Association Between Frequency of Pruritic Symptoms and Perceived Psychological Stress

A Japanese Population-Based Study

Yosuke Yamamoto, MD; Shin Yamazaki, PhD; Yasuaki Hayashino, MD, PhD; Osamu Takahashi, MD, MPH; Yasuharu Tokuda, MD, MPH; Takuro Shimbo, MD, PhD; Tsuguya Fukui, MD, MPH, PhD; Shigeaki Hinohara, MD, PhD; Yoshiki Miyachi, MD, PhD; Shunichi Fukuhara, MD, DMSc

Objective: To evaluate the relationship between frequency of pruritic symptoms experienced over a 1-month period and psychological stress.

Design: Cohort study.

Setting: Population-based study in Japan.

Participants: A total of 2224 participants at least 18 years old and without psychiatric disorders participated in the Japan Health Diary Study (October 2003), a cohort study comprising a representative sample in Japan.

Main Outcome Measures: Frequency of pruritic symptoms assessed by self-reported health diaries over the 1-month period and subsequent psychological stress measured using the Japanese version of the Perceived Stress Scale.

Results: The 2224 participants had a mean age of 44.6 years, 1212 (54.5%) were women, and 70 (3.1%) presented with pruritic symptoms. Multivariable analysis showed that patients with pruritic symptoms had significantly higher psychological stress than those without pruritic symptoms (β coefficient, 2.33; 95% confidence interval [CI], 0.53-4.14; P=.01). Furthermore, a linear trend was observed between increased psychological stress and increased severity of pruritic symptoms, with β coefficients for the first, second, and third tertiles for symptoms of 0.81 (95% CI, −1.97 to 3.59), 1.77 (95% CI, −0.82 to 4.37), and 4.86 (95% CI, 1.29 to 8.43), respectively (P value for trend, .004).

Conclusion: Our results suggest that frequency of pruritic symptoms is associated with psychological stress in the general population.

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PRURITUS, one of the most common dermatological symptoms, can cause serious discomfort and skin damage mainly via scratching. A recent study demonstrating the association between certain kinds of pruritus and increased risk of mortality, possibly due to related symptoms such as sleep disturbance, has highlighted the importance of alleviating intractable pruritus.

The relationship between pruritus and other mental health states, including depression, has also been reported in some disease-specific populations, such as patients diagnosed as having psoriasis and atopic dermatitis. Furthermore, a previous report has demonstrated that negative mental states may reduce tolerance to aversive stimuli, suggesting a possible biomedical relationship. However, most participants in the previous studies were recruited from outpatients of dermatology departments, and this relationship has not yet been investigated in a generally healthy population. In addition, the degree of pruritus was evaluated on a 5-point and cross-sectional Likert scale. Accurate evaluation of the severity of pruritus over a certain period of time may require applying another scale.

With regard to symptom documentation, the health diary is a promising tool, enabling both medical staff and patients to comprehend the alteration of subjective symptoms between consultation days. Several studies have revealed the health diary to be effective in the continuous evaluation of disease progression, particularly in patients with chronic diseases such as asthma and chronic obstructive pulmonary disease. One report on pediatric asthma further cites the value of concise, self-administered diaries in evaluation of interventions. Given that a considerable number of pruritic symptoms are indicative of chronic skin diseases such as eczema and chronic urticaria, using the degree of pruritic symptoms observed in health diaries as a scale to describe pruritus severity may prove highly effective.
We investigated the relationship between the frequency of perceived pruritic symptoms over a 1-month period and psychological stress, assessed by the Japanese version of the Perceived Stress Scale (PSS) using data from a large prospective health diary study comprised of a representative sample of the general population in Japan.12,13

METHODS

STUDY POPULATION

The Japan Health Diary Study (October 2003) was a prospective cohort study based on health diaries conducted to analyze patient-perceived symptoms and related health behaviors and utilization in communities. Data were collected from 3477 randomly selected participants among the Japanese general population, based on the findings of a nationally representative panel comprised of more than 210,000 households in Japan.11 We selected a population-weighted random sample by controlling for the size of cities, towns, and villages. The original study protocol of the Japan Health Diary Study was approved by the research ethics committee of Kyoto University Graduate School of Medicine. Additional details regarding the sampling and study methods of the Japan Health Diary Study have been previously described.12,11

In the present study, participation was limited to those who completed questionnaires about PSS. Participants with known psychiatric comorbidities were excluded because their responses to the mental health questionnaire were considered to be different from those of general healthy population. A participant was defined as having a psychiatric comorbidity if he or she had been diagnosed as having depression, schizophrenia, or other psychological diseases and regularly received outpatient treatment at the completion period. Participants younger than 18 years were also eliminated to retain reliability of completion for the diaries.

