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Hidradenitis suppurativa: chronology of the onset of the disease symptoms and their gender differences: a single-center case series of 100 patients

Hidradenitis süpürativa: hastalık semptomlarının başlangıç kronolojisi ve cinsiyet farklılıkları: 100 hastalık tek merkezli olgu serisi

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Abstract

Background and Design: The onset chronology of disease symptoms in patients with hidradenitis suppurativa (HS) and their gender differences have not yet been fully elucidated. We aimed to define the onset chronology of the disease symptoms and the socio-demographic and clinical characteristics.
Materials and Methods: This single-center case series study included 100 consecutive patients. The disease symptoms for each patient were recorded in the time order of manifestations.
Results: HS was more common in males (72%); 70% of the patients were overweight or obese. Smoking and alcohol consumption was significantly higher in males. The axilla was the most common onset area, followed by the inguinal and gluteal regions. The incidence of disease onset in the axilla in male and disease onset in the gluteus in female patients was significantly higher. Also, involvement of the pubis, perianal region, neck, back, and behind the ear was more common in males. The disease followed a more severe course in patients with the involvement of axilla, perianal, and inframammary areas ($p<0.05$).
Conclusion: Besides being the most commonly involved site, axilla was the most common disease onset area in both genders; however, the incidence of disease onset in the gluteus is higher in females and the axilla in males. The male dominance observed in our cohort followed previous results reported from Türkiye, although differing from other countries. This suggests each society's unique genetic and environmental characteristics may influence the course and evolution of the disease.
Keywords: Hidradenitis suppurativa, natural course, chronology

Öz

Amaç: Hidradenitis supurativa (HS) hastalarında hastalık semptomlarının başlangıç kronolojisi ve cinsiyet farklılıkları henüz tam olarak aydınlatılamamıştır. Hastalık belirtilerinin başlangıç kronolojisi ve hastalarımızın sosyo-demografik ve klinik özelliklerini tanımlamayı amaçladık.
Gereç ve Yöntem: Bu tek merkezli olgu serisi çalışmasına ardışık 100 hasta dahil edildi. Her hasta için hastalık semptomları klinik ortaya çıkışlarının zaman sırasına göre ve diğer özellikler retrospektif olarak elde edildi.
Bulgular: Çalışmamızda HS erkeklerde daha yaygın (%72) izlenirken; hastaların %70'i aşırı kilolu veya obezdi. Sigara ve alkol tüketimi erkeklerde anlamlı olarak daha yüksekti. Koltuk altı en yaygın başlangıç bölgesiydi, bunu inguinal ve gluteal bölgeler takip etti. Erkeklerde aksillada hastalık başlangıcı ve kadın hastalarda gluteusta hastalık başlangıç insidansı anlamlı olarak daha yüksekti. Ayrıca pubis, perianal bölge, boyun, sırt ve kulak arkası tutulumları erkeklerde daha sıktı. Ayrıca koltuk altı, perianal ve meme altı tutulumu olan hastalarda hastalığın daha şiddetli seyrettiği izlendi ($p<0,05$).
Sonuç: En sık tutulan bölge olmasının yanı sıra aksilla her iki cinsiyette de en sık hastalık başlangıç bölgesiydi ve kadınlarda gluteusta, erkeklerde aksillada hastalık başlama insidansı daha yüksekti. Çalışmamızda gözlemlenen erkek egemenliği, diğer ülkelerden farklı olmakla birlikte, Türkiye'den bildirilen önceki sonuçlarla tutarlıydı. Bu, her toplumun benzersiz genetik ve çevresel özelliklerinin hastalığın seyrini ve evrimini etkileyebileceğini düşündürmektedir.
Anahtar Kelimeler: Hidradenitis süpürativa, doğal seyir, kronoloji

