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ORIGINAL ARTICLE

The self-assessed psychological comorbidities of prurigo in European patients: a multicentre study in 13 countries

E. Brenaut,[1,*] J.A. Halvorsen,[2] F.J. Dalgard,[3,4] L. Lien,[4] F. Balieva,[5] F. Sampogna,[6] D. Linder,[7] A.W.M. Evers,[8] G.B.E. Jemec,[9] U. Gieler,[10] J. Szepietowski,[11] F. Poot,[12] I.K. Altunay,[13] A.Y. Finlay,[14] S.S. Salek,[15] C. Szabo,[16] A. Lvov,[17] S.E. Marron,[18] L. Tomas-Aragones,[19] J. Kupfer,[20] L. Misery[1]

[1]Department of Dermatology, University Hospital, Brest, France
[2]Department of Dermatology, Oslo University Hospital, Oslo University, Oslo, Norway
[3]Department of Dermatology and Venereology, Skåne University Hospital, Lund University, Malmö, Sweden
[4]National Centre for Dual Diagnosis, Innlandet Hospital Trust, Brumunddal, Norway
[5]Department of Dermatology, Stavanger University Hospital, Stavanger, Norway
[6]Clinical Epidemiology Unit, Istituto Dermopatico dell'Immacolata (IDI)- IRCCS FLMM, Rome, Italy
[7]Section of Biostatistics, University of Oslo, Oslo, Norway
[8]Department of Health, Medicine and Neuropsychology, Leiden University, Leiden, The Netherlands
[9]Department of Dermatology, Zealand University Hospital, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark
[10]Department of Dermatology, Justus Liebig University, Giessen, Germany
[11]Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wroclaw, Poland
[12]Department of Dermatology, Universite Libre de Bruxelles, Brussels, Belgium
[13]Dermatology and Veneteology Clinic, Şişli Hamidiye Etfal Training and Research Center, University of Health Science, Istanbul, Turkey
[14]Department of Dermatology, Cardiff University School of Medicine, Cardiff, UK
[15]School of Life and Medical Sciences, University of Hertfordshire, Hatfield, UK
[16]Department of Dermatology and Allergology, University of Szeged, Szeged, Hungary
[17]Moscow Scientific and Practical Centre of Dermatovenereology and Cosmetology, Moscow, Russia
[18]Department of Dermatology, Royo Villanova Hospital, Zaragoza, Spain
[19]Department of Psychology, University of Zaragoza, Zaragoza, Spain
[20]Institute of Medical Psychology, Justus Liebig University, Giessen, Germany
*Correspondence: E. Brenaut. E-mail: emilie.brenaut@chu-brest.fr

Abstract

Background Prurigo is defined by the presence of chronic pruritus and multiple localized or generalized pruriginous lesions.

Objective The aim of this study was to assess the psychological burden of prurigo in patients of European countries.

Methods In this multicentre European study, 3635 general dermatology outpatients and 1359 controls were included. Socio-demographic data and answers to questionnaires (regarding quality of life, general health, anxiety and depression and suicidal ideation) were collected.

Results There were 27 patients with prurigo; of these, 63% were men, and the mean age was 58.6 years. Among patients with prurigo, 10 of 27 (37%) suffered from anxiety and 8 of 27 (29%) from depression. Suicidal ideation was reported in 5 of 27 (19%) patients, and for four of these five patients, suicidal ideation was related to their skin disease. These frequencies were higher in the 10 commonest dermatological diseases (including psoriasis, atopic dermatitis and leg ulcers). The impact on quality of life was severe, with a mean Dermatologic Life Quality Index (DLQI) of 12.4, with an extreme impact on quality of life for 23% of patients and a very large impact for 27% of patients.

Conclusion The psychological comorbidities of prurigo are common, greater than those of other skin diseases, and their impact on quality of life is significant. Thus, it is important to study this condition and to find new treatments.