MEASUREMENTS

The main variables evaluated were the state of perceived pruritic symptoms and PSS score. In the Japan Health Diary Study, participants were asked to record each day all perceived symptoms into their health diaries for 1 month, from October 1 to October 31, 2003. Severity of pruritus was assessed by the frequency of recorded pruritic episodes in the health diaries over the specified period. Whether participants recorded a pruritic episode in the diaries was assessed by data managers who were independent of the authors. Mental health was assessed using the Japanese version of the PSS, a 5-item questionnaire regarding perceived mental stress validated against the Cornell Medical Index and the depression scale of the Minnesota Multiphasic Inventory and considered to be highly reliable among the general population and patients with various psychiatric disorders.9,10 The data from the PSS were assessed 1 week after the completion of the health diaries, with higher PSS scores representing greater psychological stress, included questions regarding participants' feelings and thoughts over the previous month, such as: "In the last month, how often have you felt nervous and 'stressed'?"

STATISTICAL ANALYSIS

The relationship between the state of pruritic symptoms and subsequent PSS score was assessed by linear regression analysis, with adjustments made for age, sex, presence of nondermatological perceived symptoms, and 6 comorbid conditions present at baseline (hypertension, cardiovascular and cerebrovascular disease, diabetes mellitus, cancer, and skin disease). Participants with comorbid conditions were defined as those who had been diagnosed as having the conditions and regularly received outpatient care at the completion period.

To examine the relationship between frequency of pruritic symptoms and subsequent PSS score, 3 categorized dummy variables were prepared according to the tertile of frequency for those participants who described pruritic symptoms in the diaries. In all the models described in the previous paragraph, participants who belonged to the first, second, and third tertiles were also compared with the remaining participants who cited no pruritic symptoms, with adjustments made for the possible confounders as described in the previous paragraph. Results were derived as β coefficients, which denoted the differences in PSS scores between participants with and without pruritic symptoms with adjustment made for confounders. Using regression models based on a previously reported method, a test of linear trend across these tertiles was performed by treating tertiles as a continuous variable with a value equivalent to their median score.15

To examine the relationship between health-related behavior and PSS score, 2 dummy variables were prepared according to the presence or absence of consultation behavior and drug use after perception of pruritic symptoms. The relationship between health-related behavior following perception of symptoms and subsequent PSS score was analyzed via linear regression with adjustment for the possible confounders described herein.

Assuming that perceived pruritic symptoms were also related to mental health in participants who reported multiple general symptoms in the health diaries, the relationship between the state of pruritic symptoms and subsequent PSS score was evaluated in 1598 patients citing more than 2 general symptoms in the health diaries, using the same regression model described herein, with adjustments for the same possible confounders. A multiple imputation approach using a chained equations method was used to account for missing values of confounding factors.15,16 with results showing that 16 participants (0.7%) had missing confounder values; a test was performed for univariate analysis. All logistic regression models considered cluster effects at regions, and all analyses were performed using Stata statistical software (version 9.2; StataCorp LP, College Station, Texas).

Of the 3658 participants enrolled in the Japan Health Diary Study, 3477 completed the diary. Of these, 1025 younger than 18 years and 13 with a known comorbidity of mental disorders were excluded. Thus, we enrolled 2439 participants (70.1%). Of these, data meeting the inclusion criteria for pruritic symptoms and psychological stress were available for 2224 patients (91.2%). The 2224 patients had a mean age of 44.6 years, 1212 (54.5%) were women, and 70 (3.1%) reported pruritic symptoms in their health diaries. Table 1 shows patient characteristics, categorized by the presence or absence of pruritic symptoms.

RELATIONSHIP BETWEEN PRURITIC SYMPTOMS AND PSYCHOLOGICAL STRESS

Results showed that the mean PSS scores were 24.4 and 21.8, with and without pruritic symptoms, respectively (P = .003). In participants who reported dermatological
symptoms in the health diaries (n=272), the mean PSS scores were 24.4 and 21.9 with and without pruritic symptoms, respectively (Figure 1).

