




# Changes in patient-perceived aggravating factors during the course of atopic dermatitis

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## Abstract

**Objective:** This study aimed to clarify how patient-perceived aggravating factors change during the course of AD.

**Methods:** This study involved a questionnaire-based survey administered to 115 patients with AD at our hospital. The changes in patient-perceived aggravating factors were examined as treatment progressed by readministering the questionnaire to 36 patients 6 months later.

**Results:** The most frequent aggravating factors at the first visit were sweating, emotional stress, and house dust. The number of patients who identified food, dust mites, house dust, pollen, and pets as aggravating factors decreased during the course of the disease. However, the number of patients who identified sweating, environmental factors, emotional stress, and lack of sleep as aggravating factors did not differ from those at the first visit; this included those who newly identified these as aggravating factors.

**Conclusion:** Many patients with AD are concerned about the aggravating factors, and it may be possible to reduce aggravating factor-related anxiety by informing patients that certain aggravating factors may change during treatment. Hence, it is necessary to ask patients about the aggravating factors at the first visit and fixed intervals and resolve them immediately.

## KEYWORDS

atopic dermatitis/eczema, epidemiology

## 1 | INTRODUCTION

Atopic dermatitis (AD) is a disease in which symptoms are expected to go into “remission” if controlled for a long time through appropriate treatment.<sup>1</sup> However, eczema may reappear, depending on the patient's living environment and lifestyle. Therefore, in addition to drug therapy for anti-inflammatory purposes, it is

important to counteract aggravating factors when treating AD.<sup>1,2</sup> Aggravating factors common to many patients with AD from epidemiological studies based on patient reports include heat, sweating, mental stress, food, dust mites, and house dust.<sup>1,3</sup> Social and cultural lifestyles have changed in the past and present, and the variety and frequency of aggravating factors vary with time and region. Hence, understanding the current trends of aggravating

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factors in patients with AD is necessary to take appropriate measures against them. However, the lack of information on aggravating factors considered by Japanese patients with AD hinders AD therapy.

Aggravating factors in AD include external factors, such as transdermal or transairway exposure to substances, and internal factors, such as emotional factors.<sup>2</sup> Percutaneous allergens are associated with improved dermatitis as skin barrier function improves and allergens no longer reach the skin.<sup>2,4-6</sup> Therefore, these allergens are less likely to aggravate dermatitis. Symptoms of AD aggravation by nonallergic external stimuli, such as mechanical irritation from clothing, are also less common when the skin barrier function and skin inflammation improve.<sup>7</sup> It is also unclear whether psychological factors such as emotional stress are no longer aggravating factors as dermatitis improves. Thus, as a patient's skin condition changes, the aggravating factors perceived by the patient may change. Aggravating factors and allergy-related anxiety are psychological burdens that can help improve treatment adherence once reduced.<sup>8,9</sup> Previous studies on the aggravating factors of AD have focused on what patients consider aggravating factors at a fixed point and have not investigated whether patients' reports change over time. If it becomes clear that the factors that exacerbate the disease when the symptoms are severe can disappear as the symptoms improve, it will increase patient adherence.

Identifying the current aggravating factors in Japanese patients with AD is necessary. Additionally, understanding how these factors change is required to take more appropriate measures against them. This study aimed to clarify the recent aggravating factors of AD in Japan and how patient-perceived aggravating factors change during the course of AD by conducting a questionnaire-based survey of patients with AD.

## 2 | MATERIALS AND METHODS

Ethics approval was obtained from the Ethics Review Committee of Hiroshima University (E2022-0089).

### 2.1 | Participants

The participants were patients with AD who visited the Department of Dermatology at Hiroshima University Hospital for the first time between July 3, 2020, and November 30, 2022. Patients with sufficient information, including medical records and clinical photographs, were enrolled to determine the Investigator's Global Assessment (IGA) score. A total of 115 patients aged 3–67 years were analyzed, including 23, 74, and 18 patients aged 3–15, 16–49, and >50 years, respectively. The participants were surveyed using a prepared questionnaire. The questionnaire could be readministered after >6 months of treatment to 36 of the 115 patients.

### 2.2 | Questionnaire on aggravating factors of AD

The questionnaire was designed for selection purposes. Patients selected what they considered to be the factors aggravating their AD symptoms from a prepared list. Responses from pediatric patients incorporated the opinions of their parents.

The options included food, dust mites, house dust, pollen, sweating, environmental factors, emotional stress, lack of sleep, and pets. The questionnaire options for the second visit were the same as those for the first visit. The questionnaire is available from the Appendix S1.

