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Conflict of interest

None.

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High prevalence and little awareness in patients with chronic inflammatory skin diseases and genital involvement

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Summary

Background: Genital involvement in patients with chronic inflammatory skin diseases is frequent, yet insufficiently acknowledged.

Objective: To evaluate the prevalence of genital symptoms in psoriasis and chronic urticaria patients, effects on quality of life, physician-patient relations and disease management.

Patients and Methods: 100 patients with psoriasis and 100 with chronic urticaria from our outpatient clinic, as well as 50 healthy controls were included. Data was collected using questionnaires developed by dermatological experts.

Results: Out of 250 subjects, 74 % had already experienced genital symptoms – 70 % of psoriasis patients and 58 % of urticaria patients. Seven out of ten even complained about recurrent genital involvement. 50 % of psoriasis and 41 % of urticaria patients reported an impact on quality of life. 41 % identified genital pruritus as the main symptom, with one out of three expecting a better management for this specific problem. Furthermore, 74 % complained about a lack of awareness among physicians: 79 % of urticaria patients and 58 % of psoriasis patients reported never having been questioned about genital symptoms by their physicians.

Conclusions: The majority of patients with psoriasis and chronic urticaria suffer from genital involvement and an impaired quality of life. Patient and physician reported outcomes should include genital symptoms as an influencing factor for quality of life.

Introduction

Chronic inflammatory skin diseases are widespread and associated with a significantly negative impact on Quality of Life (QoL) [1, 2]. Genital involvement in specific skin diseases – for example psoriasis (PSO) – has already been described in literature [3–7]. However, there is still limited information and awareness about genital involvement in other skin diseases. Psoriasis is defined as a chronic inflammatory systemic disease with known exacerbations among all age groups and various comorbidities [6].

Genital PSO is characterized by demarcated plaques, often without the pathognomonic desquamation but rather macerations due to the moistness of the genital area [3, 4, 8]. With a prevalence of 1–3 %, PSO accounts for a large

percentage of the chronic skin diseases in daily care of dermatological patients [3–6, 8]. Current literature suggests a prevalence of genital lesions of about 29 to 60 % [3–6, 8], indicating that until recent years, genital PSO has been highly under-recognized and not especially observed [3, 4, 6]. Chronic urticaria (CU) is a skin disease associated with wheals and/or angioedema, accompanied by immense pruritus over a duration of more than six consecutive weeks. In one third of CU cases, the symptoms are inducible through physical or other stimuli. In the rest of the cases, the diagnosis is “chronic spontaneous urticaria (CSU)”, where the above-mentioned symptoms occur without a distinguishable trigger. Chronic spontaneous urticaria is associated with auto-allergic or autoimmune phenomena [9–14]. The prevalence for CU varies from 0.5–5 % [10, 12–15]. There are

case reports describing genital involvement in CU patients, especially in patients with angioedema, but no larger cohort of patients has been evaluated so far [16–18].

Studies conducted with PSO patients have shown a limited awareness among health professionals regarding genital manifestations and the associated psycho-sexual impacts [3, 4, 8, 19]. There is also a certain reluctance among patients concerning the communication of genital problems, due to possible feelings of shame and/or uncertainty [3, 4]. Beyond that, only limited information on effective therapies for patients with inflammatory skin diseases and genital involvement exists. In PSO patients, genital symptoms can be treated with topical agents, such as corticosteroids or vitamin D analogues [3, 4, 8]. Patients with systemic therapies (e.g. conventional medication or biologics) also show improvement of genital lesions [4, 8, 20]. Currently, ongoing (approval) studies now include specific scores for genital involvement.

In CU patients it is not always possible to identify the cause, thus making it difficult to offer a curative therapy. The main symptomatic therapy includes second generation antihistamines [10, 14, 21]. In case of antihistamine-resistance, there is the option of treatment with anti-IgE-antibodies and immunomodulatory medication [14]. There are no specific therapy recommendations regarding genital involvement in CU patients.

However, in both cases, a holistic therapeutic approach with interdisciplinary teamwork has proven to be beneficial [15, 22]. It is also essential to screen for psychological comorbidities, like depression/anxiety, and offer professional support if needed [10, 13, 15, 22–26].