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Conflicts of interest

E Brenaut is investigator for Galderma. L Misery is investigator for Galderma and is a consultant for Trevi, Sienna and Menlo. J Szepietowski is a consultant and advisor for AbbVie, Celgene, Dignity Sciences, Leo Pharma, Novartis, Pierre Fabre and Sandoz, investigator for AbbVie, Actelion, Amgen, GSK, Janssen, Merck, Novartis,

Regereron, Takeda, Trevi and speaker for AbbVie, Actavis, Janssen, Leo Pharma, Novartis, SunFarm, Sandoz, Eli Lilly. GBE Jemec has received honoraria from AbbVie, Coloplast, Pierre Fabre, Inflarx, Novartis and UCB for participation on advisory boards and grants from Abbvie, Leo Pharma, Janssen-Cilag, Regeneron, Sanofi, Astra-Zeneca and Novartis for participation as an investigator and received speaker honoraria from AbbVie, Boehringer-Ingelheim, Galderma, Leo Pharma and MSD.
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Introduction

Prurigo occurs along with chronic pruritus and presents with symmetrically distributed papules, nodules and/or plaques.[1] This disorder is characterized by intense pruritus as the dominant symptom.[2,3] The skin between the lesions is usually normal. The term prurigo, or prurigo nodularis, has been used for many decades without a clear definition. Recently, the European experts of the Task Force Pruritus of the European Academy of Dermatology and Venereology achieved a consensus regarding the definition, classification and terminology of prurigo.[4] The major criteria are chronic pruritus (≥6 weeks), history and/or signs of repeated scratching (e.g. excoriations and scars) and localized or generalized presence of multiple pruriginous lesions. These lesions occur due to a neuronal sensitization to itch and the development of an itch–scratch cycle.[4] Prurigo is related to a neuronal sensitization to itch and development of an itch–scratch cycle. Prurigo can be associated with pruritus of dermatological, systemic, neurologic, psychiatric/psychosomatic, multifactorial or undetermined origin. It is still a matter of controversy whether prurigo represents a separate entity or is a reaction pattern due to the vicious circle of repeated itching and scratching. The treatment of prurigo remains challenging because data from randomized controlled trials are sparse.[5–8] Some molecules are in development, such as neurokinin-1 receptor antagonists or antagonists for IL-31.[9] Little is known about the prevalence of comorbidities associated with prurigo, particularly psychiatric disorders, such as anxiety and depression. The aim of this study was to select available data about prurigo out of a larger dataset from the large multicentre European study of general dermatology outpatients and to assess the psychological burden of the condition in these patients.

Patients and methods

Participants

A multicentre observational cross-sectional study had been conducted in 13 European countries.[10] Consecutive dermatology outpatients were invited to participate on random days. The inclusion criteria were age >18 years, understanding the local language and not suffering from severe psychosis. A control group of healthy workers was invited to participate. Data were available for 3635 patients and 1359 controls. Each patient was clinically examined by the dermatologist, who recorded the diagnosis, its severity and comorbidities, including cardiovascular disease, chronic respiratory disease, diabetes mellitus, rheumatological disease and other diseases such as cancer. The 10 more common dermatological diseases of the entire study were psoriasis, non-melanoma skin cancer, skin infections, eczema, acne, nevi, atopic eczema, benign skin tumours, hand eczema and leg ulcers. In this study, we identified cases of prurigo and compared their data to control patients and patients with other dermatological diseases.

Questionnaires

Each participant was asked to complete a two-part document. The first part contained questions about socio-demographic variables: sex, age, ethnicity, marital status, education and self-reported socio-economic status; the second part contained the following questionnaires:

- The Dermatologic Life Quality Index (DLQI),[11] consisting of ten questions about symptoms, embarrassment, shopping and home care, clothes, social and leisure, sport, work or study, close relationships, sex and treatment. Each question is scored from 0 to 3, giving a possible score range from 0 (no impact of skin disease on quality of life) to 30 (maximum impact on quality of life). Categories are as follows: 0–1, no effect at all on patient's life; 2–5, small effect on patient's life; 6–10, moderate effect on patient's life; 11–20, very large effect on patient's life; 21–30, extremely large effect on patient's life.
- The EuroQol 5-dimensions 3-levels (EQ-5D-3L), consisting of two parts namely the EQ-5D-3L descriptive system and the EQ visual analogue scale (EQ VAS).[12] The EQ-5D-3L descriptive system comprises the following five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has three levels: no problems, some problems and extreme problems. The EQ VAS records the respondent's self-rated health on a vertical visual analogue scale where the endpoints are labelled 'best imaginable health state' and 'worst imaginable health state'.

