Original Article

Depression in Patients with Functional Itch Disorder

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Abstract

Objective: Patients with pruritus sine materia (PSM) are often misdiagnosed as idiopathic pruritus (pruritus of unknown origin) when the cause of pruritus is not found. Some of these patients may be diagnosed with functional itch disorder (FID) which is also known as psychogenic pruritus (pruritus of psychological origin). Since antidepressants can be used in the treatment of psychogenic pruritus, the differentiation of FID from idiopathic pruritus is important. The aim of this study was to investigate the prevalence of depression in patients with FID. **Materials and Methods:** A total of 117 patients with FID who were diagnosed as idiopathic pruritus or PSM in their previous assessments and 117 controls took part in the research. The psychiatric assessment for depression was conducted using the Beck Depression Inventory (BDI) and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) major depression criteria. The study employed a descriptive and cross-sectional method. **Results:** Forty-four patients with FID (37.6%) had major depression (DSM-5) and 74 patients with FID (63.2%) had clinically significant depression (BDI). The frequency of depression among FID patients was significantly higher than controls. **Conclusions:** Our findings highlight the importance of diagnosing FID in patients with PSM. The presence of FID diagnostic criteria in a patient should prompt dermatologists for a psychiatry consultation.

Keywords: Depression, functional itch disorder, pruritus sine materia, psychogenic pruritus, somatoform pruritus

Introduction

The International Forum for the Study of Itch considers the terms "itch" and "pruritus" synonymous and defines six etiological categories of pruritus: dermatological, systemic, neurological, psychogenic, mixed, and "others.[1]" Psychogenic pruritus is the kind of itch related to psychological disorders.[2] Psychogenic pruritus is known also as functional itch disorder (FID), psychogenic itch, somatoform pruritus,[3] or functional pruritus.

Psychogenic itch is not an idiopathic pruritus (pruritus of unknown origin), and it is not an elimination diagnosis. The disorder is poorly known by both psychiatrists and dermatologists. When there are no other diagnoses to propose, psychogenic itch is often mislabeled as idiopathic pruritus. The French Psychodermatology Group (FPDG) is a group of experts in dermatology, psychology, and psychiatry. This group has proposed a definition of psychogenic pruritus as "an itch disorder where itch is at the center of the symptomatology and where psychological factors play an evident role in the triggering, intensity, aggravation, or persistence of the pruritus" and has suggested calling it "functional itch disorder."[4]

To assess the diagnosis of FID, it is necessary to exclude possible internal diseases and skin diseases with both clinical and laboratory evaluations and to determine clinical characteristics, association of itch with psychological disorders.[4] According to a study, patients who scored high on depression measures reported higher degrees of pruritus compared with patients who reported not being depressive.[5] Antidepressants were found effective in the treatment of psychogenic pruritus in another study.[6] In this study, we tried to evaluate depression in patients who are diagnosed as FID according to diagnostic criteria of FPDG.

Materials and Methods

Overview

In outpatient departments, questionnaires are generally considered as the convenient tools to screen the candidates for

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psychodermatology illnesses. Our preference in choosing the convenient questionnaire to screen for depression was based on their diagnostic accuracy in screening and the feasibility of their administration. We chose a short screening instrument for depression, Beck Depression Inventory (BDI). This could be self-administered by patients before their meeting with the clinician or in the waiting area. Another screening test utilized was the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) major depression criteria which implement short interviews to screen for major depression which is practical for dermatology outpatient clinics.[7-10]

The study was designed to evaluate, within 6 months, 117 consecutive patients and 117 controls who were admitted to the department of dermatology in our hospital. The patients had pruritus >6 months with a normal laboratory examination and a negative skin prick test. None of the FID patients had any prediagnosed psychiatric, internal, or dermatological illness. None of the controls had any prediagnosed internal or psychiatric illness.

The patients with pruritus sine materia (PSM) were classified as having psychogenic pruritus using suggested diagnostic criteria from the FPDG.[4] These included three compulsory criteria: localized or generalized PSM, chronic pruritus (>6 weeks), and the absence of a somatic cause. Three additional criteria from the following seven items were present moreover: a chronological relationship of pruritus with one or several life events that could have psychological repercussions, variations in intensity associated with stress, nocturnal variations, predominance during rest or activity, associated psychological disorders, pruritus that is improved by psychotropic drugs, and pruritus that is improved by psychotherapies [Table 1].

