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The effects of particulate matter on atopic dermatitis symptoms are influenced by weather type: Application of spatial synoptic classification (SSC)

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ABSTRACT

The effects of weather and air pollution on atopic dermatitis (AD) flares have not been well investigated. To investigate the effects of particulate matter (PM) on AD symptoms by weather type, a total of 125 young children (76 boys and 49 girls) under 6 years of age with AD living in Seoul, Korea, were enrolled as a panel and followed for 17 months between August 2013 and December 2014. AD symptoms were recorded on a daily basis, including itching, sleep disturbance, erythema, dry skin, oozing, and edema. Daily weather was classified into 7 categories according to spatial synoptic classification (SSC). Personal exposure to PM with an aerodynamic diameter less than 2.5 and 10 µm (PM_{2.5} and PM₁₀, respectively) in each individual was estimated with time-weighted average concentrations considering outdoor and indoor levels of PMs and time to spend outdoors or indoors in a day. Generalized linear mixed models were used to analyze the effects of PM_{2.5} and PM₁₀ on AD symptoms, controlling for ambient temperature, humidity, age, sex, SCORAD (SCORing of AD) at enrollment, fever, day of week, and topical corticosteroid use. A total of 20,168 person-days of symptom records were collected. The presence of AD symptoms was higher on dry polar (DP) days (45.4%, $P < .0001$) than on moist tropical (MT) days (37.7%, $P < .0001$). Overall, the risk of AD symptoms significantly increased with increased exposure to PM_{2.5} and PM₁₀. Among the 7 weather types, the risks of AD symptoms caused by PM_{2.5} and PM₁₀ exposure were significantly increased on dry moderate (DM) days, while not significant on the other weather types. In addition, lagged effect of PM_{2.5} up to 4 days was found on DM days. In conclusion, dry moderate weather type, particulate matters, and their modifying effects should be simultaneously considered for proper management of AD.

1. Introduction

Air pollutants such as particulate matter (PM), nitrogen dioxide (NO₂), and ozone (O₃) are associated with allergic disease or allergic sensitization (Ahn, 2014; Baldacci et al., 2015; Eberlein-König et al., 1998; Jacquemin et al., 2015; Kim et al., 2017a; Lin et al., 2002; Matsui, 2014; Penard-Morand et al., 2010). Among them, exposure to ambient PMs is a growing concern for public health, particularly in Asia due to large amount of anthropogenic emissions from East Asia including China (Saikawa et al., 2017).

Atopic dermatitis (AD) is a chronically relapsing inflammatory skin disease, commonly occurring in children. According to a population-based study using data from the 2008–2011 Korea National Health and Nutrition Examination Survey (KNHANES), 13.50% of Korean children aged 18 years or younger have been diagnosed with AD (Lee et al., 2016a). Phases One and Three of the International Study of Asthma and Allergies in Childhood revealed that AD symptom prevalence increased in 6–7 year-old and 12–13 year-old Korean children between 2000 and 2010 (Ahn, 2016; Oh et al., 2004; Park et al., 2016). This result is consistent with the observation that AD prevalence is increasing in

Abbreviations: AhR, aryl hydrocarbon receptor; AD, atopic dermatitis; AQMS, air quality monitoring system; DEP, diesel exhaust particle; DOW, day of week; DM, dry moderate; DP, dry polar; DT, dry tropical; GAMM, generalized additive mixed model; GLMM, generalized linear mixed model; IOR, indoor-to-outdoor pollutant concentration ratio; MM, moist moderate; MP, moist polar; MT, moist tropical; NO₂, nitrogen dioxide; O₃, ozone; PM, particulate matter; PM_{2.5}, particulate matter with a diameter less than 2.5 µm; PM₁₀, particulate matter with a diameter less than 10 µm; RH, relative humidity; SCORAD, SCORing atopic dermatitis; Tr, transitional; TWA, time-weighted averages

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many developing countries (Williams et al., 2008). Although the exact pathogenesis of AD remains to be investigated, birth cohort studies have revealed that air pollutants such as tobacco smoke, PM, NO₂ or phthalate might contribute to AD development (Deng et al., 2016; Herberth et al., 2014; Hidaka et al., 2017; Jedrychowski et al., 2011; Just et al., 2012; Lu et al., 2017; Wang et al., 2013; Wang et al., 2010). Air pollutants also act as an aggravating factor in pre-existing AD. Increased exposure to PM₁₀ has been strongly associated with increased AD flares (Kim et al., 2013; Kim et al., 2017a; Kim et al., 2017b). Exposure to airborne formaldehyde increased transepidermal water loss and skin pH in children with AD (Kim et al., 2016).

Climate is another environmental factor that should be considered in the management of AD. Poorly controlled eczema and AD prevalence have been associated with weather (Byremo et al., 2006; Lee et al., 2008; Silverberg et al., 2013; Suarez-Varela et al., 2008; Weiland et al., 2004). However, most prior studies have estimated the independent effects of air pollution and weather on AD and have not incorporated interactions of these variables (Vanos et al., 2013). Indeed, atmospheric chemistry is complex within urban areas, with ambient air pollutant levels modulated by meteorological factors such as humidity, temperature, wind speed, and wave radiation (Portier et al., 2010; Vanos et al., 2013). Elevated ambient temperature is associated with mortality, with ozone acting as an effect modifier of the association (Basu, 2009). Thus, both air pollution and weather should be evaluated and monitored for the treatment of AD, because avoiding aggravating factors is the basic management principle of AD (Bieber, 2008; Boguniewicz and Leung, 2013).

Spatial synoptic classification (SSC), also called air-mass-based classification, has been used to study human health outcomes, age-related effects, and air pollution variations under various synoptic weather types (Greene et al., 1999; Hanna et al., 2011; Hebborn and Cakmak, 2015; Rainham et al., 2005). The idea behind the air-mass-based approach is that human physiology responds to the whole ‘umbrella of air’ instead of single weather elements (Kysely et al., 2010). In this regard, the air-mass-based approach can be a useful tool for AD research, in which skin symptoms are affected by weather as well as air pollution such as PMs (Kim et al., 2017a).