- The Hospital Anxiety and Depression Scale (HADS), a well-validated instrument with good psychometric properties, which has been used to assess the symptoms of anxiety disorders and depression in somatic, psychiatric and primary care patients, as well as in the general population.[13] The HADS includes seven items that assess anxiety and seven for depression, each with four possible answers. For each dimension of anxiety and depression, a score from 0 to 7 is considered normal, from 8 to 10 is considered a borderline case and from 11 to 21 is considered a case in need of further examination or treatment.

These instruments (DLQI, EQ-5D-3L and HADS) were used in the validated translations relevant to the study countries.

- To assess suicidal ideation, the item 'Have you ever thought of committing suicide?' with possible answers of 'yes' or 'no' was included. An additional question was given to the patient group: 'Have you ever thought of committing suicide because of your skin condition?' The dermatologist answered two questions: 'Do you see depressive signs in the patient?' and 'Do you see anxiety signs in the patient?' with the possible answers: 'yes' or 'no'.

Statistical analysis

All data were analysed using Microsoft Office Excel. The quantitative variables were described using the mean and standard deviation. The means of the two groups (prurigo patients and controls) were compared with Student's *t*-test. The qualitative variables were described using the frequency and were compared between the two groups with a chi-squared test or Fisher's exact test in the case of small sample sizes. For all statistical analyses, the type 1 error was set at 5%. Data of patients with prurigo were also compared with data of the 10 more frequent skin diseases (psoriasis, non-melanoma skin cancer, skin infections, eczema, acne, nevi, atopic eczema, benign skin tumours, hand eczema and leg ulcers) for the HADS score or with all skin diseases for DLQI in a descriptive way.

Results

The details of the participants' characteristics have been previously published.[10] In this study, we included 27 patients with prurigo. The socio-demographic characteristics and comorbidities of patients with prurigo and controls are presented in Table 1.

The severity of prurigo lesions was evaluated by the doctor as slight in 4 of 20 (20%) patients, mild in 10 of 20 (50%) and severe in 6 of 20 (30%). Only 14 of 26 (53%) patients claimed to know their diagnosis. Symptoms were present for more than 1 month in 26 of 27 (96%) cases. To the question, 'What is your level of concern about your skin disease?', 15 of 27 (55%) patients answered 'very much', 10 of 27 (37%) 'middle' and 2 of 27 (7%) 'little'. Patients reported a flare-up of their skin disease every day in 15 of 26 (57.7%) cases, every week in 3 of 26 (11%), every month in 3 of 26 (11%) and several times a year in 5 of 26 (19%). Concerning location, 13 of 26 (50%) patients had prurigo lesions on the torso, 12 of 26 (46%) on the hands, 7 of 26 (26%) on the scalp and 6 of 26 (23%) on the face. At the time of examination, 23 of 26 (88%) patients were presented with pruritus. The mean (±SD) reported itch intensity was 6.6 (3.1) and ranged from 0 to 10.

Table 1 Socio-demographic characteristics and comorbidities of patients with prurigo and controls

