

# Pollen Augments the Influence of Desert Dust on Symptoms of Adult Asthma Patients

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## ABSTRACT

**Background:** East Asian desert dust storms that occur during mainly spring are called Asian dust storms (ADS). Our objective was to study the association of pollen and ADS with symptoms of adult asthma patients in Japan.

**Methods:** We designed a telephone survey to investigate the upper and lower respiratory, ocular, and skin symptoms of asthma patients during ADS in February, March, and December on 2009. Peak expiratory flow (PEF) was also measured from February to May.

**Results:** We surveyed 106 patients in February, 101 patients in March, and 103 patients in December. In February and March, Japanese cedar and/or cypress pollen was also in the atmosphere during ADS, but no pollen was identified during December survey. Worsening of upper or lower respiratory, ocular, or skin symptoms was noted by 20.8% of patients in February, 33.7% in March, and 16.5% in December. Worsening of symptoms was significantly more common in March than in February or December. Two patients needed emergency treatment for exacerbation during ADS in March, but no patient needed hospitalization in any period. There was no significant difference of the daily morning PEF/personal best PEF ratio between ADS days and control days. However, in patients with worsening of upper and/or lower respiratory tract symptoms, the daily morning PEF/personal best ratio was significantly associated with the atmospheric level of particulate matter, but not with levels of pollen or other air pollutants.

**Conclusions:** Pollen augmented symptoms in adult asthma patients, but ADS on its own also were able to aggravate symptoms and pulmonary function.

## KEY WORDS

Asian dust storms, asthma, dust, peak expiratory flow, telephone survey

## INTRODUCTION

A high atmospheric level of particulate matter is associated with respiratory or cardiovascular morbidity and mortality.<sup>1,2</sup> Recently, McCreanor *et al.*<sup>3</sup> reported that patients with asthma had asymptomatic reduction of pulmonary function and an inflammatory response after walking for only 2 hours along a roadside, suggesting that airway inflammation is exacerbated by air pollution. It has also been reported that desert dust may increase the incidences and severity of asthma.<sup>4,5</sup>

Dust storms originating in the deserts of Mongolia, northern China, and Kazakhstan are called Asian dust storms (ADS). ADS are a seasonal phenomenon that affect much of East Asia and occasionally reach the east coast of the United States.<sup>6,7</sup> Recently, Uno *et al.*<sup>8</sup> reported that ADS can actually spread completely

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**Table 1** Patient characteristics

|                           |               |
|---------------------------|---------------|
| Number                    | 145           |
| Age (year)                | 63.9 ± 14.4   |
| Gender (male/female)      | 72/73         |
| Disease duration (months) | 109.3 ± 102.4 |
| Smoking status            |               |
| Never                     | 110 (75.9%)   |
| Former                    | 28 (19.3%)    |
| Current                   | 7 ( 4.8%)     |

Data are presented as the mean ± S.E.

around the globe. ADS have become a serious problem due to heavy pollution in East Asia and an increase in the frequency and duration of the storms.<sup>9</sup> Some authors have reported that Asian dust contains pollutants such as sulfur dioxide (SO<sub>2</sub>) and nitrogen dioxide (NO<sub>2</sub>).<sup>10,11</sup> Therefore, health problems related to ADS have attracted attention. Kanatani *et al.*<sup>12</sup> reported that ADS were associated with an increased risk of hospitalization for children with asthma. Studies performed in Taiwan have shown an increase of mortality, emergency treatment for cardiovascular disease, and hospitalization for pneumonia in association with ADS.<sup>13-15</sup> In Korea, ADS are associated with an increase of acute respiratory tract symptoms and changes of peak expiratory flow (PEF) in children with asthma,<sup>16</sup> and Kwon *et al.*<sup>17</sup> reported an increase of mortality from two days after ADS. In China, Meng *et al.* also reported an increase of hospitalization for pneumonia during ADS.<sup>18</sup> On the contrary, other studies have found no significant association of ADS with hospital attendance/admission or the onset and mortality of cardiovascular, cerebrovascular, pulmonary disease, and conjunctivitis/rhinitis.<sup>19-28</sup>

Our previous study revealed that ADS caused worsening of symptoms in adults with asthma,<sup>29</sup> as Kanatani has reported for children.<sup>12</sup> However, our previous study could not completely exclude the effects of pollen, because most ADS occur from February to May, when airborne cedar pollen and cypress pollen levels are high in Japan. In this study, we investigated the relation between airborne pollen, ADS, and particulate matter in adult Japanese patients with asthma.

