CLINICAL REPORT

Occurrence, Chronicity and Intensity of Itch in a Clinical Consecutive Sample of Patients with Skin Diseases: A Multi-centre Study in 13 European Countries

Christina SCHUT[1], Florence J. DALGARD[2,3], Jon A. HALVORSEN[4], Uwe GIELER[5], Lars LIEN[3,6], Lucia TOMAS ARAGONES[7], Francoise POOT[8], Gregor B. E. JEMEC[9], Laurent MISERY[10,11], Lajos KEMÉNY[12], Francesca SAMPOGNA[13], Henriët VAN MIDDENDORP[14], Flora BALIEVA[15], Dennis LINDER[16], Jacek C. SZEPIETOWSKI[17], Andrey LVOV[18], Servando E. MARRON[19], İlknur K. ALTUNAY[20], Andrew Y. FINLAY[21], Sam SALEK[22] and Jörg KUPFER[1]

[1]Institute of Medical Psychology, Justus-Liebig-University, Gießen, Germany, [2]Department of Dermatology and Venereology, Skåne University Hospital, Lund University, Malmö, Sweden, [3]Innlandet Hospital Trust, National Center for Dual Diagnosis, Brumundal, Norway, [4]Department of Dermatology, Oslo University Hospital, University of Oslo, Institute of Clinical Medicine, Oslo, Norway, [5]Justus-Liebig-University Giessen, Giessen, Germany, [6]Department of Public Health, Hedmark University College, Elverum, Norway, [7]Department of Psychology, Faculty of Education University of Zaragoza, Aragon Health Sciences Institute (IACS), Zaragoza, Spain, [8]Department of Dermatology, University Hospital Erasme, Brussels, Belgium, [9]Department of Dermatology, Zealand University Hospital, Roskilde, Health Sciences Faculty, University of Copenhagen, Copenhagen, Denmark, [10]Department of Dermatology, University Hospital of Brest, [11]Laboratory of Neurosciences, University of Western Brittany, Brest, France, [12]Department of Dermatology and Allergology, MTA-SZTE Dermatological Research Group, University of Szeged, Szeged, Hungary, [13]Clinical Epidemiology Unit, Istituto Dermopatico dell'Immacolata (IDI)-IRCCS, Rome, Italy, [14]Health, Medical and Neuropsychology unit, Faculty of Social and Behavioural Sciences, Leiden University, Leiden, The Netherlands, [15]Department of Dermatology, Stavanger University Hospital, Stavanger, [16]Section of Biostatistics, University of Oslo, Oslo, Norway, [17]Department of Dermatology, Venereology and Allergology, Wrocław Medical University, Wroclaw, Poland, [18]Department of Clinical Dermatology and Cosmetology, Moscow Scientific and Practical Center of Dermatovenereology and Cosmetology, Moscow, Russia, [19]Dermatology Department, Royo Villanova Hospital, Aragon Health Sciences Institute (IACS), Zaragoza, Spain, [20]Dermatology and Venereology Clinic, University of Health Sciences, Istanbul Sişli Hamidiye Etfal Health Training and Research Center, Şişli – Istanbul, Turkey, [21]Dermatology and Academic Wound Healing, Division of Infection and Immunity, Cardiff University School of Medicine, College of Biomedical and Life Sciences, Cardiff, and [22]School of Life and Medical Sciences, University of Hertfordshire, College Lane, Hatfield, UK

Itch is an unpleasant symptom, affecting many dermatological patients. Studies investigating the occurrence and intensity of itch in dermatological patients often focus on a single skin disease and omit a control group with healthy skin. The aim of this multi-centre study was to assess the occurrence, chronicity and intensity (visual analogue scale 0–10) of itch in patients with different skin diseases and healthy-skin controls. Out of 3,530 dermatological patients, 54.3% reported itch (mean ± standard deviation itch intensity 5.5 ± 2.5), while out of 1,094 healthy-skin controls 8% had itch (3.6 ± 2.3). Chronic itch was reported by 36.9% of the patients and 4.7% of the healthy-skin controls. Itch was most frequent (occurrence rates higher than 80%) in patients with unclassified pruritus, prurigo and related conditions, atopic dermatitis and hand eczema. However, many patients with psychodermatological conditions and naevi also reported itch (occurrence rates higher than 19%).

Key words: itch occurrence; itch intensity; itch chronicity; skin diseases; European perspective.

Accepted Sep 18, 2018; E-published Sep 18, 2018

Acta Derm Venereol 2019; 99: 146–151.

Corr: Christina Schut, Institute of Medical Psychology, Justus-Liebig-University Gießen, Klinikstraße 29, DE-35392 Gießen, Germany. E-mail: Christina.Schut@psycho.med.uni-giessen.de

SIGNIFICANCE

This European multi-centre study investigated the occurrence, chronicity and intensity of itch in a large sample of outpatients with different skin diseases and healthy-skin controls. In this study 54.3% of patients and 8% of healthy-skin controls had itch at the time of investigation. Chronic itch was reported by 36.9% of patients and 4.7% of healthy-skin controls. The mean itch intensity in patients was 5.5 ± 2.5 (on a scale from 0–10) compared with 3.6 ± 2.3 in healthy-skin controls. Thus, itch is a very common, intense symptom among dermatological outpatients for which better specific therapies are needed.