	Patients with prurigo *n* = 27	Controls *n* = 1359	*P*-value
Countries, No. (%)			
Belgium	2 (7.4)	131 (9.6)	
Denmark	3 (11.1)	122 (9.0)	
France	1 (3.7)	20 (1.5)	
Germany	2 (7.4)	133 (9.8)	
Hungary	0	134 (9.9)	
Italy	5 (18.5)	46 (3.4)	
Netherlands	4 (14.8)	0	
Norway	6 (22.2)	218 (16.0)	
Poland	2 (7.4)	125 (9.2)	
Russia	0	120 (8.8)	
Spain	0	116 (8.5)	
Turkey	1 (3.7)	109 (8.0)	
United Kingdom	1 (3.7)	85 (6.3)	
Age, years (MD = 1/18)			
Range	28–84	18–89	
Mean ± SD	58.6 ± 15.1	41.1 ± 13.6	<0.001
Sex, No. (%) (MD = 0/3)			
Female	10 (37.0)	903 (66.6)	0.001
Marital status, No. (%) (MD = 5/3)			
Single	2 (9.1)	362 (26.7)	
Married/partner	15 (68.2)	840 (62.0)	0.017
Separated/divorced	2 (9.1)	119 (8.8)	
Widowed	3 (13.6)	34 (2.5)	
Educational level, No. (%) (MD = 0/8)			
Low	8 (29.6)	375 (27.8)	
Higher	18 (66.7)	399 (29.5)	<0.001
University	1 (3.7)	577 (42.7)	
Stressful events during last 6 months, No. (%) (MD = 0/13)	10 (37.0)	412 (30.6)	0.47
Symptoms of depression/anxiety as assessed by the dermatologist, No. (%)			
Depression (MD = 4/7)	5 (21.7)	182 (13.5)	0.22
Anxiety (MD = 4/9)	6 (26.1)	356 (26.4)	0.98
Comorbidities, No. (%)			
Heart disease (MD = 2/303)	5 (20.0)	78 (7.4)	0.037
Respiratory (MD = 5/307)	3 (13.1)	47 (4.5)	0.078
Diabetes (MD = 2/305)	4 (16.0)	24 (2.3)	0.003
Rheumatological disease (MD = 3/305)	1 (4.2)	48 (4.6)	1

MD, missing data (patients/controls).

Table 2 Anxiety, depression and suicidal ideation in patients with prurigo and controls

	Patients with prurigo *n* = 27	Controls *n* = 1359	*P*-value
HADS anxiety			
Range	0–17	0–18	
Mean ± SD	8.3 ± 4.8	4.7 ± 3.5	
≥ 11 (anxiety clinical case)	10 (37.1%)	150 (11.1%)	<0.001
HADS depression			
Range	1–16	0–16	
Mean ± SD	7.6 ± 4.1	4.3 ± 3.2	
≥ 11 (depression clinical case)	8 (29.6%)	58 (4.3%)	<0.001
Suicidal ideation (MD=1)			
Suicidal ideation	5 (19.2%)	88 (8.3%)	0.03
Suicidal ideation concerning the skin disease (among those with suicidal ideation)	4 (80.0%)	N.A	
Suicidal ideation concerning the skin disease (in the whole sample)	4 (15.4%)	N.A	

MD, missing data (patients/controls); N.A, not applicable.

Data about anxiety, depression and suicidal ideation for patients with prurigo and controls are presented in Table 2.

Ten of 27 (37.1%) patients with prurigo suffered from anxiety were diagnosed with a HADS anxiety score≥ 11, which was significantly higher ($P < 0.001$) not only than that of the controls, but also for the 10 more common dermatological conditions of the cohort of patients; in fact, 22.7% (139/612) of patients with psoriasis, 21.0% (29/138) of patients with hand eczema, 17.6% (28/159) of patients with atopic eczema, 17.5% (20/114) of patients with leg ulcers suffered from anxiety.

Similarly, 8 of 27 (29.6%) patients with prurigo suffered from depression were diagnosed with a HADS depression score ≥11, which was significantly greater ($P < 0.001$) than that of the controls (4.3%) and of the 10 other more common dermatological conditions of the cohort of patients: 24.3% (28/115) of patients with leg ulcers, 15.1% (21/139) of patients with hand eczema, 13.8% (84/608) of patients with psoriasis and 10.1% (16/158) of patients with atopic eczema suffered from depression.