This study aimed to investigate how the effects of PM exposures on AD symptoms are influenced by weather types. For this goal, we first built a panel of AD children, gathered daily AD symptoms, and then, assessed personal exposure to PMs on a daily basis. Finally, we estimated the risk of PMs on AD symptoms by SSC weather type.

2. Material and methods

2.1. Study population and AD symptoms

A total of 125 children with AD (76 boys and 49 girls under six years) living in Seoul, Korea, were enrolled as a panel. They were followed for 17 months between September 2013 and December 2014. AD diagnosis was determined according to the Hanifin and Rajka criteria (Hanifin and Rajka, 1980). The severity of AD was assessed by the SCORing Atopic Dermatitis (SCORAD) index (European Task Force on Atopic Dermatitis, 1993). Total IgE and specific IgE against common food and inhalant allergens in peripheral blood were measured using ImmunoCAP (ThermoFisher Scientific, Waltham, MA), and sensitization was defined when the level was over 0.35 kU/L. Common allergens included egg white, cow's milk, soybean, wheat, peanut, *Dermatophagoides pteronyssinus*, and *D. farinae*.

Parents or guardians were instructed to record AD symptoms on a daily basis using a symptom diary designed to easily measure AD symptom severity by describing the extent of subjective symptoms (itching and sleep disturbance) and the degree of objective signs (erythema, dryness, oozing, and edema) on a scale of 0–4. The presence of AD symptoms was defined when each subjective symptom score was 2 or greater and accompanied by at least two objective signs. All patients

took a daily bath or shower and applied moisturizers frequently during the study period. Intermittent use of low potency topical corticosteroids and oral antihistamines was allowed when needed. Those who were allergic to an inhalant or food allergen avoided exposure to the offending allergens.

Written informed consent was obtained from the parent or guardian of each participating child. The study protocols were reviewed and approved by the Institutional Review Board (IRB) at Samsung Medical Center (IRB No. 2013–05–009).

2.2. Synoptic weather types

Information on the daily synoptic weather types for Seoul was accessed from the spatial synoptic classification (SSC) website (<http://sheridan.geog.kent.edu/ssc.html>). The SSC system is a semi-automated statistical approach designed to group daily weather conditions under one of several distinct categories (Sheridan, 2002). The SSC is determined by surface-based observations at individual monitoring stations based on air temperature, dew point temperature, sea level pressure, cloud cover, and wind velocity measurements at four equally spaced times throughout the day (0300, 0900, 1500, 2100 h). Sliding seed days are used to represent the expected and observed meteorological conditions at each location throughout the year for each weather type. Each seed day was quantified by the typical meteorological variables for the location and time of year, with ranges specified to indicate threshold values for each weather type. The weather types include dry moderate (DM), dry polar (DP), dry tropical (DT), moist moderate (MM), moist polar (MP), and moist tropical (MT), plus a transitional (Tr) category representing a shift from one weather type to another. A description of each weather type can be found in Sheridan (2002) and Rainham et al. (2005). The characteristics of each weather type was seen in Supplementary Table S1.

Air masses usually take on the characteristics of the underlying surface in their source region. On moving from its source region, an air-mass can be subject to warming, cooling, and the addition or removal of water. However, when an air-mass crosses the same area at a similar speed and time of year, its characteristics will be similar, allowing days with similar weather characteristics to be classified as the same air-mass type (Davis and Kalkstein, 1990).

2.3. Exposure assessment to particulate matters

Exposure to PMs with an aerodynamic diameter less than 2.5 and 10 µm (PM_{2.5} and PM₁₀, respectively) by each individual was estimated with time-weighted average (TWA) concentrations. We estimated the TWA concentrations based on outdoor and indoor levels of PMs and time to spend each outdoor or indoor (time-activity) of each individual. The process to estimate personal exposure to PM_{2.5} and PM₁₀ is as below.

2.3.1. Outdoor levels of PM₁₀ and PM_{2.5}

We obtained hourly PM₁₀ and PM_{2.5} data from 25 air quality monitoring system (AQMS) stations operated by the Seoul Metropolitan Government Research Institute of Public Health and Environment. We then calculated 24 h-average levels of PM₁₀ and PM_{2.5} for each AQMS station. Based on the administrative district where the patient resided, we matched the daily AD symptom data of each patient with the 24 h-average levels of PM₁₀ and PM_{2.5} to determine outdoor PM exposure.

2.3.2. Indoor/outdoor ratio (IOR)

To estimate indoor PM levels for the patients, IORs for PM₁₀ and PM_{2.5} were calculated based on a previous study conducted in Seoul (Lee et al., 2016b). Sixteen parents of AD children measured indoor and outdoor PM levels at their homes for 48 h. Information regarding indoor activities, housing and residents, and meteorological parameters from the Korean Meteorological Administration (KMA) were also collected as

predictor candidates. Correlation analysis and multi-step multivariate linear regression analysis were performed to develop a model for the IORs of PM_{2.5} and PM₁₀.

The formulae for IORs are as follows;

$$\text{IOR for PM}_{10} = 0.621 + 0.0136 \cdot T - 0.00721 \cdot \text{FL} \quad (1)$$

$$\text{IOR for PM}_{2.5} = 0.629 + 0.0102 \cdot T - 0.00654 \cdot \text{FL} \quad (2)$$

where T and FL are the ambient temperature and the floor level, respectively.

Coefficients of determination (R^2) of the regression models for PM_{2.5} and PM₁₀ were 0.65 and 0.66, respectively (Lee et al., 2016b). Based on Eqs. (1) and (2), the indoor levels of PM_{2.5} and PM₁₀ concentrations for each patient's house were estimated by multiplying the predicted IOR by the outdoor concentrations obtained from the AQMS stations.

