

## Pruritus in Chronic Plaque Psoriasis: a Questionnaire-based Study of 230 Italian Patients

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**SUMMARY** In the past, several textbooks defined psoriasis as a non-pruritic dermatosis, but the most recent data in the literature emphasizes the high frequency of pruritus in psoriasis and its impact on the quality of life of patients with psoriasis.

Aim of this study was to explore the sensory and affective dimensions of pruritus as well as to assess the impact of itch on quality of life and to evaluate the influence of lifestyles, habits, and various anti-pruritic therapies on pruritus in a large group of psoriatic subjects.

The structured Yosipovitch itch questionnaire was given to 240 psoriatic patients. 230 patients returned a complete and detailed questionnaire. Pruritus was referred to by 80% of the patients. Psoriasis area and severity index (PASI) was significantly higher in itching-patients ( $P=0.04$ ). In half of the patients, itching appeared daily, particularly in the evening. Significant aggravating factors of pruritus were stress, skin dryness, hot water, sweating, elevated ambient temperature, exercise, abundant meals, bad moods, lying position, and contact with clothes. Cold water is the only factor that showed to significantly relieve the pruritus. Anti-pruritic therapies had limited effect.

Pruritus is a common, bothersome, and poorly responsive symptom in patients with psoriasis.

**KEY WORDS:** psoriasis, pruritus, questionnaire-based study

### INTRODUCTION

Psoriasis is a common inflammatory skin disease with a multi-factorial etiology and a pathogenesis that is not completely understood. The disease is often associated with an impairment of quality of life, and pruritus has shown to be one of the most putative factors (1). Although pruritus is not considered to be one of the major symptoms in psoriasis vulgaris, recent literature shows a frequent association between the two conditions with a prevalence of itching in psoriatic patients ranging from 63% to 90% (1-5). The mechanisms underlying pruritus in

psoriasis are still not fully understood, but the most common theory has emphasized the importance of impaired innervations and neuropeptides imbalance in psoriatic skin (5). Other possible hypotheses are the increased expression of interleukin 2 and vascular abnormalities (6). Furthermore, recent data indicates that pruritus could also be evoked by the opioid system, prostanoids, interleukin 31, serotonin, or proteases (6). The McGill Pain Questionnaire (MPQ) (7) has been used for several decades for the measurement and evaluation of the different dimensions of pain.

Since pain and itch have an important overlap of peripheral mediators and receptors (8), a structured itch questionnaire based on MPQ was edited by Yosipovitch *et al.* to measure the sensory and affective dimensions of pruritus and to assess the impact of itch on quality of life and the influence of anti-pruritic treatments, daily activities, and habits on pruritus (9). Initially, this questionnaire was validated only in uremic and atopic subjects (9,10), but a study on 40 psoriatic patients has recently validated this new questionnaire in psoriasis as well (11). However, the study has explored only the subjective dimensions of psoriatic pruritus and their associations with psychological symptoms and quality of life, neglecting the effects of anti-pruritic treatments on psoriatic itching and the assessment of possible aggravating and relieving factors (11). In the present study, we used the Yosipovitch questionnaire to explore the sensory and affective dimensions of pruritus as well as to assess the impact of itch on quality of life and to evaluate the influence of lifestyles, habits, and various anti-pruritic therapies on pruritus in a larger group of psoriatic patients.

## PATIENTS AND METHODS

### Patients

240 adult Caucasian patients with psoriasis (131 men and 109 women) referred to the outpatient Dermatology Clinics of the University Hospital of Udine and Trieste between April 2008 and November 2008 were invited to participate in the study. The only inclusion criterion was the presence of plaque psoriasis. Exclusion criteria were: i) current or previous history of other dermatologic diseases, ii) current or previous history of systemic itching disease (e.g. hepatic, renal, neurologic, or blood disease). After clinical evaluation, the Yosipovitch questionnaire was given to the patients. Everyone was instructed to fill out the questionnaire and to return it when complete. The study was conducted in accordance with the requirements of the local Ethic Committee.

