Communication

Not peer-reviewed version

Ionic Components of Particulate Matter 2.5 May Affect Daily Prevalence of Skin Symptoms in Patients With Allergies

Hiroshi Odajima * , Hiroshi Matsuzaki , Yuko Akamine , Kaoru Kojima , Ayako Sugiyama , Yoko Murakami , Ayako Yoshino , Akinori Takami , Kazuichi Hayakawa , Akinori Hara , Hiroyuki Nakamura

Posted Date: 11 June 2024

doi: 10.20944/preprints202406.0427.v1

Keywords: air pollution; ionic component; PM2.5; skin symptoms; daily prevalence

Article

Ionic Components of Particulate Matter 2.5 May Affect Daily Prevalence of Skin Symptoms in Patients With Allergies

Hiroshi Odajima [1,*], Hiroshi Matsuzaki [1], Yuko Akamine [1], Kaoru Kojima [1], Akiko Sugiyama [2], Yoko Murakami [1,3], Ayako Yoshino [4], Akinori Takami [4], Kazuichi Hayakawa [5], Akinori Hara [6] and Hiroyuki Nakamira [6]

[1] Department of Pediatrics, National Hospital Organization Fukuoka National Hospital, Fukuoka 811-1394, Japan
[2] Department of Dermatology, National Hospital Organization Fukuoka National Hospital, Fukuoka 811-1394, Japan
[3] Department of Pediatrics, Hiroshima Red Cross Hospital & Atomic-bomb Survivors Hospital, Hiroshima 730-8619, Japan
[4] Regional Environment Conservation Division, National Institute for Environmental Studies, Tsukuba 305-8506, Japan
[5] Low-Level Radioactivity Laboratory, Institute of Nature and Environmental Technology, Kanazawa University, Nomi 923-1224, Japan
[6] Department of Hygiene and Public Health, Faculty of Medicine, Institute of Medical, Pharmaceutical and Health Sciences, Kanazawa University, Kanazawa 920-8640, Japan
* Correspondence: odajih@mqc.biglobe.ne.jp; Tel.: +81-92-565-5534

Featured Application: The present study found a significant relationship between the prevalence of skin symptoms and the concentration of particulate matter 2.5 and its ionic components. Few studies have evaluated this topic, so the present study may be an important stepping stone for future research.

Abstract: (1) Background : To date, no studies have epidemiologically examined whether the concentration of particulate matter (PM) 2.5 and its ionic components is related to the prevalence of skin symptoms. Therefore, this study aimed to clarify this association in patients with allergic diseases. (2) Methods: From February 1 to May 31, 2020, we evaluated the daily prevalence of skin symptoms in outpatients with allergic diseases being treated at Fukuoka Hospital, Fukuoka, Japan, and measured the concentration of PM2.5 and its ionic components. (3) Results: Univariate analysis showed a statistically significant association between skin symptoms and the concentration of PM2.5 and the ionic components SO_4^{2-}, NH_4^+, K^+, and Mg^{2+}, and multivariate analysis showed a statistically significant association between the daily prevalence of skin symptoms and the concentration of the ionic components SO_4^{2-} or Mg^{2+}. (4) Conclusions: Our findings indicate that the concentration of some PM2.5 ionic components may affect skin symptoms in patients with allergic diseases.

Keywords: air pollution; ionic component; PM2.5; skin symptoms; daily prevalence

1. Introduction

Air pollutants have been reported to affect allergic diseases, especially airway diseases [1]. Previously, we reported a relationship between airway symptoms and PM2.5 and its ionic components [2]. In clinical practice, patents with allergic diseases sometimes say that their skin symptoms are worse on days with a high concentration of air pollutants, but few studies have evaluated the effects of air pollution on the prevalence of the skin symptoms [3]. Furthermore, to our knowledge no study has examined whether the specific ionic components of PM2.5 affect skin symptoms.

 doi:10.20944/preprints202406.0427.v1

Because PM2.5 and its ionic components are associated with the prevalence of respiratory symptoms, we hypothesized that they may be associated also with the prevalence of skin symptoms in patients with allergic diseases. Therefore, this study aimed to clarify the association between the prevalence of skin symptoms and the concentration of PM2.5 and its ionic components in such patients.