2.3.3. Time-activity

Time-activity indicates time to spend and location (indoor or outdoor in this case) profile. To obtain the time spent indoors and outdoors for each participant, a time-activity diary was given to patients. The time-activity diary consists of time activity profile every 30 min. Diaries were filled in for weekdays, Saturdays, and Sundays, and were used as representative patterns for the study period. Based on the time-location data, the times spent indoors and outdoors were calculated for each individual. Daily TWAs of PM_{2.5} and PM₁₀ exposure were calculated for each patient from the time spent indoors, indoor concentrations of PM_{2.5} and PM₁₀ driven by the IOR, and ambient PM concentrations.

2.4. Statistical analysis

Considering the repeated assessment of AD symptoms, we adopted a generalized linear mixed model (GLMM) with binomially distributed errors to estimate the associations of personal exposure to PMs and parent-reported AD symptoms. Confounding factors of temperature, relative humidity (RH), age, sex, SCORAD at enrollment, presence of fever as a proxy for infection, use of topical corticosteroids, and day of week (DOW) were controlled when fitting the GLMM. In the overall data, season was also adjusted. We treated PMs as a fixed effect and each participant as a random effect in the model. The effects of PMs on AD symptoms were estimated according to increases in PMs by inter-quartile range (IQR) of whole data (12.7 µg/m³ for PM_{2.5} and 24.0 µg/m³ for PM₁₀).

We also used penalized regression curves of a generalized additive mixed model (GAMM) to examine the linearity of the relationships of PMs with AD symptoms after adjustment for the same confounding factors as in the GLMM.

To consider the delayed effect of air pollutants on the presence of skin symptoms, the effects of lagged predictor variables for PM_{2.5} and PM₁₀ were analyzed, including unlagged (lag 0) and lagged by 1, 2, 3, 4, and 5 days (lag 1, lag 2, lag 3, lag 4, and lag 5, respectively).

All procedures were conducted using R version 3.0.0 (The Comprehensive R Archive Network: <http://cran.r-project.org>) using the “lme4” package (version 3.1.2) for GLMM and the “mgcv” package (version 1.8.3) for GAMM model fitting. All tests were two-sided, and an alpha level less than 0.05 was considered significant.

3. Results

Among 125 children enrolled in the panel, a dataset was made including 114 children who had reported their symptoms and had all information needed in the analyses. A total of 20,168 person-days of data were collected from 114 children during the study period (Table 1). Among them, 13,064 person-days (64.8%) were from boys and 7,104 person-days (35.2%) were from girls. There were no significant differences in age, height, weight, total IgE, and SCORAD at enrollment between boys and girls. However, boys (50.7%) used topical

Table 1

Characteristics of the study population during the study period.

	Total	Boys	Girls	P-value*
No. of subjects	125	76	49	
Age (years)	1.9 ± 1.6	1.8 ± 1.6	2.1 ± 1.7	0.4108
Height (cm)	83.5 ± 14.8	83.4 ± 14.8	83.8 ± 15.1	0.8773
Weight (kg)	11.8 ± 4.1	12.0 ± 4.4	11.5 ± 3.7	0.4588
Total IgE (kU/L)	353.1 ± 743.7	337.3 ± 665.6	378.9 ± 863.8	0.7875
SCORAD at enrollment	28.6 ± 11.1	28.7 ± 11.6	28.3 ± 10.3	0.8106
Presence of fever (%)	2.9	3.0	2.6	0.0567
Use of TCS (%)	47.1	50.7	40.5	< .0001
No. of records (person-days)	20,168	13,064	7,104	

Data are expressed as mean ± standard deviation. *Each variable was compared between boys and girls using a *t*-test. The Mann-Whitney *U* tests were used to analyze the differences in the presence of fever and the use of TCS. SCORAD, SCORing of Atopic Dermatitis. TCS, topical corticosteroid.

corticosteroids more than girls (40.5%) ($P < .0001$).

During the study period, from August 1, 2013 to December 31, 2014 (518 days), the levels of ambient PM_{2.5} and PM₁₀ were, on average, 24.6 µg/m³ [standard deviation (SD): 14.2] and 46.0 µg/m³ (SD: 26.9), respectively (Supplementary Table S2). Average ambient temperature and RH were 13.3°C (SD: 9.2) and 62.6% (SD: 14.4), respectively. The most frequent weather type was DM (198 days, 38.2%), followed by DP (92 days, 17.8%). Days of DT, MM, MP, MT, and Tr numbered 33 (6.4%), 65 (12.5%), 12(2.3%), 78 (15.1%), and 40 (7.7%), respectively. Similarly, the largest amount of data was recorded on DM days, accounting for 8,418 (41.7%) out of 20,168 person-days in total.

Time spent indoors for children with AD was approximately 22.8 h a day (SD: 0.9 h) during weekdays and 22.1 h (SD: 1.8 h) during weekends, indicating that children with AD stayed indoors for 93.5% of the day, on average (Supplementary Table S3). IORs for PM_{2.5} and PM₁₀ in our patients were 0.71 (SD: 0.10) and 0.76 (SD: 0.08), respectively (Supplementary Table S4). As shown in Table 2, the TWAs of PM_{2.5} and PM₁₀ varied by weather type. Among the seven weather types, the TWAs of PM_{2.5} and PM₁₀ were highest on DT days for both PM_{2.5} (27.9 µg/m³) and PM₁₀ (65.2 µg/m³) and lowest on DP days for PM_{2.5} (12.7 µg/m³) and on MP days for PM₁₀ (21.9 µg/m³).

The presence of AD symptoms was 42.1% in total. Among the seven weather types, the presence of AD symptoms was found most frequently on DP days (45.4%, $P = .0004$) and least frequently on MT days (37.7%, $P < .0001$).

Fig. 1 addresses the relationships between PM exposure and AD symptoms in the GAMM with adjustment for ambient temperature, ambient RH, age, sex, SCORAD at enrollment, presence of fever, use of topical corticosteroids, and DOW. Overall, AD symptoms appeared to increase linearly as PM exposure increased in all weather types except DP and transitional days for PM₁₀.