The Global Burden of Disease Study 2010 (1) estimated that 33.7 million years lived with disability (YLD) are caused by skin and subcutaneous diseases. According to this study, which analysed data from 187 countries, skin conditions represent "the fourth leading cause of nonfatal disease burden" (2), affecting 1.9 billion people at any time (2, 3). Itch, defined by Hafenreffer as "an unpleasant cutaneous sensation that provokes the desire to scratch" (4) has long been neglected and unrecognized, even though it represents a common symptom in patients with skin diseases (5–7). Thus, there is a need to better document itch in patients with skin disease in order to encourage the development of new treatments, allocate resources more appropriately and develop better care for patients with itch.

The distribution and burden of itch in dermatological patients is mainly known from single-centre studies (8, 9) or studies focusing on a single skin disease (e.g. 10, 11). Also, studies on the occurrence of itch are often uncontrolled (8–12). Recently, the European Society for Dermatology and Psychiatry (ESDaP) completed a large European observational cross-sectional multi-centre study to better document the psychological burden (i.e. anxiety and depression, negative life events and suicidal ideation) of patients with skin disease (13). In this study, patients

doi: 10.2340/00015555-3040
Acta Derm Venereol 2019; 99: 146–151

with skin diseases from 15 out-patient dermatological clinics in 13 different countries (i.e. Belgium, Denmark, France, Germany, Hungary, Italy (2 study centres), the Netherlands, Norway (2 study centres), Poland, Russia, Spain, Turkey, the UK) were included. The large database generated by this study also enables exploration of the symptom itch in the group of all skin patients, as well as the assessment of the distribution of itch in different skin diseases. Moreover, the data allows the comparison of the occurrence, chronicity and intensity of itch between patients with skin diseases and healthy-skin controls.

The aims of the study are: (*i*) to describe the occurrence of current (acute) and chronic itch (itch lasting longer than 6 weeks) as well as the intensity of current itch in skin patients compared with healthy-skin controls; (*ii*) to describe the occurrence of current (acute) and chronic itch (itch lasting longer than 6 weeks) as well as the intensity of current itch among patients with different skin diseases; (*iii*) to determine whether skin patients with itch differ from skin patients without itch and healthy-skin controls regarding age, sex and the occurrence of physical comorbidities.

MATERIALS AND METHODS

Study design

A secondary analysis of data that have already been published (13) was conducted. However, it should be emphasized that data on the occurrence, chronicity and intensity of itch from this database have not been published previously. The investigation was an observational cross-sectional multicentre study with 15 sites in 13 European countries (13). Out-patients in secondary and tertiary care were recruited from 15 dermatological clinics between November 2011 and February 2013. The study protocol was that, at each clinic, consecutive patients were invited to participate in the study until 250 patients were included (for the exact numbers recruited in each country, see (13)). The participation rate was 79.9% (13). The inclusion criteria were age at least 18 years and being able to read and write the local language. Experiencing severe psychosis or receiving psychiatric treatment were exclusion criteria. A control group of 1,359 participants was recruited via advertisements among hospital employees at the same institution, but not from the dermatology department. Persons in the control-group were subjectively skin-healthy and regarded themselves not in need of consulting a dermatologist due to any skin condition. Controls who reported having a skin condition were excluded.

Each participant completed the same questionnaires. In skin patients, the dermatological diagnosis was made by a dermatologist. Usually one, but in some cases two or more, dermatological diagnoses were recorded. If there were doubts as to whether a skin disease was present (e.g. no diagnosis, no flares or no itch) the patient was not included in the study. The diagnoses were allocated to 27 categories adapted from the Lambeth study (14). The decision about what category the diagnosis should be allocated to was made by 3 dermatologists who are experts in the field of itch research (FD; UG; JAH). The category "unclassified pruritus" was chosen in those cases where patients visited the clinic due to itch, but no explicit diagnosis had yet been given.

The presence of other physical conditions (cardiovascular diseases, chronic respiratory diseases, diabetes, rheumatological diseases and others) was identified by asking the patient or by reviewing the patient's file. The controls were not examined and information on physical comorbidities was self-reported (for details see (13)).

Questionnaires

Itch and its characteristics were assessed with the following items: "Does your skin itch now?" (yes/no), if yes "For how long?" (under 6 weeks/over 6 weeks), whereby itch lasting for less than 6 weeks represents acute itch, while itch lasting for longer than 6 weeks represents chronic itch (15)) and "How intense is your itching?" with responses given on a visual analogue scale from 0 ("none") to 10 ("worst imaginable"). The VAS was used to measure itch intensity, because it has been shown to be a reliable and valid tool to measure the subjective symptom itch (16). In addition, self-reported socio-demographic data, such as age, sex, socio-economic status and marital status, were recorded.