The main purpose of this study is to investigate the prevalence of genital symptoms and the impact on QoL in patients with PSO and CU. Secondary questions focus on the extent of QoL impairment, physician-patient relations, management and therapy requests. As a consequence, awareness should be raised concerning the under-recognized topic of genital lesions in patients with chronic skin disease. Ultimately, this study should help to optimize patient management including treatment.

Patients and methods

Study design and patients

This questionnaire study was conducted in the dermatology department at the university hospital of Mainz, Germany. 100 patients with PSO and 100 patients with CU were included, as well as 50 controls without skin diseases. Data were collected between January and June 2016. Ethical approval was granted by Ethics committee Rhineland-Palatinate.

A non-diagnosis related questionnaire was developed. Validation was conducted with the support of dermatologists

including experts in the field of chronic inflammatory skin diseases. Their suggestions were taken into account and included in the final questionnaire.

Subjects (18 years or older) with a diagnosed chronic inflammatory skin disease (PSO or CU) as well as 50 healthy controls were included by clinical research physicians of our department. Patients were recruited through our specialized outpatient clinic; controls were gathered among contacts of the patients and of clinical staff. Patients with an inflammatory skin disease other than PSO or CU were excluded. Participation was voluntary. Subjects were presented a non-diagnosis related, paper-based questionnaire with a total of ten questions, including: dichotomous questions, single selection questions, multiple-choice questions, free text questions and scaled questions (using a Visual Analogue Scala, VAS). The questions addressed the following issues: prevalence of genital symptoms, type and frequency of genital problems, impact on QoL, sense of shame, consultation by physicians and therapy requests. Statistical analysis was carried out based on the anonymized data.

Statistical analysis

All data collected from the questionnaire was attributed to a corresponding variable. The answers to the multiple-choice-questions were analyzed as categorical variables. The questions concerning duration of disease, frequency of (genital) symptoms and extent of QoL impairment were analyzed as continuous variables.

For descriptive analysis, absolute and relative frequencies for the comparison of two categorical variables were computed using cross tabulations with bar charts. For continuous, normally distributed variables the mean and standard deviation was calculated, as well as the median with quartiles for non-normally distributed variables. For showing the correlation of two ordinal variables Spearman's rank-order correlation was calculated and for the comparison of two categorical variables Pearson's chi-squared test was used. The differentiation of central tendencies of two independent ordinal scaled variables was conducted using a Mann-Whitney U test. All analyses are of explorative character. *P*-values below 5 % are considered significant, although no adjustments were made for multiple tests. For this reason, *P*-values should be interpreted with caution. SPSS software (version 22.0.01) was used for statistical analysis.

Results

Patient characteristics

In total, 200 patients, and 50 healthy volunteers were enrolled. Out of the 100 patients with psoriasis, 50 were male and 50 were female. In the urticarial group there were 39 males

and 61 females and in the control group there were 24 females and 26 males. The median age of the whole study population was 49 years (range 18–83 years), in the PSO group 50 years (range 23–51 years), in the CU group 45 years (range 19–75 years) and in the control group 50 years (range 18–80 years) (Table S1, Online supplement only).

Presence of genital symptoms

Out of 250 subjects included, 59.6 % (149 out of 250) had already suffered from symptoms in the genital area in the past. This included 70 % (70 out of 100) of PSO patients, 58 % (58 out of 100) of CU patients and 42 % (21 out of 50) of controls.

Chi-square testing revealed a significant difference concerning the prevalence of genital symptoms in patients with chronic inflammatory skin diseases (PSO and CU) compared to those without (controls) ($P = 0.004$). The prevalence of genital lesions in patients with PSO was significantly greater than in controls ($P = 0.01$), whereas no significant difference comparing CU and controls could be found ($P = 0.064$).

Frequency of genital symptoms

For the examination of the frequency of genital symptoms, free text answers were compiled and divided into following groups: “once, repeatedly, continually, other”. The majority of our study population stated that they had suffered “repeatedly” from genital symptoms, as shown in Figure 1. In addition, certain tendencies can be identified: Controls often reported genital involvement as singular occurrences in their lifetime, whereas only PSO patients described genital symptoms as being “continual”.