### Assessments

All patients suffering from psoriasis, regardless of the presence of pruritus, were invited to fill out the first section of the questionnaire to obtain information on:

- Personal demographic details (patient's gender, age, etc.).
- Brief psoriatic history (age of onset of psoriasis and its current severity based on the validated Psoriasis

and Severity Index (PASI) calculated by the dermatologist during the visit).

- Presence of itching linked to psoriasis (yes or no).

The patients with psoriasis who were affected by pruritus were asked to complete the second section of the questionnaire in order to investigate the characteristics and the sensory and affective aspects of pruritus, i.e. the variables that could influence its perception and its impact on quality of life:

History of pruritus:

- Duration.
- Frequency of pruritus (daily, weekly, fortnightly, monthly, or randomly).
- Time of the day when pruritus most frequently appeared (morning, afternoon, evening, or night). Patients with nightly pruritus were asked to mark how their itch disturbed sleeping in the night on a 10-cm visual analogue scale (VAS) scale.
- Accompanying symptoms.

Patients were requested to indicate one of the following choices: pain, sweating, feeling unwell, headache, heat sensation, cold sensation, and none.

Severity of pruritus:

- Severity of pruritus was assessed on a 10-cm VAS with end-points anchored by "no itch" and "as bad as could possibly be". The subjects were asked to state the intensity of itch in four situations: at the peak of psoriasis, at the lowest intensity of psoriasis, currently (i.e. at time of interview), the most severe itch, and after a normal mosquito bite, which was chosen as a reference point.

The localization of pruritus:

- Patients were requested to mark the areas affected by itch on a body diagram. The percentage of body surface area involved was then estimated with the rule of nines used commonly in burn assessment. Furthermore, the patients were asked to indicate if itch was located only on the psoriatic plaque or also on healthy skin.

Verbal descriptor scale of itch sensation and affective dimension:

- Both the itch sensation and affective dimension were investigated. Patients were asked to indicate one of the descriptions reported in a list. In particular, the description of the sensation of itch was constructed from a list of 6 words: tickling, stinging, crawling, stabbing, pinching, and burning; while the affective dimension was composed of a set of 4 words commonly mentioned by patients suffering from itch: bothersome, annoying, unbearable, and worrisome.

The effect of daily activities and habits on pruritus:

- Patients were asked to indicate whether stress, skin dryness, hot water, cold water, sweating, hot ambient temperature, cold ambient temperature, exercise, abundant meal, low mood, a lying position, contact with clothes, sleep, rest, regular meal, or sitting position caused increased intensity, did not affect, or relieved their itch.

Influence of drugs on the psoriatic itch:

- The effect of anti-histamines and other anti-pruritic treatments (topical emollients and corticosteroids) on itching were recorded. The various drugs were documented and their efficacy was marked as follows: 0 = no effect, 1 = short term effect (less than 24 h), 2 = long term effect.

Impact of psoriatic pruritus on quality of life:

- Patients were asked whether there had been a reduction in mood, sleep, sexual desire, sexual activity, concentration, and appetite after the onset of itch.

## STATISTICAL ANALYSIS

Characteristics of the patients and of the psoriasis, as reported in the first section of the questionnaire, were described in all the enrolled subjects and potential differences between patients with and without pruritus were evaluated using t-tests for continuous variables with normal distribution according to the Kolmogorov-Smirnov test (such as age), Wilcoxon's rank sums test for those with non-normal distribution (such as the PASI score), and chi-square tests and Fisher's exact test (in case of expected number of cases <5 in one or more cells of contingency tables) for categorical variables. PASI and VAS scores among subjects with pruritus were described using the mean and standard deviation (SD). Other characteristics of pruritus, investigated in the second section of the questionnaire, were described using frequencies. The statistical significance of modifications of pruritus induced by selected exposures was assessed through the sign test.