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Introduction

Hidradenitis suppurativa (HS) is an inflammatory disease characterized by painful deep-seated nodules, abscesses, and sinus tracts that develop after puberty in apocrine gland-rich areas, often in the axillary, inguinal, and anogenital areas[1]. HS can be regarded as a disease of adults, as it is rarely seen before puberty or in the elderly. The disease is most commonly seen between the ages of 20 and 29 and reported more frequently in women[2]. Its incidence in literature varies between 0.03 and 4.1%[3]. A strong relationship has been reported with smoking and obesity in this complex inflammatory skin disorder[4,5]. HS substantially reduces numerous health parameters, functionality, and quality of life[6]. The treatment of HS presents significant challenges. The two main factors affecting the treatment approach are inflammation and fibrosis, causing scarring. Treatment approaches include lifestyle changes along with topical treatments, oral antibiotics, retinoids, biological treatments, hormonal treatments, laser treatments, and/or surgical interventions.

The natural course of HS is not known precisely. The initial symptom, the chronological order of subsequent symptoms, and the duration of these symptoms may vary among patients. The clinical course is more severe in male patients. Early age of onset, involvement of multiple anatomical regions, and concomitant diseases have been associated with the severity of the disease. The severity and location of the disease might differ between genders. However, the literature shows significant differences regarding the factors affecting severity[2,7-10].

We aimed to define the chronology of the onset of the disease symptoms and the socio-demographic and clinical characteristics in a single-centre cohort of patients with HS.

Material and Methods

Study Design and Patients

A total of 100 consecutive patients with a diagnosis of HS followed in the Dermatology Outpatient Clinic of the Department of Dermatology and Venereology, University Faculty of Medicine between 2019 and 2022 were included in the study. The study was approved by the Ethics Committee of the Akdeniz University Faculty of Medicine (approval number: KAEK-814, date: 21.10.2020). Patients who could not remember the order of appearance of symptoms were excluded. Socio-demographic and clinical characteristics of the patients (age, gender, occupation, family history, educational status, marital status, smoking, alcohol use and body mass index, age at the onset of disease, duration of illness, sites of involvement, time order of the symptoms, concomitant diseases, and treatments) were obtained retrospectively from the HS-registry program developed by Alpsoy E, Ergen F, and Ulker M. Disease severity was documented as Hurley staging (HSt) and Physician's Global Assessment score (HS-PGA), and psychological effects of HS were evaluated with the Dermatology Life Quality Index (DLQI) and visual analog scale (VAS) pain score.

Statistical Analysis

Descriptive statistics were presented as frequency (n) and percentage (%) for categorical variables and mean ± standard deviation or median [minimum-maximum (min-max)] values for continuous variables. The assumption of normality was checked with the Shapiro-Wilk test. Fisher's Exact test or Pearson's chi-square test was used to analyze the relationships between categorical variables. Mann-Whitney U test was used for non-parametric comparison of continuous variables of the two groups, and Student's t-test was used for parametric comparison. Kruskal-Wallis test was used in the non-parametric comparison of continuous variables of three or more groups, and Bonferroni correction was made in post-hoc tests for significant cases. Spearman correlation test was used for the relationships between ordinal or non-normally distributed continuous variables. Univariate and multivariate ordinal logistic regression analysis was performed to determine independent risk factors associated with the Hurley stage in patients, and the results are presented with odds ratio (OR) and 95% confidence intervals (CI). All analyses were performed using the IBM SPSS 23.0 program (IBM Corp. Armonk, NY). P values less than 0.05 were considered statistically significant.

Results

HS was more common in males (72%). The mean age of disease onset was 23.6±10.9 years; the median disease duration was 7 (min-max: 0.5-41) years. 77% of patients had a smoking history, and 70% were overweight and/or obese. 22% of our patients had a family history. Regarding comorbidities, 13% of patients had hypertriglyceridemia, 12% had diabetes, 11% had a psychiatric disease, and 7% had hypertension. Smoking (p=0.003) and alcohol consumption (p=0.024) were significantly higher in males than females. All socio-demographic characteristics of patients are shown in Table 1.