Fig. 2 shows the effects of daily PM exposure on AD symptoms by weather type. (All OR values are seen in Supplementary Table S5). Overall, the risk of AD symptoms significantly increased with increased exposure to PM_{2.5} [adjusted odds ratio (aOR) = 1.078; 95% confidence interval (CI), 1.018–1.141] and PM₁₀ (aOR = 1.063; 95% CI, 1.006–1.123) by IQR (12.7 µg/m³ for PM_{2.5} and 24.0 µg/m³ for PM₁₀). Among the seven weather types, the risk of AD symptoms due to PM_{2.5} was significantly increased on DM days (aOR = 1.165; 95% CI, 1.068–1.270). The risk of AD symptoms due to PM₁₀ was also significantly increased on DM days (aOR = 1.095; 95% CI, 1.001–1.198). The adverse PM effects on AD symptoms were strong on humid cold days (MP) for both PM_{2.5} (aOR = 1.407; 95% CI, 0.618–3.206) and PM₁₀ (aOR = 1.701; 95% CI, 0.590–4.903), although they were not statistically significant.

Table 2Time-weighted averages of PM_{2.5} and PM₁₀ exposure, temperature, relative humidity, and presence of AD symptoms according to weather type.

Weather type	No. of records (person-day) (%)	PM _{2.5} ($\mu\text{g}/\text{m}^3$)	PM ₁₀ ($\mu\text{g}/\text{m}^3$)	Temperature ($^{\circ}\text{C}$)	Relative humidity (%)	Presence of symptom	
						(%)	P-value*
Overall	20,168 (100.0)	17.8 $\pm$ 10.2	34.4 $\pm$ 20.8	13.3 $\pm$ 9.2	62.6 $\pm$ 14.4	42.1	–
DM	8418 (41.7)	18.8 $\pm$ 10.4	36 $\pm$ 18.6	14.4 $\pm$ 7.3	60.6 $\pm$ 8.9	41.9	0.8004
DP	3,467 (17.2)	12.7 $\pm$ 7.7	24.9 $\pm$ 10.2	1.4 $\pm$ 5.5	47.8 $\pm$ 9.5	45.4	0.0004
DT	1,101 (5.5)	27.9 $\pm$ 11.5	65.2 $\pm$ 34.4	19.9 $\pm$ 3.5	48.2 $\pm$ 9.5	43.4	0.4131
MM	3,010 (14.9)	16.8 $\pm$ 10.5	30.4 $\pm$ 20.7	17.6 $\pm$ 6.0	82.3 $\pm$ 9.6	40.0	0.0296
MP	434 (2.2)	13.6 $\pm$ 7.3	21.9 $\pm$ 11.0	0.6 $\pm$ 2.8	73.1 $\pm$ 8.3	44.7	0.3032
MT	2,224 (11.0)	21.5 $\pm$ 10.0	39.5 $\pm$ 19.8	22.7 $\pm$ 3.8	71.8 $\pm$ 5.8	37.7	< .0001
Tr	1,514 (7.5)	14.5 $\pm$ 8.6	29.6 $\pm$ 14.9	10.2 $\pm$ 8.6	62.2 $\pm$ 13.4	44.6	0.0647

Data are expressed as mean $\pm$ standard deviation. * The presence of symptoms was compared between overall and each weather type by using the chi-squared test. DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; Tr, transitional; PM_{2.5}, particulate matter with a diameter less than 2.5 μm in aerodynamic diameter; PM₁₀, particulate matter with a diameter less than 10 μm in aerodynamic diameter.

We also found that there was a statistically significant time lag effect of up to the previous 5 days for both PM_{2.5} and PM₁₀ for all days and for DM days (Fig. 3). Complete information on the lagged effects of PMs on all and DM days are included in Supplementary Table S6.

4. Discussion

In the present study, we investigated how weather modifies the effect of PM exposure on AD symptoms by applying the SSC weather type. We found that PM_{2.5} and PM₁₀ exposure is strongly associated with the presence of AD symptoms, and the effects of PMs on AD

