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Report

Drivers of disease severity and burden of hidradenitis suppurativa: a cross-sectional analysis on 553 German patients

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Abstract

Background Hidradenitis suppurativa (HS) is an inflammatory disease of the inverse skin regions with an age peak at around 40 years and an estimated prevalence of 1%. Nodules and abscesses can develop into fistules and scarring, which cause severe pain. HS is a progressive, life-defining disease that leads to physical limitations, inability to work, and social isolation. There is still little data on the drivers of disease severity and burden.

Method The cross-sectional study is based on the baseline data of 553 participants of the health care research project "EsmAiL," which was carried out as a multicenter randomized controlled trial. It included adult HS-patients presenting with at least three inflammatory lesions and at least a moderate impact on quality of life.

Results Disease activity increases with age. Men are more severely affected than women but feel less burdened. Obesity negatively influences disease activity and disease burden. Affected individuals have a higher level of education than the age adjusted population, but the unemployment rate is significantly higher. Disease activity significantly reduces quality of life and promotes depression and anxiety.

Conclusions HS is a severe and debilitating dermatosis. As a result of the well-established factors involved, HS requires a multi-causal approach to management, in addition to medical and surgical treatment. This must take into account all available therapeutic options, as well as patient education to reduce risk factors and pain, and psychological support. HS requires interdisciplinary and multi-professional care. To prevent disease progression, a structured treatment plan is needed.

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Introduction

Hidradenitis suppurativa (HS)/acne inversa (Ai) is an inflammatory disease mainly affecting the axillae, groin, anogenital, and perianal areas.

About 1% of the population suffers from HS.[1,2] The disease is characterized by a chronic recurrent course in which inflamed nodules, abscesses, and fistulas repeatedly occur, resulting in irreversible tissue damage. According to the present lesions, HS can be classified into three degrees of severity (Hurley stages I–III).[3] In the literature, the Hurley Stage distribution is given as 45.5% Hurley I, 41.5% Hurley II, and 13.0% Hurley III.[4]

Studies show very long times to diagnosis of up to 7–9 years.[5] On the one hand, the feeling of shame leads many affected persons to conceal the symptoms; on the other hand, minor inflammations are often not associated with HS and thus misdiagnosed, mistreated, or not treated at all.[6]

Even though it is a life-defining disease, for a long time, research interest in HS was scarce—a search in Medline, for example, shows that as of May 2023, there are only 3441 entries with "HS" in the title,* almost two-thirds of which were published within the last 5 years. In comparison, a search for "psoriasis" yields 31,117 entries, about 10 times as many.

Under the lead of the Department of Dermatology at the University Medical Centre Mainz, the project "Evaluation of a

*Search for "hidradenitis suppurativa" or "acne inversa" or "akne inversa" in titel (on 16.05.2023).

structured and guideline-based multimodal care concept for people with acne inversa" (EsmAiL), funded by the Innovation Fund of the GBA, was launched to improve the outpatient care of patients with HS. In the project, medical practices, clinics, and wound centers of different specialties were qualified nationwide to become so-called "acne inversa centers" (AiZ). This study assesses the baseline data of the study population in order to investigate the following inquiries:

1 Are there any socioeconomic factors and/or risk factors associated with the disease activity and disease burden of HS?
2 Is higher disease activity associated with higher depression, anxiety, quality of life impairment, and work disability?

Methods

Study design and population

The cross-sectional analysis includes the baseline data of the study population in EsmAiL. The study was previously approved by the ethics committees involved and registered in the German Clinical Trials Registry (DRKS) before the first patients were included (DRKS00022135). For the initial assessment, physicians of several specialties were qualified to be so-called "screeners" who were trained in the usage of the intended HS classifications and survey instruments. To participate in EsmAiL, interested patients had to register with the study team and afterward received an appointment with one of the 15 trained screeners who collected the baseline data independently (see the publication of the results of the RCT "EsmAiL" for more details[7]).

