

Structural changes of pelvic/hip entheses and their evolution over time in psoriatic arthritis patients starting bDMARDs

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Abstract

Objective: This study aimed to investigate the frequency and progression of pelvic and hip enthesal structural changes in PsA patients initiating biologic therapy.

Methods: Records from the Hacettepe University Rheumatology Biologic Therapy Registry (HUR-BIO) were retrospectively reviewed. PsA patients with pelvic radiographs obtained within ± 1 year of biologic therapy initiation were included. Radiographs were assessed according to the modified New York criteria, and enthesal involvement at the ischium, symphysis pubis, iliac wings and greater/ lesser trochanter was graded from 0 (none) to 4 (florid new bone formation). Grade 2 or higher was considered clinically relevant. Demographic and clinical characteristics were compared between patients with/ without structural changes and progression of these lesions were assessed.

Results: A total of 108 patients (68.5% female; mean age 41.5 ± 11.6 years; mean PsA duration 2.2 years) were included. Baseline mNY positivity was detected in 45.4%. Bilateral relevant enthesal involvement was observed in 21.9% at the ischium, 15.3% at the symphysis pubis, and 7.7% at the iliac wings. Greater trochanteric enthesopathy was 2% on the right side. Male patients, with higher BMI and older age with family history tended to have more structural lesions. After a mean follow-up of 38.6 months, data from 48 patients were available. Most progression was limited to a one-grade increase at the ischium (28%).

Conclusion: Major pelvic enthesal lesions, predominantly at the ischium and symphysis pubis, are relatively common in PsA but show minimal radiographic progression under biologic therapy.

Keywords: xray, psoriatic arthritis, enthesitis, pelvis

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory musculoskeletal disease characterized by a heterogeneous pattern of clinical manifestations affecting multiple that are considered when treating patients, such as peripheral arthritis, axial disease, enthesitis, dactylitis, and skin and nail involvement

[1]. Among these, enthesitis, the inflammation at the tendon or ligament insertion into bone, is considered a hallmark feature of PsA [2]. Although enthesitis is most commonly assessed and reported using ultrasound, evaluation of deeper regions such as the pelvis and hips requires alternative imaging modalities. Magnetic resonance imaging (MRI) is valuable for detecting active enthesal inflammation; however, its use is limited by

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higher costs, longer acquisition times, and logistical constraints [2]. Over the long term, structural changes can also be visualized radiographically, including cortical bone irregularities, erosions, calcifications, and new bone formation, which may serve as indicators of enthesal involvement in the pelvic and hip regions.

Previous studies have suggested that pelvic enthesal involvement, frequently in PsA [3,4]. However, the literature on the prevalence, distribution, and clinical characteristics of patients with structural pelvic enthesal involvement remains limited, and the longitudinal progression of these lesions has not been systematically evaluated.

Therefore, the aim of this study was to assess pelvic enthesal involvement, including the ischium, iliac wings, symphysis pubis, and the greater and lesser trochanters, on conventional radiography, and to examine its progression over time in a cohort of PsA patients treated with biologic DMARDs.

2. Materials and Methods

2.1. Patient Selection

The Hacettepe University Rheumatology Biologic Database (Hacettepe) is a single-center registry established in 2005, which includes patients with inflammatory arthritis receiving biologic DMARDs

(bDMARDs). For this study, patients from the HUR-BIO PsA cohort who had at least one anteroposterior (AP) or Ferguson-view pelvic X-ray obtained within ± 1 year of bDMARD initiation were included, regardless of the presence or absence of sacroiliitis on imaging (Figure 1). All patients had a clinical diagnosis of psoriatic arthritis (PsA) confirmed by the treating rheumatologist, and it was recorded whether they fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR).

2.2. Patient and Clinical Data Collection

The following data were recorded: sex, age, and age at PsA diagnosis. Additional baseline variables included smoking status, and presence of obesity (BMI >30) at the time of bDMARD initiation. Clinical features such as history of dactylitis (yes/no), enthesitis (based on the Leeds Enthesitis Index), and nail involvement (including pitting, onycholysis, and hyperkeratosis) were noted. Patient-reported outcomes (PROs) and C-reactive protein (CRP) levels were also recorded at the visit when bDMARD therapy was initiated.

2.3. Ethical Approval

The study was approved by the Ethics Committee of the Hacettepe University Faculty of Medicine (Approval No: KA-22005) and conducted in accordance with the ethical principles of the 1964 Declaration of Helsinki. Informed consent was obtained from all participating patients.