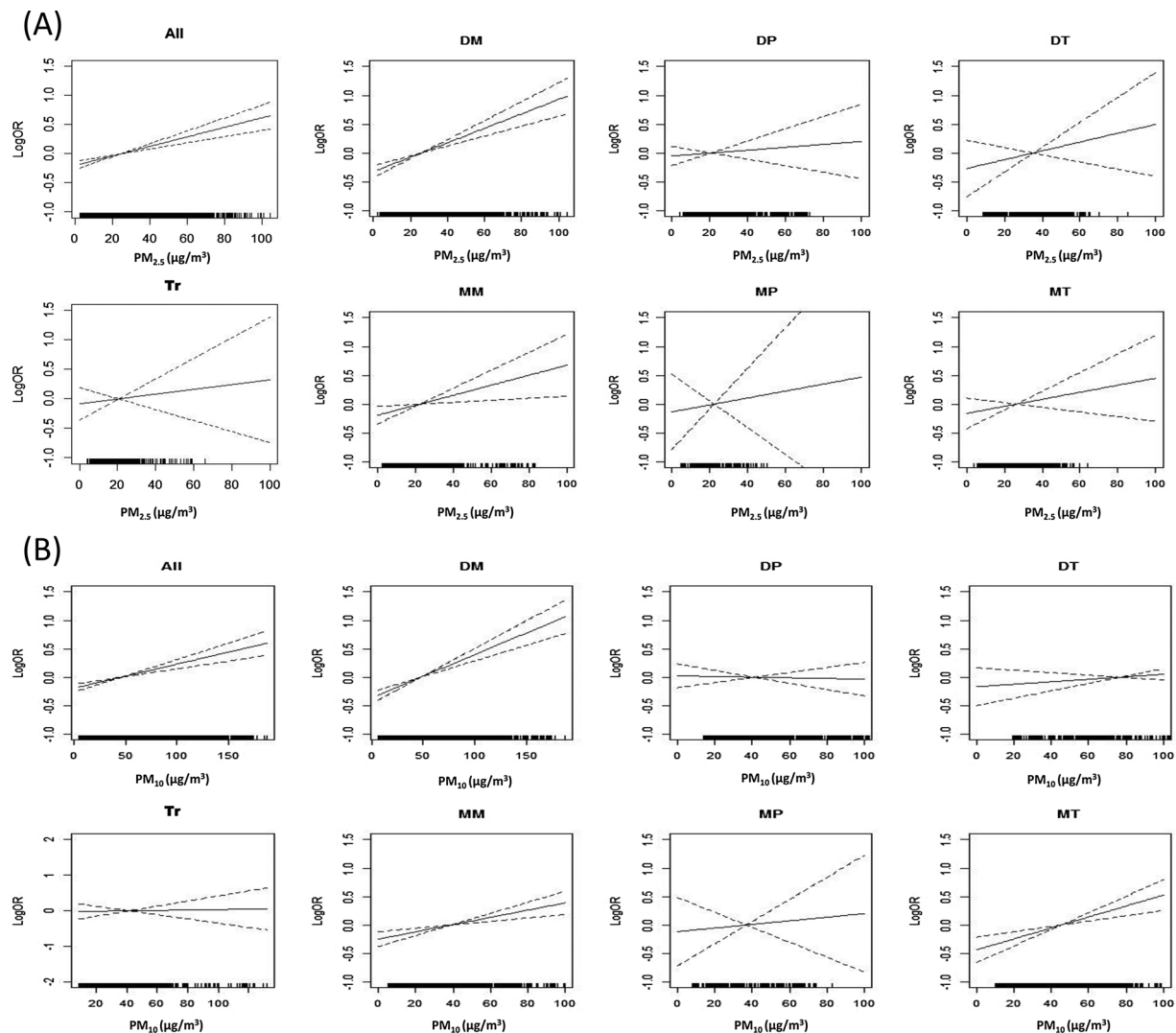


Fig. 1. Relationships of personal exposure to PM_{2.5} (A) and PM₁₀ (B) with AD symptoms according to weather type. PM_{2.5}, particulate matter less than 2.5 μm in aerodynamic diameter; PM₁₀, particulate matter with a diameter less than 10 μm in aerodynamic diameter; AD, atopic dermatitis; DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; Tr, transitional.

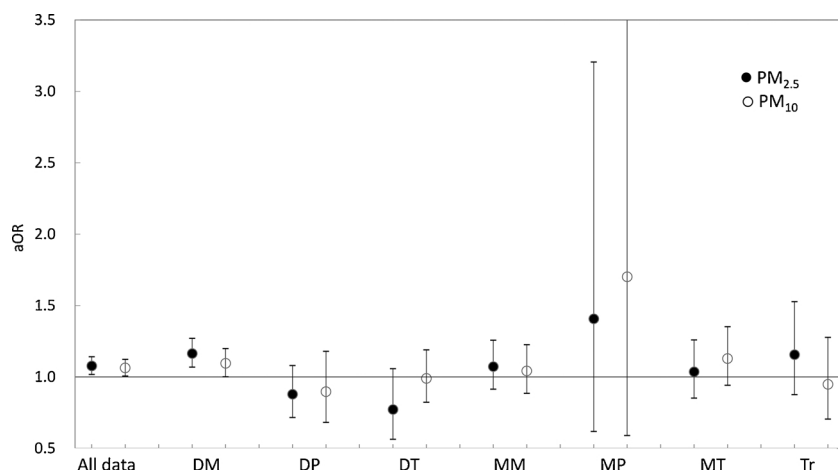


Fig. 2. Effects of PM_{2.5} and PM₁₀ on AD symptoms according to weather type. PM_{2.5}, particulate matter with a diameter less than 2.5 μm in aerodynamic diameter; PM₁₀, particulate matter with a diameter less than 10 μm in aerodynamic diameter; AD, atopic dermatitis; DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; Tr, transitional; aOR, adjusted odds ratio.

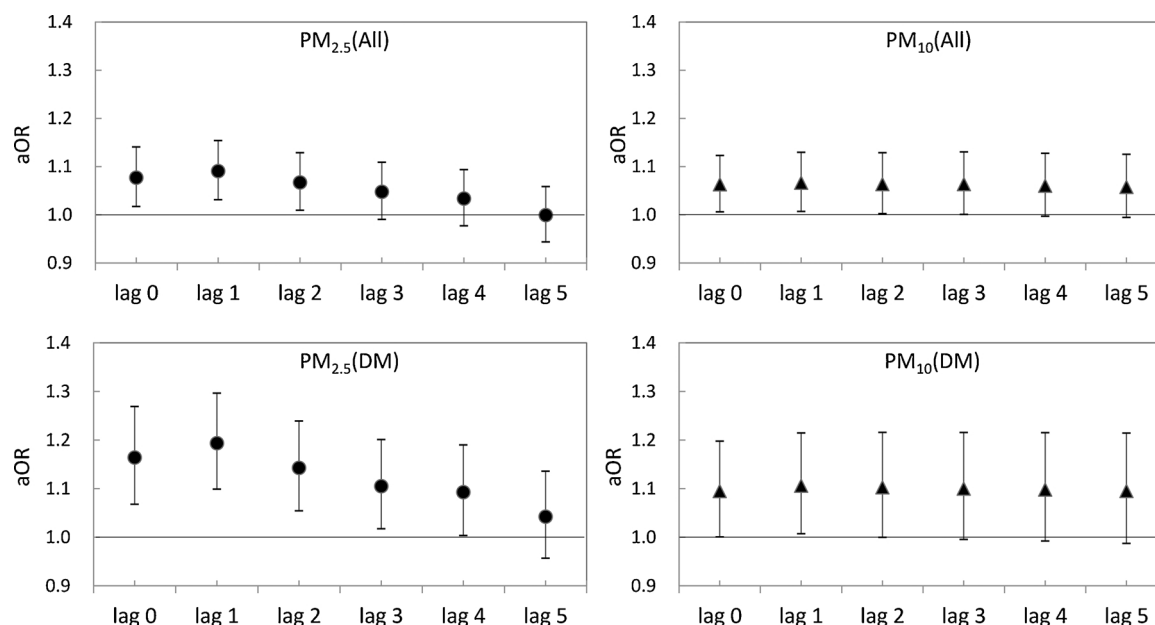


Fig. 3. Lagged effects of PM_{2.5} and PM₁₀ on AD symptoms for overall weather types (A) and DM days (B). PM_{2.5}, particulate matter with a diameter less than 2.5 μm in aerodynamic diameter; PM₁₀, particulate matter with a diameter less than 10 μm in aerodynamic diameter; AD, atopic dermatitis; DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; Tr, transitional; aOR, adjusted odds ratio; lag 0, lag 1, lag 2, lag 3, lag 4, and lag 5 indicate unlagged, lagged by 1, 2, 3, 4, and 5 days, respectively.