2. Materials and Methods

2.1. Study Design

From February 1 to May 31, 2020, we performed a prospective cohort study to investigate the relationship between the daily prevalence of skin symptoms in patients with allergic diseases and the concentration of PM2.5 and its ionic components. The study was approved by the ethics committee of National Hospital Organization Fukuoka National Hospital (Fukuoka Hospital) and performed in accordance with the Declaration of Helsinki.

2.2. Participants and Study Procedures

We started recruiting outpatients with allergic diseases being treated at Fukuoka Hospital in Fukuoka, Japan, on December 1, 2019, and examined patients from February 1 to May 31, 2020. Participants gave written informed consent to participate in the study.

Participants were given a diary and asked to use it to record their daily skin symptoms and to answer the question "Did your skin get worse?" At each outpatient visit, a specialist nurse confirmed that participants were recording their symptoms correctly. At the end of the data collection period, we analyzed the daily prevalence of skin symptoms in those participants who recorded worsening symptoms, which were defined as answering "yes" to the question whether their skin had worsened.

2.3. Measurement of PM2.5 and Its Ionic Components

PM2.5 and its ionic components were measured daily using a large-capacity air sampler HV-RW-k1 (Shibata Scientific Co., Ltd., Tokyo) installed on the rooftop of Fukuoka Hospital. Sampler filters were changed daily at 10 a.m. by trained laboratory technicians and stored at -20 degrees Celsius. The filters were sent to the National Institute for Environmental Studies every two weeks to measure PM2.5 and its ionic components. Details of the PM2.5 measurement method and component analysis are provided in a separate report [4].

Fukuoka City has a population of 1.5 million people and is a city blessed with a relatively warm climate. Although there are no large-scale factories in the city, air pollution is brought in from China on the wind, mainly in early spring. Fukuoka Hospital is located in a corner of Ogi facing the sea. Because air blows from the ocean, through the city center, toward the mountains, and collects at the base of the mountains, air measurements at the hospital are likely to accurately reflect the air quality in the city as a whole.

The study period was set from February 1st to May 31st, because according to environmental health monitoring data, PM2.5 concentrations in this region were particularly high during this period [5]. China's air pollution has improved in major cities since 2013, and PM2.5 concentrations have decreased in Japan as well, but despite this, PM2.5 concentrations were high in Fukuoka from February to May. Transboundary pollution is thought to be one of the causes [5].

2.4. Statistical Analysis

Statistical analyzes were performed using R-3.6.1 (Foundation for Statistical Computing, Vienna, Austria). First, we performed univariate linear regression using Spearman's test to examine the relationship between PM2.5 or its ionic components and skin symptoms. Next, in order to ascertain which variables are independently associated with skin symptoms, a retrospective step was performed in which variables found to be significantly associated with skin symptoms in univariate analysis were excluded in order of their relevance. A multiple regression method was used.

Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 11 June 2024 doi:10.20944/preprints202406.0427.v1

Differences were considered statistically significant if a p value (two-tailed) less than 0.05 was obtained.

3. Results

From December 1, 2019, to January 31, 2020, we screened 78 patients, 72 of whom (male, n=38; female, n=34) were eligible for the study and agreed to participate from February 1 to May 31, 2020. Six of the 78 patients were excluded because they had no allergic disease.

The mean (SD) age was 10.6 (6.19) years (median, 9 years; range, 3-42 years). Participants had been diagnosed with the following allergic diseases: asthma, n=65; atopic dermatitis, n=29; allergic rhinitis, n=47; allergic conjunctivitis, n=4; and sinusitis, n=7.

3.1. PM2.5 and Its Ionic Components

The characteristics of PM2.5 and its ionic components are shown in Table 1.

Table 1. Concentrations of PM 2.5 and its ionic components measured from January 1 to April 31, 2020, at Fukuoka National Hospital, Fukuoka, Japan.