## METHODS

### PATIENTS

We enrolled 145 outpatients aged >18 years with moderate asthma who were managed at Tottori University Hospital from December 2008 to January 2009 (Table 1). All patients satisfied the criteria in the Global Initiative for Asthma (GINA) guidelines for diagnosis of asthma.<sup>30</sup> They had a history of intermittent wheezing and airway hyperresponsiveness to methacholine or >20% diurnal fluctuation of peak expiratory flow (PEF). Moderate asthma was defined

according to National Institute of Child Health and Human Development and the National Heart, Lung, and Blood Institute.<sup>31</sup> All patients lived in Yonago City, Tottori Prefecture, Japan, and all gave informed consent to the study.

### DEFINITION OF ADS AND MEASUREMENT OF AIR POLLUTANTS

Yonago City is located on the west side of Japan in a rural area and has a population of approximately 160,000. There are no major sources of air pollution apart from a paper mill and motor vehicles.

In Japan, ADS are defined by visibility of less than 10 km due to dust arising from the deserts of East Asia. In this study, the ADS events for Yonago City were defined according to announcements made by the Japan Meteorological Agency and the Ministry of the Environment. Particulate matter in the atmosphere (PM<sub>10</sub>) and the levels of SO<sub>2</sub> and NO<sub>x</sub> were measured by Tottori Prefectural Institute of Health and Environment.

### AIRBORNE POLLEN

Airborne pollen was measured with a Durham sampler placed on the roof of a building (10 m above ground level) in a position that allowed free air movement on all sides. Slides covered with glycerine jelly containing fuchsin were exposed to the air for 24 hours. Then pollen grains on the slides (in an 18 × 18 mm area) were counted after staining with Calbela's solution. The total daily pollen count was expressed as the number of pollen particles/cm<sup>2</sup>.

### PEF MONITORING

From January to May 2009, all patients measured their morning PEF every day using a peak flow meter (Mini-Wright, Harlow, England, American Thoracic Society scale) and recorded the best value from three attempts. PEF was measured within 30 minutes of rising and before inhalation of corticosteroids and β<sub>2</sub>-agonists or taking oral drugs. The highest morning PEF from January to May 2009 was defined as the personal best value.

### TELEPHONE SURVEY

The telephone survey was performed two days after the first ADS event, as was our previous survey.<sup>29</sup> We inquired whether patients had experienced exacerbation of upper and lower respiratory tract symptoms, ocular symptoms, or skin symptoms during the ADS event. We asked about the following symptoms: (1) worsening cough, sputum, wheezing, dyspnea, and use of short-acting β<sub>2</sub>-agonists and hospital attendance for lower respiratory tract symptoms; (2) tearing, itching, mucus, and pain as ocular symptoms; (3) stuffiness, sneezing, pharyngalgia, and itching as upper respiratory tract symptoms; and (4) itching, redness, and pain as skin symptoms. We judged that