Adult HS patients of all severity levels were eligible to participate. At baseline assessment, at least three inflammatory lesions (inflammatory nodule, abscess, or draining fistula) had to be present, and the disease had to have at least a moderate influence on quality of life, as measured by the dermatological quality of life index (DLQI > 5).[8] After a thorough explanation about the study, patients provided written consent. Participation was voluntary and could be withdrawn at any time. All screeners were blinded to the inclusion criteria of disease activity and disease burden.

Statistical methods

Instruments were chosen based on the current literature. For ordinal classification, the Hurley severity classification[3] was used. For disease activity, the International Hidradenitis Suppurativa Severity Score System (IHS4)[9] and the current pain on the Numeric Rating Scale (NRS)[11] were collected.

For disease burden, the Dermatological Quality of Life Index (DLQI),[8] the Hospital Anxiety and Depression Scale (HADS),[10] and the number of days of work inability were documented. Socioeconomic variables were marital status, educational level, and occupational status. Body mass index (BMI), smoking status, and most common comorbidities were used as risk factors.

For the documentation of the clinical findings, the screeners filled out the data entry forms. Questionnaires were given out to patients to collect Patient Reported Outcomes (PROs) and demographic data. In addition, immediately after randomization, participants received digital questionnaires regarding their disease history, days of work inability, and personal situation. The questionnaires were subjected to a prior cognitive pretest with 10 patients.

For the descriptive analyses, absolute and relative frequencies for discrete variables and mean values with associated standard deviation as well as median (minimum, maximum) for continuous variables were reported. Subgroups of the sample were analyzed using the non-parametric Kruskal-Wallis test and, if necessary, examined in a post-hoc analysis with the pairwise Wilcoxon test. For multiple testing, Bonferroni was used for adjustment. Depending on the distribution of the outcome variables, a linear regression or a Poisson regression was calculated for the association between variables and risk factors. For all variables, the effect size was given with an associated 95% CI. The study size resulted from the sample size calculation of the EsmAiL-study[7]; no separate sample size calculation was performed. The data were analyzed by the Institute of Medical Epidemiology, Biometry and Informatics of the Medical Faculty of the Martin Luther University Halle-Wittenberg as an independent institution.

Results

Participants

Recruitment took place throughout Germany in the period from September 29, 2020 to July 31, 2021 by the 15 trained screeners.

A total of 726 patients were screened, 553 of whom met the inclusion criteria. In terms of severity, of the 553 included participants, 72 were classified as Hurley stage I (13.0%), 343 as Hurley stage II (62.0%), and 138 as Hurley stage III (25.0%) at baseline (Table 1). In line with other literature, the proportion of women was high (78.3%), and the average age of the sample was 39.0 ± 10.5 years (Table 1).

Socioeconomic factors and risk factors

Average inflammatory activity (IHS4) amounted to 18.2 ± 18.6 points and increased significantly with Hurley stage (Hurley I: 7.5 ± 6.09 points; Hurley II: 14.6 ± 12.6 points; Hurley III: 32.9 ± 25.7; $P < 0.001$ points). The average pain level of patients was 6.8 ± 2.2 points and showed no significant association with the Hurley stage. The mean values of the sample regarding the DLQI and HADS were 17.8 ± 6.5 and 17.3 ± 7.8 points (Table 1).

With regard to socioeconomic factors, marital status, and occupational status, a high proportion of patients were single (48.6%) and 31.3% did not practice any profession (Table 1). Regarding risk factors, the sample showed a high proportion of