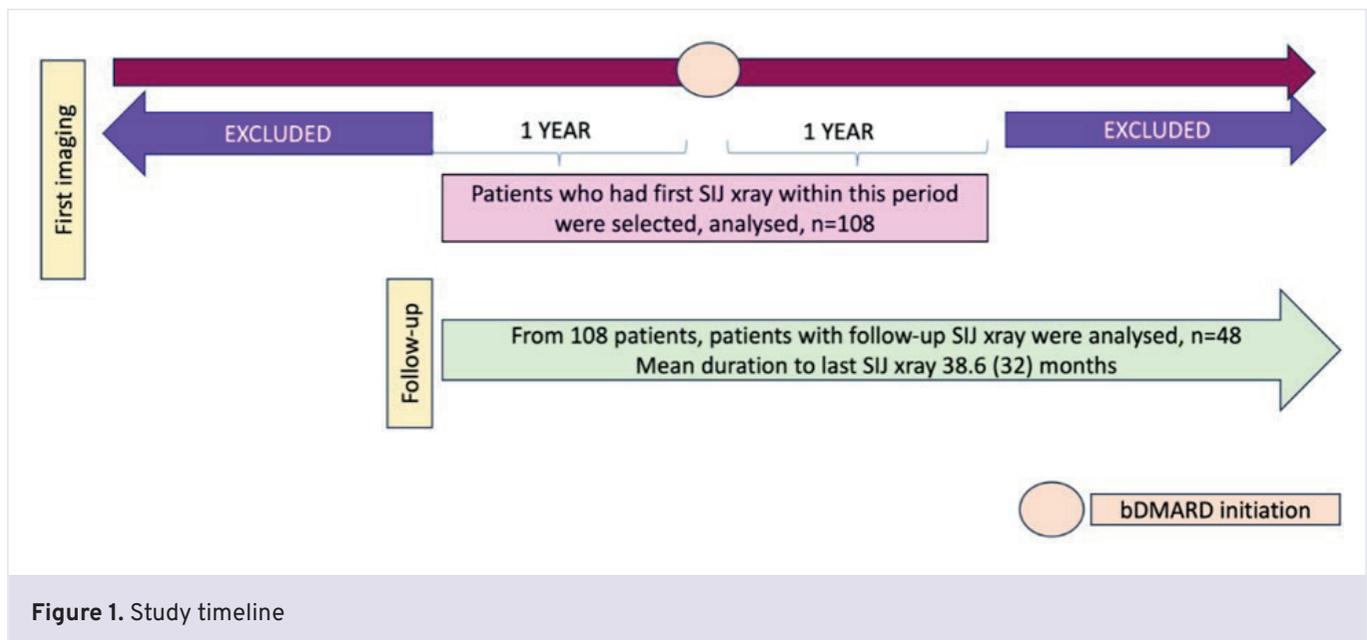


Figure 1. Study timeline

2.4. Pelvic and Lumbar X-ray Assessment and Definitions

Pelvic X-rays were reviewed by an experienced rheumatologist (UK). In cases of suspicion regarding structural findings, the images were jointly re-evaluated by two rheumatologists (UK and LK) until a consensus was reached. Radiographs were assessed according to the modified New York (mNY) criteria (grades 0–4). In addition, enthesal changes were graded at the ischium, symphysis pubis, iliac wings and greater and lesser trochanter as follows: Grade 0: none, Grade 1: minimal, Grade 2: moderate, Grade 3: advanced, and Grade 4: florid new bone formation [4]. Grades 2 and higher were considered to represent clinically relevant changes [4]. When parts of the pelvis were outside the imaging field or obscured by overlying structures, the findings were recorded as “missing.” Among the selected patients, those with available follow-up radiographs were evaluated longitudinally using baseline and final images to determine structural progression. Figure 2 provides an example of grading for the ischium

2.5. Statistical Analysis

All analyses were performed using Stata SE v18 (StataCorp, College Station, TX, USA). Data normality was evaluated both visually (histograms, probability plots) and analytically (Kolmogorov–Smirnov test, skewness, and kurtosis). Continuous variables were summarized as mean (standard deviation, SD) or median [interquartile range, IQR], while categorical variables were expressed as frequencies and percentages.