The most frequently affected area was the axilla (81%), followed by the inguinal (59%) and gluteal (47%) areas. In males, HS involvement was more common in pubis (p=0.012), perianal region (p=0.045), neck (p=0.017), back (p=0.019), and behind the ear (p=0.031) (Table 2). Scalp involvement was seen only in males, and inner thigh involvement was more common in females, although statistically insignificant (p=0.058; p=0,080, respectively). When disease onset areas were evaluated, the most common onset area was the axilla (55%), followed by the inguinal region (26%) and the gluteal regions (25%). Onset in the axillary region in males was significantly higher than in females (p=0.049), while gluteal region onset of the disease was significantly more in females (p=0.040) (Table 3).

Forty-three percent of patients had a history of acne vulgaris; acne conglobata was seen in 19%, dissecting cellulitis in 5%, and pilonidal sinus in 31%. The majority of the patients (71%) were HSt II. The median VAS-pain score was 6 (min-max: 0-10), and the mean DLQI score was 13 (min: 0-max: 30). According to the HS-PGA scoring system, disease severity was evaluated as "moderate" in most patients (45%). Although there was no difference between genders regarding Hurley stages, VAS pain scores and DLQI scores, the HS-PGA stage was defined as "minimal" significantly more in females (17.9%) than males (1.4%) (p=0.043). There was no difference in other stages of HS-PGA (Table 4).

HS progressed more severely in the axilla [(OR: 6.997; 95% CI: 1.892-25.878; p=0.004), perianal region (OR: 5.189; 95% CI: 1.207-22.311; p=0.043), and the mammalian area (OR: 4.85; 95% CI: 1.234-19.07; p=0.024) (Table 5).

Table 1. Socio-demographic and clinical characteristics of patients

Categories	Total (n=100)	Male (n=72)	Female (n=28)	P
Age ± SD, years (min-max)	33.7±12.3	34.5±11.6	31.7±14	0.302
Age at disease onset ± SD, years (min-max)	23.6±10.9	24±10.3	22.8±12.7	0.622
Duration of disease ± SD, years (min-max)	7 (0.5-41)	7 (0.5-41)	6.5 (1-29)	0.380
Marital status				
Single	55 (55)	40 (55.6)	15 (53.6)	0.858
Married	45 (45)	32 (44.4)	13 (46.4)	
Smoking status	77 (77)	61 (84.7)	16 (57.1)	**0.003**
Number of smoking pack years ± SD. (min-max)	16 (0.5-80)	20 (0.5-80)	13.3 (1-40)	0.271
Regular alcohol consumption	31 (31)	27 (37.5)	4 (14.3)	**0.024**
BMI*	27.97±6.39	28.5±6.1	26.62±7.02	0.188
<25	30 (30)	18 (25)	12 (42.9)	0.147
25-30	41 (41)	30 (41.7)	11 (39.3)	
>30	29 (29)	24 (33.3)	5 (17.9)	
HS family history	22 (22)	16 (22.2)	6 (21.4)	0.931
Acne Systemic disease	43 (43) 68 (68)	31 (43.1) 51 (70.8)	12 (42.9) 17 (60.7)	0.986 0.330

Results are given as mean ± SD, median (min-max) or n (%), Student's t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's exact test.
*BMI: Body mass index, min: Minimum, max: Maximum

Table 2. Areas of involvement for all patients and according to gender

Location of lesions, n (%)	Total (n=100)	Male (n=72)	Female (n=28)	p
Axillae	81 (81)	60 (83.3)	21 (75)	0.340
İnguinal	59 (59)	41 (56.9)	18 (64.3)	0.503
Inner thigh	30 (30)	18 (25)	12 (42.9)	0.080
Pubic	29 (29)	26 (36.1)	3 (10.7)	**0.012**
Perineal	6 (6)	5 (6.9)	1 (3.6)	0.999
Perianal	20 (20)	18 (25)	2 (7.1)	**0.045**
Gluteal	47 (47)	33 (45.8)	14 (50)	0.708
Mammarian	27 (27)	18 (25)	9 (32.1)	0.470
Genital	17 (17)	14 (19.4)	3 (10.7)	0.383
Face	10 (10)	9 (12.5)	1 (3.6)	0.275
Neck	13 (13)	13 (18.1)	0 (0)	**0.017**
Back	23 (23)	21 (29.2)	2 (7.1)	**0.019**
Post-auricular	11 (11)	11 (15.3)	0 (0)	**0.031**
Scalp	10 (10)	10 (13.9)	0 (0)	0.058