	Unit	Mean	SD	Median	Min	Max
PM2.5,	μg/m^3	14.9	7.75	13.5	2.86	45.55
Cl^-,	μg/m^3	0.04	0.07	0.015	0.00	0.356
NO_3^-,	μg/m^3	1.00	1.04	0.69	0.01	7.52
SO_4^{2-},	μg/m^3	2.90	2.01	2.27	0.59	12.31
Na^+,	μg/m^3	0.42	0.20	0.39	0.06	0.97
NH_4^+,	μg/m^3	0.75	0.82	0.52	0.02	5.89
K^+,	μg/m^3	0.27	0.13	0.26	0.08	0.90
Ca^{2+},	μg/m^3	0.01	0.01	0.01	0.004	0.059
Mg^{2+},	μg/m^3	0.34	0.28	0.29	0.09	2.88

3.2. Univariate Analysis

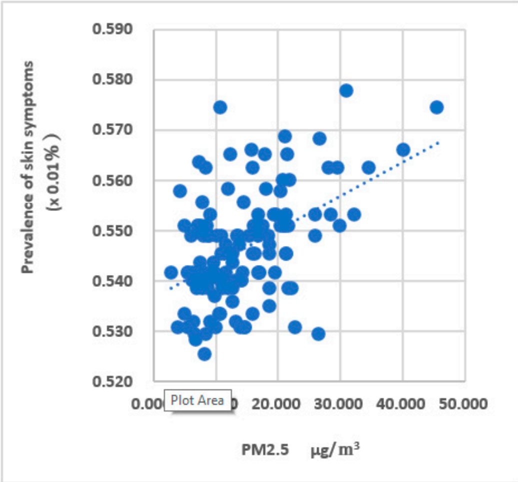
The results of the univariate analysis of the relationship between the prevalence of skin symptoms and the concentrations of PM2.5 and its ionic components are shown in Table 2 and Figure 1. We found a statistically significant relationship between the prevalence of daily skin symptoms and the concentration of PM2.5, SO_4^{2-}, NH_4^+, K^+, and Mg^{2+}.

Table 2. Relationship between the daily prevalence of skin symptoms and the concentration of PM2.5 and its ionic components.

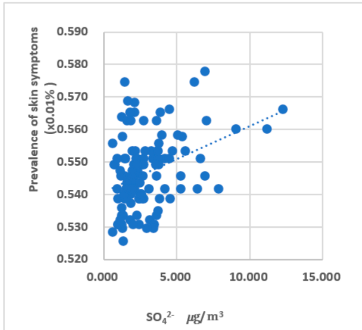
	rs	P
PM2.5	0.3905**	9.50E-06
Cl-	0.0343	0.7084
NO_3^-	0.1014	0.2684
SO_4^{2-}	0.3263**	0.0003
Na^+	0.1525	0.095
NH_4^+	0.3214**	0.0003
K^+	0.2292*	0.0115
Ca^{2+}	0.0651	0.4778
Mg^{2+}	0.3018**	0.0008

PM2.5, particulate matter 2.5; rs, Spearman's rank correlation coefficient; .*p<0.05, **p<0.01, Spearman's test, n=121, two tailed.

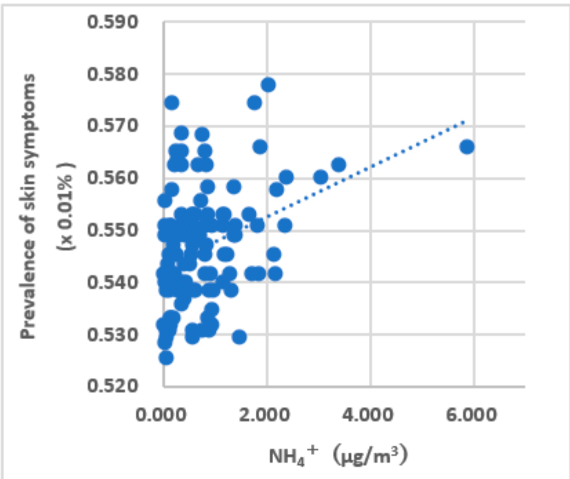
Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 11 June 2024 doi:10.20944/preprints202406.0427.v1