Multivariable linear regression analysis revealed that patients reporting pruritic symptoms in the diaries had significantly higher perceived stress than those without pruritic symptoms (β coefficient, 2.33; 95% confidence interval [CI], 0.53-4.14; P=.01) (Table 2). Higher perceived stress was also associated with increased age and the presence of nondermatological symptoms. In contrast, lower perceived stress was associated with comorbid cardiovascular disease. Compared with patients without pruritic symptoms, those in the first, second, and third tertiles for frequency of pruritic symptoms had high perceived stress, with β coefficients of 0.81 (95% CI, -1.98 to 3.59; P=.57), 1.77 (95% CI, -0.82 to 4.37; P=.18), and 4.66 (95% CI, 1.29 to 8.43; P=.008), respectively (P value for trend, .004) (Figure 2).

### Table 2. Factors Associated With Psychological Stress as Assessed by PSS Score, Using a Multivariable Linear Regression Model

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>β Coefficient (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritic symptoms (vs no)</td>
<td>2.33 (0.53 to 4.14)</td>
<td>.01</td>
</tr>
<tr>
<td>Age, per 1-y increase</td>
<td>-0.11 (-0.13 to -0.09)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sex, male (vs female)</td>
<td>-0.05 (-0.07 to 0.50)</td>
<td>.78</td>
</tr>
<tr>
<td>Perceived general symptoms other than dermatological symptoms (vs no)</td>
<td>1.49 (0.59 to 2.40)</td>
<td>.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.37 (-0.94 to 1.68)</td>
<td>.58</td>
</tr>
<tr>
<td>Diabetes mellitus (vs no)</td>
<td>0.78 (-1.46 to 3.02)</td>
<td>.49</td>
</tr>
<tr>
<td>Cerebrovascular disease (vs no)</td>
<td>2.22 (-1.13 to 5.58)</td>
<td>.19</td>
</tr>
<tr>
<td>Cardiovascular disease (vs no)</td>
<td>-2.58 (-5.20 to 0.05)</td>
<td>.06</td>
</tr>
<tr>
<td>Cancer (vs no)</td>
<td>1.94 (-1.14 to 5.03)</td>
<td>.22</td>
</tr>
<tr>
<td>Skin disease (vs no)</td>
<td>0.98 (-0.49 to 2.44)</td>
<td>.19</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; PSS, Perceived Stress Scale.

Of the participants with pruritic symptoms, 48 (68.6%) displayed health-related behaviors (they began prescription drug use or visited a physician’s office) after perceiving pruritic symptoms. Furthermore, these participants reported significantly higher psychological stress than those without pruritic symptoms (β coefficient, 2.44; 95% CI, 0.07-4.82; P=.04). However, participants with symptoms who did not engage in health-related behavior were likely to experience even higher psychological stress than those without pruritic symptoms, albeit not to a statistically significant degree (β coefficient, 2.09; 95% CI, −0.25 to 4.42; P=.08).

### Subgroup Analysis of Participants Describing More Than 2 General Symptoms in Their Health Diaries

Multivariable analysis of those participants describing more than 2 general symptoms in the diaries (n=1598) showed an association between the presence of pruritic symptoms and increased psychological stress (β coefficient, 2.41; 95% CI, 0.64-4.17; P=.008). In addition, results also showed that patients in first, second, and third tertiles for frequency of pruritic symptoms had significantly higher perceived stress than those without symptoms, with β coefficients of 1.30 (95% CI, −1.56 to 4.17; P=.37), 1.48 (95% CI, −1.13 to 4.10; P=.27), and 4.70 (95% CI, 1.33-8.07; P=.006), respectively (P value for trend, .004).

### Comment

Our study conducted in a large sample of the general population found a significant association (see Table 2 for P values) between the state of pruritic symptoms and perceived psychological stress as assessed by self-administered questionnaire. In particular, results showed that this association was clearly defined because the β
coefficients of the first, second, and third tertiles for frequency of pruritic symptoms in each model increased in a dose-dependent manner. This trend was also observed in a subgroup of patients who reported more than 2 general symptoms, suggesting that the relationship between pruritic symptoms and psychological stress may be independent of other health problems. After classifying participants according to health behavior (those who used prescription drugs or visited a physician’s office), analysis showed that those with health-related behaviors had higher β coefficients than those without. Our findings provide further support for a relationship between pruritus and psychological stress, based on our supposition that pruritic symptoms that require drug use or an office visit might be intractable and may therefore subsequently affect a patient’s mental health.

