

Desert Dust Exposure Is Associated with Increased Risk of Asthma Hospitalization in Children

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Rationale: Desert dust particles, including quartz, which causes inflammatory responses in the airway in animal studies, are transported to widespread regions around the globe. Epidemiologically, areas impacted by desert dust storms, such as communities in the Middle East and the Caribbean, seem to have higher incidences of asthma than might be expected.

Objectives: We investigated the magnitude of association between airborne mineral dust concentration and hospitalization of children for asthma exacerbation by using Light Detection And Ranging (LIDAR) with a polarization analyzer for an exposure measurement, which can distinguish mineral dust particles from other particles.

Methods: A case-crossover design was used. The exposure measurement was LIDAR's nonspherical extinction coefficient. The outcome measurement was hospitalization of children aged 1 to 15 years for asthma exacerbation in eight principal hospitals in Toyama, a local area in Japan bordering the Japan Sea, during February to April, 2005 to 2009.

Measurements and Main Results: During the study period, there were 620 admissions for asthma exacerbation, and 6 days with a heavy dust event (daily mineral dust concentration > 0.1 mg/m³). Conditional logistic regression showed a statistically significant association between asthma hospitalization and a heavy dust event. The crude odds ratio (OR) of the heavy dust event for hospitalization on the day was 1.88 (95% confidence interval [CI], 1.04–3.41; *P* = 0.037), and the OR of heavy dust event during the previous week was 1.83 (95% CI, 1.31–2.56; *P* = 0.00043). The OR adjusted by other air pollutant levels, pollen, and meteorological factors was 1.71 (95% CI, 1.18–2.48; *P* = 0.0050).

Conclusions: Heavy dust events are associated with an increased risk of hospitalizations for asthma.

Keywords: Asian dust; Kosa; mineral dust; African dust; quartz

Aerosol particles are produced by a variety of processes, both natural and anthropogenic. Among them, desert dust constitutes about 40% of the aerosol mass injected into the troposphere (1).

Quartz, an amorphous and crystalline silica, included in dust sand, is known to cause respiratory disease in occupationally exposed people and highly exposed people who live close to deserts (2–5). It causes inflammatory responses with the release of inflammatory cytokines in the lungs of rats in experimental studies (6–8).

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AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Desert dust particles, including quartz, which cause inflammatory responses in the airway in animal studies are transported to widespread regions around the globe. However, no studies have investigated the magnitude of desert dust effects on asthma exacerbation with quantitative objective measures of desert dust in the air.

What This Study Adds to the Field

Desert dust exposure was associated with the increased risk of asthma hospitalization for children with asthma. The risk was particularly high for boys.

Desert dust is transported to wide regions of the world. Dust originating from the Sahara desert can be transported across the Atlantic Ocean and reach northeastern South America, the Caribbean, Central America, and southeastern United States (9). Dust originating from the Taklimakan desert was transported more than one full circle around the globe in about 13 days (10). Epidemiologically, areas impacted by desert dust storms, such as communities in the Middle East and the Caribbean, seem to have higher incidences of asthma than might be expected (2, 11–13). Although several clinical studies tried to relate desert dust to asthma, none had a quantitative objective measure of desert dust in the air (14–19) except one that measured the amount of some minerals in the air (20). On the other hand, extensive studies of the atmospheric aerosol particle load in the troposphere have been conducted in the last decades using the Light Detection and Ranging (LIDAR) technique in North America, Western Europe, and Asia (10, 21–27). LIDAR is an optical remote sensing technology that measures properties of scattered light to find range and/or other information on a distant target. The LIDAR system with a polarization analyzer can distinguish mineral dust particles (nonspherical particles) from non-mineral dust particles (spherical particles) (28–32). Although particulate matter 2.5 μm or smaller in size and particulate matter 10 μm or smaller in size differentiate the size of particles but do not differentiate mineral dust from nonmineral dust, the LIDAR system with a polarization analyzer does not differentiate the size of particles but does differentiate the shape of particles. Thus, the LIDAR system can specifically measure quantity of mineral dust. In Asia, observations of tropospheric aerosol particles are continuously being conducted using a network of LIDARs at 23 locations in Japan, Korea, and China.