Between-group comparisons for continuous data were conducted using the Student’s t-test or Mann–Whitney U test, depending on the distribution. Paired t-tests or Wilcoxon signed-rank tests were used for within-group comparisons. Categorical variables were analyzed using the Chi-square test or Fisher’s exact test, as appropriate. Results for count data were reported as valid percentages.

3. Results

3.1. Patient characteristics, differences according to the pelvic enthesal involvement severity

A total of 108 patients were included in the study, of whom 74 (68.5%) were female. The mean (SD) age at the time of the first pelvic radiograph was 41.5 (11.6) years, and the mean PsA disease duration was 2.2 years. CASPAR criteria positivity was observed in 66 (61.1%) of patients. A history of enthesitis at any time was reported in 23 (43.4%). Based on baseline pelvic radiographs, 49 (45.4%) of patients were positive according to the modified New York (mNY) criteria.

Regarding clinically relevant pelvic enthesopathies, bilateral involvement was detected in 16 (21.9%) patients at the ischium, 13 (15.3%) patients at the symphysis pubis, and 6 (7.7%) patients at the iliac wings. Clinically relevant major trochanter enthesopathy was observed in 2 (2.2%) patients on the right. On

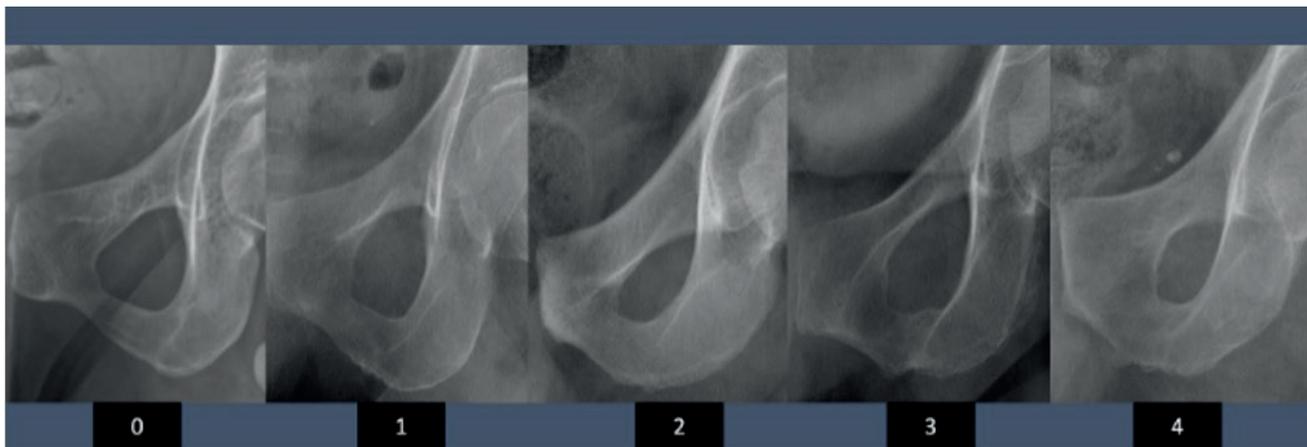


Figure 2. Grading example for ischium

the left side only 3 (3.3) patients had grade 1 major trochanter enthesopathy whereas no minor trochanter enthesopathy was identified.

When patients with and without clinically relevant pelvic enthesitis were compared, the proportion of females was significantly lower in the \geq grade 2 group than in the $<$ grade 2 group (53.3% vs 76.0%, $p = 0.02$), indicating a higher prevalence of males among patients with advanced enthesal involvement. Patients with \geq grade 2 enthesitis were also older at the time of first pelvic radiography [44.4 (9.8) vs 40.6 (12.3)] years, $p = 0.09$ and at PsA diagnosis [42.2 (10) vs 37.9 (11.3) years, $p = 0.06$], although these differences did not reach statistical significance. Disease duration was comparable between groups (mean 2.2 years in both, $p = 0.40$).

A trend toward higher BMI was observed among patients with advanced enthesitis (BMI > 30 in 43.3% vs 26.2%, $p = 0.09$), and a positive family history of psoriasis or PsA was numerically more frequent (58.8% vs 38.9%, $p = 0.17$). Smoking history was similar between groups (52% vs 47%, $p = 0.81$). Clinically, dactylitis was slightly

less common among patients with advanced enthesitis (23.8% vs 33.3%, $p = 0.43$), whereas a history of enthesitis was, as expected, more often recorded in this group (50% vs 38.2%, $p = 0.47$). On imaging, sacroiliitis according to the modified New York criteria was also more frequent in patients with \geq grade 2 enthesitis (53.3% vs 41.8%, $p = 0.29$) (Table 1). Overall, both groups showed comparable findings in terms of disease activity parameters (Table 2).