### 2.3 | Assessment of AD severity

Two dermatologists obtained information from the medical records and clinical photographs of patients to determine the IGA score for each patient.

### 2.4 | Statistics analyses

Chi-squared test was performed to detect differences in each aggravating factor according to age and IGA. The values were considered significant at  $p < .05$ .

## 3 | RESULTS

### 3.1 | Frequency of aggravating factors of AD at the first visit

The most frequent aggravating factor at the first visit was sweating, followed by emotional stress and house dust (Table 1). Environmental factors indicated seasonal changes and differences between cold and warm temperatures. Other factors included alcohol consumption and menstruation.

TABLE 1 Frequency of each aggravating factor at the first visit.

Factor	Number (%)
Sweating	67 (58)
Emotional stress	55 (48)
House dust	41 (36)
Pollen	36 (31)
Dust mites	33 (29)
Lack of sleep	33 (29)
Food	24 (21)
Pets	24 (21)
Environmental factors	23 (20)
Others	51 (44)

Note: The number and percentage of patients who recognized each factor as an aggravating factor ( $N = 115$ ).

### 3.2 | Frequency of aggravating factors of AD according to age group

The aggravating factors according to the different age groups are shown in Table 2. Among children aged <15 years, sweating (13 patients) was the most frequent symptom followed by food consumption (seven patients) (Table 2). Emotional stress (five patients) was less frequent in this group than in the other age groups (Table 2). Sweating was the most frequent aggravating factor in the 16–49-year-old age group, followed by emotional stress, which was observed in more than half of the patients. Approximately 30% of this group recognized a lack of sleep and environmental factors as aggravating factors, along with dust mites and pollen (Table 2). Emotional stress was the most frequent factor (12 patients) in patients aged >50 years, followed by sweating (nine patients) and house dust (nine patients) (Table 2).

### 3.3 | Frequency of aggravating factors according to AD severity

The aggravating factors for each IGA score at the first visit were compared (Table 3); 48, 45, and 22 patients scored 4, 3, and 2, respectively. None of the patients had an IGA score of 1 or 0 on their first visit. Sweating was the most frequently reported aggravating factor, regardless of AD severity. Emotional stress was considered the second-most aggravating factor for all severities. No significant differences were observed in the frequencies of aggravating factors according to AD severity (Table 3).

### 3.4 | AD severity and aggravating factors at reassessment

Changes in the factors that patients perceived to aggravate with treatment progression were examined. In total, 36 patients whose questionnaires were readministered 6 months after the first assessment

were analyzed: four, 28, and four patients were aged 3–15, 16–49, and >50 years, respectively. This reassessment included 20 males and 16 females. The IGA scores of 7, 4, 19, 5, and one of the 36 patients were 0, 1, 2, 3, and 4, respectively. Their IGA scores had improved or remained unchanged from the time of the first visit in all patients.

New aggravating factors were identified in 19 patients. However, in many patients, the number of aggravating factors presented by the patient had decreased since the first visit. The number of patients who recognized food, dust mites, house dust, pollen, and pets as aggravating factors decreased over the course of the disease (Figure 1). However, the number of patients who identified sweating, environmental factors, emotional stress, and lack of sleep as aggravating factors did not differ significantly from that at the first visit; this included patients who newly identified these as aggravating factors (Figure 1).

Differences in changes between patients with well-controlled AD (IGA score: 0 or 1) and those who still experienced dermatitis (IGA score: 2–4) at the second visit were examined (Figure 2). Eleven patients had IGA scores of 0 or 1, and 25 had IGA scores of 2–4. The proportion of patients who recognized external factors, including food, dust mites, house dust, pollen, and pets, as aggravating factors decreased regardless of dermatitis at the second visit (Figure 2A,B). As aggravating factors, emotional stress and lack of sleep did not significantly decrease in either group (Figure 2A,B).

## 4 | DISCUSSION

This study investigated the aggravating factors in Japanese patients with AD. Aggravating factors of AD differed depending on geographical factors such as climate and the culture and age groups of the target patients in a 2004 survey of patients with AD aged 12–24 years in the UK. Sweating, hot weather, fabrics, and dust were recognized as rash-exacerbating factors by approximately 30% of patients; only 4.9% of patients stated that food was an aggravating factor.<sup>10</sup> A 2021 Swiss study on aggravating factors

TABLE 2 Frequency of each aggravating factor grouped by age.