Participants and measures

The study was carried out after obtaining the approval of the local ethical committee in our institution, and patients signed an informed consent form before participating in the study (Kecioren Training and Research Hospital, Institutional Review Board #1050/13-01-2016). All the patients in this study were diagnosed as idiopathic pruritus or PSM in their previous assessments. Eligibility criteria for patients were as follows: the presence of general pruritus with a negative skin prick test, no systemic drug treatment, age of 16 years or older, and disease duration longer than 6 months. The reasons for exclusion were relevant skin disease, internal diseases such as diabetes, thyroid disease, and/or active hepatitis, and positive skin prick test.

Table 1: Diagnostic criteria for functional itch disorder from the French Psychodermatology Group (4)

Three compulsory criteria
Localized or generalized pruritus sine material (without primary skin lesion)
Chronic pruritus (>6 weeks)
No somatic cause
Three of seven optional criteria
A chronological relationship between the occurrence of pruritus and one or several life events that could have psychological repercussions
Variations in intensity associated with stress
Nycthemeral variations
Predominance during rest or inaction
Associated psychological disorder
Pruritus that could be improved by psychotropic drugs

In the absence of primary skin findings, the physical examination focused on looking for evidence of a systemic disease and findings of conjunctival pallor, thyromegaly, splenomegaly, or stigmata of liver disease. Lymph nodes were palpated for signs of lymphadenopathy. In both patient and control groups, blood and urine analyses were performed during previous visits for exposing possible etiology of pruritus. In addition, all the patients and controls had skin prick test composed of common 13 skin allergens (tree mix, Betulaceae, grass mixtures, pine and grain pollens, cereal mix, *Dermatophagoides farinae, Dermatophagoides pteronyssinus, Alternaria, Aspergillus* mix, cockroach, mosquito, cat hair, and dog hair).

To compare the collected data of patients with FID with the group of patients with a diagnosed skin condition, 117 participants with a chronic (longer than 6 months) skin disease without any complaint of pruritus were enrolled as the comparison group.

Questionnaires

Both psychiatric and demographic-clinical questionnaires were used for each of the FID patients and controls. The demographic-clinical questionnaire was composed of two questions on demographic data (age and sex) and two questions on clinical data (type of additional diseases and duration of diseases). The psychiatric assessment for depression was conducted using a validated questionnaire, BDI, and interrogated DSM-5 major depression criteria.

Beck Depression Inventory and Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition major depression criteria

The BDI, created by Beck *et al.* in 1961, is a 21-question multiple-choice self-report inventory, one of the most widely used psychometric tests for measuring the severity of depression.[8,11] Each question has a set of at least four possible responses, ranging in intensity. When the test is scored, a value of 0–3 is assigned for each answer and the total score is compared to a key to determine the severity of depression. The standard cutoff scores are as follow: 10–18 indicates mild depression (MID), 19–29 indicates moderate depression (MOD), and 30–63 indicates severe depression (SED). Higher total scores indicate more severe depressive symptoms.[11] In addition to this, to observe more severe depressive symptoms, we used DSM-5 major depression criteria. It is the most widely used criteria for diagnosing major depression, and it is found in the American Psychiatric Association's DSM-5.[10]

Statistical analysis

In investigating data compatibility to normal range, Shapiro–Wilk test was used. In comparison of groups not in normal range, Mann–Whitney U-test was used for two groups. Univariate analyses of the categorical variables were summarized as percentages and compared with the Chi-square test. Pearson's Chi-square test, Pearson's exact Chi-square test, and Fisher's exact Chi-square test were used in cross-analysis. The odds ratios were calculated by cross-tabulation. Spearman's correlation coefficients were calculated for the variables that were not commodious to normal distribution and determined direction and magnitude of correlation between variables. For all the comparisons, a two-tailed value of $P < 0.05$ was considered statistically significant. Calculations were performed using SPSS 21 for Windows (IBM Corp., Armonk, NY, USA).

Results

Sample characteristics

All the consecutive FID patients who met the inclusion criteria were enrolled in the study. A study group of 117 patients with FID and a control group of 117 patients with other skin disorders that lack pruritus complaint were included in the study. In the control group, the prevalence rates of the specific dermatological conditions in the sample were as follows: acne (n = 26), melasma (n = 22), verruca plantaris (n = 24), tinea unguium (n = 25), and vitiligo (n = 20). The questionnaires were completed by all the patients in the study and control groups.