**Table 2** Daily averages of air pollution levels

|                                       | February and March in 2009 |               |                   | December in 2009 |         |
|---------------------------------------|----------------------------|---------------|-------------------|------------------|---------|
|                                       | Control days               | ADS days      | <i>P</i> values   | Control days     | ADS day |
| PM <sub>10</sub> (μg/m <sup>3</sup> ) | 27.8 ± 13.8                | 65.3 ± 16.7   | <i>P</i> < 0.0001 | 25.2 ± 11.5      | 98      |
| SO <sub>2</sub> (ppb)                 | 2.16 ± 2.67                | 5.44 ± 3.75   | <i>P</i> < 0.005  | 4.16 ± 4.99      | 7       |
| NO <sub>x</sub> (ppb)                 | 32.40 ± 24.77              | 34.68 ± 20.80 | NS                | 30.73 ± 21.83    | 21      |
| Temperature (°C)                      | 7.3 ± 2.9                  | 10.9 ± 4.7    | <i>P</i> < 0.005  | 7.1 ± 3.7        | 8.2     |
| Humidity (%)                          | 70.0 ± 8.9                 | 63.1 ± 11.3   | <i>P</i> < 0.05   | 74.3 ± 8.9       | 63      |
| Atmospheric pressure (hPa)            | 1018.1 ± 5.2               | 1012.4 ± 4.4  | <i>P</i> < 0.005  | 1017.5 ± 3.9     | 1014.8  |
| Pollen (cm <sup>2</sup> /day)         | 58.8 ± 134.0               | 114.9 ± 114.3 | NS                | —                | 0       |

**Table 3** Average of pollen levels (cm<sup>2</sup>/day)

|                               |               |
|-------------------------------|---------------|
| ADS days for February in 2009 | 63.7 ± 61.4   |
| ADS days for March in 2009    | 217.3 ± 138.7 |
| ADS days for December in 2009 | 0             |

Data are presented as the mean ± S.E.

worsening of symptoms had occurred if a patient mentioned worsening of even one symptom, but excluded patients who had respiratory tract infection or suspected infection. We defined respiratory tract infection as being present in patients with any of the following: (1) pyrexia, trachyphonia, or sore throat; (2) those who stated that they had respiratory tract infection based on their own interpretation of symptoms; and (3) if family members and/or colleagues had caught a cold.

### DATA ANALYSIS

Results are shown as the mean ± standard error (SE). SPSS software (Japanese version 16.0 for windows; SPSS Japan Inc., Tokyo, Japan) was used for statistical analysis. Comparisons between groups were done with the Mann-Whitney nonparametric test, while the  $\chi^2$  test was employed for categorical data. Multivariate logistic regression analysis was also performed to compare patients with or without worsening of symptoms. Control days for February and March were defined as the days when ADS did not occur during those months in 2009. Likewise, we defined control days for December as the days when ADS did not occur during that month in 2009.

To assess the relation between PEF values and levels of air pollutants or weather conditions, we performed multiple regression analysis. We hypothesized that the effect of air pollutants and weather on PEF could be delayed, so we performed two analyses. For the same day analysis, PEF values were analyzed with the level of air pollutants and weather conditions on the same day. For the one day lag analysis, we averaged data for the previous day and the same day (temperature, atmospheric pressure, pollen, PM<sub>10</sub>, SO<sub>2</sub>, and NO<sub>x</sub>) when analyzing the effect of air pollut-

ants and weather conditions on PEF. In this study, we were unable to measure absolute humidity. Because humidity is strongly influenced by temperature, it was omitted from analysis. Significance was accepted at *P* < 0.05 for all analyses.

## RESULTS

### RELATIONS AMONG ADS EVENTS, AIRBORNE POLLEN, AND AIR POLLUTANTS

Eleven ADS event days were identified during 2009, including February 11-15, February 20-21, March 16-18, and December 26 in 2009. From February to March 2009, Japanese cedar pollen and cypress pollen were present in the atmosphere during each ADS event.

Table 2 shows the daily average levels of air pollution. In February and March, PM<sub>10</sub> and SO<sub>2</sub> levels were significantly higher on ADS days than control days. The temperature was also significantly higher and humidity was significantly lower on ADS days than control days. Because there was only one ADS event day in December, statistical analysis of this event was not done.

Table 3 shows the average pollen levels during the ADS events. Japanese cedar pollen was detected from February 2, and cypress pollen was also detected from March 8. We also searched for pollen on December 26-27, but no pollen was identified.

### RESULTS OF THE TELEPHONE SURVEYS

We conducted telephone surveys on February 13-14, March 18-19, and December 27-28 in 2009; 106/145 patients participated in the first survey, 101 patients participated in the second survey, and 103 patients participated in the third survey. While 39 patients in the first survey, 44 patients in the second survey, and 42 patients in the third survey could not be contacted during period of the telephone survey. Table 4 shows patient characteristics for the three surveys—there were no significant differences among them.