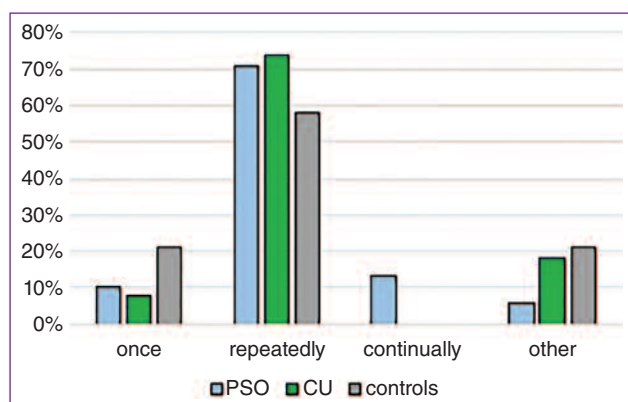


Figure 1 Frequency of genital symptoms. The x-axis shows how often subjects suffered from genital symptoms (“once”, “repeatedly”, “continually”, “other”) divided by group (PSO, CU, controls). The y-axis shows the corresponding results in percent ($n = 130$).

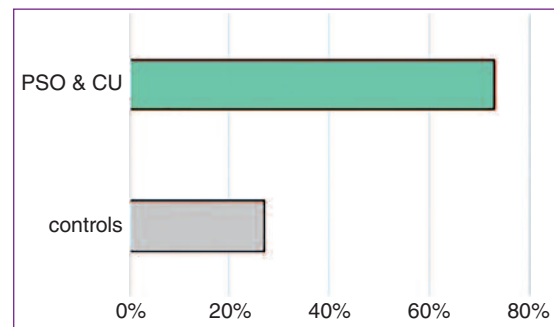


Figure 2 Impact of genital symptoms on QoL. The x-axis shows study subjects who declared an impact on their QoL because of genital symptoms in percent. The y-axis shows the groups (PSO & CU vs. controls) ($n = 250$).

Impact on QoL

In our study population, 40 % declared that their genital involvement has had an impact on their QoL (73 % PSO/ CU patients and 27 % of controls) (Figure 2). When asked about the severity of QoL impairment, PSO patients experienced the most significant impact (3.54 on VAS; 95 % CI [2.96–4.12]), followed by CU patients (2.47 on VAS; 95 % CI [2.02–2.91]) and controls (1.7 on VAS; 95 % CI [1.21–2.18]) (Figure 3). There was no significant difference between severity of QoL impairment comparing patients with PSO vs. patients with CU ($P = 0.19$). However, there was a difference between central tendencies regarding severity of QoL impairment among PSO patients vs. controls ($P < 0.001$) as well as CU patients vs. controls ($P = 0.007$).

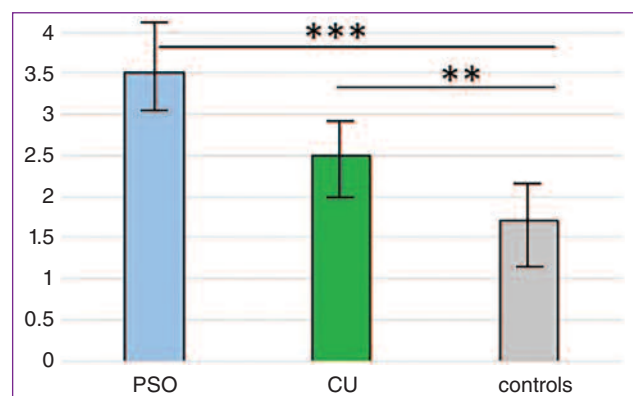


Figure 3 Severity of QoL impairment. The x-axis shows the groups PSO, CU and controls. The y-axis represents the severity of QoL impairment due to genital symptoms in absolute figures, objectified through VAS ($***P < 0.001$; $**P < 0.01$). Error bars indicate confidence intervals ($n = 250$).

Duration of disease

Regarding the duration of disease, a difference between central tendencies could be found in PSO vs. CU patients ($P = 0.032$), with PSO patients having a longer history of disease (PSO arithmetic mean 16.17 years; CU arithmetic mean 5.81 years).

We found a positive correlation ($r_s = 0.142$) between duration of disease and severity of QoL impairment. This suggests that the duration of disease may have an influence on genital involvement: patients with genital lesions had on average a longer history of disease than those without.