The present study took place in Toyama, Japan, a local prefecture occasionally susceptible to Asian dust events in the spring. Asian dust is a windblown dust originating from the

deserts of Mongolia and China. It is a seasonal event, and Asian cities experience yellowish air on several days in the spring when the dust is blowing. We investigated the magnitude of the effect of mineral dust particles on children's asthma exacerbation using the LIDAR measurement. The primary hypothesis was that heavy dust events are associated with an increased risk of hospitalizations for asthma.

METHODS

Study Design

The present study used a case-crossover design (33–35). Four controls were matched to each hospitalization, ± 2 weeks and ± 4 weeks. The study protocol was approved by the Human Research Protection Program of the University of California, San Diego.

Hospitalization Data

Data were obtained from the hospitalization records of eight principal hospitals in Toyama, Japan. Potential cases were children aged 1 to 15 years who had at least one hospitalization with the admission diagnosis of asthma in any of the eight principal hospitals in Toyama between February and April, from 2005 to 2009. Hospitalization referred to actual inpatient admission and did not include emergency visits that did not end in admission.

Dust, Air Pollution, and Meteorological Data

The mineral dust data were based on measurement by the LIDAR system with a polarization analyzer (10, 28, 36).

A heavy dust event day *a priori* was defined as the day when the daily (24 h) average dust extinction coefficient in Toyama, measured by LIDAR less than 1 km height from the ground, recorded more than 0.1/km, which corresponded to 0.1 mg/m³ mineral dust particles, the standard threshold for particulate matter (28, 36).

Statistical Analysis

Initially, a conditional logistic regression analysis was performed using hospitalization as the dependent variable, and heavy dust event as the independent variable changing the hazard/control period from 1 to 7 days to determine the crude odds ratio (OR) of heavy dust events for asthma hospitalization. We examined possible climatic confounders (daily average temperature, temperature difference from the previous day, temperature difference within the day, air pressure, air pressure difference from the previous day, humidity, and wind speed) if each had an increased OR for asthma hospitalization with various cut-off values and various lag structures up to lag 0 to 6 (Days 0–6). Then we performed cross-correlations of the variables and conducted a conditional logistic regression to determine the climatically adjusted OR using hospitalization as the dependent variable and, as independent variables, heavy dust event and all climatic variables that showed apparent increase ($P < 0.1$) of OR for asthma hospitalization among the above. We examined other air pollutants (gaseous NO₂, SO₂, and photochemical oxidants [Ox], non-mineral dust particles, and pollen) if each had an increased OR for asthma hospitalization with various cut-off values and various lag structures up to lag 0 to 6 (Days 0–6). Then these other air pollutants were each examined by a two-compartment model approach to determine if they had an effect on the OR of heavy dust event to asthma hospitalization. Finally, we conducted a conditional logistic regression to obtain the best fit OR using heavy dust event, the climatic variables described above, and other air pollutants described above as independent variables.

The same conditional logistic regression analysis was conducted on each subgroup of sex and age defined *a priori* (ages 1–5 yr, 6–12 yr, 13–15 yr).

We also conducted the same conditional logistic regression using a heavy dust event defined by a more conventional method, suspended particulate matter (daily average particulate matter level ≥ 0.1 mg/m³), as an exposure measurement. R version 2.9.2 was used for statistical analysis. Additional detail on the method for making these measurements is provided in an online data supplement.

RESULTS

Subjects

During the study period, there were a total of 620 initial hospitalizations for asthma in children who were 1 to 15 years of age. The hospitalization characteristics are described in Table 1. There were more male than female pediatric asthma admissions, consistent with previously published global and regional reports (37). Half of the admissions were for children aged 2 to 5 years. Admissions were most frequent in the month of April and in 2006.