3.2. Progression of pelvic enthesal involvement

After a mean (SD) follow-up duration of 38.6 (32) months, follow-up data were available for 48 patients. Among these, the most frequently used first-line b/tsDMARDs were adalimumab (45.8%, $n=22$), etanercept (20.8%, $n=10$), and certolizumab (16.7%, $n=8$). For second-line treatment, adalimumab (18.8%, $n=9$), golimumab (10.4%, $n=5$), and certolizumab (8.3%, $n=4$) were the most commonly prescribed agents. In the third-line setting, etanercept (8.3%, $n=4$), adalimumab (6.3%, $n=3$), and golimumab or secukinumab (2.1%, $n=1$ each) were the most frequently used. Use of biologic

Table 1. Demographic and clinical characteristic of patients at bDMARD initiation

	All patients n=108	Patients with $<$ grade 2 enthesitis* (n=67)	Patients with \geq grade 2 enthesitis ^ (n=30)	P value
Female gender, n (%)	74 (68.5)	51 (76)	16 (53.3)	0.02
Age at the time of first SIJ radiography, mean (SD), years	41.5 (11.6)	40.6 (12.3)	44.4 (9.8)	0.09
Age at the time of first bDMARD initiation, mean (SD), years	41.5 (11.7)	40.5 (12.3)	44.4 (9.8)	0.09
PsA diagnosis age, mean (SD), years	39.1 (11.2)	37.9 (11.3)	42.2 (10)	0.06
PsA disease duration, mean (SD), years	2.2 (3.7)	2.2 (4.1)	2.2 (2.9)	0.40
PsO/PsA family history, n (%)	24 (40)	14 (38.9)	10 (58.8)	0.17
BMI > 30 , n (%)	33 (31)	17 (26.2)	13 (43.3)	0.09
Smoking (ever), n (%)	43 (51.8)	24 (47)	12 (52)	0.81
Dactylitis (ever), n (%)	21 (30)	14 (33.3)	5 (23.8)	0.43
Enthesitis (ever), n (%)	23 (43.4)	13 (38.2)	6 (50)	0.47
Nail involvement, n #	28	13	11	NA
Sacroileitis according to mNY criteria, n (%)	49 (45.4)	28 (41.8)	16 (53.3)	0.29

*patients with at least one enthesal site is scored less than grade 2

^ patients with at least one enthesal site is scored grade 2 or more

In 11 patients, all of the enthesal sites were scored missing

The rest of the cases other than positive ones were missing and for this reason percentages were not provided

SIJ: Sacroiliac joint, bDMARD: biologic disease modifying anti-rheumatic drugs, BMI: Body mass index, PsA: Psoriatic arthritis, PsO: Psoriasis, mNY: Modified new york

Table 2. Disease activity parameters of patients at bDMARD initiation

	All patients n=108	Patients with < grade 2 enthesitis* (n=67)	Patients with >= grade 2 enthesitis ^ (n=30)	P value
BASDAI, mean (SD)	5.6 (2.0)	5.4 (2.0)	5.9 (2.0)	0.25
BASFI, mean (SD)	3.5 (2.2)	3.5 (2.4)	3.3 (2.1)	0.81
DAS-28, mean (SD)	3.6 (1.0)	3.6 (1.0)	3.8 (1.0)	0.22
DAPSA-28, mean (SD)	17.8 (6.8)	16.9 (5.8)	19.6 (7.9)	0.19
CRP, mean (SD)	1.2 (1.7)	1.0 (1.1)	1.5 (2.5)	0.13
HAQ-DI, mean (SD)	0.6 (0.5)	0.6 (0.5)	0.7 (0.5)	0.28

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index DAS-28, Disease Activity Score-28; DAPSA: the Disease Activity Index for Psoriatic Arthritis, CRP, C-reactive protein (mg/dl), HAQ-DI, Health Assessment Questionnaire Disability Index
 *patients with at least one enthesial site is scored less than grade 2
 ^ patients with at least one enthesial site is scored grade 2 or more
 In 11 patients, all of the enthesial sites were scored missing

agents beyond the third line was uncommon, with only a few patients receiving a fourth (n = 3) or fifth (n = 1) b/tsDMARD. In these later treatment lines, golimumab, secukinumab, tofacitinib, and infliximab were each used in a single patient.