Ethics

The protocol for the European study was approved by the Regional Committee for Medical Research Ethics in Norway REK 2011/1087. Local ethical approval was obtained, where necessary, in the other countries. The study was conducted in accordance with the Declaration of Helsinki and ICH/EU good clinical practice.

Statistical analyses

Data were entered into a database at each site and sent to the Statistical Center in Giessen, Germany. The data were consolidated into a single file. SPSS version 22 software (IBM Corp, released 2013) was used to process and analyse the data. To characterize the sample, we report numbers, percentages with 95% confidence interval (CI), or mean values with standard deviation (SD). To compare patients and healthy-skin controls, we used *t*-tests for continuous variables and χ^2 tests for dichotomous or categorical variables. We describe the occurrence of physical comorbidities with number and percentages with 95% CI. Multivariate logistic regression analyses were conducted to study the associations between the occurrence, chronicity and groups, adjusted for sex and age. Odds ratios (ORs) were calculated using the regression coefficients β from the regression models. The exponential of the coefficient represents the OR. Because of the great number of regression analyses, the *p*-values were corrected using the Bonferroni-correction according to Holm (17), as done in a recently published study (18).

RESULTS

Subjects

A total of 3,635 patients from 15 different study centres and 1,359 healthy-skin controls took part in the study (also see (13)). Of these, 3,530 patients (97.1% of all examined patients) and 1,094 healthy-skin controls (80.5% of all healthy-skin controls) responded to the question on the presence of itch. This group of 4,624 subjects constituted the sample in the present study. Regarding the analyses of 27 different skin diseases, patients with 2 or more dermatological diagnoses (441 subjects) were excluded, thus 3,089 patients (having one dermatological diagnosis each) were included in these analyses.

Sociodemographic characteristics of patients and healthy-skin controls are presented in **Table I**. There were no significant differences between patients with and

Table I. Sociodemographic characteristics and physical comorbidities (excluding skin diseases) of patients with itch, patients without itch and healthy-skin controls

	Patients with itch (n = 1,917/3,530)		Patients without itch (n = 1,613/3,530)		Healthy-skin controls (n = 1,094)		Test patients with itch vs. patients without itch	Test patients with itch vs. healthy-skin controls	Test patients without itch vs. healthy-skin controls
Sex, n (%)									
Female	1,077 (56.3)		907 (56.5)		705 (64.6)		$\chi^2(1)=0.02$	$\chi^2(1)=19.80$***	$\chi^2(1)=17.51$***
Male	837 (43.7)		698 (43.5)		387 (35.4)				
Age, years, mean ± SD	47.2 ± 17.5		46.7 ± 18.3		40.5 ± 13.3		t(3300)=0.93	t(2744.6)=11.00***	t(2648.1)=10.11***
Socio-economic status, n (%)									
Low	403 (21.4)		227 (14.3)		176 (16.2)		$\chi^2(2)=28.80$***	$\chi^2(2)=12.16$**	$\chi^2(2)=2.08$
Middle	1,325 (70.2)		1,215 (76.6)		809 (74.3)				
High	159 (8.4)		144 (9.1)		104 (9.6)				
Marital status, n (%)									
Single	442 (25.3)		413 (27.4)		293 (26.8)		$\chi^2(3)=19.71$***	$\chi^2(3)=33.25$***	$\chi^2(3)=8.70$*
Married	1007 (57.7)		920 (61.0)		679 (62.2)				
Separated	163 (9.3)		106 (7.0)		92 (8.4)				
Widowed	132 (7.6)		69 (4.6)		28 (2.6)				
Physical comorbidities (excluding skin diseases), overall	n (%), 95% CI	MD	n (%), 95% CI	MD	n (%), 95% CI	MD	OR (95% CI)	OR (95% CI)	OR (95% CI)
	573 (31.5), 29.5–33.4	100	385 (25.0), 22.7–27.1	71	164 (15.7), 13.5–17.7	47	1.48 (1.25–1.75)	1.76 (1.43–2.18)	1.17 (0.93–1.46)

*p < 0.05, **p < 0.01, ***p < 0.001 (retrieved by t-tests).
Data from patients with one (n = 3,089) and two or more (n = 441) dermatological diagnoses. Healthy-skin controls were persons both with and without itch.
SD: standard deviation; MD: missing data; OR: odds ratio (adjusted for age and sex); 95% CI: 95% confidence interval.

without itch regarding age or sex (p > 0.05). There were fewer females in the group of patients compared with the group of healthy-skin controls (p < 0.001). The group of dermatological patients was significantly older than the healthy-skin control group (p < 0.001). In addition, the socio-economic status varied between patients with itch and healthy-skin controls (p < 0.1). Also, the marital status differed between groups (p < 0.05). Moreover, physical comorbidities were significantly more common in patients with itch compared with both patients without itch or healthy-skin controls (also see Table I). Of the patients with itch, 31.5% (95% CI 29.5–33.4) had at least one physical comorbidity, while only 15.7% (95% CI 13.5–17.7) of the healthy-skin control group had at least 1 physical comorbidity. The OR for comorbidities was 1.76 (95% CI 1.43–2.18) in patients with itch compared with healthy-skin controls (adjusted for age and sex).