The difference in PSS scores between participants with pruritic symptoms and those without pruritic symptoms in this study was 2.33. In comparison with other factors, this difference in PSS scores was almost the same as that between women in the general population Sendai City and new outpatients in the Department of Psychosomatic Medicine of Tohoku University Hospital in Japan and between depressed patients with personality disorders and those without, suggesting relatively high psychological stress in participants with pruritic symptoms.10,17

Perceived severity of pruritus may change depending on various factors, such as the state of skin disease and changes in skin physiologic characteristics. A recent study18 has suggested that severity may even change between day and night, possibly owing to dysfunction of the circadian rhythm of itch mediators. Ordinary cross-sectional measurements using a visual analog or a several-point Likert scale are therefore believed to be incapable of fully grasping the state of pruritus over a certain period of time. Instead, diary cards for perceived pruritic symptoms have been used in several randomized controlled trials to record patient-reported outcomes and evaluate the effect of drugs on participants with pruritic symptoms.19,20

Figure 2. The β coefficients of participants reporting pruritic symptoms in their health diaries if they belonged to each group categorized according to tertiles of the frequency of pruritic symptoms (vs participants without pruritic symptoms).

Psychological stress has been reportedly associated with several skin diseases, including psoriasis, atopic dermatitis, and acne vulgaris.9,25 A pathophysiological association was observed between deterioration in epidermal barrier function and increased psychological stress, suggesting pathogenesis of stress-associated skin disorders.26 One recent study involving outpatients with acne vulgaris who visited hospitals complaining of acne vulgaris revealed a dose-dependent relationship between acne severity and stress levels as assessed by PSS.27 However, to our knowledge, no investigations have focused on the relationship between pruritus and perceived psychological stress in the general population.

With regard to the association between psychological symptoms and skin conditions, a number of studies have examined the relationship between depression and several dermatoses.28,29 Several studies3,30 have noted that patients with psoriasis and acne, as well as outpatients from dermatology departments, are likely to have depressive symptoms. Other reports suggest a relationship between atopic dermatitis and depressive symptoms.31 However, most studies investigated changes in skin appearance caused by skin disease rather than pruritus itself as a causative factor of psychological symptoms.

To our knowledge, the present study is the first investigation of the relationship between severity of pruritus and psychological symptoms in the general population. Results from the present study were generalized through the use of national representative samples. Positive results from the subgroup analysis, which was conducted to determine the reliability of our main result, were also satisfactory.

Several limitations to the present study warrant mention. First, the health diaries in which pruritic symptoms were recorded were self-reports and therefore subjective. Furthermore, health diaries for pruritic symptoms were not strictly validated against other scales, although a recent study suggests an association between Scoring Atopic Dermatitis (SCORAD) scores and der-
matological symptoms assessed using diary cards. Second, on information on the symptom severity was not requested and may be subject to misclassification bias, which might lead our results to null. Third, although psychological stress was sufficiently measured by PSS, assessment using this method does not fulfill the criteria of definitive diagnosis of any psychiatric disorders. Fourth, we did not investigate the relationship between pruritic symptoms and psychological stress in other countries outside of Japan. Global generalization of our results therefore requires additional investigation. Finally, as a general limitation of observational studies, adjustment of unknown confounding factors highly associated with the investigated relationships was not possible.

In conclusion, results from our study using a large representative sample of general populations showed a significant epidemiological association between frequency of pruritic symptoms and perceived psychological stress. Additional investigations, including validations against other scales like visual analog scale, are now necessary to validate the use of health diaries in actual dermatological practice.

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Correspondence: Yosuke Yamamoto, MD, Department of Epidemiology and Healthcare Research, Graduate School of Medicine, Kyoto University, Yoshida Konoe-cho, Sakyo-ku, Kyoto 606-8501, Japan (yamamotoy2@gmail.com).

Author Contributions: Dr Yamamoto had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Yamamoto, Yamazaki, Hayashino, Takahashi, Tokuda, Shimbo, Fukui, Hinohara, Miyachi, and Fukuhara. Acquisition of data: Takahashi, Tokuda, Shimbo, Hinohara, and Fukuhara. Analysis and interpretation of data: Yamamoto, Yamazaki, Takahashi, Miyachi, and Fukuhara. Drafting of the manuscript: Yamamoto, Yamazaki, Hayashino, and Fukuhara. Critical revision of the manuscript for important intellectual content: Yamazaki, Hayashino, Takahashi, Tokuda, Shimbo, Fukui, Hinohara, Miyachi, and Fukuhara. Statistical analysis: Yamamoto, Yamazaki, Hayashino, Takahashi, Tokuda, and Fukuhara. Obtained funding: Shimbo, Fukui, Hinohara, and Fukuhara. Administrative, technical, and material support: Yamamoto, Yamazaki, Hayashino, Takahashi, Tokuda, Hinohara, and Fukuhara. Study supervision: Yamazaki, Hayashino, Shimbo, Fukui, Miyachi, Hinohara, and Fukuhara.

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