Table 1 Patient characteristics for $n = 533$ participants

	Mean ± SD/ absolute frequency	Median [min; max]/ relative frequency
Demographic factors		
Age	39.0 ± 10.47	38.0 [18; 77]
Gender		
Male	120	(21.7%)
Female	433	(78.3%)
Smoking behavior		
Smoker	353	(63.9%)
Former smoker	103	(18.6%)
Non-smoker	97	(17.5%)
Cigarettes/day ($n = 333$)	14.3 ± 7.53	14.0 [1; 50]
Body mass index	32.2 ± 7.27	31.2 [17.9; 59.3]
Comorbidities	1.6 ± 0.96	1 [0;7]
Acne conglobata	20	(3.6%)
Hypertension	108	(19.5%)
Chronic inflammatory bowel disease	35	(6.3%)
Depression	152	(27.5%)
Type II diabetes	133	(24.1%)
Inflammatory joint disease	67	(12.1%)
Dyslipidemia	29	(5.2%)
Cardiovascular disease	18	(3.3%)
Polycystic ovary syndrome	26	(4.7%)
Thyroid dysfunction	105	(19.0%)
Other	186	(33.6%)
Socioeconomic factors		
Marital status ($n = 508$)		
Single	247	(48.6%)
Married	202	(39.8%)
Divorced/widowed	59	(11.6%)
Educational level ($n = 508$)		
School education (incl. A-levels)	179	(35.2%)
Apprenticeship	203	(40.0%)
Higher education	126	(24.8%)
Work status		
Employed	380	(63.72%)
Not employed	173	(31.28%)
Disease situation		
IHS4	18.2 ± 18.56	12.0 [3; 135]
Hurley Stage		
Hurley I	72	(13.0%)
Hurley II	343	(62.0%)
Hurley III	138	(25.0%)
Pain NRS	6.8 ± 2.16	7.0 [0; 10]
DLQI	17.8 ± 6.5	18.0 [6; 30]
HADS (total)	17.3 ± 7.82	17.0 [1; 42]
HADS anxiety	9.4 ± 4.09	9.0 [0; 21]
HADS depression	7.9 ± 4.44	7.0 [0; 21]
Days of work inability ($n = 380$)	16.4 ± 35.00	3.0 [0; 365]

smokers (63.9%) as well as a high BMI of 32.2 kg/m^2 on average (Table 1). The most common comorbidities were depression (27.5%), type II diabetes (24.1%), and hypertension (19.5%) (Table 1).

The results of the regression analyses showed that the IHS4 increased significantly with age. Furthermore, although men had a higher IHS4, they seemed to be less burdened by the disease, since pain, as well as the DLQI and HADS, were significantly positively associated with the female gender (Table 2).

Affected people who were not in marriage had lower inflammatory activity but felt similarly burdened as married people in all other respects. An educational attainment higher than a high school diploma was associated with a lower IHS4, and patients with a university degree or a Ph.D. reported lower anxiety and depression. Unemployment was associated with both increased inflammatory activity as well as increased disease burden (Table 2).

With regard to the risk factors, former smokers showed reduced inflammatory activity compared to smokers. The effect was not significant in non-smokers, but non-smokers showed lower values for pain severity and HADS. Overweight, measured by BMI, was positively associated with the IHS4, as well as with the DLQI and HADS, but did not show a significant correlation with pain level.

Disease burden and work ability

One in four of the patients in the analyzed sample suffered from depression, which was the most common comorbidity. The high emotional burden was confirmed by the results of the HADS and the DLQI. The scores for depressiveness and quality-of-life impairment increased with Hurley stage ($P = 0.040$ for HADS depression, $P < 0.001$ for DLQI, Figure 1). However, HS did not only have a massive impact on the private lives of the participants but also on their ability to work. The days of work inability because of the disease per year amounted to 16.4 ± 35.0 on average and increased with Hurley stage ($P = 0.64$, Figure 1).

The analysis showed that both the IHS4 and the pain level were significantly positively associated with the DLQI and the depression domain of the HADS. Higher pain also significantly corresponded to a higher anxiety domain of the HADS and more days of work inability (Table 3).