The results of the three surveys are displayed in Table 5. Worsening of upper or lower respiratory, ocular, or skin symptoms was reported by 22/106 patients (20.8%) in the February survey, 34/101 patients

**Table 4** Differences of patients characteristics in each survey

|                                         | February survey | March survey | December survey | P value |
|-----------------------------------------|-----------------|--------------|-----------------|---------|
| Number                                  | 106             | 101          | 103             | NS      |
| Age (years)                             | 61.3 ± 14.5     | 61.7 ± 14.8  | 62.3 ± 14.3     | NS      |
| Gender (male/female)                    | 47/59           | 48/54        | 48/56           | NS      |
| Existence of atopy                      | 41 (38.7%)      | 40 (39.6%)   | 37 (35.9%)      | NS      |
| Presence of other allergic diseases     |                 |              |                 |         |
| Allergic rhinitis                       | 27 (25.5%)      | 26 (25.7%)   | 22 (21.4%)      | NS      |
| Cedar pollen and cypress pollen allergy | 12 (11.3%)      | 11 (10.9%)   | 11 (10.7%)      | NS      |
| Perennial allergic rhinitis             | 15 (14.2%)      | 15 (14.9%)   | 11 (10.7%)      | NS      |
| Allergic conjunctivitis                 | 4 ( 3.8%)       | 4 ( 4.0%)    | 4 ( 3.9%)       | NS      |
| Atopic dermatitis                       | 3 ( 2.8%)       | 4 ( 4.0%)    | 3 ( 2.9%)       | NS      |
| Non-allergic rhinitis                   | 4 ( 3.8%)       | 4 ( 4.0%)    | 2 ( 1.9%)       | NS      |
| Usual maintenance treatment             |                 |              |                 |         |
| Inhaled corticosteroid                  | 106 ( 100%)     | 101 ( 100%)  | 102 ( 100%)     | NS      |
| Oral corticosteroid                     | 0 ( 0%)         | 0 ( 0%)      | 0 ( 0%)         | NS      |
| Inhaled long-acting $\beta_2$ -agonists | 66 (62.3%)      | 64 (63.4%)   | 58 (56.3%)      | NS      |
| Leukotriene antagonist                  | 25 (23.6%)      | 27 (26.7%)   | 29 (28.2%)      | NS      |
| Teophylline                             | 5 ( 4.7%)       | 5 ( 5.0%)    | 3 ( 2.9%)       | NS      |
| Antihistamines                          | 11 (10.4%)      | 12 (11.9%)   | 11 (10.7%)      | NS      |

Data are presented as the mean ± S.E.; NS, not significant.