Itch occurrence, chronicity and intensity in skin patients compared with healthy-skin controls

In total, 54.3% (1,917 out of 3,530) of the patients with skin diseases reported that they currently had itch, compared with 8.0% (88 out of 1,094) of the healthy-skin controls. The OR of reporting itch when having a skin disease was 13.64 (95% CI 10.82–17.20) compared with healthy-skin controls. Chronic itch was reported by 36.9% of the patients and 4.7% of the healthy-skin controls. The overall mean ± SD itch intensity was 2.96 ± 3.3 in patients and 0.29 ± 1.18 in healthy-skin controls. The mean ± SD intensity of itch among patients reporting itch was 5.50 ± 2.51 (**Table II**).

Itch occurrence and chronicity in patients with different skin diseases

The occurrence rates of current and chronic itch among the different patient groups are shown in **Table III**. The occurrence of itch was highest in patients with unclassified pruritus (96.2%), prurigo (88.9%), atopic dermatitis (86.0%), hand eczema (82.3%), other eczemas (77.7%) and urticaria (75.9%). The patient groups with the highest occurrence of chronic itch were patients with unclassified pruritus (78.0%), prurigo and related conditions (72.2%), atopic dermatitis (66.7%) and other eczemas (56.5%). In patients with hand eczema the occurrence of chronic

Table II. Occurrence, chronicity and intensity of itch in dermatological patients in 13 European countries and in healthy-skin controls as well as the associations (OR) between the occurrence/chronicity of itch in patients and the occurrence/chronicity of itch in healthy-skin controls

	Patients (n = 3,530)		Healthy-skin controls (n = 1,094)		Patients/healthy-skin controls
	n/valid cases (%), 95% CI	Missing/out of	n/valid cases (%), 95% CI	Missing/out of	OR (95% CI)
Occurrence	1,917/3,530 (54.3), 52.5–55.9		88/1,094 (8.0), 6.6–9.8		13.6 (10.8–17.2)
Chronicity					
Overall	1,225/3,316 (36.9), 35.3–38.6	214/3,530	51/1,075 (4.7), 3.5–6.0	19/1,094	11.4 (8.5–15.3)
In those with itch	1,225/1,703 (71.9), 69.9–74.1	214/1,917	51/69 (73.9), 62.9–84.5	19/88	0.8 (0.5–1.5)
Intensity	Mean (SD)		Mean (SD)		B (95% CI)
Overall	2.96 (3.30)	44/ 3530	0.29 (1.18)	1/1094	2.67 (2.47–2.88)
In those with itch	5.50 (2.51)	44/1917	3.64 (2.29)	1/88	1.84 (1.30–2.39)
In those with chronic itch	5.92 (2.41)	22/1225	4.08 (2.37)	0/51	1.80 (1.11–2.48)

Data constitutes patients with 1 (n = 3,089) and 2 or more (n = 441) dermatological diagnoses.
OR: odd ratio (adjusted for sex and age); CI: confidence interval; SD: standard deviation; B: regression coefficient.

itch was very high, with 53% of patients experiencing itch lasting longer than 6 weeks.

In all skin patients the occurrence rates of current itch were at least doubly high as in the group of healthy-skin controls. Even in patients with naevi, 19.9% of patients reported having current itch compared with 8% of the healthy-skin controls. Also, the number of patients with psychodermatological conditions who reported having itch was very high: 54.5% reported having current itch and 40% reported having chronic itch.

Itch intensity in patients with different skin diseases

The intensity of itch among the different patient groups is given in Table SI[1].

The highest mean intensity of itch was found in the following diagnostic groups: unclassified pruritus (VAS score: 7.03), prurigo (VAS score: 6.15), atopic dermatitis (VAS score: 5.35), hand eczema (VAS score: 4.73) and urticaria (VAS score: 4.73).

The itch intensity among those reporting itch was highest in unclassified pruritus (VAS score: 7.31), prurigo (VAS score: 6.97), psychodermatological conditions (VAS score: 6.33), urticaria (VAS score: 6.31), atopic dermatitis (VAS score: 6.22) and hidradenitis suppurativa (VAS score: 6.03).

While the mean itch intensity was very low in healthy-skin controls (VAS score: 0.29), it was above 1 in all patient groups, except for patients with naevi (VAS score: 0.77) and patients with benign skin tumours (VAS score: 0.98).

DISCUSSION

This is the first large multi-centre study in Europe comparing the occurrence, chronicity and intensity of itch between patients with skin diseases and healthy-skin controls. Approximately half of the patients visiting a dermatological outpatient clinic in Europe reported that they experience itch. About 37% of them reported having itch lasting longer than 6 weeks.