symptoms vary by weather type. In other words, the adverse effects of PMs were significant on moderate days. Although the presence of AD symptoms was more frequently found on cold days (DP and MP days) in Seoul (Table 2), the effect of PM_{2.5} was significant only on DM days (Fig. 2). To the best of our knowledge, this is the first study to evaluate the role of weather in the association between air pollution and AD.

The air-mass-based approach to classify daily weather in this study takes into account all of the data from weather situation rather than single elements (Kysely et al., 2010). Air-mass-based synoptic circulation patterns are known to affect ambient levels of air pollution as well as the relationship between air pollution and human health. For example, Vanos et al. (2013) found that weather type had the greatest modifying effect on mortality risk due to ozone (O₃). The associations between O₃, PM_{2.5}, and asthma hospitalizations differed under specific synoptic weather types in 10 Canadian cities (Hebbern and Cakmak, 2015). The SSC can be used to define geographic regions and to account for the spatial variability in health effects of air pollution after examining O₃ exposure and cardiovascular-related mortality in the Canadian Census Health and Environment Cohort (CANHEC) by SSC zone (Cakmak et al., 2016). Therefore, our finding that the influence of

PMs on AD symptoms was significant mainly on DM days might be due to the modifying effect of weather on air pollution. On the other hand, 8,519 records (41.7%) analyzed in the present study occurred on DM days, suggesting that there might be a selection bias. However, the effect of PM₁₀ was significant on MM and MT days, but not on DP days with a greater number of records. Therefore, it seems unlikely that our result can be simply attributed to a selection bias.

In Seoul, DM is predominant among the 7 weather types. During the 518 days of study period from August 2013 to December 2014, 38.2% were DM days and 17.8% were DP days. When we analyzed the most frequent weather type by day of the year using daily SSC data from 1985 to 2014 in Seoul, Korea, the most frequent weather type was DM (212 days, 58.1%) followed by DP (83 days, 22.8%) (Supplementary Fig. S1). DM days were mostly found in spring and fall, with DP days in winter and MM and MT days observed in July and August. Overall, our result demonstrates that avoidance of exposure to PMs should be emphasized in Seoul to reduce AD flares especially in spring and fall, while attention needs to be paid to environmental factors other than PMs in winter and summer. This suggests that environmental factors such as air pollution and weather must be monitored in each geographical area for

the proper management of AD because of high regional variation.

Our finding that PM exposure is associated with aggravation of AD symptoms is consistent with previous studies. Epidemiologic studies have revealed that outdoor PM levels correlate positively with the prevalence and exacerbation of AD (Kim et al., 2013; Kim et al., 2017a; Morgenstern et al., 2008; Song et al., 2011). A recent study on the mechanism (Hidaka et al., 2017) showed that the activation of the aryl hydrocarbon receptor (AhR) by air pollutants induced expression of the neurotrophic factor artemin, allodynia, epidermal hyper-innervation, and inflammation in a transgenic mouse model with a constitutively active form of AhR. In that study, epicutaneous application of diesel exhaust particles (DEPs), the main source of traffic-related air pollution, caused pruritus and AD-like phenotypes via AhR-mediated induction of artemin in keratinocytes. They also demonstrated that AhR activation and subsequent upregulation of *ARTN* was induced by administration of DEPs in human epidermal keratinocytes and HaCaT cells. PMs can also act as an adjuvant in allergic diseases. Polycyclic aromatic hydrocarbons (PAHs), the major components of DEPs, induced interleukin (IL)-4 secretion in basophils from birch pollen-allergic patients in the absence of allergens (Lubitz et al., 2010). It is noteworthy that epidemiologic, animal, and *in vitro* studies suggest that PM may contribute to the development or worsening of AD.

Few studies have evaluated the associations between PMs and AD symptoms according to particle size. PM_{2.5} was more associated with oxidative stress in rat lung epithelial cells than was PM₁₀, suggesting it may have a greater effect on asthma than PM₁₀ (Choi et al., 2004). In a panel study by Song et al. (2011), significant association was found between the concentration of ultrafine particles (< 0.1 µm in diameter) and itching in children with AD, but not with PM_{2.5} or PM₁₀. A systematic review and meta-analysis demonstrated that the OR of PM_{2.5} (OR = 1.05; 95%CI 0.95–1.16; I² = 46%) was higher than that of PM₁₀ (OR = 0.96; 95%CI 0.83–1.11; I² = 62.7%) in AD (Ngoc et al., 2017). It is conceivable that smaller particles may play an important role in the pathophysiology of AD, because fine particles are absorbed through dermal contact (Wei et al., 2010). In the present study, the percent change of the risk of PM_{2.5} and PM₁₀ was 16.5% (95% CI, 6.8–27.0) and 9.5% (95% CI, 0.1–19.8), respectively. The effect of PM_{2.5} on DM days seemed greater than that of PM₁₀. Our data does not mean that PM_{2.5} has a more harmful effect than PM₁₀, but implies that increased risk of AD symptoms by PM exposure may be considerably attributed to PM_{2.5}. In addition, chemical components of PM pose a risk of adverse skin effects. PAHs within particulate matter easily penetrate into the skin because of their lipophilic nature (Kao et al., 1985) and consequently exert a detrimental effect. Higher rates of moderate-to-severe eczema are associated with exposure to copper, lead, or zinc in PM_{2.5} (Kathuria and Silverberg, 2016). Continuous monitoring of PMs according to the size and measurements of its chemical components may be advisable to prevent exacerbation of AD in children.