**Table 5** Results of the telephone survey

|                                                                                                   | February survey | March survey | December survey |
|---------------------------------------------------------------------------------------------------|-----------------|--------------|-----------------|
| Number                                                                                            | 106             | 101          | 103             |
| Patients with worsening of either symptom                                                         | 22 (20.8%)*     | 34 (33.7%)   | 17 (16.5%)**    |
| Patients with worsening of lower respiratory tract symptom                                        | 15 (14.2%)      | 23 (22.8%)   | 12 (11.7%)***   |
| Cough                                                                                             | 9 ( 8.5%)       | 11 (10.9%)   | 8 ( 7.8%)       |
| Sputum                                                                                            | 10 ( 9.4%)      | 14 (13.9%)   | 5 ( 4.9%)       |
| Wheezing                                                                                          | 2 ( 1.9%)       | 5 ( 0.5%)    | 0 ( 0%)         |
| Dyspnea                                                                                           | 5 ( 4.7%)       | 7 ( 6.9%)    | 2 ( 1.9%)       |
| Patients with worsening of upper respiratory tract symptom                                        | 14 (13.2%)      | 20 (19.8%)   | 8 ( 7.8%)*      |
| Sneezing                                                                                          | 11 (10.4%)      | 17 (16.8%)   | 6 ( 5.8%)       |
| Stuffiness                                                                                        | 3 (21.4%)       | 4 ( 4.0%)    | 3 ( 2.9%)       |
| Itching                                                                                           | 5 ( 4.7%)       | 8 ( 7.9%)    | 2 ( 1.9%)       |
| Patients with worsening of ocular symptom                                                         | 9 ( 8.5%)       | 16 (15.8%)   | 2 ( 1.9%)*      |
| Tearing                                                                                           | 0 ( 0%)         | 3 ( 3.0%)    | 0 ( 0%)         |
| Itching                                                                                           | 9 ( 8.5%)       | 16 (15.8%)   | 2 ( 1.9%)       |
| Mucus                                                                                             | 1 ( 0.9%)       | 3 ( 3.0%)    | 0 ( 0%)         |
| Pain                                                                                              | 0 ( 0%)         | 1 ( 1.0%)    | 0 ( 0%)         |
| Patients with worsening of skin symptom                                                           | 0 ( 0%)         | 0 ( 0%)      | 0 ( 0%)         |
| Hospitalization for exacerbation of asthma                                                        | 0 ( 0%)         | 0 ( 0%)      | 0 ( 0%)         |
| Hospital visit for worsening of lower respiratory tract symptom                                   | 0 ( 0%)         | 2 ( 2.0%)    | 0 ( 0%)         |
| Use of short-acting $\beta_2$ agonist for worsening of lower tract respiratory symptom during ADS | 6 ( 5.7%)       | 13 (12.9%)   | 5 ( 4.9%)       |

ADS, Asian dust storms. \* $P < 0.03$ , versus March survey; \*\* $P < 0.005$ , versus March survey; \*\*\* $P < 0.05$ , versus March survey.

(33.7%) in the March survey, and 17/103 patients (16.5%) in the December survey. The frequency of worsening of symptoms was significantly higher in March than in February or December. Worsening of

lower respiratory tract symptoms was reported by 15 patients (14.2%) in February, 23 patients (22.8%) in March, and 12 patients (11.7%) in December, with a significant difference between the March and Decem-

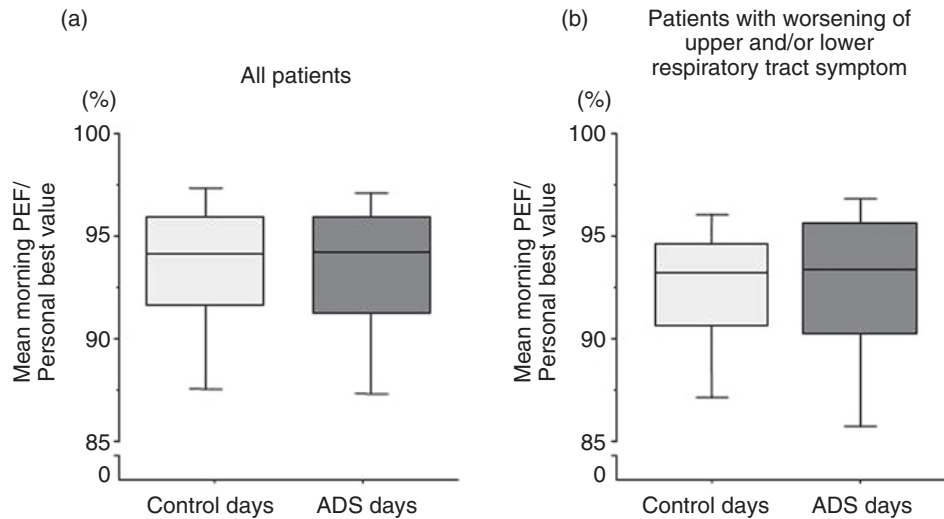


**Fig. 1** Results of monitoring PEF. (a) In all patients, the mean morning PEF to personal best ratio was  $92.9 \pm 5.4\%$  in the ADS days versus  $93.2 \pm 5.2\%$  in the control days. (b) In patients with worsening of lower respiratory tract symptoms, the mean morning PEF/personal best ratio was  $92.5 \pm 3.8\%$  in the ADS days versus  $92.5 \pm 3.2\%$  during the control period. There was no significant difference between ADS days and control days in both of all patients and patients with worsening of lower respiratory tract symptom.

ber surveys ( $P < 0.05$ ).