Aggravating factor	3–15 Age (N = 23), number (%)	16–49 Age (N = 74), number (%)	>50 Age (N = 18), number (%)	Chi-square	p-Value
Food	7 (30)	13 (18)	4 (22)	1.7827821	.410085
Dust mites	5 (22)	24 (32)	4 (22)	1.41762605	.492228
House dust	5 (22)	27 (36)	9 (50)	3.57831959	.167101
Pollen	6 (26)	26 (35)	4 (22)	1.48653928	.475556
Sweating	13 (57)	45 (61)	9 (50)	0.73160381	.69364
Environmental factors	2 (9)	19 (26)	2 (11)	4.21571028	.121498
Emotional stress	5 (22)	38 (51)	12 (67)	9.2018837	.010042
Lack of sleep	4 (17)	25 (34)	4 (22)	2.74138606	.253931
Pets	5 (22)	14 (19)	5 (28)	0.70120601	.704263
Others	8 (35)	34 (46)	9 (50)	1.1622077	.559281

Note: Twenty-three, 74, and 18 patients were aged 3–15, 16–49, and >50 years, respectively. Statistical analysis was performed using the chi-squared test. Emotional stress (five [22%]) was less common in those under 15 than in other age groups.

TABLE 3 Frequency of each aggravating factor grouped by severity.

Aggravating factor	IGA4 (N=48), number (%)	IGA3 (N=45), number (%)	IGA2 (N=22), number (%)	Chi-square	p-Value
Food	10 (21)	7 (16)	7 (32)	2.36644721	.30629
Dust mites	14 (29)	14 (31)	5 (23)	0.51652426	.772393
House dust	19 (29)	17 (38)	5 (23)	2.013948192	.365323
Pollen	14 (29)	13 (29)	9 (41)	1.16784494	.557706
Sweating	31 (65)	23 (51)	13 (59)	1.741227771	.418694
Environmental factors	11 (23)	10 (22)	2 (9)	2.030460859	.362319
Emotional stress	25 (52)	19 (42)	11 (50)	0.95663931	.619824
Lack of sleep	17 (35)	10 (22)	6 (27)	2.00307421	.367314
Pets	12 (25)	8 (18)	4 (18)	0.852596478	.652922
Others	22 (46)	17 (18)	12 (55)	1.75692665	.415421

Note: Twenty-two, 45, and 48 patients had IGA scores of 2, 3, and 4, respectively. Statistical analysis was performed using the chi-squared test. There was no significant difference in the number of subjects per factor according to the severity of dermatitis.