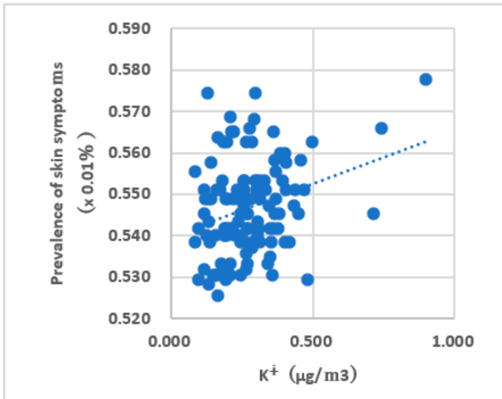
1-1



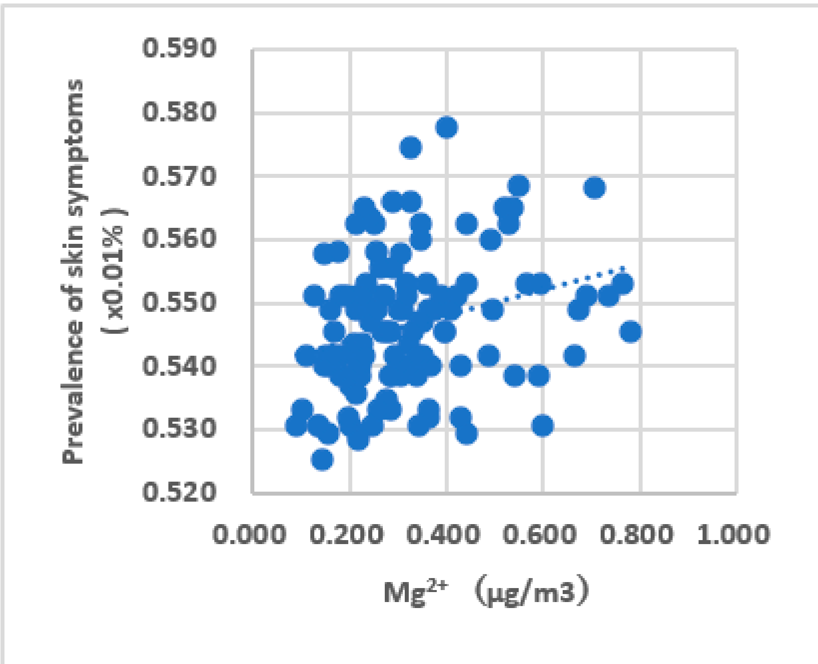
1-2



1-3



1-4



1-5

Figure 1. Scatter plot of the relationship between the prevalence of daily skin symptoms and the daily mean concentration of PM2.5 and its ionic components;.

The results shown in Parts 1-1 to 1-5 of the figure are as follows (all analyses were two-tailed):

Figure 1-1, The relationship between the prevalence of skin symptoms and PM2.5, rs=0.326, p=0.0003;

Figure 1-2, The relationship between the prevalence of skin symptoms and SO_4^{2-}, rs=0.391, p=9.5E-06;

Figure 1-3, The relationship between the prevalence of skin symptoms and NH_4^+, rs=0.321, p=0.00032;

Figure 1-4, The relationship between the prevalence of skin symptoms and K^+, rs=0.229, p=0.0115;

Figure 1-5; The relationship between the prevalence of skin symptoms and Mg^{2+}, rs=0.302, p=0.0008

PM2.5, particulate matter 2.5s

3.3. Multivariate Analysis

We performed a multivariate analysis of the items that were significant in the univariate analysis (Table 3). Neither PM2.5 nor any of the ionic components other than SO_4^{2-}, NH_4^+, K^+, and Mg^{2+} were included in the analysis because they were highly correlated with PM2.5 or other these ions (data not shown).

According to the results of the multivariate analysis, the prediction formula for the prevalence of skin symptoms was as follows:

prevalence of skin symptoms = 0.538 + 0.0017 x SO_4^{2-} + 0.00108xMg^{2+}.