The occurrence of current itch in dermatological patients (54%) reported in this study is higher than the occurrence found previously in a German study, in which 334 patients from a single dermatological practice had a point prevalence of current itch of 36.2% (8). It is hypothesized that the difference may be explained by the high proportion of neoplasms ($n=88$) in the previous study as only 23.9% of neoplasms were accompanied by pruritus. In the current study, patients with psoriasis

[1]https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-3040

Table III. Occurrence and chronicity of itch in patients experiencing 1 of 27 different skin diseases and healthy-skin controls. Associations (OR) between the occurrence of itch in patients and occurrence of itch in healthy-skin controls, adjusted for age and sex

Diagnostic categories (*n*)	Occurrence *n* (%), 95% CI	Patients/healthy-skin controls OR (95% CI)	Occurrence of chronic itch overall[a]		Occurrence of chronic itch in those with itch[b]	
			Missing/ out of, *n*	*n* (%), 95% CI	Missing/ out of, *n*	*n* (%), 95% CI
Patients overall (3,089)	1,664 (53.9), 52.0–55.6	13.5 (10.7–17.0)*	172/3,089	1,065 (36.5), 34.9–38.3	172/1664	1,065 (71.4), 68.9–73.7
Unclassified pruritus (53)	51 (96.2) 90.4–100	285.4 (67.2-1212.4)*	3/53	39 (78.0), 66.0-88.2	3/51	39 (81.3), 70.2-92.0
Prurigo and related conditions (18)	16 (88.9), 72.2–100.0	85.9 (18.9–389.4)*	0/18	13 (72.2), 50.0–93.3	0/16	13 (81.3), 61.1–100
Atopic dermatitis (150)	129 (86.0), 79.9–91.2	67.0 (40.0–112.0)*	6/150	96 (66.7), 58.6–74.5	6/129	96 (78.0), 70.9–85.2
Hand eczema (124)	102 (82.3), 75.6–88.9	52.7 (31.5–88.0)*	7/124	62 (53.0), 44.3–62.5	7/102	62 (65.3), 55.6–75.0
Other eczemas (197)	153 (77.7), 71.5–83.4	39.4 (26.1–59.6)*	11/197	105 (56.5), 49.5–63.7	11/153	105 (73.9), 66.4–80.6
Urticaria (54)	41 (75.9), 63.3–86.3	37.0 (19.0–71.9)*	5/54	21 (42.9), 30.0–56.2	5/41	21 (58.3), 42.9–73.2
Seborrhoeic dermatitis (54)	40 (74.1), 60.8–85.5	32.9 (17.2–63.0)*	2/54	19 (36.5), 22.5–50.0	2/40	19 (50.0), 34.8–66.0
Psoriasis (567)	399 (70.4), 66.4–74.2	29.82 (22.02–40.39)*	37/567	263 (49.6), 45.0–53.8	37/399	263 (72.7), 68.0–77.0
Bullous diseases (62)	40 (64.5), 53.2–76.2	25.4 (13.4–48.0)*	2/62	23 (38.3), 25.9–50.8	2/40	23 (60.5), 45.0–76.6
Psychodermatological conditions (22)	12 (54.5), 33.4–76.1	13.8 (5.7–33.2)*	2/22	8 (40.0), 20.0–61.9	2/12	8 (80.0), 50.0–100
Granuloma annulare (11)	6 (54.5), 25.0–81.8	12.8 (3.8–43.6)*	0/11	5 (45.5), 18.2–75.0	0/6	5 (83.3), 50.0–100
Connective tissue disorders (79)	41 (51.9), 40.0–62.2	13.2 (7.9–22.3)*	0/79	30 (38.0), 28.0–48.1	0/41	30 (73.2), 58.3–86.8
Infections of the skin (205)	103 (50.2), 43.3–57.0	11.7 (8.2–16.8)*	13/205	59 (30.7), 24.3–37.6	13/103	59 (65.6), 55.7–75.3
Lichen planus (36)	18 (50.0), 33.3–66.7	11.54 (5.6–23.8)*	1/36	14 (40.0), 23.5–55.3	1/18	14 (82.4), 61.1–100
Leg ulcer (103)	48 (46.6), 36.9–56.2	9.0 (5.4–15.3)*	5/103	36 (36.7), 27.5–46.7	5/48	36 (83.7), 71.4–93.7
Hidradenitis suppurativa (40)	18 (45.0), 29.3–61.0	9.8 (5.0–19.0)*	3/40	10 (27.0: 13.2; 42.1	3/18	10 (66.7), 41.2–87.5
Others (286)	126 (44.1), 38.2–50.0	8.6 (6.2–11.9)*	17/286	70 (26.0), 20.6–31.4	17/126	70 (64.2), 54.8–72.9
Rosacea (54)	23 (42.6), 29.1–55.4	8.9 (4.9–16.1)*	1/54	11 (20.8), 10.4–32.0	1/23	11 (50.0), 29.2–71.9)
Other hair conditions (62)	25 (40.3), 27.4–51.8	8.1 (4.6–14.2)*	6/62	15 (26.8), 15.8–38.2	6/25	15 (78.9), 58.6–95.0)
Alopecia areata (22)	8 (36.4), 17.4–57.1	6.6 (2.7–16.2)*	1/22	7 (33.3), 13.6–55.0	1/8	7 (100), 100–100
Non-melanoma skin cancer (304)	105 (34.4), 28.9–39.7	6.1 (3.9–9.5)*	26/304	64 (23.0), 18.1–28.0	26/105	64 (81.0), 72.2–89.3
Acne (187)	57 (30.5), 24.2–37.3	5.6 (3.5–8.9)*	6/187	42 (23.2), 17.3–29.5	6/57	42 (82.4), 70.6–92.5
Hyperhidrosis (11)	3 (27.3), 0–54.5	4.4 (1.1–17.2)*	0/11	2 (18.2), 0–45.5	0/3	2 (66.7), 0–100
Vitiligo (23)	6 (26.1), 8.7–43.5	4.3 (1.6–11.5)*	0/23	2 (8.7), 0–21.7	0/6	2 (33.3), 0–75.0
Benign skin tumours (131)	31 (23.7), 16.8–30.9	3.7 (2.3–5.9)*	3/131	14 (10.9), 5.4–16.8	3/31	14 (50.0), 31.4–66.7
Malignant melanoma (57)	13 (22.8), 12.3–33.9	3.3 (1.6–6.6)*	2/57	9 (16.4), 6.9–26.4	2/13	9 (81.8), 57.1–100
Nevi (141)	28 (19.9), 13.0–26.6	2.9 (1.8–4.6)*	10/141	12 (9.2), 4.8–15.0	10/28	12 (66.7), 43.8–88.9
Healthy–skin controls (1094)	88 (8.0), 6.6–9.8	1	19/1,094	51 (4.7), 3.5–6.1	19/88	51 (73.9), 62.7–84.4