Worsening of upper respiratory and ocular symptoms was significantly more frequent in March than in December ( $P < 0.03$ ). There was also a significant difference in the number of patients with worsening of ocular symptoms between the March and February surveys. Two patients needed emergency treatment for exacerbation of lower respiratory tract symptoms during ADS in March. In all three surveys, about 40% of patients with worsening of lower respiratory tract symptoms used short-acting  $\beta_2$  agonist and noted improvement.

#### CHANGES OF PEF

In all patients, the mean morning PEF/personal best ratio was  $92.9 \pm 5.4\%$  on ADS days versus  $93.2 \pm 5.2\%$  on control days (Fig. 1a). In patients who had one or more episodes of worsening of upper and/or lower respiratory tract symptoms in three surveys, the mean morning PEF/personal best ratio was  $92.5 \pm 3.8\%$  on ADS days versus  $92.5 \pm 3.2\%$  on control days (Fig. 1b). There was no significant difference between ADS days and control days for all patients or for the patients with worsening of upper and/or lower respiratory tract symptoms.

#### COMPARISON BETWEEN PATIENTS WITH OR WITHOUT WORSENING OF UPPER AND/OR LOWER RESPIRATORY TRACT SYMPTOMS DURING ADS EVENTS

Worsening of upper and/or lower respiratory tract

symptoms was defined as being present if a patient mentioned worsening of such symptoms even once in the three surveys. There was a significant difference in the prevalence of allergic rhinitis and non-allergic rhinitis between patients with or without worsening of upper and/or lower respiratory tract symptoms (Table 6). On the other hand, there were no significant differences of age, gender, allergic conjunctivitis, or atopic dermatitis.

#### ASSOCIATION WITH PEF AND AIR POLLUTANTS

Associations among the daily morning PEF/personal best ratio, air pollutants, and weather conditions were investigated by multiple regression analysis from February 1 to March 31 in 2009 (Table 7). In all patients, no significant association was detected between the daily morning PEF/personal best ratio and the levels of  $PM_{10}$ , pollen,  $SO_2$ , and  $NO_x$ , or the average temperature and atmospheric pressure. In patients with worsening of upper and/or lower respiratory tract symptoms (defined as even one mention of worsening respiratory tract symptoms in the three surveys), the daily morning PEF/personal best ratio was significantly associated with  $PM_{10}$  and temperature, but not with the levels of pollen,  $SO_2$ , or  $NO_x$ , and atmospheric pressure. An increase of  $PM_{10}$  led to a decrease of morning PEF.

#### DISCUSSION

In the present study, the daily morning PEF/personal

**Table 6** Comparison of patients with or without worsening of upper and/or lower respiratory tract symptoms

|                                     | Patients without worsening of any symptoms | Patients with worsening of upper and/or lower respiratory tract symptoms | P value         |
|-------------------------------------|--------------------------------------------|--------------------------------------------------------------------------|-----------------|
| Number                              | 69                                         | 38                                                                       | NS              |
| Age (years)                         | 62.3 ± 14.8                                | 60.9 ± 14.7                                                              | NS              |
| Gender (male/female)                | 32/37                                      | 17/21                                                                    | NS              |
| Existence of atopy                  | 21 (30.4%)                                 | 19 (50.0%)                                                               | NS              |
| Presence of other allergic diseases |                                            |                                                                          |                 |
| Allergic rhinitis                   | 18 (26.1%)                                 | 20 (52.6%)                                                               | <i>P</i> < 0.03 |
| Allergic conjunctivitis             | 3 ( 4.3%)                                  | 1 ( 2.6%)                                                                | NS              |
| Atopic dermatitis                   | 1 ( 1.4%)                                  | 3 ( 7.9%)                                                                | NS              |
| Non-allergic rhinitis               | 0 ( 0%)                                    | 3 ( 7.9%)                                                                | <i>P</i> < 0.03 |

Data are presented as the mean ± S.E.; NS, not significant.