Specific symptoms

In our study population, and among all our groups (PSO, CU and controls), the main genital symptom was identified as pruritus (36.4 % of the whole study population, 41 % of PSO patients, 41 % of CU patients, 18 % of controls). Other genital symptoms noted in our study population were: Dryness (19.2 %), fungal infection (17.6 %), oozing/burning sensations (9.6 %), pain (6.4 %) and “others” (10.8 %). It should be noted that PSO patients suffered more from dryness and burning sensations compared to the other groups (dryness: PSO 28 %, CU 16 %, controls 8 %), while all three groups suffered approximately equally from fungal infection (PSO 16 %, CU 21 %, controls 14 %) and pain (PSO 7 %, CU 5 %, controls 8 %).

Therapy requests

When patients were asked which specific genital symptom they wished to have focused therapy for, the majority consequently answered with “pruritus”. It should be noted that only 72 out of 250 patients/controls answered this question (33.3 % of the whole study population $n = 72$ answered with “pruritus”, 31.6 % of PSO patients $n = 38$ and 38.7 % of CU patients $n = 31$).

Physician-patient-communication

Interestingly, 78.8 % of the CU patients had never been questioned about prior or existing problems in the genital area by their physicians. In comparison only 57.6 % of PSO patients reported never having been asked about this topic (Figure 4).

Additionally, 29.9 % of CU patients reported they would *not* notify their physicians about genital symptoms proactively but would rather expect the topic to be addressed by their doctors. In contrast, only 13.0 % of PSO patients and 8.0 % of control subjects would not report problems on their own (Figure 5).

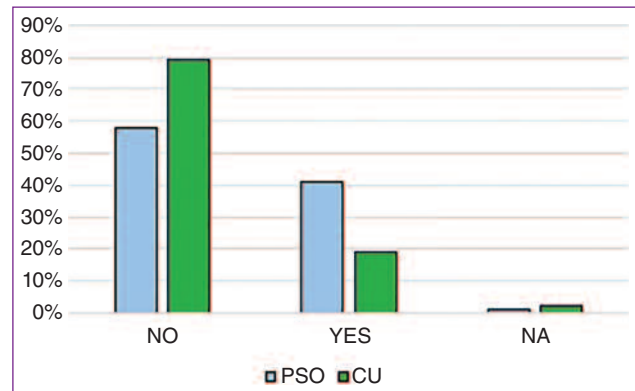


Figure 4 Inquiry by physician. Patients and controls were asked whether their doctors had ever inquired about genital symptoms. The x-axis shows the answers: “No”, “Yes”, “NA” divided by group (PSO, CU). The y-axis shows the corresponding percentage ($n = 248$).

Reasons for poor communication

In our study population, the main reason for poor physician-patient communication was listed as “sense of shame” (36.0 % of the whole study population, 33.3 % of PSO patients, 33.3 % CU patients, 50 % of controls). Other reasons included: privacy (20 %), inhibitions (16 %), physician dependent (8 %) and “others” (20 %). The results among the groups were similar. However, it should be noted that among CU patients, “privacy” (33.3 %) was the second main reason for poor physician-patient-communication and that controls only answered with “sense of shame” (50 %), “inhibition” (25 %) and “others” (25 %).

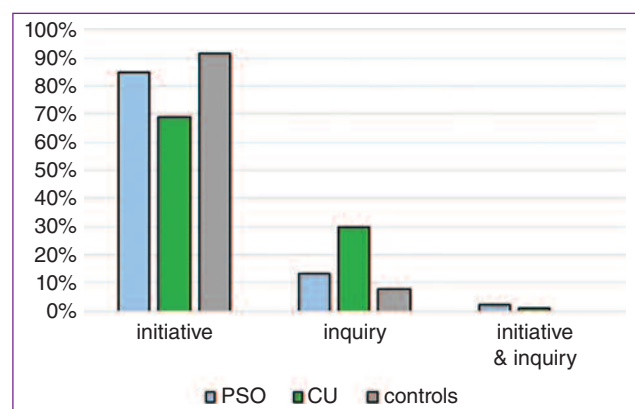


Figure 5 Patient-physician communication. Patients and controls were asked whether they would report genital symptoms proactively to their physician or whether they expected to be asked. The x-axis shows the answers: “initiative”, “inquiry”, “initiative & inquiry” divided by group (PSO, CU, controls) and the y-axis the corresponding percentage ($n = 247$).