Finally, 5 of 27 (19.2%) patients with prurigo reported past or present suicidal ideation, which was significantly higher ($P = 0.03$) than that of controls (8.3%) and of the 10 more common dermatological conditions of the cohort; in fact, 17.8% (21/118) of patients with leg ulcers, 17.3% (106/613) of patients with psoriasis, 15.0% (25/167) of patients with atopic eczema and 14.2% (20/141) of patients with hand eczema reported suicidal ideation. The data about anxiety, depression and suicidal ideation for the other dermatological conditions are presented in a previously published study.[10]

We analysed the concordance of the diagnosis of anxiety and depression between the dermatologist and that suggested by the HADS questionnaire in the 27 patients with prurigo. The HADS questionnaire suggested that there was no depression in 16 patients and the dermatologist in 12 of these 16 patients (75%). The HADS questionnaire concluded that there was no anxiety in 14 patients and the dermatologist in 11 of these 14 patients (78%). The true-positive value (represented by the percentage of dermatologists recognizing signs of depression or anxiety in depressed or anxious patients defined by HADS ≥11) was 50% for anxiety and 20% for depression, and the false-negative value was 66% for depression and 64% for anxiety. The dermatologists underestimated depression and anxiety in 6 of 23 patients (26%), respectively. On the other hand, dermatologists overestimated depression in 4 of 23 patients (17%) and anxiety in 3 of 23 patients (13%).

The mean DLQI was 12.4 ± 8.6, with a range from 0 to 30. The distribution of the score categories of DLQI is presented in Fig. 1. Compared to the 25 other skin diseases, prurigo had a large impact on quality of life, the same as hidradenitis suppurativa (DLQI = 12.4 ± 7.3) and greater than that of atopic dermatitis (11.4 ± 7.1) and pruritus (11.2 ± 7.3). The values for all the other skin diseases were under 10.

The results of the EQ-5D-3L descriptive system are presented in Fig. 2. The EQ VAS was 57.4 ± 16.5. Among the dermatological diseases studied, prurigo had the third worst self-reported

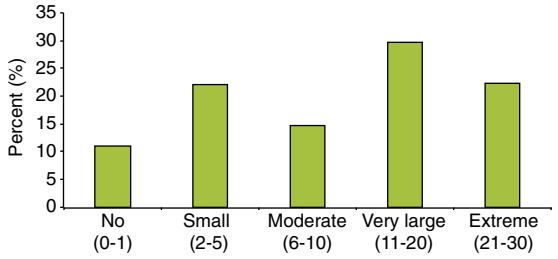

Figure 1 Dermatologic Life Quality Index (DLQI) score categories in patients with prurigo: impairment on the quality of life.

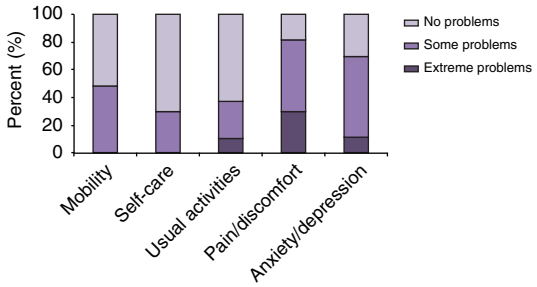

Figure 2 Results of the 5 dimensions of the EQ-5D-3L descriptive system for patients with prurigo.

health, with a score of 57.4, behind leg ulcers (56.0 ± 20.2) and hidradenitis suppurativa (56.9 ± 20.7).

Discussion

Studies on the psychological consequences of prurigo are scarce. In our study, anxiety, depression and suicidal ideation were more common in patients with prurigo than in patients with the 10 other more common dermatological diseases (psoriasis, non-melanoma skin cancer, skin infections, eczema, acne, nevi, atopic eczema, benign skin tumours, hand eczema and leg ulcers).