The relationship between the values calculated by this formula and the measured values was statistically significant (n=121, p=0.00026, r=0.326; Figure 2).

Table 3. Results of multivariate analysis of the daily prevalence of skin symptoms and the concentrations of PM2.5 and the ionic components that showed a significant relationship in univariate analysis.

Residuals	**Min**	**1Q**	**Median**	**3Q**	**Max**
	-0.018841	-0.006410	-0.000877	0.005179	0.030017
x	Estimate	Std. error	t value		Pr(>ltl)
(Intercept)	0.5380167	0.0018365	292.956		<2e-16***
SO_4^{2-}	0.0016986	0.0004693	3.620		0.000436***
Mg^{2+}	0.0108384	0.0033995	3.188		0.001833**

1Q, first quartile; 3Q, third quartile; Residual Standard error: 0.01009 on 118 degrees of freedom; Multiple R-squared, 0.2005; adjusted R-squared, 0.1869; F-statistic, 14.79 on 2 and 118 DF; p value = 1.848e-06.

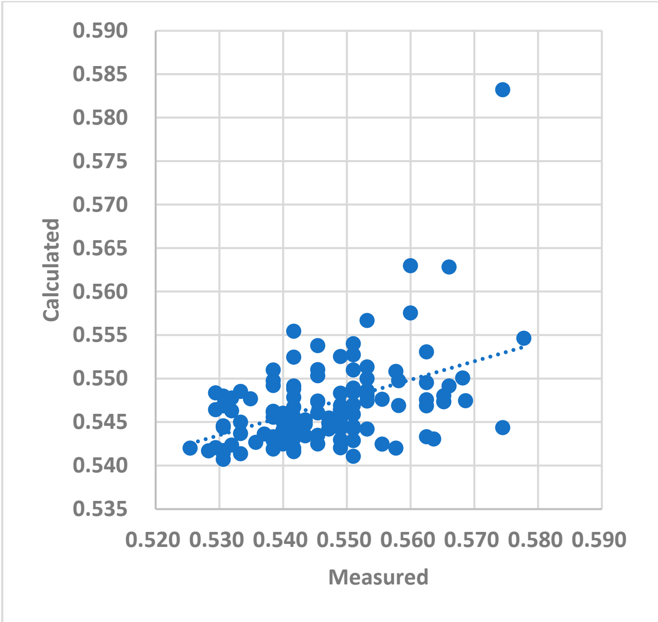


Figure 2. Correlation between the calculated and the recorded prevalence of daily skin symptoms.

The prevalence of skin symptoms was calculated by the following formula obtained from multivariate analysis: 0.538+0.0017 x SO_4^{2-} + 0.0108 x Mg^{2+}.

The relationship between skin symptoms calculated by this formula and daily skin symptoms recorded by patients was statistically significant (n=121, rs=0.326, p=0.00026 [two tailed]). These results indicate that daily skin symptoms depend to some extent on the concentration of SO_4^{2-} and Mg^{2+} in PM2.5.

4. Discussion

The study found an association between the prevalence of everyday skin symptoms in allergy patients and the overall concentration of PM2.5 and some of the its ionic components.

Allergic diseases have been on the rise over the past several decades, but asthma and atopic dermatitis have not increased in Japan over the past 10 to 20 years [6]. Although the reasons for the increase in allergic diseases are not clearly understood, we reported that the prevalence of childhood asthma may be related to the concentration of suspended particulate matter in the atmosphere, including PM2.5. [7]. We also reported that the ionic component concentration of PM2.5 was associated with nasal symptoms, respiratory symptoms, and maximum expiratory flow rate [3]. We sometimes hear from atopic dermatitis patients that their skin symptoms worsen on days when PM2.5 concentrations are high. However, no epidemiological investigation was conducted and it was ignored. Based on the above, we hypothesized that air pollution may be related to the symptoms of atopic dermatitis, and that daily changes in skin symptoms may be related to changes in the concentration of PM2.5 and its ionic components.