Pearson chi-squared test, Fisher's Exact test

Discussion

We analyzed for the first time the onset chronology of disease symptoms and their gender differences. Our results show the axilla is the most common onset area, followed by the inguinal and gluteal regions. The incidence of disease onset in the axilla in men and disease onset in the gluteus in women was significantly higher than in the other gender. Besides disease frequency, HS severity and cigarette/alcohol consumption were more prominent in males than females. Regarding disease severity, axillary, perianal, and mammalian region involvement were independent risk factors for high disease severity.

The natural history of the disease, including onset manifestations and their order, is not precisely known. The presentation of the disease symptoms varies considerably between studies and regions. The present study demonstrated the most frequently affected region was the axilla, followed by the inguinal and gluteal areas. While this

Table 3. Disease onset region of the patients

Area of disease onset, n (%)	Total (n=100)	Male (n=72)	Female (n=28)	p
Axillae	55 (55)	44 (61.1)	11 (39.3)	**0.049**
Inguinal	26 (26)	18 (25)	8 (28.6)	0.715
Inner thigh	14 (14)	8 (11.1)	6 (21.4)	0.207
Pubis	6 (6)	4 (5.6)	2 (7.1)	0.671
Perineal	3 (3)	2 (2.8)	1 (3.6)	0.999
Perianal	5 (5)	5 (6.9)	0 (0)	0.318
Gluteal	25 (25)	14 (19.4)	11 (39.3)	**0.040**
Mammarian	5 (5)	2 (2.8)	3 (10.7)	0.132
Genital	2 (2)	1 (1.4)	1 (3.6)	0.484
Other	10 (10)	10 (13.9)	0 (0)	0.058

Pearson ki-kare test, Fisher's Exact test

Table 4. Hurley stage, VAS, DLQI and Hs-PGA scores of patients

Categories	Total (n=100)	Male (n=72)	Female (n=28)	p
Hurley stage				
1	16 (16)	11 (15.3)	5 (17.9)	0.201
2	71 (71)	49 (68.1)	22 (78.6)	
3	13 (13)	12 (16.7)	1 (3.6)	
VAS	6 (0-10)	6 (0-10)	7 (0-10)	0.186
DLQI	13 (0-30)	13 (0-30)	12.5 (1-28)	0.887
HS-PGA				
Clean	5 (5)	5 (6.9)[a]	0 (0)[a]	**0.043**
Minimal	6 (6)	1 (1.4)[a]	5 (17.9)[b]	
Mild	25 (25)	17 (23.6)[a]	8 (28.6)[a]	
Moderate	45 (45)	33 (45.8)[a]	12 (42.9)[a]	
Severe	7 (7)	6 (8.3)[a]	1 (3.6)[a]	
Very severe	12 (12)	10 (13.9)[a]	2 (7.1)[a]	

Results are given as median (min-max) or n (%). Mann-Whitney U test, Fisher's Exact test.
Different lowercase exponential letters in a row indicate statistically significant difference between groups.
VAS: Visual analog scale, DLQI: Dermatology Life Quality Index, HS-PGA: Hidradenitis Suppurativa-Physicians Global Assessment, min: Minimum, max: Maximum

was similar to the previous multi-center report from Türkiye[11], the gluteal region was shown as the most common localization in studies conducted in Japan and Korea, followed by the axilla and inguinal region[8,9]. Thus, involvement sites and their frequency seem influenced by genetic and probably environmental characteristics. Smoking and alcohol consumption, which play a role in the development of in developing the disease, show significant differences between societies. These environmental factors, which were detected with a high frequency among male patients in our study, may have played a role in the frequency and severity of the disease between genders.