Data consists of patients with 1 dermatological diagnosis, patients with 2 and more dermatological diseases were excluded from these analyses; $n=3,089$. The conditions are ranked according to itch occurrences. (Exception: data of the group of all patients (patients overall) are presented first and data of healthy-skin controls are presented last). *Occurrence rates significantly differed between patients and healthy-skin controls ($p<0.05$; alpha-corrected after Holm). [a]Occurrence of chronicity in the whole group. [b]Occurrence of chronicity only among those who report itch. OR: odds ratio; CI: confidence interval.

constituted the largest group of patients with 567 cases, 70.4% of whom reported itch. Moreover, in contrast to the previous study, in our study in 13 out of 27 diagnostic groups the number of patients with pruritus was greater than the number of patients without pruritus. In the previous study, more than half of the patients reported pruritus in only 2 (atopic eczema and dermatitis) out of 9 diagnostic groups (8).

A study of 1,428 dermatology outpatients from Turkey demonstrated an occurrence of chronic itch of 30.9% (9), which is in line with our finding that 37% of the dermatological skin patients experienced chronic itch. A Dutch study of 826 skin patients assessed in a general practice setting found that 53.3% of the assessed patients reported a mean itch intensity >2 on a VAS during the last 4 weeks (19). We speculate that the difference may be explained by the differing time spans studied, i.e. a shorter duration (4 weeks) over which itch was assessed in the Dutch study.

The occurrence of itch among controls in our study (8.0%) is similar to the occurrence that has been reported for the general population previously (8.4% and 6.5%) in 2 large studies in Denmark and Norway (12, 20). Regarding chronic itch, we found that 4.7% of the controls reported having chronic itch, a much smaller percentage than those reported in 2 German population-based studies (13.5% or 15.4%, respectively; (21, 22)). One has to keep in mind, however, that our controls cannot be regarded as representative for the general population, as our controls did not have any skin condition.

In the current study itch was most prevalent in patients diagnosed with unclassified pruritus, prurigo, atopic dermatitis, hand eczema, other eczemas and urticaria. The occurrence and chronicity of itch across different skin diseases has already been reported, but mainly in patients with psoriasis and eczema: In a large US questionnaire-based study including 17,425 respondents, itch was reported by 79% of the psoriasis patients (11). In atopic eczema, the occurrence of daily itching was 87% and 91% in 2 studies in which 100 or 304 patients were investigated (10, 23). Moreover, it was found that in chronic idiopathic urticaria, itch occurred in 68% of patients on a daily basis (24). In a recent study investigating 78 patients with lichen planus, 69.2% of the patients reported experiencing itch during the examination (25). In a questionnaire-based study assessing 1,541 adult patients with vitiligo, 35% of the patients reported itch or burning (26). In patients with hidradenitis suppurativa, itch occurred in 57.3% of the patients (27). These studies in most cases report occurrence rates that are comparable to ours. However, many of them are single-centre studies often including small numbers of patients. In contrast, our study had a large sample size and the simultaneous inclusion of many patient groups, some not previously reported.

With the current study, we were able to show that the occurrence of itch is also quite high in diseases usually not characterized by itch, e.g. infections of the skin, leg ulcers, naevi, skin cancer, rosacea and alopecia areata. In these skin diseases, the occurrence of itch was at least 2.88 times higher than in healthy-skin controls.