Mineral Dust Levels and Other Air Pollutant Levels

Daily average mineral dust levels greater than 0.1 mg/m³ were recorded on 6 days in Toyama during the study period (Figure 1). Other air pollutant levels and meteorological observations during the study period are shown in Table 2. Correlations between mineral dust levels and air pollutants or meteorological variables are presented in Table E1 in the online supplement. There were no particularly strong correlations among them. In the local area during the study period, cedar was the major source of pollen, and cypress pollen was also observed in a lesser amount.

Relationship between Heavy Mineral Dust Exposure and Asthma Hospitalization

Figure 2 shows the crude ORs for the relationship between asthma hospitalizations and a heavy dust event on the day of the admission (lag 0) and on the previous cumulative 1 to 7 days (lag 0–1 to lag 0–7). A statistically significant association was shown between asthma hospitalization and a heavy dust event. The crude OR of the heavy dust event for hospitalization on the day was 1.88 (95% CI, 1.04–3.41; $P = 0.037$). The positive association was maintained regardless of the hazard period studied. The crude OR of heavy dust event on any day during the previous week (lag 0–6) was 1.83 (95% CI, 1.31–2.56; $P = 0.00043$).

A crude association between climatic observations and asthma hospitalization is shown in Table E2. Asthma hospitalization had apparent associations ($P < 0.1$) with average temperature, air pressure difference from the previous day, and humidity. We conducted a conditional logistic regression with hospitalization as the dependent variable and as independent variables, heavy dust event and climatic variables with apparent association for asthma hospitalization described above, and we obtained the climatically adjusted OR of 1.86 (95% CI, 1.32–2.62; $P = 0.00037$) for heavy dust event during the previous week.

Table 3 shows the OR and climatically adjusted OR for the heavy dust event (lag 0–6) taking into consideration one of the

TABLE 1. DEMOGRAPHICS OF HOSPITALIZATIONS

		No. (%)		No. (%)		
				Month		
Sex						
Male	367	(59)	Feb	175	(28)	
Female	253	(41)	Mar	199	(32)	
Total	620	(100)	Apr	246	(40)	
			Total	620	(100)	
Age, yr	Male	Female	All	Year		
1	133	52	185 (30)	2005	151 (24)	
2–5	178	132	310 (50)	2006	170 (27)	
6–12	52	65	117 (19)	2007	90 (14)	
13–15	4	4	8 (1)	2008	118 (19)	
Total	367	253	620 (100)	2009	91 (15)	
Mean	3.2	4.2	3.6	Total	620 (100)	
Median	2	3	2			

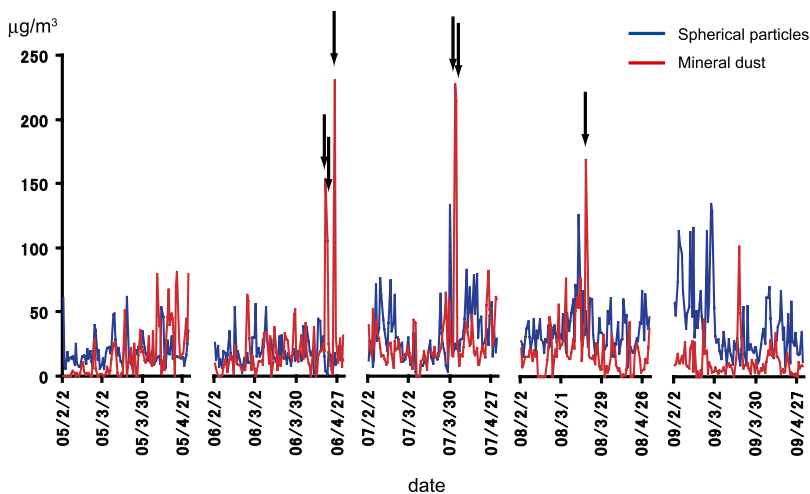


Figure 1. Daily levels of mineral dust particles (nonspherical particles) and nonmineral dust particles (spherical particles) during the study period. Red represents mineral dust level, and blue represents nonmineral dust level. Arrows represent the days with more than 0.1 mg/m³ mineral dust particle levels.