## RESULTS

### Patients' dispositions and baseline characteristics

The demographic characteristics of patients with psoriasis are shown in the Table 1. Four patients did not take part in the study for personal reasons (2 not interested and 2 lacked time) and six patients had to be excluded from our final analysis because of incomplete questionnaires. 230 patients (124 men

and 106 women) returned a complete and detailed questionnaire and were included in the final analysis. The mean age of all patients was  $55.9 \pm 16.9$ , and the mean age at the onset of psoriasis was  $35.9 \pm 18.1$ . All patients were affected by plaque type psoriasis. The mean of PASI score was  $9.2 \pm 7.6$

### Demographic details and brief psoriatic history

Forty-six (20%) patients (30 men and 16 women) with psoriasis did not have pruritus; the mean age of the patients  $55.8 \pm 17.3$ , and mean age at the onset of psoriasis was  $30.3 \pm 12$ . The mean PASI score was  $7.5 \pm 4.9$ .

One hundred and eighty-four patients (80%) suffered from pruritus. It was more frequent in women

**Table 1.** Sociodemographic and clinical characteristics of patients with and without pruritus

Characteristics	No itch (46)	Itch (184)
<b>Male (n)</b>	30	94
<b>Female (n)</b>	16	90
<b>Age (mean±SD)</b>	55.8±17.3	56±16.9
<b>Race</b>		
<b>Caucasian (%)</b>	100	100
<b>Age at onset of psoriasis (mean±SD)</b>	30.3±12	32.3±14
<b>Type of psoriasis</b>		
<b>Plaque (%)</b>	100	100
<b>Psoriasis area and severity index (PASI) score (mean±SD)</b>	7.5±4.9	11.9±9.9
<b>Family Status</b>		
<b>Single (%)</b>	22	35
<b>Married (%)</b>	74	70
<b>Divorced (%)</b>	4	5
<b>Years of Education (mean±SD)</b>	8.55±2.24	9.1±2.35
<b>Work Status</b>		
<b>Working (%)</b>	51	58
<b>Not working (%)</b>	49	42

(94%) than in men (90%) but the difference was not significant ( $P=0.29$ ). The mean age of the patients was  $56 \pm 16.9$  and the mean age at the onset of psoriasis was  $32.3 \pm 14$ . The mean PASI score was  $11.9 \pm 9.9$ .

The differences in age, sex, and onset of psoriasis between the two groups were not significant.

The mean PASI score was significantly higher in itching-patients than in those without pruritus ( $P=0.04$ ).

### Characteristics of pruritus

The mean duration of pruritus was  $19.7 \pm 8.6$  years. In 20 (11%) patients pruritus appeared before the onset of psoriasis, in 63 (34.3%) after, and in 86 (46.9%) simultaneously. The other 15 (7.8%) patients could not recall when it had appeared. It manifested on a daily basis in 92 patients (50%), on a weekly basis in 39 (21.2%), on a fortnightly basis in 29 (15.8%), on a monthly basis in 15 (8.1%), and randomly in 9 (4.9%). The time of day when pruritus most frequently occurred was in the evening (39%), followed by the night (32.8%), afternoon (15.6%), and morning (12.6%). In the group of patients with nightly prevalence, the pruritus altered the quality of sleep in 56.3% of cases, with a mean VAS value of  $4 \pm 2$ . Most of the patients (97%) reported an accompanying sensation with pruritus, such as heat (32.4%), pain (18.6%), sweating (13.5%), feeling unwell (12%), cold (10.5%), or headache (10%). The other 3% of the patients with pruritus did not have accompanying symptoms. Pruritus was reported most often only on the plaque of psoriasis (70.3%), whereas the others patients (29.7%)

also reported pruritus on the healthy skin. Very often, patients reported pruritus on several anatomic sites; the most common were the lower limbs (59.3%), followed by the scalp (54.7%), upper limbs (48.4%), and trunk (46.9%). The mean VAS severity of pruritus was  $6.3 \pm 2.1$  at the peak of psoriasis,  $0.5 \pm 1.0$  least intensity,  $1.1 \pm 1.7$ , at the current time,  $6.6 \pm 2.5$  at the most severe moment, and  $3.4 \pm 2.6$  after a mosquito bite. The most common sensory descriptions of the itch were pinching (33%), burning (23.9%), tickling (18.7%), and stinging (13.5%), while other sensation such as crawling and stabbing were less common (7.8% and 3.1%, respectively). The affective descriptor of itch was bothersome in 81 patients (44%), annoying in 66 (35.9%), unbearable in 20 (10.9%), and worrisome in 17 (9.2%).