In terms of gender differences, although axillary, inguinal, and gluteal regions were the most common localizations in both genders in the current study and in the previous literature[2,12], HS involvement was more common in pubis, perianal region, neck, back, and behind the ear locations in males in the current study. This is in line with the observation that the involvement of unusual localizations is more common in males. In previous studies from Korea and Japan, axillary and inguinal area involvement was more common in women and gluteal involvement in men[8,9]. Schrader et al.[2] also reported that gluteal region involvement is more common in males (50% in males, 38% in females). In our study, we did not observe a significant difference between genders regarding the frequency of gluteal involvement, similar to the other multicenter study conducted in Türkiye (p=0.708)[10]. This could be due to the limited number of females in the current study. The difference in pubis and perianal area involvement between the genders may be due to the tendency of women not to report genital area involvement because of embarrassment, etc. This may have resulted in an incorrectly low frequency of genital involvement among women.

Regarding disease onset areas, the present study showed the incidence of disease onset in the axillar area in men and disease onset in the

Table 5. Factors associated with disease severity

	Univariable		Multivariable	
Categories	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
Age at disease onset	0.989 (0.952-1.028)	0.578	-	-
Sex (ref: female)	1.84 (0.717-4.722)	0.205	-	-
Number of smoking (pack years)	1.027 (0.998-1.057)	0.070	1.027 (0.987-1.068)	0.188
BMI (ref: <25)				
25-30	1.212 (0.431-3.406)	0.715	-	-
>30	1.333 (0.432-4.113)	0.617	-	-
Duration of disease	1.097 (1.035-1.162)	**0.002**	1.044 (0.969-1.123)	0.257
Areas of involvement (ref:none)				
Axillae	5.472 (1.819-16.457)	**0.002**	6.997 (1.892-25.878)	**0.004**
Inguinal	5.136 (1.86-14.18)	**0.003**	2.387 (0.672-8.47)	0.178
Inner thigh	5.292 (1.832-15.291)	**0.002**	2.361 (0.639-8.721)	0.197
Pubis	5.955 (1.988-17.841)	**0.001**	2.294 (0.591-8.901)	0.230
Perineal	8.906 (1.644-48.251)	**0.011**	0.571 (0.049-6.635)	0.655
Perianal	8.594 (2.612-28.279)	**<0.001**	5.189 (1.207-22.311)	**0.027**
Gluteal	2.089 (0.862-5.063)	0.103	-	**-**
Mammarian	8.134 (2.562-25.819)	**<0.001**	4.85 (1.234-19.07)	**0.024**
Genital	5.351 (1.636-17.498)	**0.006**	1.467 (0.323-6.654)	0.619
Other	3.811 (1.424-10.2)	**0.008**	2.485 (0.799-7.727)	0.116
Systemic disease (ref:no)	1.742 (0.698-4.351)	0.235	-	-
Family history (ref:no)	0.93 (0.338-2.563)	0.889	-	-

Variables with p<0.1 in univariate analysis were included in the multivariate model
CI: Confidence interval, BMI: Body mass index, OR: Odds ratio

gluteal region in women was significantly higher than the other gender. These results could help physicians suspect HS earlier when a patient has a history of an inflammatory nodule or abscess involving these regions. This is paramount, as when the diagnosis is established earlier, the long-term morbidity of the disease could be reduced.

Axillary, perianal, and mammarian region involvement was an independent risk factor for high disease severity (p<0.05), similar to the findings of Schrader et al.[2] However, there are differences in previous reports, such as the multicenter study by Özkur et al.[10] showing the involvement of the genital, inguinal, and neck regions' correlation with the severity of the disease and Yang et al.[8] study demonstrating the perineum and gluteal region more frequently in severe patients.