There are not many studies that have evaluated the relationship between skin symptoms and air pollutants, especially PM2.5, which has recently become a problem, and its ionic components, or the impact of these air pollutants on allergic diseases other than asthma. Several studies have been conducted on the effects of air pollutants on dermatitis. It has been reported that the prevalence of eczema increases when NO_2 concentrations are high and patients live near major roads (e.g. highways) [8–10]. A Korean study reported that exposure to PM2.5 increases eczema symptoms [11]. It has been reported that the prevalence of allergic diseases decreases by 0.39% when the NO_2 concentration decreases by 1 ppb, and by 0.14% when the suspended particulate matter concentration decreases by 1 mg/m3 [12].

 doi:10.20944/preprints202406.0427.v1

There are many reports on the relationship between air pollution and allergic diseases. However, many of these reports show comparisons of disease prevalence in areas or days with high or low concentrations of air pollutants.

This report investigated daily changes between diseases prevalence and air pollution concentrations. There are not many reports from this perspective. Research from this perspective requires a high degree of corporation from participants, but since the data come from the same person, it is unlikely that the background will change. This may be the strength of this study.

This study was conducted from February to April 2020. Markham et al. [13] compared pediatric emergency department visits from March to August 2020 during the COVID-19 pandemic with visits in the same months in the three years before the pandemic, and found that hospitalizations for organic diseases reported a significant decrease. It has been reported that the number of organic diseases that were common has decreased significantly. The results of this epidemiological study suggest that the prevalence of respiratory diseases may have been influenced by conditions associated with the pandemic, such as reduced traffic. This suggests that protective measures to prevent the spread of COVID-19, such as social distancing and wearing masks, may have been effective in reducing the spread of the virus and bacteria [12].

Previously, we also reported that mask wearing had a positive effect on symptoms in allergy patients [14]. Wearing a mask was effective in reducing the prevalence of respiratory symptoms and improving peak expiratory flow. However, even under such circumstances, the effects of PM2.5 and its ionic components on skin symptoms have been confirmed.

The COVID-19 pandemic is also impacting allergies through changes (or restrictions) to daily life, such as reduced attendance at school or work, fewer opportunities to meet others, and less travel. However, changes in daily life during the study period are unlikely to affect the effects of air pollutants on the skin.

A limitation of this study may be the lack of detailed diagnostic criteria for subtle symptom changes in skin lesions. However, this time, we conducted a broader investigation into the worsening of skin symptoms to test the hypothesis that PM2.5 and its ionic components may influence the overall skin symptoms of allergic patients. This study revealed that PM2.5 and its ionic components are likely to affect skin symptoms. Furthermore, we found that this effect has at least a short-term effect (acute effect). (See also Figure in Graphical Abstract).

Another limitation of this study was that this study was conducted in limited area. However, we got the positive relationship between the skin symptoms and the concentration of some air pollutants. Although there may be a problem with universality in a limited area, it is considered to be advantageous for looking at the effects over a certain period of time. However, future studies in many regions are required.

Yet another limitation of this study is the small number of participants. However, our study had the above-mentioned strengths and statistically significant results existed. In fact, we hope that the next study will overcome the weaknesses of this study.

We have already reported that the prevalence of AD was on the decline in 2002 [15], and a survey of first-grade elementary school students in Himeji City, Japan also showed a clear decrease [16]. Yura et al, according to a large-scale survey of first-year elementary school students, the increase of AD has stopped since the 1990s, and there are no longer any differences between grades [17]. As mentioned above, epidemiological surveys in Japan have shown that the prevalence of AD is on the decline. This trend may be explained by the decreasing trend in air pollution, especially PM2.5 and its ion concentrations in Japan. However, we believe that the prevalence of AD is not solely determined by air pollution. However, the results of this study show that the concentration of PM2.5 and some of its ionic components have a statistically significant positive correlation with the prevalence of AD. This suggests that PM2.5 and its ionic components may be one of the important factors in AD. As AD worsens, the incidence of symptoms is increasing. Furthermore, regarding the daily prevalence of AD worsening, a significant correlation was observed between the measured value and the calculated value using the formula obtained from the multivariate test. This indicates that the symptoms of AD's disease worsen as the concentration of PM2.5 and its ionic components increases, and repeated symptoms are known to be an exacerbating factor. This is estimated to have increased the prevalence of the condition. It is possible that the recent decline in the prevalence of AD may be related to the decline in PM2.5 concentration.