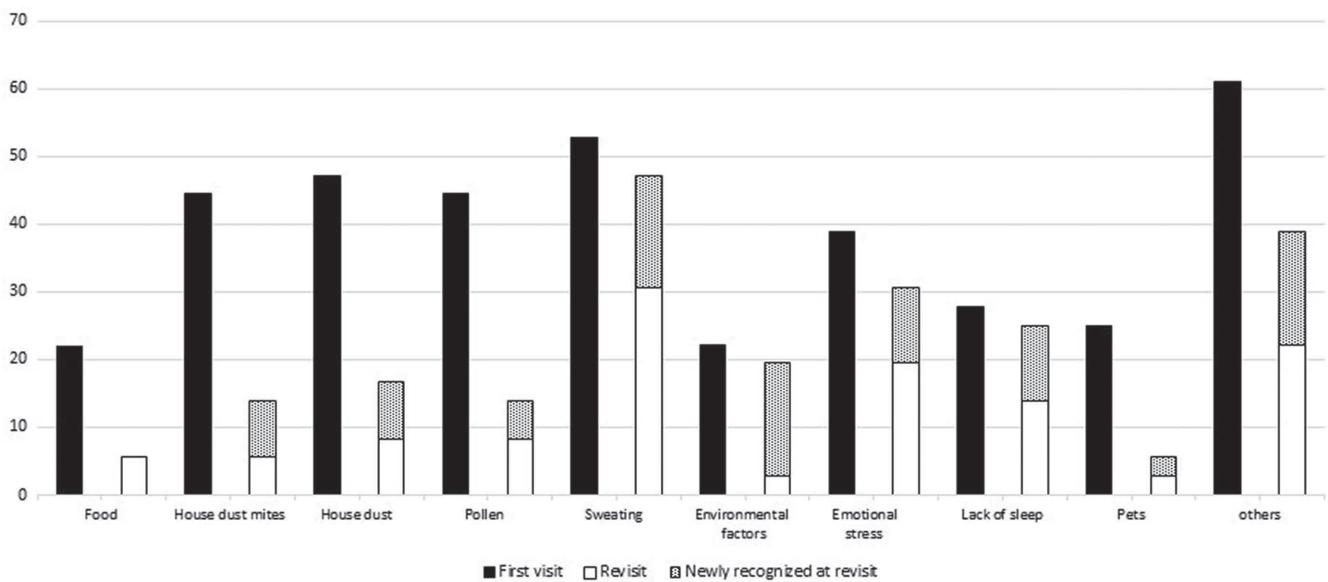


FIGURE 1 Comparison of frequencies of each aggravating factor between the first visit and second visit. Black indicates the percentage of patients who responded at the first visit, and white indicates the percentage of patients who responded at the second visit. The dots are the percentage of patients with newly recognized aggravating factors at the second visit (N=36). The number of patients who identified food, dust mites, house dust, pollen, and pets as aggravating factors decreased during treatment. Other factors were not significantly different from those of the first visit.

and AD-related itching assessed aggravating factors in 34 patients with AD aged 20–70 years. Skin dryness was the most common (79%), followed by dust exposure (65%), emotional distress (50%), and sweating (41%).<sup>11</sup>

In the present study, sweating (58%) was the most common aggravating factor, higher than observed in the UK and Switzerland (Table 1). This may be because sweat exposure is unavoidable in Japan, which is more humid than Europe. Interestingly, some aggravating factors were characterized by age. Emotional stress was less frequent among patients aged <15 years and more frequent among those aged >16 years. Children may be less aware of these subjective factors than adults are; hence, a simple questionnaire survey may

not be sufficient for future study on the impact of emotional stress on children with AD.

Additionally, no bias was observed in the frequency of factors aggravated by the severity of dermatitis at the first visit (Table 2). The degree of dermatitis has been suggested to be independent of the frequency of the aggravating factors.

In this study, 89% of the patients had different patient-reported aggravating factors between their first visit to our clinic and 6 months later. One possible reason for recognizing new aggravating factors could be that medical professionals administered a questionnaire to patients, which increased their awareness of aggravating factors and made them more sensitive. However, interestingly, in 47% of