Discussion

Our study clearly shows that recurrent genital symptoms in patients with chronic inflammatory skin diseases (PSO or CU) are more common and under-recognized than previously assumed. Although the two analyzed diseases appear to differ greatly in terms involved skin structures (i.e. psoriasis has epidermal and dermal involvement whereas urticaria is mainly a dermal disease) genital pruritus was identified as one of the main, recurrent genital symptoms for which there was a demand for more specific therapies.

Another important aspect highlighted in our study is the impairment of QoL: both PSO and CU, are associated with a significant negative impact on QoL [3–6, 8–10, 12, 13, 19, 27–29]. In our collective, 40 % stated that genital symptoms have had a negative impact on their QoL. Out of these, PSO patients showed the greatest impairment of QoL (VAS 3.6/ CU patients: 2.5/controls: 1.7). It should also be noted that, according to the literature, PSO patients often additionally suffer from negative effects on their sexual health, through disease-associated sexual dysfunction and/or reduced sexual activity [3, 4, 8, 19]. No publications of CU patients on this topic are available. Psoriasis and CU patients are known to frequently suffer from psychological comorbidities. It is therefore imperative to continually evaluate QoL, disease activity and disease burden. This may not only reveal the patients' subjective views but may also help assess therapeutic success [9, 11, 12, 15, 28, 30, 31]. A helpful tool for assessing the effects on QoL is the Dermatology Quality Index. However, genital lesions and possible impairments should always be discussed additionally during consultation to raise awareness, reduce inhibition levels and adjust the management of these patients.

An interesting correlation could be drawn between duration of inflammatory skin disease and prevalence of genital symptoms. In our study, PSO patients showed the longest duration of disease and the highest prevalence for genital lesions. Furthermore, a majority of PSO patients indicated having suffered repeatedly from symptoms in the genital area and showed the greatest impairment of QoL. It would seem that the longer the duration of disease, the more likely the (recurrent) development of genital symptoms and the greater the influence on QoL. In the literature, a similar conclusion could be drawn among CU patients: It is suspected that a longer duration and higher activity of disease are associated with a greater impact on everyday life, possibly leading to social isolation [11].

Unfortunately, our study confirmed results from the literature regarding the low awareness among physicians of genital lesions in chronic skin diseases [3, 4, 8, 19, 31]. The majority of our study population (70.6 %) reported that their physicians had never inquired about genital symptoms before. However, it should be noted that most patients included in our study came to our outpatient clinic for a primary

consultation. Patients with PSO appear to have been interviewed about genital lesions more frequently. It needs to be discussed whether genital lesions in psoriasis are better known, thus being a more evident part of the medical history. Another aspect may be a longer disease duration with possibly more frequent dermatological consultations.

On the other hand, we also found a distinct willingness in the majority of our study population to openly discuss problems of the genital area with their physician. A possible explanation for this result could be the setting of our study: patients were interviewed in a special consultation, with possibly more time and/or awareness for their specific problems. Since the genital area is one of the most vulnerable anatomical regions of the body a high involvement in any systemic chronic skin disease is anticipated and should be addressed.

Limitations

The sample size was 250 (200 patients, 50 healthy volunteers). All participants were asked if they currently have or ever had genital symptoms in the past. A greater sample size would be needed to achieve more significant results. This is an exploratory analysis. *P*-values < 0.05 are considered significant but present only relevant differences. Furthermore, in the urticarial group the percentage of women was slightly higher – future studies should aim for an equal gender distribution. Another point of criticism is the possible preselected patient cohort in our outpatient specialized clinic for PSO and CU, which thus may not properly represent the general population. Additionally, although all included PSO patients had psoriasis vulgaris and all included urticaria patients had CU, we did not focus on additional subtypes (for example: was the CU with/without an inducible component and/or angioedema? Was the psoriasis with/without additional psoriasis arthropathica and/or psoriasis inversa?).

An interesting approach to further research would be to include other inflammatory skin diseases (e.g. atopic dermatitis) and/or different age groups (children, young adults during puberty, women during menopause). Furthermore, it would be interesting and necessary to specify the genital lesions (e.g. with a specific scoring system – like for psoriasis on the scalp or hand/feet area) and to examine the symptoms in more detail: are they disease dependent or disease accompanying lesions due to different triggers? Regarding QoL, there are also several further, interesting research approaches, for example using special questionnaires and/or evaluating possible (psychological) comorbidities concerning this topic.

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