Our findings warrant future studies using more stringent evaluation criteria and including a more detailed analysis of the relationship between the proportion of all ionic components of PM2.5 and skin symptoms. Indicated. Furthermore, if future research reveals the effects of ionic components on the skin, it will become clear whether the effects are simply physical stimulation or chemical effects, which may lead to the prevention of skin symptoms. It is believed that great effects can be expected not only in the cause but also in the treatment.

5. Conclusions

We studied the influence of PM2.5 and its ionic components on the prevalence of daily skin symptoms in outpatients with allergic diseases. Univariate analysis showed a statistically significant short-term association between skin symptoms and concentrations of PM2.5 and its ionic components. As a result of multivariate analysis, a significant relationship was observed between skin symptoms and NH_4^+ and Mg^{2+}, and it was considered important to examine the relationship between skin symptoms and ionic components.

Author Contributions: Author contributions: Conceptualization, H.O and H.M.; methodology, H.O., H.M., Y.A., K.K., A.S., Y.M., A.Y., A.T., K.H. and H. N.; software, H.O. and H.M.; validation, H.O., A.Y. and A.T.; formal analysis, H.O., H.M., A.Y. and A.T.; investigation, H.O., H.M., K.K., A.S., A.Y., and A.T.; resources, H.O., H.M., Y.A., Y.M., A.S.; data curation, H.O., H.M., Y.A., A.S., K.K. and Y.M.; writing original draft preparation, H.O.; writing-review and editing, H.O., H.M., Y.A., K.K., A.S., Y.M., A.Y., A.T., K.H., A.H., and H.N.; visualization. H.O. and H.M.; supervision, H.O., project administration, H.N., K.H., A.T. and H.O.; funding acquisition, H.N., K.H., A.T. and H.O.; All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Environment Research and Technology Development Fund (JPMEERF20195051, JPMEERF20202003, JPMEERF20225M02) of the Environmental Restoriction and Conservation Agency of Japan.

Institutional Review Board Statement : The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of National Hospital Organization Fukuoka National Hospital (protocol code F31-03 and date of approval 15 May 2019).

Informed Consent Statement: Informed consent was obtained from all participants involved in the study. Written informed consent was obtained from the patients to publish this paper.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available because of privacy concerns.

Acknowledgments: We thank the study participants for recording their symptoms every day, the laboratory technologist for regularly checking and examining the air sampler, and Misako Yamamoto for preparing the analysis of the diary symptoms.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data;in the writing of the manuscript; or in the decision to publish the results.

References

1. Koenig IQ, Air pollution and asthma, J Allergy Clinic Immunol 1997,104:7167-122.
2. Odajima H, Matsuzaki H, Akamine Y, Kojima K, Murakami Y, Yoshino A, Takami A, Hayakawa K, Hara A, Nakamura H, The ionic component of PM2.5 may be associated with respiratory symptoms and peak expiratory flow rate, Appl. Sci. 2022, 12(19), 10082; https://doi.org/10.3390/app121910082]
3. Fadadu RP, Abuabara K, Balmes JR, Hanifin JM, Wei ML, Air pollution and Atopic dermatitis, from Molecular Mechanisms to Population level Evidence: A Review Int J Environ Res Public Health, 2023; 20: 2526, doi: 10,33901.
4. Ayako Yoshino A, Takami A, Shimizu A, Sato A, Hayakawa K, Tang N, Kim-Oanh Pham KO, Hara A, Nakamura H, Odajima H, Analysis of Chemical Components of Fine Particulate Matter Observed at