Discussion

The results confirm that HS patients are often young women who suffer from high disease activity and burden. Compared to other dermatological conditions such as pyoderma gangrenosum, which has an average pain level of 4.5,[11] the analyzed sample shows a significantly higher degree of pain (Table 1). Moreover, depression and anxiety as well as quality-of-life impairments are higher in HS patients than in those suffering from the more popular psoriasis[12,13] (Table 1). In relation to the

Table 2 Association of disease activity and burden of disease with socioeconomic and risk factors

	Outcome: IHS4 (Poisson-Regression) e^{β} with 95% CI, *P*-value	Outcome: Pain (Linear Regression) β with 95% CI, *P*-value	Outcome: DLQI (Linear Regression) β with 95% CI, *P*-value	Outcome: HADS (Linear Regression) β with 95% CI, *P*-value
Marital status (Ref: married)				
Single	0.93 (0.89 to 0.97), **$P = 0.002$**	0.35 (−0.08 to 0.78), $P = 0.114$	−0.73 (−2.04 to 0.59), $P = 0.278$	0.60 (−0.95 to 2.14), $P = 0.451$
Divorced/widowed	0.88 (0.82 to 0.94), **$P < 0.001$**	−0.01 (−0.63 to 0.62), $P = 0.980$	0.33 (−1.57 to 2.23), $P = 0.736$	0.92 (−1.32 to 3.15), $P = 0.421$
Educational level (Ref: School education)				
Apprenticeship	0.90 (0.86 to 0.94), **$P < 0.001$**	0.04 (−0.39 to 0.47), $P = 0.860$	0.39 (−0.91 to 1.69), $P = 0.556$	−0.68 (−2.21 to 0.86), $P = 0.385$
Higher education	0.89 (0.84 to 0.94), **$P < 0.001$**	−0.45 (−0.95 to 0.04), $P = 0.069$	−0.84 (−2.34 to 0.65), $P = 0.268$	−2.40 (−4.16 to −0.64), **$P = 0.008$**
Work status (Ref: Employed)				
Not employed	1.06 (1.02 to 1.11), **$P = 0.006$**	0.13 (−0.27 to 0.53), $P = 0.512$	1.30 (0.08 to 2.52), **$P = 0.036$**	2.77 (1.34 to 4.21), **$P < 0.001$**
Smoking status (Ref: Smoker)				
Non-smoker	1.00 (0.94 to 1.05), $P = 0.944$	−0.54 (−1.03 to −0.05), **$P = 0.033$**	−0.51 (−2.02 to 1.00), $P = 0.504$	−1.88 (−3.66 to −0.11), **$P = 0.038$**
Former-smoker	0.88 (0.83 to 0.93), **$P < 0.001$**	−0.32 (−0.82 to 0.17), $P = 0.204$	−0.25 (−1.76 to 1.26), $P = 0.747$	−1.39 (−3.17 to 0.39), $P = 0.125$
BMI	1.02 (1.02 to 1.02), **$P < 0.001$**	0.02 (−0.002 to 0.05), $P = 0.076$	0.12 (0.04 to 0.20), **$P = 0.003$**	0.14 (0.05 to 0.23), **$P = 0.003$**
Confounder				
Age in years	1.01 (1.01 to 1.01), **$P < 0.001$**	0.01 (−0.01 to 0.03), $P = 0.220$	0.01 (−0.06 to 0.07), $P = 0.827$	0.08 (0.01 to 0.15), **$P = 0.032$**
Gender (Ref: male)				
Female	0.75 (0.72 to 0.79), **$P < 0.001$**	0.94 (0.48 to 1.40), **$P < 0.001$**	2.34 (0.94 to 3.74), **$P = 0.001$**	2.23 (0.58 to 3.88), **$P = 0.008$**

$e^{\beta} > 1$, expected outcome value increases; $e^{\beta} < 1$, expected outcome value decreases.

age-adjusted population, diabetes mellitus type II, depression, obesity, and hypertension are overrepresented in people with HS,[14] which increases the risk of cardiovascular sequelae and associated mortality.[15]

The study adds new insights with respect to the drivers of disease activity and burden. The regressions show that IHS4 increases significantly with age (Table 2), which fosters the assumption about the progressive nature of the disease. Although the sample contains significantly more women (79.1%), they have a significantly lower IHS4 than men (−24.8%). This either means that men experience a more severe progression or, more likely, seek medical advice later.[16] Even though men on average have a higher inflammatory activity, they are significantly less burdened by the disease than women in terms of pain, quality of life, anxiety, and depression (Table 2). Two clear conclusions can be drawn from these data. First, men should be a clear target for raising awareness of the disease and decreasing barriers to accessing care. Second, for women destigmatization of the disease appears to be a central target for full comprehensive treatment.