A psychometric study from Dazzi *et al.*[14] compared 20 patients with prurigo nodularis to 20 voluntary subjects. Specific questionnaires were used as follows: the General Health Questionnaire, State-Trait Anxiety Inventory – form Y, Beck Depression Inventory II and Eysenck Personality Questionnaire. Symptoms of trait anxiety and depression were significantly more common in the group of patients with prurigo than in the control group (51.3% vs. 39.5% and 19.2% vs. 7.0%, respectively), but there was no significant difference for state anxiety. A recent epidemiological study based on an analysis of a register included 877 patients with prurigo nodularis and 8770 controls.[15] The frequencies of anxiety and depression and consumption of anxiolytics and antidepressants were significantly higher in patients with prurigo compared to controls, and there was no association between prurigo and committed suicide. Depression was found in 8.5% of patients with prurigo, and anxiety was only found in 2.1%. This result could be explained in several ways: the diagnosis was probably not always registered in the database, and there was probably an underdiagnosis. Another study compared the psychological comorbidities of 94 patients with prurigo not to controls but to 91 patients with psoriasis.[16] There was no significant difference with regard to alexithymia, somatization symptoms, hypochondrias, anxiety (present in 18% of patients with prurigo vs. 11% with psoriasis) and depression (present in 22% of patients with prurigo and 21% of patients with psoriasis). Psychological comorbidities can be considered to be a consequence of prurigo, but depression and anxiety can induce pruritus and thereby lead to prurigo.[17]

Concerning the agreement between dermatologist and HADS, the true-positive rate was lower in patients with prurigo compared to the entire cohort of patients analysed in a previous study for depression (20% vs. 44%, respectively) but higher for anxiety (50% vs. 35%, respectively).[18]

In a previously published study on the same cohort of patients, our patients with prurigo had one of the three lowest mean EQ VAS scores (57.4).[19] This value was similar to that of rheumatoid arthritis pain (56.4) and 25.7 points lower than for healthy controls.[20] Impairment for each of the five dimensions of the EQ5D for patients with prurigo compared to controls highlighted an increased odds ratio (between 8.6 and 3.3) for all dimensions (in descending order): pain/discomfort, self-care, depression/anxiety, mobility and activity. Among the 35 dermatological diseases studied, for self-care, prurigo was the worst after blistering disease, and for pain/discomfort, prurigo was the worst after hidradenitis suppurativa.[21]

Among all of the dermatological diseases studied, prurigo had the worst impact on quality of life, with a mean DLQI at 12.4, the same as hidradenitis suppurativa. Impairment of quality of life was severe: for half of the patients, it was considered as very or extremely large. Also, the burden caused by dermatological therapy was high in patients with prurigo: it was reported in 60.7% of patients, the second worst after atopic dermatitis (63.4%) in the entire study[21]. In a previous study including 30 patients with prurigo nodularis treated with pimecrolimus, the mean DLQI was 11.5.[22]

The prevalence of prurigo in our study is 0.74%. No study is available concerning the prevalence of this rare disease. Jorgensen identified 877 cases of prurigo in all Danish patients with a hospital (in- or outpatient) diagnosis of prurigo nodularis before 2011, but the denominator is unknown.

Men were somewhat more numerous (59.3%) than women in our group of patients. Prurigo is usually considered to be more common in women. In a cohort of 108 patients with prurigo nodularis, females represented 63.9% of the sample.[23] Epidemiological data are lacking, so it is difficult to draw conclusions concerning the difference between sexes.[5] The mean age of patients in our study was 57, and prurigo usually appears in middle age (40–60 years old). The mean age was 61.5 years in Iking's study[23]. Patients with prurigo reported a significantly lower level of education than controls (60.9% vs. 27.8%). Some comorbidities, such as heart disease and diabetes, were significantly more common in patients with prurigo than in controls. These comorbidities or the drugs used to treat them could be a cause of prurigo. There is little information on comorbidities but diabetes was present in 7.4% of patients in Iking's cohort.[23]

This study has some limitations. The sample size is limited, but prurigo is a rare disease. Previous prospective studies included 20–108 patients.[14,23] Moreover, prurigo was only defined very recently, so there is probably a heterogeneity of diseases named prurigo in our study, because there was no consensual definition at the time of the study.[4] However, the diagnosis was made by a dermatologist.

Prurigo remains relatively unexplored, but researchers are increasingly interested in this disease. In particular, the European experts of the Task Force Pruritus published an expert consensus on the definition, classification and terminology of chronic prurigo.[4] The treatment of prurigo remains challenging but some molecules are in development.[5–8]

In conclusion, this study highlights prurigo's significant impact on quality of life, including the high frequency of anxiety, depression and suicidal ideation. Thus, this condition should be further studied to find new approaches to management.

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