Eighty (68.4%) of patients were female and 37 (31.6%) of patients were male. The mean age of the patients was 43.4, with a standard deviation of ±16.1 (ranged between 16 and 82). The mean duration of pruritus was 27.96 months, with a standard deviation of ±20.42 (ranged between 6 and 120). Eighty-one (69.2%) of controls were female and 36 (30.8%) of patients were male. The mean age of the controls was 37.64, with a standard deviation of ±17.03 (ranged between 16 and 79).

Beck Depression Inventory

Seventy-four patients with FID (63.2%) and 59 controls (50.4%) had a total score ≥10, and the difference between the two groups was statistically significant (P = 0.047). It included mild (32.4%), moderate (33%), and severe (17%) depression in patients with FID according to the standard cutoff scores. On the other hand, there was no difference in disease severity (MID, MOD, and SED) between the two groups (χ^2 = 3.689; P = 0.158) [Table 2]. When the responses to questions were compared between controls and FID patients, patients with FID revealed higher scores to some questions. The responses that are statistically significant were summarized in Table 3. The most common symptom was feeling sad. Seventy-eight patients with FID (66.7%) described themselves as feeling sad (χ^2 =10.182; P = 0.037) [Table 3].

Table 2: The frequency of positively and/or negatively diagnosed patients and controls according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition and Beck Depression Inventory questionnaires, *n* (%); *Pearson's Chi-square test; and odds ratio

Inventory Questionnaires	Severity	Patients, *n* (%)	Controls, *n* (%)	χ^2, *P**	OR
DSM-5	−	73 (62.4)	90 (76.9)	5.84	2.04
	+	44 (37.6)	27 (23.1)	0.016	
BDI	MID	24 (32.4)	28 (47.5)	3.689	
	MOD	33 (44.6)	23 (39.0)	0.158	
	SED	17 (23.0)	8 (13.5)		

*According to DSM-5 major depression criteria, +: In table refers to the patients who fulfilled at least five major depression criteria including at least one depressed mood and loss of interest or pleasure in the same 2-week period, According to BDI questionnaire scores, MID refers to 10-18 points, MOD refers to 19-29 points, and 30-63 points refers to SED. OR: Odds ratio, MID: Mild depression, MOD: Moderate depression, SED: Severe depression, BDI: Beck Depression Inventory, DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

Table 3: The percentage, frequency, and χ^2 and *P* values of the high-score responses to questions of the Beck Depression Inventory in functional itch disorder patients in comparison with controls

Questions	Frequency (%) (*n*=117)	χ^2, *P**
Feeling sad	78 (66.7)	10.182, 0.037
Discourage about the future	67 (57.3)	9.241, 0.026
Feeling failure as a person	61 (52.1)	18.565, 0.001
Crying	66 (56.4)	14.120, 0.003
Losing interest in other people	65 (55.6)	10.703, 0.013
Difficulty in making decisions	54 (46.2)	10.980, 0.012
Feeling tired	50 (42.7)	14.305, 0.003
Losing weight	62 (53)	9.749, 0.021
Losing interest in sex	42 (35.9)	8.325, 0.040

*Pearson Chi-square test

Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition major depression criteria

Forty-four patients with FID (37.6%) and 27 patients from the control group (23.1%) fulfilled at least five major depression criteria including at least one depressed mood and loss of interest or pleasure in the same 2-week period (χ^2 = 5.84; P = 0.016; odds ratio [OR] = 2.04) [Table 2]. Fifty-nine patients with FID (50.4%) expressed a more depressed mood than controls (χ^2 = 9.374; P = 0.003; OR = 2.3). Ninety-two patients with FID (78.6%) described themselves as having a loss of interest or pleasure (χ^2 = 20.332; P = 0.001; OR = 3.7) while 53% of patients with FID (n = 62) had insomnia or hypersomnia (χ^2 = 4.402; P = 0.049; OR = 1.7).

Discussion

Psychodermatology describes an interaction between dermatology and psychiatry; the incidence of psychiatric

disorders among dermatological patients is estimated between 30% and 60% in the literature.[12-15] The presence of a concomitant psychiatric illness is predominantly observed in patients with various dermatological diseases, and PSM is among them.[15] Pruritus without any skin lesion is named as PSM. A detailed patient history is particularly important in patients with generalized pruritus who lack primary skin lesions because the differential diagnosis for this presentation is broad and includes organic and psychiatric disorders that are associated with significant morbidity.[16] In chronic PSM without any somatic cause, one must consider FID.[3] In this study, it was well understood that most of the patients who were followed as idiopathic PSM met the diagnostic criteria of FPDG. Thus, these conditions might not be idiopathic and may have a psychological background.