In our study, acne history was 43%. Kimball et al.[13] reported that diseases related to follicular occlusion tetrad were also more common in patients with HS. The frequency of acne vulgaris was reported to be higher in studies from Türkiye (23-67.3%) than in studies from America and Japan (2.9-27.7%). Including all acne patients, not just patients with a history of severe acne, may be the reason for this difference[7,8,11,14,15]. In our cohort, 19% of patients had acne conglobata, while 5% had dissecting cellulitis, and 31% had a history of pilonidal sinus. Evidence suggests these diseases share the same pathological process initiated by follicular occlusion in areas rich in apocrine sweat glands and occurring concomitantly[16].

Pain is one of the most bothersome symptoms for patients with HS[17]. Pain was described by 96% of our patients. The mean VAS score was 6, although there was a weak positive correlation between VAS scores and the HSt (r=0.208, p=0.038). These results were similar to a recent study evaluating 1,795 patients[18], although they reported higher pain scores in female patients, which was different in our study (no significant difference between genders; p=0.186). This could be due to the limited number of females in our study.

It has been increasingly demonstrated that HS tremendously affects patients' quality of life. The median DLQI score was 13 in our study, similar to the study by Schneider-Burrus et al.[19] There was no significant difference in terms of genders. However, a moderate positive correlation was demonstrated between HSt and DLQI scores of patients (r=0.400; p<0.001), also shown by Schneider-Burrus et al.[19]

These results emphasize that patients with HS have a lower quality of life, which correlates with disease severity. Thus, treatment and control of disease symptoms are important for the general quality of life for both genders.

As in previous studies from Türkiye, male predominance (2.5:1) was also remarkable in our study. While in Europe, HS is more frequently associated with the female gender (male/female: 1:3)[20], reports from Korea and Japan also showed a male predominance (male/female: 2.5-3:1)[8,21], Male predominance in our study might be related to the higher severity of the disease in men, as severely affected patients are more likely to attend tertiary hospitals. Moreover, particularly the involvement of private areas, such as the genital region, might have affected women in terms of consultation with doctors and could explain the lower incidence in Asian countries. However, geographic, racial, and ethnic differences in HS prevalence and incidence may also play a role[22].

In our study, family history was found in 22% of patients. In previous studies from Europe, a significant genetic contribution to the pathogenesis of HS was shown with a family history reported in around 30-40% of patients[2,23]. However, a multicenter study from Korea has reported family history as 0.07% (8), and two studies from Japan found the incidence of family history 4% and 2%, respectively[21,23]. Although the exact reason for these differences is unknown, genetic differences could be an important factor[22]. In our study, the mean age of disease onset was 19.8±7.2 years in patients with a family history. Meanwhile, it was 24.6±11.5 years in patients without a family history (23.6±10.9 for whole patients). Deckers et al.[24] also drew attention to the early age of disease onset in patients with a positive family history, as seen in our study.

Study Limitations

Limitations of the current study might include having a cross-sectional design, not having a control group, using self-reported history regarding the onset and evolution of the disease, and including only patients seeking treatment in mainly tertiary health institutions. Thus, these factors should be considered when generalizing the results of this study to the entire population. However, the major strengths of our study are having a large sample of patients with HS, using validated disease severity scores and data from a disease-specific electronic database.

Conclusion

To our best knowledge, the chronology of disease onset areas was first examined in the current study. Therefore, these results may contribute to the literature regarding the natural history and clinical characteristics of HS, which is important to understand disease evaluation for better management of HS and prevention of morbidities.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of the Akdeniz University Faculty of Medicine (approval number: KAEK-814, date: 21.10.2020).

Informed Consent: Retrospective study.

Peer-review: Externally peer reviewed.

Authorship Contributions

Concept: K.M., A.B., E.A., Design: K.M., A.B., E.A., Data Collection or Processing: K.M., A.B., E.A., Analysis or Interpretation: K.M., A.B., E.A., Literature Search: K.M., A.B., E.A., Writing: K.M., A.B., E.A.

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