As children spend most of their time indoors in Seoul, measuring indoor PM levels and time spent indoors is very important in the analysis of PM's effect on health. Although we did not measure daily indoor levels for the entire study period and for all residential places, we estimated the TWA levels of PM exposure based on indoor and outdoor PM levels and time spent in each place. As a result, we were able to assess the PM exposure levels more accurately and determine the adverse effect of PMs on AD symptoms. While the estimated indoor levels have uncertainties, the coefficients of determination (R²) of the regression models for estimated and measured indoor levels were 0.65 and 0.66 for PM_{2.5} and PM₁₀, respectively, which are acceptable.

5. Conclusions

A significant harmful effect of PM_{2.5} and PM₁₀ on AD symptoms was found particularly on dry and moderate days in Seoul, Korea which has a temperate climate, and therefore avoidance of exposure to PMs should be emphasized in Seoul to reduce AD flares, according to the weather

types. Our findings suggest that continuous monitoring of PMs may be advisable to prevent exacerbation of AD in children. Importantly, dry moderate weather type, particulate matters, and their modifying effects should be simultaneously considered for proper management of AD flares.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.ijheh.2018.05.006>.

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Supplementary materials

The effects of particulate matter on atopic dermatitis symptoms are influenced by weather type: Application of spatial synoptic classification (SSC)

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Table S1

Characteristics of 7 weather types according to spatial synoptic classification (SSC)

Weather type	Characteristics
DM (dry moderate)	DM air is mild and dry. It has no traditional analog, but is often found with zonal flow in the middle latitudes, especially in the lee of mountain ranges. It also arises when a traditional air mass has been advected far from its source region and has thus modified considerably.
DP (dry polar)	DP is generally advected from polar regions around a cold-core anticyclone, and is usually associated with the lowest temperatures observed in a region for a particular time of year, as well as clear, dry conditions.
DT (dry tropical)	DT represents the hottest and driest conditions found at any location. There are two primary sources of DT: either it is advected from the desert regions, such as the Sonoran or Sahara Desert, or it is produced by rapidly descending air, whether via orography (such as the chinook) or strong subsidence.
MM (moist moderate)	MM is considerably warmer and more humid than MP. The MM air mass typically appears in a zone south of MP air, still in an area of overrunning but with the responsible front much nearer. It can also arise within an mT air mass on days when high cloud cover suppresses the temperature.
MP (moist polar)	MP is typically cloudy, humid, and cool. MP air appears either by inland transport from a cool ocean, or as a result of frontal overrunning well to the south of the region.
MT (moist tropical)	MT is warm and very humid. It is typically found in warm sectors of mid-latitude cyclones or in a return flow on the western side of an anticyclone; as one approaches the tropics this weather type dominates.
Tr (transitional)	Tr days are defined as days in which one weather type yields to another, based on large shifts in pressure, dew point, and wind over the course of the day.

(Source: <http://sheridan.geog.kent.edu/ssc.html>)

Table S2

Summary statistics of indoor and outdoor concentrations for PM_{2.5} and PM₁₀ during the study period (August 1, 2013 to December 31, 2014)*

(Unit: µg/m³)

		Mean	Standard deviation	Minimum	1Q	Median	3Q	Maximum.
PM_{2.5}	Indoor (estimated)	17.4	10.0	1.8	10.0	15.1	22.4	72.3
	Outdoor (measured)	24.6	14.2	2.3	14.5	21.0	31.7	104.3
PM₁₀	Indoor (estimated)	33.7	20.5	4.0	19.3	28.6	42.9	168.6
	Outdoor (measured)	45.8	27.0	5.0	26.9	39.0	58.3	187.2

*Indoor levels of PMs were estimated based on outdoor level of PMs and indoor to outdoor ratio (IOR); 1Q, first quartile; 3Q, third quartile.

Table S3

Time spent indoors and outdoors for atopic dermatitis (AD) children

	Indoor	Outdoor
Weekday (hr)	22.8±0.9	1.2±0.9
Saturday(hr)	22.1±1.9	1.9±1.9
Sunday(hr)	22.1±1.7	1.9±1.7

Table S4

Indoor to outdoor ratio (IOR) for residents of atopic dermatitis (AD) patients.

	Mean	Standard deviation	Minimum	Maximum
PM_{2.5}	0.71	0.10	0.38	0.89
PM₁₀	0.76	0.08	0.54	0.96

Table S5Effects of PM_{2.5} and PM₁₀ on atopic dermatitis (AD) symptoms by weather type*

Weather type	PM_{2.5}		PM₁₀	
	OR (95% CI)	<i>P</i> -value	OR (95% CI)	<i>P</i> -value
Overall	1.078 (1.018, 1.141)	0.011	1.063 (1.006, 1.123)	0.029
DM	1.165 (1.068, 1.270)	0.001	1.095 (1.001, 1.198)	0.048
DP	0.879 (0.716, 1.079)	0.219	0.897 (0.682, 1.179)	0.435
DT	0.772 (0.563, 1.058)	0.107	0.989 (0.823, 1.189)	0.908
MM	1.072 (0.915, 1.257)	0.390	1.042 (0.885, 1.225)	0.622
MP	1.407 (0.618, 3.206)	0.416	1.701 (0.590, 4.903)	0.325
MT	1.036 (0.852, 1.260)	0.722	1.128 (0.941, 1.352)	0.192
Tr	1.156 (0.876, 1.527)	0.306	0.948 (0.704, 1.278)	0.728