FID is also known as psychogenic pruritus.[3] In psychogenic pruritus, the reason of pruritus becomes psychogenic; there are cycles of stress leading to pruritus as well as pruritus contributing to stress.[17] Although there are some studies which report that psychogenic pruritus is noted in patients with psychiatric conditions such as depression, anxiety, aggression, obsessive–compulsive disorders, psychoses, and substance use,[18-22] there exists no study evaluating depression frequency in patients who are diagnosed as FID. In this regard, untreated patients with chronic PSM in this study were classified as having FID using suggested ten diagnostic criteria (3 – compulsory and 7 – optional) from the FPDG[4] [Table 1]. We preferred to use these criteria which were validated by an international study for a more objective and standard diagnosis.[3]

Instead of the term "psychogenic pruritus," the FPDG[4] proposes the use of other terms such as "functional itch disorder" and "somatoform pruritus." In addition to this, in underlying FID where no somatic or psychiatric diagnosis coexists, FPDG proposes the use of "functional disorders" rather than "somatoform disorders." The onset of an associated psychological symptom or a psychiatric disorder should not necessarily be found when FID is diagnosed but may be revealed later in case of an associated mental disorder.[3] Parallel with this, we found that forty-four patients with FID (37.6%) had major depression and seventy-four patients with FID (63.2%) had clinically significant depression. Regarding international classifications of psychiatric diseases, psychogenic pruritus is not cited in the Tenth Revision of the International Classification of the Diseases;[23] however, pruritus is reported under the diagnosis "other somatoform disorders" (F45.8). The term "psychogenic pruritus" was not used also in the DSM-4,[24] but it could be recognized among the following four diagnoses listed in the DSM-4: conversion disorder, undifferentiated somatoform disorders (300.81), unspecified somatoform disorder (300.82), and pain disorder associated with psychological factors (307.80).

It is not easy to determine whether it is a psychogenic pruritus, neuropathic pruritus, idiopathic pruritus, or somatoform pruritus. Neuropathic itch refers to pruritus caused by neuronal or glial damage,[25] whereas psychogenic itch is related to psychological disorders.[2] Neuropathic pruritus is caused by lesions of the afferent neural pathways. There are some clues to differentiate neuropathic itch; the distribution often corresponds to a particular spinal segment, often a sensory deficit or an aberration in sensory perception such as allodynia (nonpainful stimuli evoke pain), allokinesis (sensation of itch produced by innocuous stimuli that would not ordinarily induce itch), or hyperpathia (evoked pain grossly out of proportion to painful stimuli) present.[25,26] In this study, a thorough physical examination was conducted, and patients' history was taken in detail in order to rule out neuropathic pruritus. Other differential diagnoses of psychogenic pruritus are psychogenic urticaria and psychogenic dermographism; however, there are temporary and recurrent visible urticarial lesions in those cases. Another important differential diagnosis is self-inflicted skin lesions (SISLs)[27] such as psychogenic excoriations[28] and dermatitis artefacta. The psychopathology in SISLs is impulsive and compulsive; the main symptom is not pruritus but scratching. In contrast, psychogenic pruritus is related to an illusion of pruritus where pruritus is the main complaint. Another differential diagnosis is abusive skin excoriations observed in the pediatric population.

In a study of 100 psychiatric inpatients, the prevalence of generalized pruritus was 42%.[29] Psychogenic pruritus is encountered in patients with primary psychiatric disorders. It is known as a clinical pattern of the somatoform disorders that have subjective complaints by the patients.[26,30,31] One study reports that 6.5% of outpatients at a clinic specializing in psychodermatology suffered from "somatoform pruritus" (using a definition close to those in DSM-4).[32] On the other hand, the frequency of FID is not known because the differential diagnosis of FID is difficult and FID is often mislabeled as idiopathic pruritus.[3]

