2-13)	11 (6-17)	0.0003
HRQoL			
0-10	39 (67.2)	237 (46.7)	
11-20	19 (32.8)	183 (36.1)	
21-30	0 (-)	87 (17.2)	<0.0001[d]
DLQI/IHS4[e]			
Mean (SD)	1.5 (2.9)	1.9 (2.9)	
Median (IQR)	0.6 (0.2-1.2)	0.9 (0.3-2.0)	0.042
SF36-PCS			
Mean (SD)	43.7 (9.3)	42.2 (10.8)	
Median (IQR)	44.3 (38.1-50.6)	43.3 (35.5-50.7)	0.655
SF36-MCS			
Mean (SD)	40.4 (11.7)	35.6 (12.8)	
Median (IQR)	41.6 (31.5-49.9)	34.8 (26.0-45.9)	0.021

HS, Hidradenitis Suppurativa; GHQ, General Health Questionnaire; SD, Standard Deviation; IQR, Interquartile Range; DLQI, Dermatology Life Quality Index; HRQoL, Health-Related Quality of Life; IHS4, International Hidradenitis Suppurativa Severity Score System; SF36, Short Form Health Survey 36; PCS, Physical Component Summary; MCS, Mental Component Summary.

[a]Mann-Whitney U test

[b]Totals may vary because of missing values

[c]1 point of GHQ-likert to 1 point of IHS4

[d]Fisher's exact test

[e]1 point of DLQI to 1 point of IHS4