other pollutants (two-pollutant model). For each two-pollutant model, we examined various models with various lag structures from 0 to 0 to 6 days, and various cut-off levels, but the single-pollutant effect of heavy dust event was only slightly attenuated by other pollutants and remained significant after adjustment in all models. Table 3 shows the OR of heavy dust events for asthma hospitalization in the two-pollutant model using results from a model that showed the strongest association with asthma hospitalization for each other pollutant. The final model for obtaining the adjusted OR of heavy dust event for asthma hospitalization was determined to be the one with the climatic variables and other pollutant variables described above. The best fit OR of heavy dust event for asthma hospitalization was 1.71 (95% CI, 1.18–2.48; *P* = 0.0050).

We also conducted the same conditional logistic regression using a heavy dust event defined by suspended particulate matter as an exposure measurement, and a statistically significantly increased OR was shown using this method (Figure E4).

Figure 3 presents the crude OR of heavy dust event for asthma hospitalizations in each sex group and subgroup defined *a priori* (ages 1–5 yr, 6–12 yr, and 13–15 yr). The associations were particularly strong for boys. The risk for hospitalization on the day of heavy dust event was particularly high for boys (OR, 2.32; 95% CI, 1.10–4.87) and for elementary school ages (OR, 3.33; 95% CI, 1.02–10.92), whereas the risk for hospitalizations the following week seemed similar among the subgroups.

DISCUSSION

In this study, heavy mineral dust exposure was significantly associated with an increased risk of asthma hospitalization in children. Although we presumed in the study protocol that a high association would be observed during 3 days after mineral dust exposure, a high association was maintained even after 4 to 6 days after the exposure. This is, as far as we know, the first report that showed a clear association between mineral dust exposure and increased risk of asthma hospitalization. Previously reported efforts to investigate the association between desert dust exposure and asthma exacerbation included two studies in the Caribbean islands on Sahara dust, one in Australia on local dust, and one in Taiwan and three in Korea on Asian dust (15–20). All but the Korean studies showed subtle linkage, or did not show obvious associations with visits or admissions for asthma. The studies from Korea showed a significant decrease in peak flow for children and adults with asthma on Asian dust days, although a quantitative definition of Asian dust days was not presented in the reports, and effects of other air pollutants were not taken into consideration (17, 19, 20). In all these studies, there were some days that had particulate matter greater than 0.1 mg/m³ during the study periods. Possible explanations for the variety of results would be difference in exposure measurement, study design, and the general knowledge of people about the risk of dust, and local variation of size, chemical, mineralogical, and microbiological composition of dust particles.

TABLE 2. FREQUENCY DISTRIBUTION OF THE DAILY LEVELS FOR AIR POLLUTANTS AND METEOROLOGICAL OBSERVATIONS DURING THE STUDY PERIOD

	Days	Mean	SD	25th percentile	Med	75th percentile
Mineral dust particles, µg/m ³	400	21.27	25.66	7.82	15	25.08
Non-mineral dust particles, µg/m ³	446	28.05	20.55	4.6	22.87	35.77
Suspended particulate matter, µg/m ³	446	17.52	11.68	9	14	23
NO ₂ , ppm	446	12.61	5.85	8	12	17
SO ₂ , ppm	446	0.86	0.69	0	1	1
Ox, ppm	446	35.17	9.79	29	36	41
Pollen, /cm ²	400	31.8	76.7	0	3	21
Average temperature, °C	446	7.64	4.86	3.8	7.2	11.2
Temperature difference from the previous day, °C	446	0.15	2.9	-1.4	0.3	1.8
Temperature difference within the day, °C	446	9.1	3.7	6.2	8.8	1.2
Average air pressure, hPa	446	1,014.7	6.34	1,010.1	1,015.2	1,019.5
Air pressure difference from the previous day, hPa	446	-0.01	0.29	-3.90	0.55	4.20
Wind speed, m/s	446	6.7	2.6	4.6	6.2	8.4
Humidity, %	446	74.4	12.4	66	76	84

Definition of abbreviations: Ox = photochemical oxidants.