In our study, 44 patients with FID (37.6%) and 27 patients from the control group (23.1%) fulfilled at least five major depression criteria in this study. Seventy-four patients with FID (63.2%) had a total score ≥10 and were diagnosed as having clinically significant depression. The main psychiatric disorders encountered in dermatology patients are anxiety, depression (mood disorders), and body dysmorphic disorder.[33] Hughes *et al.* reported that 30% of dermatology outpatients and 60% of dermatology inpatients suffered from a psychiatric disorder.[34] Ludwig *et al.* found that in a public health outpatients' service of a dermatology clinic, the frequency of anxiety was 40.3% and the frequency of depression was 43.7%.[35] Al Shahwan *et al.* reported that the frequency of mood disorders in Arab dermatology outpatients was 29% for anxiety and 14% for depression.[36] In our study, the frequency of depression was statistically higher in patients with FID than controls, while the frequency of depression was also high in controls. Depression is noted in patients with acne (n = 26) and vitiligo (n = 20) in the control group because the main dermatological disorders with concomitant psychiatric illnesses are known as dermatitis, acne, pruritus,

eczema, atopic dermatitis, urticaria, alopecia, psychocutaneous disorders, psoriasis, and vitiligo.[15,32-44]

Disfiguring skin disorders with chronic pruritus (>6 weeks) such as atopic dermatitis and prurigo nodularis are often associated with social problems and with psychic disorders such as depression or anxiety.[1,45] One study mentions that persistent skin diseases had a higher psychiatric comorbidity in comparison to the intermittent and incidental skin diseases.[46] In our study, the frequency of depression was 63.24% in patients with FID. When DSM-5 major depression criteria were taken into account, 37.6% of patients were noted to have major depression. This is in line with the findings in a study on patients with psychogenic pruritus (consisting of lichen simplex chronicus, neurotic excoriation, prurigo nodularis, and pruritus that is intermittent, short term, and severe and without physical signs) where all the patients were found to have affective disorders (depressions, anxieties, and mixed anxiety and depressive disorders) and 18% (12/65) also had associated personality disorders.[47]

There is little knowledge about the influence of chronic pruritus itself on comorbid symptoms of depression. In a study with 284 participants[48] with chronic pruritus (atopic dermatitis, prurigo nodularis [pruritus with multiple scratch lesions], and chronic pruritus of other origins [chronic pruritus with little or no scratch lesions]), patients with chronic pruritus had a more negative body concept than healthy individuals. Higher levels of depression and anxiety were related to a more negative body image. Patients with chronic pruritus of other origins had higher scores in terms of grooming, daily activities, and acceptance of one's body by others than patients with atopic dermatitis. On the other hand, there is also a little knowledge about the influence of depression on chronic pruritus. In a study, patients who scored high on depression measures reported higher degrees of pruritus compared with patients who reported not being depressive.[5]

Contrary to our findings, in another study[37] with 114 adult males with dermatological disorders, the percentage of depression was 66.6% in patients with pruritus while no depression was observed in chronic fungal infections. The depression is commonly associated with psychogenic pruritus, and these patients with psychogenic pruritus secondary to depression may also present with prominent anxiety and agitation supporting our study.[49] The prevalence of major depression in our study was higher when DSM-5 was utilized as a screening test instead of BDI. It could be a result of the fact that BDI is a self-reported questionnaire while DSM-5 criteria are clinician-administered and thus might give a more accurate evaluation.

We found a high frequency of depression in patients with FID. Although there has been no clinical trial of pharmacological treatment for psychogenic itch,[50] antidepressant drugs such as tricyclic antidepressants (mainly doxepin) and selective serotonin reuptake inhibitors (fluoxetine, sertraline, paroxetine, citalopram, fluvoxamine, and escitalopram)[6] are recommended and have an acceptable risk of adverse effects. Results of our study, with a high prevalence of depression in FID patients, might be supportive in favor of antidepressant use in treatment of this peculiar patient group.

There are some limitations in our study. We preferred to use a screening test such as BDI questionnaire to screen for the psychiatric conditions accompanying the itch in a group of dermatology outpatients because they are readily available, convenient, and time-saving when compared with a psychiatry consultation. Nevertheless, including a professional specializing in psychiatry would have been optimal in terms of making accurate diagnosis of the psychiatric conditions. Furthermore, addition of a third group of healthy patients could make the comparison of FID patients with normal population available while increasing the statistical power of the study; however, we were unable to include a third group because of our methodology and the institutional review board decisions. Although this study provides some more scientific data on the relationship between the psychological disorders and FID, more studies are needed to conclude on this matter, given the scant information available in the literature.[12-15]

Conclusion

Our findings highlight the importance of diagnosing psychogenic pruritus (FID) in patients with PSM. The presence of FID diagnostic criteria in a patient should prompt dermatologists for a psychiatry consultation for evaluation of a psychological comorbidity.

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Conflicts of interest

There are no conflicts of interest.

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