The mean itch intensities found in the current study in patients with atopic dermatitis, urticaria, psoriasis or seborrheic dermatitis were all lower than the ones found in a large US study (28). The difference in itch intensities between these studies is not surprising as the US patients were highly selected patients with very intense itch due to their visit to a specialized tertiary itch centre.

The strengths of our study are the large sample size, inclusion of a large spectrum of skin diseases with some in which the epidemiology of itch has not been reported previously, the standardized assessment of the occurrence, chronicity and intensity of itch as recently recommended (29) and the continental scope of the data reflecting a wide range of cultural and socio-economic settings.

The weaknesses of the study include a possible selection bias, as the clinics where patients were recruited are predominantly academic settings. Moreover, it would have been preferable to validate self-reported diagnoses by doctors. Persons in the control group categorized themselves as skin healthy without being seen by a dermatologist. Thus, it is possible that persons were included in the control group, who regarded themselves as skin healthy, but actually had some kind of skin disease. It is also of note that all persons in the control group were part of the working population as they were recruited from hospital stuff, while we do not know how many of the skin patients were working. Moreover, the study design did not allow us to distinguish between untreated patients and those who had already received treatment for their skin disease. Comparing these 2 groups in future studies would allow assessment as to whether the relationship between itch and physical comorbidities was greater in patients experiencing itch for a long time than in patients that had just received the diagnosis. Also, we did not further differentiate between different kinds of bullous diseases. As there are apparently large differences in itch between bullous pemphigoid, dermatitis herpetiformis and pemphigus, these differences should be assessed prospectively in future studies. In addition, almost one-third (31.5%) of patients with itch had at least one physical comorbidity. Since itch is a symptom of some systemic diseases (e.g. renal failure, lymphoma, endocrine disease) and can be a side-effect of many drugs used to treat physical diseases (30), it would also be interesting to differentiate between itching and non-itching comorbidities in future studies. Some groups of patients were small: 8 groups of patients had less than 50 participants, which led to big confidence intervals in the analysis. However, we still chose to report the occurrence, chronicity and intensity of itch in these patients in order to not exclude any patients.

For a thorough discussion of the strength and weaknesses of the design, see Dalgard et al. (13).

In conclusion, this multi-centre study, which included dermatological patients and healthy-skin controls, emphasizes that itch is a common symptom among dermatological out-patients with many different skin diseases. It thus highlights the need for better itch-specific therapies and tailored management strategies.

ACKNOWLEDGEMENTS

Funding. South-Eastern Norway Regional Health Authority granted scholarship for the study to FJD, but had no influence on the study design, in the collection of data and data analysis, and interpretation of data, in the writing of the report, and in the decision to submit the paper for publication.

Conflicts of interest. LM report Astellas, Celgene, Expanscience, Johnson&Johnson, Novartis, Pierre Fabre, Sanofi. FS has been a consultant for Janssen and Abbvie. FP has been consultant for Leo-Pharma. AYF has received honoraria for consultancy with travel expenses from Galderma, Novartis, Napp, Sanofi, Archimedes, Amgen. GBEJ is a consultant and investigator for AbbVie and Novartis, has received unrestricted grants from AbbVie, Leo Pharma and Novartis; sits on Advisory Boards of AbbVie; InflaRx, LEO Pharma, Novartis, Janssen Pharmaceuticals, Pierre Fabre, and UCB; and is Investigator for AbbVie, InflaRx, Novartis, Regeneron, Sanofi and UCB.