When implementing a care concept, it is relevant to know which factors are most associated with disease activity and disease burden. Smoking and obesity are generally recognized as the two primary risk factors.[17] Indeed, smokers and obese people are also significantly overrepresented in the EsmAiL cohort. The IHS4 is significantly associated with BMI (2.1% increase per unit BMI) and is 11.8% lower in former smokers than in smokers. However, interestingly, the IHS4 of non-smokers is not significantly different from that of smokers (Table 2).

The burden of disease (DLQI and HADS) is significantly positively associated with BMI but should be considered clinically less relevant because of the low coefficients (0.12 and 0.14 per BMI unit). Smoking behavior does not seem to have any effect on the burden of disease (Table 2). These results suggest that adjuvant therapies for weight loss and nicotine abstinence in HS patients have the potential to reduce disease activity, but weight loss clearly should be the first target (Table 2). This knowledge is highly relevant in practical implementation. It is well-known that reducing nicotine consumption often leads to weight gain. Therefore, purely from an HS point of view, weight loss should be recommended first as an adjuvant therapy, as this seems to have a greater effect on the disease.

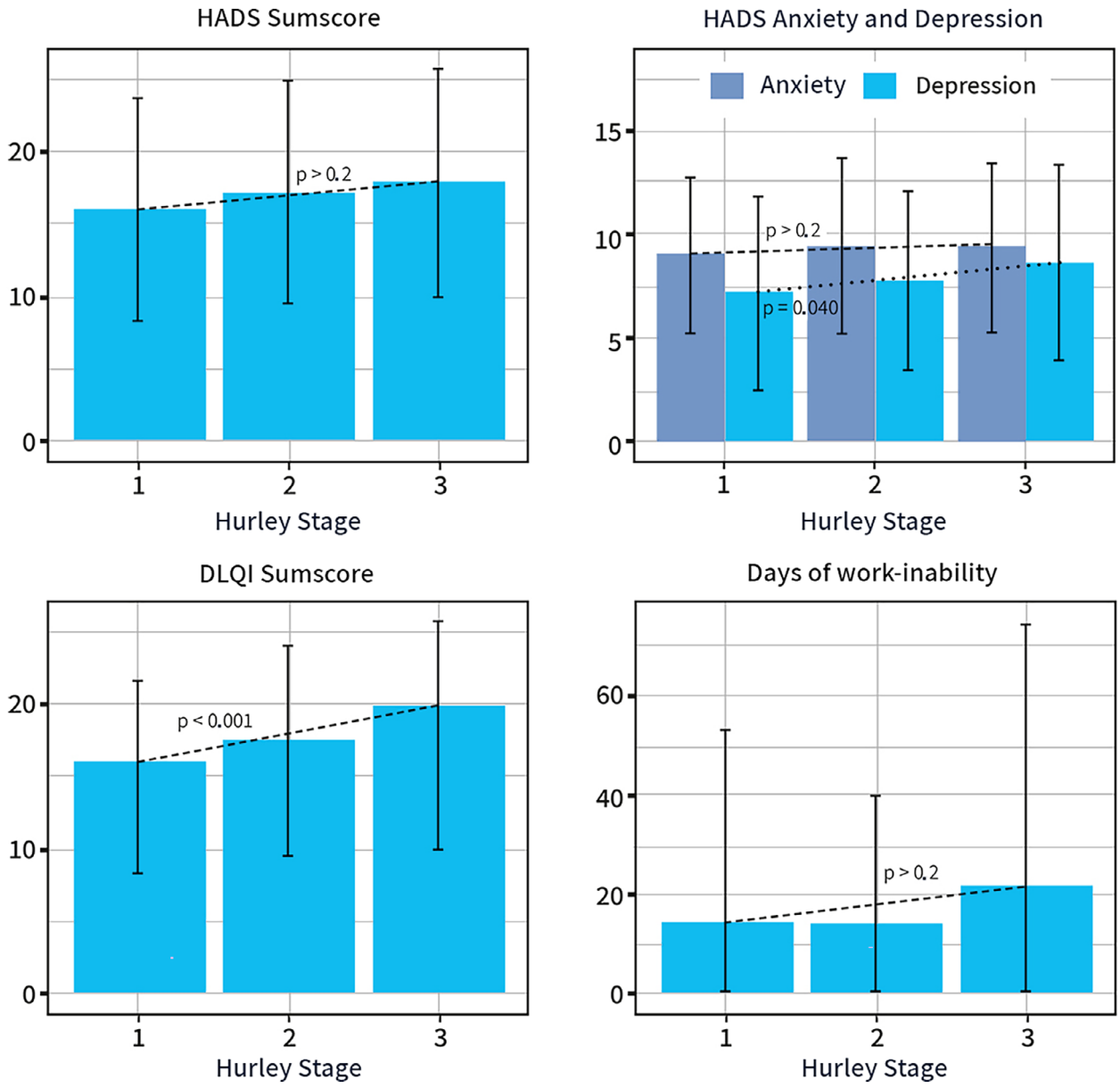

Figure 1 Values for HADS sumscore, HADS domains anxiety and depression, DLQI, and days of work inability for Hurley stages I, II, and III

In addition to the risk factors, socioeconomic aspects were also examined. It is striking that single people are clearly over-represented in the EsmAiL sample. It is to be assumed that patients with HS are less likely to enter into relationships because of shame and fear of stigmatization. There are more than twice as many unemployed people among those affected by HS than in the age-adjusted normal population.[14] Even those employed were unable to work for an average of 16.4 days due to HS. Studies suggest that frequent work inability and movement restrictions caused by the disease regularly lead to unemployment.[2,18,19] Furthermore, patients with HS experience significantly slower income growth[20] and are often assigned to a lower socioeconomic status in recent population studies.[21,22] Although low socioeconomic status may negatively influence disease development, it is more likely that attaining this lower status is a consequence of the disease. This conclusion is supported by our results that the people in the EsmAiL sample have similar or even higher educational qualifications than the general population.[14] As a result of the performed regressions, professionals and people with a higher level of education have lower inflammatory activity and burden in the HADS (Table 2). This presumably results from better access to the health care system through easier procurement of information and ultimately the possibility of financing therapy options.

Table 3 Association of depressiveness, anxiety, quality of life, and work ability with disease activity