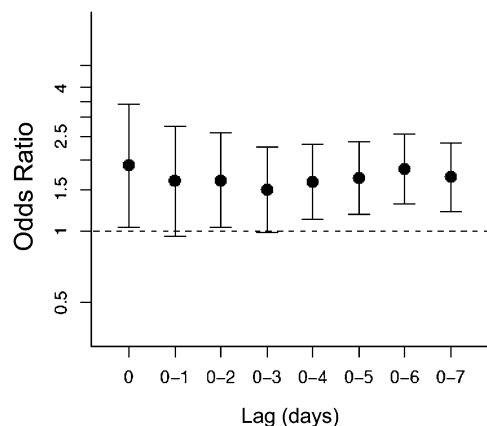


Figure 2. Crude odds ratios for the relationship between asthma hospitalizations and heavy mineral dust exposure (daily average level > 0.1 mg/m³) on the day of the admission (lag 0) or the previous 1 to 7 days (lag 0–1 to lag 0–7). Error bars represent 95% confidence intervals.

The size distribution of Asian dust particles being lifted into the air and carried to Japan had a peak of 4 μm , and ranged mostly from 0.5 to 10 μm in diameter. Particles this size can penetrate into the lower respiratory system and particles less than 2.5 μm in diameter can enter the gas-exchange region of the lung (2).

Asian dust contains silica and alumina as the main component (6). Quartz, an amorphous and crystalline silica, and aluminum have been reported to cause inflammatory responses with the release of inflammatory cytokines in the lungs of rats (7, 8, 38). Furthermore, Asian dust contains various chemical compounds, including sulfate (SO_4^{2-}) or nitrate (NO_3^-), derived from alkaline soil, which capture acidic gases, such as sulfur oxides (SO_2) and nitrogen oxides (NO_2), during its transportation (39). Hiyoshi and colleagues reported that Asian dust and ovalbumin administered into mice demonstrated an enhanced adjuvant effect of sand dust on ovalbumin-specific IgG1 production when administered together with sulfate (40).

Another important constituent is organics, such as bacteria, fungi, viruses, and other microorganisms. During Asian dust events in Taejeon, Korea, the bacterial cfu concentration increased on average 4.3 times over that observed under normal atmospheric conditions (41). Griffin reported that Asian dust included the known allergenic fungi (2). Dust-borne microorganisms in particular can directly impact the immune system of individuals sensitive to those agents, and lipopolysaccharide or β -glucan included in the microorganisms are known pattern-associated molecular patterns that activate dendritic cells to mount an immune response (42). A study by Ichinose and

colleagues demonstrated that inhalation of dust sand from Tengger Desert (China), which had higher amounts of β -glucan than dust from the Maowusu Desert (Inner Mongolia), caused greater eosinophil infiltration in the murine airway than did dust from the Maowusu Desert (43). Another study further showed that the heated desert sand, in which microbiological materials and sulfate were excluded by heating, had less effect on allergic lung inflammation (44). Accordingly, quartz, sulfate, and microbiological materials would be included in the pathogenicity of desert sand.

The measured quartz content in a major dust storm is very similar between Asian dust and African dust (60.95% in North Africa and 60.26% in China), and the concentrations of culturable bacteria and fungi and fungal spores in dust storms are greatly elevated relative to background in most investigated places (2, 45). Accordingly, it is quite possible that not only in East Asia but also in many other areas where windborne desert dust is observed, desert dust exposure greatly contributes to asthma admissions of children.