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012; 380: 2163–2206.
2. Hay RJ, Johns NE, Williams HC, Bolliger IW, Dellavalle RP, Margolis DJ, et al. The global burden of skin disease in 2010: an analysis of the prevalence and impact of skin conditions. J Invest Dermatol 2014; 134: 1527–1534.
3. Hay RJ, Augustin M, Griffiths CEM, Sterry W. The global challenge for skin health. Br J Dermatol 2015; 172: 1469–1472.
4. Hafenreffer S. De pruritu. nosodochium in quo cutis, eique adhaerentium partium, affectus omnes, singulari methodo, et cognoscendi et curandi fidelissime traduntur. Ulm: Kühn, 1660.
5. Leader B, Carr CW, Chen SC. Pruritus Epidemiology and Quality of Life. In: Cowan G, Yosipovitch G, eds. Pharmacology of itch. Handbook of experimental pharmacology. Berlin: Springer-Verlag, 2015: 226: p. 15–38.
6. Weisshaar E, Dalgard F. Epidemiology of itch. Adding to the burden of skin morbidity. Acta Derm Venereol 2009; 89: 339–350.
7. Dalgard F, Weisshaar E. The epidemiology of pruritus. In: Misery L, Ständer S. Pruritus. London: Springer, 2010: p. 69–75.
8. Kopyciok MER, Ständer HF, Osada N, Steinke S, Ständer S. Prevalence and characteristics of pruritus: a one-week cross-sectional study in a German dermatology practice. Acta Derm Venereol 2016; 96: 50–55.
9. Sarikaya Solak S, Kivanc Altunay I, Mertoglu Caliskan E. Chronic pruritus in Turkish dermatology outpatients: prevalence, sociodemographic and clinical characteristics. G Ital Dermatol Venereol 2016; 107: 178–185.
10. Yosipovitch G, Goon ATJ, Wee J, Chan YH, Zucker I, Goh CL. Itch characteristics in chinese patients with atopic dermatitis using a new questionnaire for the assessment of pruritus. In J Dermatol 2002; 41: 212–216.
11. Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T. The impact of psoriasis on quality of life results of a 1998 National Psoriasis Foundation Patient-Membership Survey. Arch Dermatol 2001; 137: 280–284.
12. Miller IM, Zarchi K, Ellervik C, Jemec GB. Self-reported skin morbidity in Denmark: a population-based cross-sectional study. Eur J Dermatol 2016; 26: 281–286.
13. Dalgard F, Gieler U, Lucia T-A, Lien L, Poot F, Jemec GB, et al. The psychological burden of skin diseases: a cross-sectional multicenter study among dermatological out-patients in 13 European countries. J Invest Dermatol 2015; 135: 984–991.
14. Rea JN, Newhouse ML, Halil T. Skin disease in Lambeth. A community study of prevalence and use of medical care. Br J Prev Soc Med 1976; 30: 107–114.
15. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. Acta Derm Venereol 2007; 87: 291–294.
16. Phan NC, Blome C, Fritz F, Gerss J, Reich A, Ebata T, et al. Assessement of pruritus intensity: Prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. Acta Derm Venereol 2012; 92: 502–507.
17. Aicken M, Gensler H. Adjusting for multiple testing when reporting research results: the Bonferroni vs Holm Methods. Am J Public Health 1996; 86: 726–728.
18. Balieva F, Kupfer J, Lien L, Gieler U, Finlay AY, Tomás-Aragonés L, et al. The burden of skin diseases assessed with the EQ5DTM: a European multicentre study in 13 countries. Br J Dermatol 2017; 176: 1170–1178.
19. Verhoeven EWM, Kraaimaat FW, van de Kerkhof PCM, van Weel C, Duller P, van der Valk PG, et al. Prevalence of physical symptoms of itch, pain and fatigue in patients with skin diseases in general practice. Br J Dermatol 2007; 156: 1346–1349.
20. Dalgard F, Svensson A, Holm JO, Sundby J. Self-reported skin morbidity in Oslo. Associations with sociodemographic factors among adults in a cross-sectional study. Br J Dermatol 2004; 151: 452–457.
21. Matterne U, Apfelbacher CJ, Loerbroks A, Schwarzer T, Büttner M, Ofenloch R, et al. Prevalence, correlates and characteristics of chronic pruritus: a population-based cross-sectional study. Acta Derm Venereol 2011; 91: 674–679.
22. Matterne U, Apfelbacher CJ, Vogelgsang L, Loerbroks A, Weisshaar E. Incidence and determinants of chronic pruritus: a population-based cohort study. Acta Derm Venereol 2013; 93: 532–537.
23. Dawn A, Papoiu ADP, Chan YH, Rapp SR, Rassette N, Yosipovitch G. Itch characteristics in atopic dermatitis: results of a web-based questionnaire. Br J Dermatol 2009; 160: 642–644.
24. Yosipovitch G, Ansari N, Goon A, Chan YH, Goh CL. Clinical characteristics of pruritus in chronic idiopathic urticaria. Br J Dermatol 2002; 147: 32–36.
25. Welz-Kubiak K, Reich A, Szepietowski JC. Clinical aspects of itch in lichen planus. Acta Derm Venereol 2017; 97: 505–508.
26. Silverberg JI, Silverberg NB. Association between vitiligo extent and distribution and quality-of-life impairment. JAMA Dermatol 2013; 149: 159–164.
27. Vossen ARJV, Schoenmakers A, van Straalen KR, Prens EP, van der Zee HH. Assessing pruritus in hidradenitis suppurativa: a cross-sectional study. Am J Clin Dermatol 2017; 18: 687–695.
28. Mollanazar NK, Sethi M, Valdes Rodriguez R, Nattkemper LA, Ramsey FV, Zhao H, Yosipovitch G. Retrospective analysis of data from an itch center: Integrating validated tools in the electronic health record. J Am Acad Dermatol 2016; 75: 842–844.
29. Ständer S, Zeidler C, Riepe C, Steinke S, Fritz F, Bruland P, et al. European EADV network on assessment of severity and burden of Pruritus (PruNet): first meeting on outcome tools. J Eur Acad Derm Venerol 2016; 30: 1144–1147.
30. Pereira MP, Kremer AE, Mettang T, Ständer S. Chronic pruritus in the absence of skin disease: pathophysiology, diagnosis and treatment. Am J Clin Dermatol 2016; 17: 337–348.