	Outcome: HADS (linear regression) β with 95% CI, *P*-value	Outcome: anxiety (linear regression) β with 95% CI, *P*-value	Outcome: depression (linear regression) β with 95% CI, *P*-value	Outcome: DLQI (linear regression) β with 95% CI, *P*-value	Outcome: days of work inability (linear regression) β with 95% CI, *P*-value
IHS4	0.02 (−0.01 to 0.06), $P = 0.214$	−0.01 (−0.03 to 0.01), $P = 0.559$	0.03 (0.01 to 0.05), **$P = 0.006$**	0.07 (0.01 to 0.07), **$P < 0.001$**	−0.07 (−0.26 to 0.13), $P = 0.507$
Pain-NRS	0.61 (0.30 to 0.92), **$P < 0.001$**	0.29 (0.12 to 0.45), **$P < 0.001$**	0.32 (0.14 to 0.50), **$P < 0.001$**	1.11 (0.85 to 1.33), **$P < 0.001$**	1.78 (0.06 to 3.51), **$P = 0.043$**
Confounder					
Age in years	0.07 (−0.01 to 0.14), $P = 0.067$	.004 (−0.04 to 0.04), $P = 0.847$	00.06 (0.02 to 0.10), **$P = 0.002$**	−0.02 (−0.09 to 0.02), $P = 0.532$	0.18 (−0.26 to 0.62), $P = 0.419$
Gender (Ref: male) female	1.79 (0.12 to 3.45), **$P = 0.035$**	0.99 (0.11 to 1.88), **$P = 0.027$**	0.79 (−0.14 to 1.72), $P = 0.096$	1.78 (0.81 to 3.38), **$P = 0.007$**	3.920 (−5.01 to 12.85), $P = 0.389$
Marital status (Ref: Married)					
Single	0.35 (−1.19 to 1.88), $P = 0.658$	0.19 (−0.82 to 1.53), $P = 0.648$	0.15 (−0.70 to 1.79), $P = 0.720$	−1.18 (−2.23 to 0.13), $P = 0.054$	3.45 (−8.53 to 19.24), $P = 0.412$
Divorced/ widowed	0.90 (−1.31 to 3.12), $P = 0.423$	0.36 (−0.62 to 1.00), $P = 0.551$	0.55 (−0.70 to 1.02), $P = 0.388$	0.34 (−1.32 to 2.10), $P = 0.702$	5.36 (−4.81 to 11.71), $P = 0.448$
Educational level (Ref: School education)					
Apprenticeship	−0.57 (−2.09 to 0.95), $P = 0.462$	−0.29 (−1.10 to 0.515), $P = 0.477$	−0.28 (−1.13 to 0.58), $P = 0.524$,	0.56 (−0.60 to 1.74), $P = 0.354$	0.87 (−7.63 to 9.37), $P = 0.841$
Higher education	−2.50 (−4.23 to 0.78), **$P = 0.005$**	−1.13 (−2.05 to −0.22), **$P = 0.016$**	−1.38 (−2.34 to −0.41) **$P = 0.005$**	−0.29 (−1.42 to 1.25), $P = 0.673$	−2.19 (−11.78 to 7.40), $P = 0.654$
Work status (Ref: employed)					
Not employed	2.65 (1.22 to 4.08), **$P < 0.001$**	1.139 (0.38 to 1.90), **$P = 0.003$**	1.51 (0.71 to 2.31), **$P < 0.001$**	1.10 (0.09 to 2.30), $P = 0.054$	n.a., n.a.

One out of four affected persons in the sample suffers from depression. This high prevalence is confirmed in other studies.[23] The analysis of the sample shows that the IHS4 has marginal positive associations with the DLQI and the depression domain of the HADS. More severe pain also has a minor effect in magnitude on the HADS but substantially reduces quality of life and increases days off work (Table 3). Additionally, pain seems to be a relevant factor for all disease severities. In a previous population analysis, 4% of HS patients were found to be abusing substances because of the chronicity of their pain.[24] Strategies for the management of HS-associated pain that consider the risks of dependence are currently not well-established[25–27] but clearly depict an unmet need because of the substantial impact of pain on mental health (Table 3).

Limitations

A potential selection bias results from the fact that participants learned about the study through marketing in various channels. This means that the patients are likely above-average informed. It was to be expected that these patients would be more severely affected and searching for help compared to the average population. It should be emphasized that this bias is reinforced by the inclusion criteria of the EsmAiL trial concerning lesions and DLQI. In the literature, the expected Hurley stage distribution is reported as 45.5% Hurley I, 41.5% Hurley II, and 13.0% Hurley III,[4] confirming a shift in the EsmAiL sample towards higher severity grades (especially Hurley II) (Table 1). The results should be interpreted with this fact in mind.

Outlook

Hidradenitis suppurativa is a burdensome, complex disease that leads to severe physical and psychological impairments and increasingly puts a strain on the ability to work and on the daily lives of those affected. To prevent progression, a multimodal, individualized set of available treatment options is needed, which also considers risk factor reduction and pain management since treatment options are often limited. The EsmAiL project evaluated whether appropriately designed care can be implemented in specially trained AiZs and whether it is dominant compared to standard care.[7]

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