Fukuoka, Japan, in Spring 2020 and Their Transport Paths, Appl. Sci. 2022, 12(22), 11400; https://doi.org/10.3390/app122211400.
5. Ministry of the Environment, Environmental Health Department, Insurance Affairs Office. Environmental Health Surveillance Survey Report on Air Pollution, Separate Volume: Fine Particulate Matter (PM2.5), 2020 9 Environmental Health Department: Tokyo, Japan 2020; pp.7,24.
6. Kurosaka F, Shimizu K, Oka K et al. The prevalence of allergic disease -The prevalence of atopic disease is decreasing from the surveillance in Himeji-. Jan J Pediatric Allergy Clinical Immunology 2014; 28:50-57(in Japanese).
7. Odajima H, Kawano T, Wakatsuki M, Akamine Y, Okabe K, Oki T, Matsuzaki H, Murakami Y, Iwata M, Taba N, et al. Annual changes in the prevalence of asthma may be related to air pollution in Fukuoka: 29 years of observation. ERS Open Res. 2020,6,00166-2020.
8. Morgenstern V, Zutavern A, Crys J, Brorkow I, Koletzko S, Kramer U, et al, GINI Study Group. Atopic diseases, allergic sensitization, and exposure to traffic related air pollution in children. A m J Respire Crit Care Med. 2008; 177:1331-7.
9. Patella V, Florio G, Palmieri M, Bousquet J, Tonacci A, Giuliano A, Gangemi S. Atopic dermatitis severity during exposure to air pollutants and weather changes with an Artificial Neural Network (ANN) analysis. Pediatr Allergy Immunol. 2020 Now; 31(8):938-945. Doi: 10.111/pai.13314. Epub 2020 Aug 10,RP
10. Abuabara K, Balmes JR, Hanifin JM, Wei ML. Short-term effects of weather and air pollution on atopic dermatitis symptoms in children: A panel study in Korea Kim Y-M, Kim J, Han Y, Jeon B-H, Chong H-K, Ahn K, PMID: 28384276 PMCID: PMC5383262 DOI: 10.1371/journal.pone.0.175229 Review Int J Environ Res Public Health. 2023 Jan 31;20(3):2526.doi: 10.3390/ijerph20032526.
11. Kim J, Kim EH. Oh I, Jung K, Han Y. Cheong HK, et al, Symptoms of atopic dermatitis are influenced by outdoor air pollution. J Allergy Clin Immunol 2013; 132: 495-8.)
12. Hasunuma H, Ishimaru Y, Yoda Y, Shima M. Decline of ambient air pollution levels due to measures to control automobile emissions and effects on the prevalence of respiratory and allergic disorders among children in Japan. Environ Res. 2014; 131: 111-8.
13. Markham JL, Richardson T, Deporre A, Teufel Rjii, Hersh Al, Feegler EW et al. Inpatient Use and Outcomes at children's Hospital during the early Covid-19 pandemic. Pediatrics 2021;147: e2020044735.
14. Odajima H, Matsuzaki H, Akamine Y, Kojima K, Murakami Y, Yoshino A et al. Efficacy of Mask Wearing in Preventing the deleterious Health Effect of the Ionic Components of PM2.5-Possibility Seen in Allergic Patients. Appl. Sci. 2022, 12(21), 11185; https://doi.org/10.3390/app122111185.
15. A study group on the prevalence of allergic diseases, The West Japan Study Group of Allergy in Chldren, On the prevalence of allergic diseases in school children -Comparison between the Studies in 1992 and 2002 with the Same Methods and Same Districts- Jan J Pediatr Allergy Clin Immunol、2003. 17：255-68.
16. Kurosaka F, Nakatani Y, Terata T et al. Current cat ownership may be associated with the lower prevalence of atopic dermatitis, allergic rhinitis, and Japanese cedar pollinosis in schoolchildren in Himeji, Japan. Pediatr Allergy Immunol 2006; 15:22-28
17. A Yura , T Shimizu, Trends in the prevalence of atopic dermatitis in school children. longitudinal study in Osaka Prefecture, Japan, from 1985 to 1997. Br J Dermatol 2001;145(6):966-73. 2001.