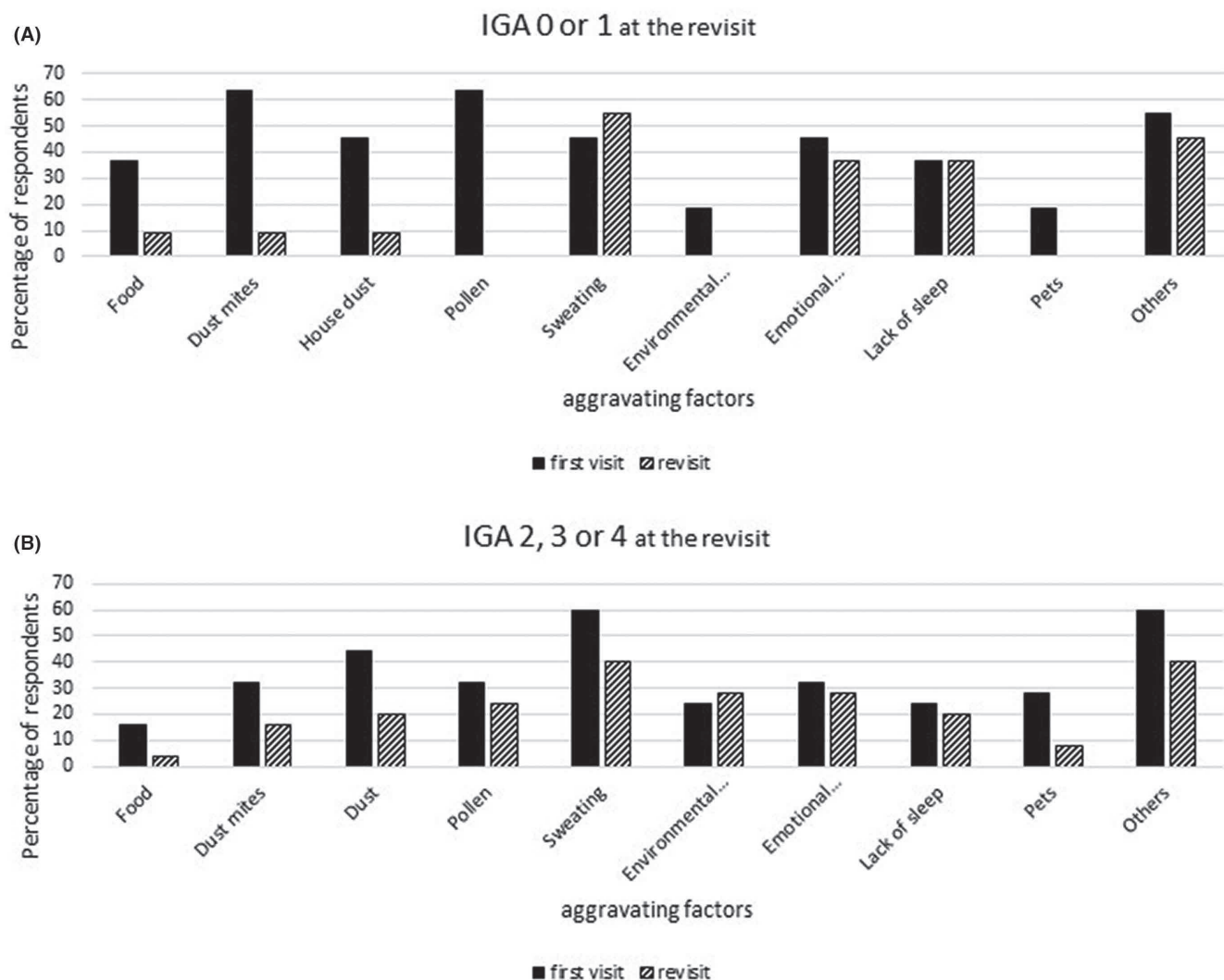


FIGURE 2 Frequency of each aggravating factor in patients with IGA scores (A) 0 and 1 and (B) 2–4 at the second visit. Seven, four, nineteen, five, and one patient(s) had IGA scores of 0, 1, 2, 3, and 4, respectively.

the patients, the number of aggravating factors decreased. Skin inflammation improves skin barrier dysfunction, preventing external aggravating factors such as allergens from entering the skin.<sup>2,4–6</sup> Accordingly, it can be inferred that improving dermatitis reduces the external aggravating factors. Dust mites, house dust, and environmental factors were less frequent aggravating factors for patients with an IGA score of 2 on the first visit than for those with more severe symptoms. However, many aggravating factors were present at similar rates, regardless of AD severity (Figure 2A,B). Furthermore, the proportion of these external aggravating factors decreased at the second visit regardless of the IGA scores (Figure 2A,B), suggesting that factors other than the improvement of barrier function can influence aggravating factors.

Among the external factors, the proportion of patients for whom sweating was aggravating did not decrease much at the second visit compared with house dust (Figure 1). The difference between sweating and other external aggravating factors in AD is a subject for future investigations. Stress and lack of sleep, which are considered internal factors, remained aggravating in many patients during

the second visit (Figure 1). There is a distinction between factors that cease to aggravate during treatment and those that remain aggravating.

In addition to improving dermatitis, patient education and trust in healthcare professionals may reduce aggravating factors. For example, accurate information on the aggravating factors may reduce unnecessary patient concerns. Patient adherence to treatment for atopic dermatitis can be greatly improved through trust in healthcare professionals.<sup>12</sup> Therefore, patients can practice measures against aggravating factors, which are important pillars of AD treatment for atopic dermatitis, through a trusting relationship with their healthcare provider. Appropriate measures against aggravating factors may also help to reduce the patient's perceived aggravating factors. Sweating, mental stress, and lack of sleep may have been difficult for the patients to address.

The limitation of this study is that the questionnaire was administered at a single institution, and the number of patients was small. This study was based on patient reports; hence, assumptions and misunderstandings regarding aggravating factors cannot be ruled

out. Seasonal differences in sweat factors were not analyzed as aggravating factors. The correlation between the proportion of aggravating factors and dermatitis severity was not statistically analyzed due to the limited number of cases.

In the present study, some aggravating factors in many patients with AD were reduced at the second visit. It has been reported that eliminating exacerbating factor-related burdens can improve treatment adherence.<sup>8,13</sup> Informing patients that treatment can reduce the aggravating factors of AD may reduce the disease burden of aggravating factor-related anxiety and improve treatment adherence.

#### CONFLICT OF INTEREST STATEMENT

Akio Tanaka received honoraria from Eli Lilly, Kaken Seiyaku, Sanofi, Taiho Pharma, AbbVie, Kyorin Pharmaceutical, Mitsubishi-Tanabe, Torii Pharmaceutical, Pfizer, and Maruho as a speaker and received research grants from Eli Lilly, Sanofi, Teijin Pharma, Taiho Pharma, Mitsubishi-Tanabe, Torii Pharmaceutical, and Maruho. All other authors declare no conflicts of interest.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available.

#### ETHICS STATEMENT

Informed Consent: N/A.

Approval of the research protocol: This study was approved by the Ethics Review Committee of Hiroshima University (E2022-0089).

Registry and the Registration No.: N/A.

Animal Studies: N/A.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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