### Aggravating and relieving factors of pruritus

Factors that aggravated or relieved pruritus are shown in Table 2. Stress ( $P<0.0001$ ), skin dryness ( $P<0.0001$ ), hot water ( $P=0.002$ ), sweating ( $P=0.003$ ), hot ambient temperature ( $P=0.007$ ), exercise ( $P=0.009$ ), an abundant meal ( $P=0.01$ ), bad mood ( $P=0.032$ ), a supine position ( $P=0.048$ ), and contact with clothes ( $P=0.052$ ) were identified as significant aggravating factors of pruritus. Cold water is the only factor that showed to significantly relieve the pruritus ( $P=0.029$ ). Sleep, rest, regular meals, sitting position, and cold ambient temperature had no effect on pruritus.

**Table 2.** The effect of daily factors on pruritus in patients with psoriasis

Daily activity	Aggravated (% patients)	Relieved (% patients)	No effect (% patients)
Stress	84	15	1
Dryness	78	12	10
Hot water	65	25	10
Sweating	62	29	9
Hot ambient temperature	58	30	12
Exercise	60	34	6
Abundant meal	57	32	11
Low mood	52	34	14
Lying position	50	33	12
Clothes	51	38	11
Cold water	27	63	10
Sleep	8	15	77
Rest	12	16	72
Regular meal	2	1	97
Sitting position	5	8	87
Cold ambient temperature	9	3	88

### Effect of drugs on psoriatic pruritus

Antihistamines were used by 45 pruritic patients (24.5%). Of these 34.5% reported a short-term effect and 65.5% reported no effect. None of the patients reported long-term effects. Among the topical anti-pruritic treatments, the emollients were utilized most commonly, in 53% of patients with pruritus, 65% of whom reported no effect, and 35% a short-term effect; no patients reported long term effects. Corticosteroids were used by 88 patients with pruritus (48%), 55% of whom reported a short-term effect; no patient reported long-term effects, and 45% reported no anti-pruritic effect.

### Impact on quality of life

The majority (56.5%) of the patients have reported that their quality of life decreased after the onset of psoriatic pruritus. In particular, 96 patients (52.2%) reported a reduction in mood, 39 (21.2%) a reduction in sleep, 24 (13%) a reduction in sexual desire, 18 (9.8%) a reduction in sexual activity, 72 (39.1%) a reduction in concentration, and 17 (9.2%) a reduction in appetite.

### DISCUSSION

Despite several textbooks' definition of psoriasis as a non-pruritic dermatosis (12), the most recent data shows a high incidence of pruritus in this disease, ranging from 63% to 90% (1-5). Our study, which encompassed larger group of patients than the previous studies, confirms that pruritus is a common symptom in plaque psoriasis.

In our study, PASI scores were significantly higher in patients with itch than in those without pruritus (mean  $11.9 \pm 9.9$  vs.  $7.5 \pm 4.9$ ,  $P=0.04$ ). Our finding is consistent with results reported by Szepietovski *et al.* (13) and Chang *et al.* (14), and in contrast with the reports of Nakamura *et al.* (15) and Yosipovitch (16). Psoriasis and pruritus have a complex and not yet fully understood pathogenesis influenced by several and shared molecules and cytokines. In both cases, nerve growth factor (NGF) and several neuropeptides, such as substance P (SP) and calcitonin gene-related protein (CGRP), play an important pathogenetic role. Their involvement in psoriatic itch has been demonstrated by a study that showed some differences between pruritic patients with and without pruritus in the quantity of dermal nerves, in SP-receptors, CGRP-receptors, and high-affinity NGF-receptors (TrkA) which were elevated in pruritic psoriatic lesions compared with non-pruritic psoriatic lesions (6). The up-regulation of SP-receptors and CGRP-receptors could also be related to severe psoriasis, given that SP and

CGRP are chemotactic to neutrophils and mitogenic to keratinocytes and endothelial cells, while up-regulation of NGF-receptor may contribute to severity of psoriasis by direct stimulation of keratinocytes, endothelial cells and nerve growth, as well as by activating T cells. Therefore, some authors have suggested that the correlation between severity of psoriasis and the occurrence of psoriatic itch would be due to the up-regulation of the receptors for NGF, SP, and CGRP (6). In any case, our statistical findings support the hypothetical correlation between severity of psoriasis and prevalence of psoriatic itch.