In our study, there were no heavy dust event days in 2005, yet 25% of the hospitalizations occurred in that year. There was a downward trend in hospitalizations from 2007 to 2009 compared with 2006, yet there were three heavy dust event days during this period. Although the desert dust exposure was shown as an independent risk for asthma hospitalization in this study, the contribution of heavy dust events to the total number of asthma hospitalization may be limited in Japan. This is reasonable considering that the heavy dust event occurred only on 6 days of the 446 days of the study period. The heavy dust events may be a more substantial contributor to the total number of asthma hospitalizations in some other parts of the world where dust events occur more frequently than in Japan.

Not only desert dust but also infections, irritants such as tobacco smoke, and other pollutants are also known to exacerbate asthma. In our study, other than heavy dust events, we found statistically significant associations with asthma hospitalization in gaseous NO_2 , gaseous SO_2 , gaseous Ox, nonmineral particles, and pollen in some cut-off levels in some lag periods. Similarly, we observed an increased OR when using particulate matter count for an exposure measurement, although this method does not clearly differentiate mineral dust from other particles. Thus, using LIDAR system, it would be possible to caution children with asthma to avoid exposure to heavy dust environments.

In the present study, the risk of mineral dust for asthma hospitalization was particularly high for boys (Figure 3A). Especially, the risk on the first day of the exposure was high for boys and for elementary school ages (6–12 yr old), whereas girls and infants (1–5 yr old) showed the increased risk later in the week (Figure 3B). The percentage of elementary school ages among all ages in boys (14%) was lower than in girls (26%). Accordingly the stronger association observed in boys

TABLE 3. ODDS RATIO OF HEAVY DUST EVENTS FOR ASTHMA HOSPITALIZATION ADJUSTED BY OTHER POLLUTANTS IN TWO-POLLUTANT MODEL

	Single-Pollutant Model	Two-pollutant Model Adjusted by				
		Non-M Dust	Pollen	NO_2	SO_2	Ox
Crude OR	1.83	1.79	2.04	1.70	1.80	1.63
95% CI	1.31–2.56	1.28–2.51	1.44–2.88	1.21–2.39	1.28–2.55	1.15–2.29
Climatically adjusted OR	1.86	1.83	2.19	1.76	1.86	1.66
95% CI	1.32–2.62	1.30–2.58	1.50–3.04	1.25–2.48	1.31–2.64	1.17–2.35

Definition of abbreviations: CI = confidence interval; Non-M dust = non-mineral dust particles; OR = odds ratio.

Non-mineral dust (on the day: lag 0 d) and pollen (on the previous day: lag 1 d) was treated as a five-level variable, NO_2 was treated as dichotomous (with cut-off value of 80th percentile and cumulative lag 0–5 d), and SO_2 (on the day: lag 0 d) was treated as a five-level nominal variable.