*The effects of PMs on AD symptoms were estimated according to increases in PMs by interquartile range (IQR) (12.7 µg/m³ for PM_{2.5} and 24.0 µg/m³ for PM₁₀); DM, dry moderate; DP, dry polar; DT, dry tropical; MM, moist moderate; MP, moist polar; MT, moist tropical; Tr, transitional; CI, confidence interval

Table S6

Lagged effects of PM_{2.5} and PM₁₀ on atopic dermatitis (AD) symptoms for the whole study period and DM days*

Weather type	Lagged days	PM _{2.5}	PM ₁₀
		OR (95% CI)	OR (95% CI)
Overall	lag 0	1.078 (1.018, 1.141)	1.063 (1.006, 1.123)
	lag 1	1.091 (1.031, 1.154)	1.067 (1.007, 1.130)
	lag 2	1.068 (1.010, 1.129)	1.064 (1.003, 1.129)
	lag 3	1.048 (0.990, 1.109)	1.064 (1.001, 1.130)
	lag 4	1.034 (0.977, 1.094)	1.060 (0.997, 1.128)
	lag 5	1.000 (0.944, 1.059)	1.058 (0.995, 1.126)
DM	lag 0	1.164 (1.068, 1.269)	1.095 (1.001, 1.198)
	lag 1	1.194 (1.099, 1.297)	1.106 (1.008, 1.215)
	lag 2	1.143 (1.055, 1.239)	1.102 (0.999, 1.215)
	lag 3	1.106 (1.018, 1.201)	1.103 (0.998, 1.218)
	lag 4	1.093 (1.004, 1.190)	1.101 (0.996, 1.219)
	lag 5	1.043 (0.957, 1.136)	1.098 (0.991, 1.218)

* The effects of PMs on AD symptoms were estimated according to increases in PMs by interquartile range (IQR) (12.7 µg/m³ for PM_{2.5} and 24.0 µg/m³ for PM₁₀); DM, dry moderate; CI, confidence interval; lag 0, lag 1, lag 2, lag 3, lag 4, and lag 5 indicate unlagged, lagged by 1, 2, 3, 4, and 5 days, respectively.

A	Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	
	January 2014	TR	DP	DM	DP	DP	DM	DM	DM	DP	DP	TR	DP	DP	DP	DP	DM	DM	DP	DP	MP	DP	DP	DM	DM	MM	DP	TR	TR	TR	TR	DP	
	February 2014	TR	MM	TR	DP	DP	DP	DM	MP	MP	DM	DP	DM	DM	DM	DM	DM	DM	DM	DM	DP	DM	DM	DM	DM	DM	DM	DM					
	March 2014	MM	DM	DM	DM	DP	DP	DP	DP	DP	DP	DM	MM	MM	DP	DM	DM	TR	MT	MM	MM	DM	DM	DM	DM	MT	MT+	DM	DT	MT	MT	DT	
	April 2014	DT	DT	TR	DP	DP	DP	DM	DM	MM	DM	DM	MM	DT	DM	MM	MM	DM	DM	DM	DM	DM	DT	DT	DT	DT	DT	MM	MM	MM	DM		
	May 2014	DM	DM	DM	DP	DP	DP	TR	MM	DM	DT	TR	MM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	MT	DM	TR	DM	DT	DT	DT	DT	DT	
	June 2014	MT	MT	MM	MT	MT	DM	MT	MM	DM	MT	MM	MM	MM	DM	DM	DM	MT	MT	MM	MT	MM	MT	MM	MM	MM	MT	DM	MT	MM	MM	DM	
	July 2014	MT	MT	MM	DM	MT	MT	DT	MT	MT	DT	DT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MM	MM	MM	MT	TR	DM	DM	MT	MT	MT+	
	August 2014	DT	DT	MM	MM	MT	MM	MM	DM	DM	TR	DM	MT	TR	MM	DM	MT	MM	MM	MM	MM	MM	MM	MT	MT	MT	MT	MT	DM	DM	DM	DM	
	September 2014	DM	MT	MM	DM	MT	DM	MT	MT	DT	DM	DM	DM	DM	DM	MT	DM	DM	DM	DM	DM	DM	DM	DM	DT	MM	DM	MT	MT	MM	MM	DM	
	October 2014	DM	MM	MM	DM	DM	DM	DM	DM	DM	DM	DM	DT	DM	DM	DM	TR	DM	DM	DM	MM	MM	DM	DM	DM	DM	MM	DP	DP	DM	DM	DM	
	November 2014	MT	TR	DP	DM	DM	DM	DM	DM	DM	DM	DM	TR	DP	DP	DP	DP	MP	DP	DM	DM	DM	MM	DM	DM	DM	DM	DM	DM	TR	DM	MM	
December 2014	TR	DP	MP	DP	DP	DP	DP	DP	DP	TR	DP	DP	DP	DP	DP	MP	TR	DP	DP	TR	TR	DP	DP	DP	DM	DM	DP	DP	DP	MP	MM	DM	DP

B	Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
	January	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP
	February	DP	DP	DP	DP	DP	DP	DM	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DM	DP	DM	DM	DM	DM	DM	DM	DM			
	March	DM	DM	DM	DM	DM	DM	DM	DM	DM	DP	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
	April	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
	May	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
	June	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	MM	MM	DM	DM	MM	DM	MM	DM	MM	DM	MM	MM
	July	MM	MM	MM	MM	MM	MM	MM	MT	MM	MM	MM	MM	MM	MM	MM	MM	MM	MM	MT	MT	MM	MT	MM	MM	MT	MT	MT	MM	MT	MT	MT
	August	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MT	MM	DM	MT	MT	MT	MT	MT	MM	MT	MM	MT	DM
	September	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
	October	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM
	November	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DM	DP	DP	DP	DM	DM	DP	DP	DM	DM	DM	DM	DM	DM	DM	DP	DP	DP	DM
December	DM	DM	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DP	DM	DM	DP	DM	DM	DP	DP	DP	DP	DP	

Fig. S1. Spatial synoptic classification (SSC) for 2014(A) and the most frequent weather types by each day of the year for 30 years from 1985 to 2014(B) in Seoul, Korea