**Table 7** Partial correlation coefficient for daily morning PEF/Personal best value associated with air pollutants

|                                       | All patients                                                             |              |         |                                 |              |         |
|---------------------------------------|--------------------------------------------------------------------------|--------------|---------|---------------------------------|--------------|---------|
|                                       | The same day                                                             |              |         | The one day lag                 |              |         |
|                                       | Partial correlation coefficient                                          | 95% CI       | P value | Partial correlation coefficient | 95% CI       | P value |
| Average temperature (°C)              | 0.203                                                                    | -0.015-0.103 | 0.140   | 0.191                           | -0.022-0.120 | 0.171   |
| Average atmospheric pressure (hPa)    | 0.184                                                                    | -0.011-0.055 | 0.183   | 0.127                           | -0.022-0.060 | 0.363   |
| PM <sub>10</sub> (μg/m <sup>3</sup> ) | -0.082                                                                   | -0.012-0.006 | 0.556   | -0.029                          | -0.013-0.011 | 0.837   |
| SO <sub>2</sub> (ppb)                 | 0.069                                                                    | -0.044-0.072 | 0.623   | -0.002                          | -0.078-0.078 | 0.991   |
| NO <sub>x</sub> (ppb)                 | -0.006                                                                   | -0.007-0.007 | 0.967   | 0.118                           | -0.005-0.012 | 0.400   |
| Pollen (/cm <sup>2</sup> /day)        | -0.134                                                                   | -0.002-0.001 | 0.336   | -0.039                          | -0.002-0.002 | 0.779   |
|                                       | Patients with worsening of upper and/or lower respiratory tract symptoms |              |         |                                 |              |         |
|                                       | The same day                                                             |              |         | The one day lag                 |              |         |
|                                       | Partial correlation coefficient                                          | 95% CI       | P value | Partial correlation coefficient | 95% CI       | P value |
| Average temperature (°C)              | 0.334                                                                    | 0.035-0.292  | 0.014   | 0.277                           | 0.004-0.312  | 0.045   |
| Average atmospheric pressure (hPa)    | 0.054                                                                    | -0.057-0.085 | 0.696   | -0.023                          | -0.096-0.082 | 0.872   |
| PM <sub>10</sub> (μg/m <sup>3</sup> ) | -0.367                                                                   | -0.048-0.008 | 0.006   | -0.418                          | -0.069-0.170 | 0.002   |
| SO <sub>2</sub> (ppb)                 | 0.194                                                                    | -0.037-0.216 | 0.160   | 0.269                           | 0.000-0.338  | 0.051   |
| NO <sub>x</sub> (ppb)                 | -0.232                                                                   | -0.027-0.002 | 0.091   | -0.207                          | -0.033-0.005 | 0.137   |
| Pollen (/cm <sup>2</sup> /day)        | -0.135                                                                   | -0.004-0.001 | 0.330   | 0.026                           | -0.004-0.004 | 0.856   |

CI, confidence interval.

best ratio was significantly correlated with PM<sub>10</sub> among patients with worsening of their symptoms on ADS days, while the pollen level was not associated with the PEF. Two subjects attended hospital for emergency treatment due to exacerbation of lower respiratory tract symptoms, but none of the patients required admission. About 40% of the patients with worsening of lower respiratory tract symptoms showed a response to short-acting β<sub>2</sub>-agonists.

We previously reported that ADS can aggravate lower respiratory tract symptoms in asthma patients, but the actual influence on symptoms is mild.<sup>29</sup> However, we could not completely exclude the influence

of pollen in that study because high atmospheric levels of Japanese cedar pollen and cypress pollen are present from February to April in Japan. Allergic rhinitis induced by cedar pollen and/or cypress pollen was reported to affect 26.5% of all Japanese in 2008,<sup>32</sup> and patients with asthma often have rhinitis,<sup>33</sup> although epidemiological studies have not clearly defined the influence of pollen on asthma.<sup>34</sup>

On December 26, no pollen was detected during ADS, and the pollen level in February was lower than that in March. Thus, our surveys revealed that the dust itself could aggravate symptoms of asthma in the absence of pollen on adult asthma, although pollen

augmented the influence of ADS. In this study as well as our previous study, none of the patients needed hospitalization for exacerbation of asthma symptoms and only two patients presented for emergency treatment, suggesting that the adverse influence of ADS was mild.