Regarding radiographic progression, a one-grade increase in ischial enthesopathy was observed in 28% of patients, whereas progression beyond one grade was not seen. At the symphysis pubis, 8.5% of patients showed a one-grade and 3% a two-grade progression. On the right iliac wing, 6% of patients demonstrated a

one-grade increase, with no progression exceeding one grade. On the left iliac wing, a one-grade progression was observed in 3% of patients, with no further increase beyond that level (Figure 3). No progression was detected at the greater or lesser trochanter sites

4. Discussion

This study presents a radiographic assessment of pelvic/hip enthesal involvement in patients with PsA, emphasizing both its frequency and longitudinal

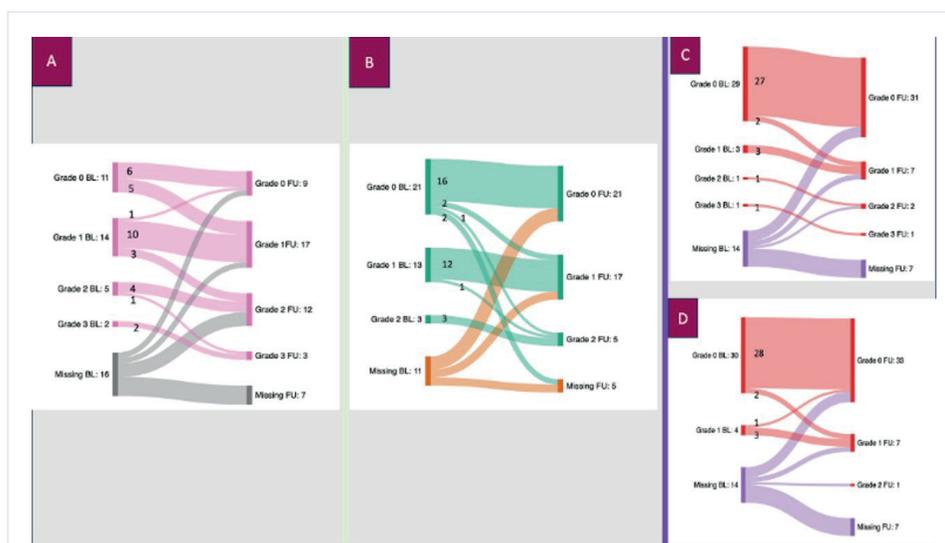


Figure 3. Changes of enthesal involvement of pelvic region A: Ischium (bilateral), B: Symphysis Pubis (bilateral), C: Iliac wing (right), D: Iliac wing (left), BL: Baseline, FU: Follow-up

changes. The bilateral ischium emerged as the most frequently affected sites, followed by the symphysis pubis, while iliac wing and trochanteric involvement were less common. Over a mean follow-up period of approximately three years, radiographic progression of pelvic enthesal lesions appeared limited, suggesting that structural damage in these regions tends to evolve slowly in a bDMARD population.

In a previous study comparing patients with PsA and rheumatoid arthritis (RA), Bitik et al. reported that radiographic ischial enthesal lesions were present in 50% of PsA patients, significantly higher than in RA. The frequency observed in our cohort was somewhat lower than the 50% reported by Bitik et al., which may be explained by differences imaging indication and methodologic differences in reporting [3]. Radiographs in the earlier study were obtained from patients with axial or heel pain, and this selection criteria may have increased the rates. Furthermore, no grading system was applied in that assessment, and the authors recorded cortical erosions and enthesophytes while excluding suspected cortical irregularities, making direct comparison with our findings difficult. In the CASPAR substudy assessing psoriatic spondylitis, Helliwell et al. reported slightly higher frequencies of advanced (grade 3-4) enthesal changes at comparable pelvic sites (ischial enthesitis 22%, symphysis 25%, and iliac enthesitis 4%) [4]. This higher prevalence may be explained by the characteristics of their cohort, which included patients with longer disease duration, which has been shown previously in axial spondyloarthritis population, and predominantly axial involvement, as reflected by the high proportion of individuals with severe sacroiliitis (grade 3-4 in 82%) [4,5].