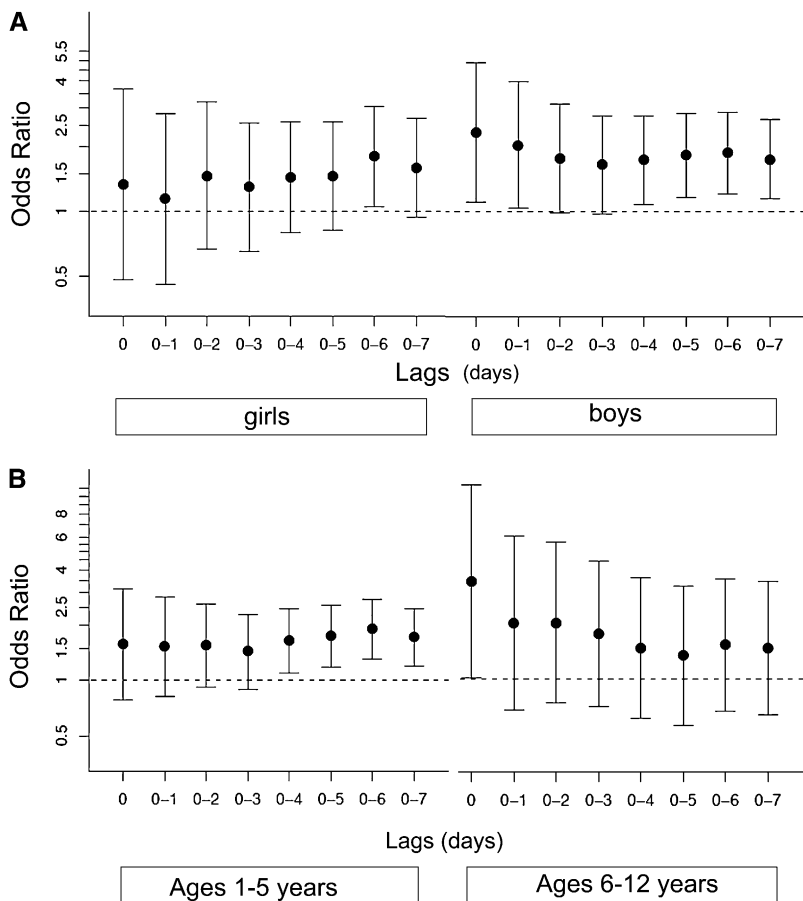


Figure 3. Crude odds ratios of heavy mineral dust exposure (daily average level > 0.1 mg/m³) for asthma hospitalizations on the day of the admission (lag 0) or the previous 1 to 7 days (lag 0–1 to lag 0–7) in each subgroup. (A) Girls (n = 253) and boys (n = 367). (B) Children aged 1 to 5 years (n = 495) and 6 to 12 years (n = 117). Error bars represent 95% confidence intervals.

cannot be explained by the distribution of ages. It is interesting that boys showed a higher OR in heavy dust events and girls showed a higher OR for other air pollutants, such as NO₂, SO₂, and Ox, in our study. The high risk on the first day observed in boys and in elementary school-aged children may have been influenced by any of several factors: length of exposure to outdoor air, exercise in outdoor air, or any immune mechanism that might make these groups more susceptible to mineral dust particles. Further investigations should be conducted to investigate if there are any differences in pathogenesis between the earlier asthma symptoms and later ones and to determine if there are especially susceptible subpopulations among patients with asthma, including adults.

Aerosolized particles have various effects on the atmospheric environment, including chemical and radiative effects, and also on the oceanic environment (2). It is not realistic to eliminate the dust events, which would negatively influence living creatures in various ways. However, we believe that we can at least minimize the detrimental effects of desert dust exposure by giving information to relevant people, so that susceptible children can protect themselves.

Our study has following limitations. First, the interpretation was limited by the occurrence of only six heavy dust event days in the study period. Second, the exposure data were not individually based but were based on measurements in the locality. Accordingly, it is possible that we underestimated the association because of miscategorizations. Third, because we chose hospitalizations for the outcome measure, the study results are generalized only to children who can be hospitalized. However, an observational study in Japan shows that 17.5% of pediatric patients with intermittent mild asthma also experience

hospitalization, and accordingly our study result will probably be applicable not only for patients with moderate to severe disease but also for patients with mild disease (46). Last, the associations we found were only for acute effects. Chronic effects should be further investigated.

As for the strength of our study, we used objective measures for both exposure and outcome, so that recall bias or presentation bias could be excluded. Additionally, we used the LIDAR nonspherical extinction coefficient for an exposure measure, so that we could focus on the effect of mineral dust particles.

In conclusion, this study suggested that heavy dust events were significantly associated with the increased risk of asthma admission for children with asthma. Physicians, patients, and the general public, including schools and preschools, should be adequately informed of the health implications of heavy desert dust exposure so that those at risk can minimize the deleterious effects.

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