On the other hand, Kanatani *et al.*<sup>12</sup> reported an increased risk of hospitalization related to ADS in children with asthma. Thus, the influence of ADS may be different between adults and children with asthma in Japan. In children, asthma symptoms may be influenced more easily than in adults due to differences of pathophysiology between adult and pediatric asthma. In addition, the criteria for hospitalization to treat acute asthma may differ between adults and children. In this study, some patients (especially the elderly) avoided the outdoors on ADS days. It is likely that children participated in outdoor activities as usual, even on ADS days. Therefore, children might have been more strongly influenced by ADS.

The mean morning PEF/personal best ratio showed no significant difference between ADS days and control days in this study, as well as in our previous study. When the levels of air pollutants were compared between ADS days and control days, significant differences were detected for SO<sub>2</sub> and PM<sub>10</sub>, thus we analyzed the association of air pollutants with PEF. In patients with exacerbation of the symptoms during ADS, only PM<sub>10</sub> was significantly correlated with PEF.

Despite the significant association between PM<sub>10</sub> and PEF, a significant difference was not detected in the mean morning PEF/personal best ratio between ADS days and control days in this study. It had been reported that PEF monitoring was not as sensitive as a symptom diary for revealing acute exacerbations of asthma.<sup>35</sup> We speculated that the influence of ADS for adult patients with asthma was mild in Japan and, as a result, the decrease of PEF during ADS was too small to detect a significant difference between ADS days and control days. In addition, the PEF decrease might not be prolonged, because patients improved using short-acting  $\beta_2$ -agonists.

The mechanism of exacerbation of symptoms by ADS may be attributed to particulate matter. Desert dust could enter the lower airways of humans, including the small airways and alveoli, because the diameter of Asian dust particles reaching Japan is 3–5  $\mu$ m. Some studies have shown that dust from deserts in Mongolia and northern China increases lung inflammation and infiltration in animals.<sup>36–38</sup> ADS may promote airway inflammation in patients with asthma. Particulate matter is also known to increase airway inflammation in asthma patients.<sup>3</sup> Thus, the association of PEF with PM<sub>10</sub> indicates that an increase of particulate matter on ADS days may provoke airway inflammation and pulmonary dysfunction in some asthma patients.

The main physiological function of the nose is to condition inhaled air so that it reaches the lower airway in a state that does not threaten homeostasis.<sup>39</sup> The nasal passages have a great capacity to warm and humidify air.<sup>40</sup> Most grains of pollen are 20–40  $\mu$ m in diameter and are unable to reach the lower airways because particles with a diameter above 5 to 10  $\mu$ m are trapped by the nasal mucosa. However, patients with allergic rhinitis become unable to breathe through the nose if pollen exacerbates inflammation and induces nasal congestion. As a result, dry air and particulate matter can directly reach the lower airways of such patients. In fact, patients with rhinitis had a higher frequency of worsening of symptoms on ADS days than patients without rhinitis in this study as well as in our previous study, which suggests that nasal obstruction is one of the mechanisms by which pollen augments the exacerbation of asthma symptoms associated with ADS. This could be the reason why worsening of lower respiratory tract symptoms was more frequent in the March survey than the December survey, although the PM<sub>10</sub> level on ADS days was higher in December than in March.

In conclusion, we found that 16%–33% of asthma patients showed worsening of upper or lower respiratory, ocular, or skin symptoms on ADS days. A concomitant increase of pollen augmented the rate of worsening of symptoms. There was no significant difference of PEF between ADS days and control days. However, in patients with worsening of symptoms on ADS days, PM<sub>10</sub> was significantly associated with PEF. Presumably, dust from Asian deserts itself may increase airway inflammation in Japanese asthma patients, but further studies are needed to define the association between ADS and health.

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## CONFLICT OF INTEREST

No potential conflict of interest was disclosed.

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