Nevertheless, in our study, the mNY criteria positivity reached up to 45% which is higher than expected in a general PsA cohort [6]. However, this should be kept in mind that these are patients who had pelvis radiography taken around bDMARD start. This may reflect particular patient population at risk of axial symptoms even there is not an inclusion criteria.

When comparing patients with and without clinically significant pelvic enthesitis, several patterns emerged that are consistent with prior observations on sex and mechanical load-related differences in enthesal disease. The lower proportion of females and the trend toward older age in the \geq grade 2 group

suggest that mechanical factors may contribute to enthesal structural damage, in line with prior studies linking enthesal new bone formation to cumulative biomechanical stress and male predominance [2,7]. The observed trend toward higher BMI among patients with advanced enthesitis supports this interpretation, as obesity is known to increase enthesal load and has been associated with greater enthesal thickness and structural change on imaging

The higher, though non-significant, frequency of positive family history of psoriasis or PsA in the advanced enthesitis group may reflect a genetic predisposition influencing enthesal response to inflammation or mechanical stress. It has already been shown that HLA-B27 positivity is associated with the presence of clinical enthesitis and also correlated with higher sonographic enthesitis scores, suggesting that this genetic background may predispose to more severe enthesal inflammation within limitation of HLAB27 is not reported in this assessment [8,9].

In our cohort, progression of enthesal structural changes was very limited, which may, at least in part, be related to the use of bDMARD therapy; however, this interpretation should be made with caution, as the study lacked a comparator group of patients not receiving biologic treatment or treated only with csDMARDs. This observation after all, aligns with previous data suggesting that bDMARDs can positively influence bone metabolism in PsA. Simon et al. demonstrated, using high-resolution peripheral quantitative CT, that PsA patients treated with bDMARDs exhibited significantly higher bone mineral density and improved bone strength compared with those receiving methotrexate or no DMARDs, indicating a direct effect of cytokine blockade on restoring bone homeostasis by reducing osteoclast activity and enhancing bone formation [10]. However, while these findings underscore the beneficial impact of biologic therapies on overall bone structure, their specific effects on enthesal sites remain insufficiently characterized. Supporting this, Mathew et al. reported that clinical enthesitis resolved in up to 86% of PsA patients treated with DMARDs within one year, yet highlighted the lack of imaging-based data to evaluate structural outcomes at the entheses [11]. Overall, the potential protective, or even regressive, effects of bDMARD therapy on structural enthesal lesions warrant further investigation.

This study has several limitations. First, the association between pelvic enthesal lesions and spinal structural damage was not explored, which has been previously shown in axSpA. Second, radiographs were scored by a single experienced reader, which may introduce observer bias despite the reader's more than 20 years of expertise in musculoskeletal imaging. Third, the cohort represents a selected population of PsA patients undergoing bDMARD initiation, and therefore, the results may not be generalizable to all PsA patients. Finally, the potential contribution of these lesions to axial pain could not be assessed, as systematic evaluation of symptom-imaging correlation was beyond the study scope. Despite these limitations, the study also has important strengths. To our knowledge, this is the first study to systematically evaluate radiographic progression of pelvic enthesal lesions over time in PsA. The inclusion of longitudinal imaging data provides valuable insight into the structural evolution of enthesal involvement in the context of biologic therapy.

To conclude, in a bDMARD cohort, pelvic/hip enthesal lesions were seen frequently. Patients with male gender is more commonly affected as well as the obese and older patients with family history had tendency to be more commonly affected. The progression on the contrary is very limited over 3 years and mainly seen at ischium.

Author contributions

Conception and design: G.A., A.S., L.K., U.K.; Data acquisition: G.A., A.S., L.K., U.K.; Data analysis: G.A., U.K.; Data interpretation: G.A., A.S., L.K., U.K.; Drafting of the manuscript: G.A.; Critical revision of the manuscript: G.A., A.S., L.K., U.K. All authors reviewed the results, approved the final version of the manuscript, and agreed to be accountable for all aspects of this study.

Ethical approval

This study was approved by the Ethics Committee of the Hacettepe University Faculty of Medicine (Date: August 23, 2022, Decision/Protocol No: 2022/13-19 KA-22005). Informed consent was obtained from all participants involved in this study.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflict of interest

The authors declare that this study was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Generative AI statement

The authors declare that no generative AI or AI-assisted technologies were used in the writing or preparation of this study.

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