Surprisingly, in 20 (11%) patients from our study pruritus appeared before the onset of psoriatic lesions. Considering that the actual or previous history of other dermatological diseases or systemic itching diseases (e.g. hepatic, renal, neurologic, or blood diseases) was adopted as an exclusion criterion in our study, it is likely that there is a hypothetical link between pruritus "sine materia" reported by these patients, and psoriasis. It is possible that at the onset of pruritus these subjects had already developed the disease, although with a minimal extension. Consequently, since NGF, SP, and CGRP could play an important role in psoriatic itch (6), the above mentioned correlation could be explained by the increased expression of NGF and the high density of nerve fibers producing SP and CGRP in the healthy skin of patients with psoriasis compared to the skin of those without the disease (17). This explicative model could also explain the presence of itch not only on psoriatic plaques but also on non-lesional skin, as reported in 29.7% of our patients with psoriasis; while other patients (70.3%) reported pruritus only on psoriatic lesions.

Amatya *et al.* (1) and Sampogna *et al.* (2) have shown a increased incidence of some characteristics of pruritus such as intensity, heat, pain, stinging, and tickling and crawling sensations in women. However, this has not been confirmed by our study. It is likely that confounding factors such as race, age and psychological influences have to be considered.

Our patients reported pruritus on several anatomic sites, most commonly on the lower limbs, followed by the scalp, upper limbs and trunk, without a significant difference in frequency. The low frequency of pruritus on the face and neck corresponded with the low frequency of psoriatic plaques in those areas.

Variation in the density of nerve innervation and the distribution of various pruritic mediators of the skin in different parts of the body could explain the different perception of pruritus.

In line with the findings of other authors (16), we

observed that pruritus tends to appear more often in the evening and night, resulting in difficulties in falling asleep in a significant percentage of all patients (21.2%) and, in the group of subjects with nightly prevalence, in an altered quality of sleep in 56.3% of cases, with a consequent impairment of their quality of life. We speculate that the lack of activity and work, which help to take the patients' mind off pruritus, together with the lying position and the warm temperature of the bed might contribute to the increased itching during the evening and night.

In contrast with the literature (16), cold water was the only significant relieving factor in this study. In our opinion, the vasoconstricting effect of the cold water could reduce the local skin release of pruritic mediators and their immission in the circulatory system.

In line with previous studies, our study identified stress, skin dryness, hot water, sweating, hot ambient temperature, exercise, an abundant meal, bad mood, lying position, and contact with clothes as significant aggravating factors of psoriatic itch, and stress and dryness as the most influential. Stress is a well known factor that, through the release of neuropeptides, can aggravate both psoriasis and pruritus (18). The other aggravating factors (exercise, warmth water, sweating, elevated temperature) increase the severity of dryness through vasodilatation and sweating with an increase of epidermal water loss.

Our study found anti-pruritic therapies to be of limited effect on psoriatic itch. In particular, according to other authors (1,13,16), antihistamines were reported as having limited and short-term effects on itch, and that only in a small number of patients; it is likely these findings are due to the limited role of histamine in the pathogenesis of pruritus in psoriasis (13,19). Among the various anti-pruritic treatments used by our patients, topical steroids were found to be the most effective in relieving pruritus, but only in the short-term, while emollients were reported as less effective in reducing psoriatic itch.

## CONCLUSION

Pruritus represents a very common and bothersome symptom in psoriasis which may negatively affect quality of life of the patients. It can occur both on the lesional skin and on the healthy skin, and may worsen psoriasis as a Koebner phenomenon. It is very difficult to treat since it is poorly responsive to conventional anti-pruritic treatment. It is likely that some life style modifications such as avoiding hot showers, elevated ambient temperatures, and abundant meals could help to relief psoriatic pruritus.

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