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Defining the Relationship between Daily Exposure to Particulate Matter and Hospital Visits by Psoriasis Patients

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Background: Although particulate matter likely provokes inflammatory reactions in those with chronic skin disorders like atopic dermatitis, no study has examined the relationship between particulate matter and psoriasis exacerbation.
Objective: This study evaluated possible associations between particulate matter and hospital visits for psoriasis patients in 7 major cities in South Korea.
Methods: We investigated the relationship between psoriasis and particulate matter. To do this, we used psoriasis patient data from the Korean National Health Insurance Service database. In addition, PM_{10} and $PM_{2.5}$ concentration data spanning a 3-year time frame were obtained from the Korea Environment Corporation.
Results: A pattern analysis generated by the sample cross-correlation function and time series regression showed a correlation between particulate matter concentration and the number of hospital visits by psoriasis patients. However, the prewhitening method, which minimizes the effects of other variables besides particulate matter, revealed no correlation between the two.
Conclusion: This study suggests that particulate matter has no impact on hospital visit frequency among psoriasis patients in South Korean urban areas.

Keywords: Particulate matter, Psoriasis

INTRODUCTION

Particulate matter (PM) is one of the most common air pollutants and is a growing public health concern[1]. PM is classified as PM_{10} (smaller than 10 μm), coarse PM (ranging from 2.5 to 10 μm), fine PM ($PM_{2.5}$, smaller than 2.5 μm), or ultrafine PM (smaller than 0.1 μm) according to the particles' aerodynamic diameter[2]. They are comprised of harmful materials such as

carbon compounds, nitrate, sulfate, acid, and heavy metals[3]. Exposure to PM affects not only the respiratory tract but also the cardiovascular system and skin[4,5].

Psoriasis is a systemic chronic disease with histological features such as epidermis hyperplasia and dermal inflammation. Psoriasis is characterized by compromised barrier function[6]. Previous studies have revealed that defects in epidermal barrier-related genes are associated with a risk of psoriasis. Persistent exposure, percutaneous penetration, and the properties of air pollutants directly affect the integrity of the skin barrier[7]. Thus, it is likely that psoriasis patients with impaired skin barriers are easily affected when their skin is exposed to increased pollutants such as PM. However, there are few epidemiological reports on this topic, and the existing evidence is insufficient. This study investigated possible relationships between psoriasis and PM by analyzing the correlation between psoriasis patient hospital visits and daily PM concentration exposure using the Korean National Health Insurance Service (NHIS) and the Korea Environment Corporation (K-eco) database.

MATERIALS AND METHODS

Data regarding the number of patients with psoriasis were obtained from the NHIS database. In general, the NHIS is the sole insurer that provides mandatory universal health insurance to virtually the entire Korean population (i.e., approximately 97% of the total population). We used the nation-wide claims data generated between January 2015 and December 2017. This study was approved by the Institutional Review Board of Kyungpook National University Hospital (IRB no. KNUH 2020-02-008) and the requirement for informed consent was waived because the NHIS database was constructed after anonymization according to strict confidentiality guidelines. The NHIS database has previously been used for epidemiological studies, and its validity is described elsewhere[8]. PM concentrations were obtained from the K-eco database. K-eco provides people and their related organizations with air quality information via a national ambient air quality monitoring network. In addition, K-eco collects and manages measurement data from approximately 451 nationwide ambient air quality monitoring stations and provides PM_{10} and $PM_{2.5}$ concentration readings through a real-time ambient air quality monitoring system.

Data were analyzed using a cross-correlation function, a time series regression, and prewhitening using the TSA package (version 1.2.1, R programming; R Foundation for Statistical Computing, Vienna, Austria). p-values <0.05 were deemed statistically significant. First, we performed a pattern analysis on the correlation between PM concentration and the number of psoriasis patient hospital visits through the sCCF (sample cross-correlation function), r_k. For two time series, $\{X_t\}$ and $\{Y_t\}$, r_k, which is an estimator of CCF $\rho_k(X,Y)=\mathrm{cor}(X_t,Y_{t-k})$, was defined by the following:

$$r_k := \frac{\sum(X_t-\bar{X})(Y_{t-k}-\bar{Y})^2}{\sqrt{\sum(X_t-\bar{X})^2}\sqrt{\sum(Y_{t-k}-\bar{Y})^2}}$$

And in the case of stationary X and Y that are independent of each other, the variance of $r_k(X,Y)$ is approximately:

$$\frac{1}{n}\left[1+2\sum_{k=1}^{\infty}\rho_k(X)\rho_k(Y)\right]$$

where $\rho_k(X)$ and $\rho_k(Y)$ are the ACF (auto correlation function) of X and Y, respectively.

Next, we estimated the number of patients with psoriasis based solely on PM concentrations, excluding the effects of holidays and so on. This result was compared to the actual trend in the number of patients with psoriasis. These data may be nonstationary; therefore, we analyzed whether there is a significant correlation between the two by minimizing the effects of variables other than PM concentration. If $\tilde{X}=\pi(B)X_t$ behaves like white noise, then the process of transforming the X's into the $\tilde{X}$'s via the linear operator, $\pi(B)$, is known as prewhitening. Prewhitening is a method that removes some useless coefficient candidates by transformation. If X and Y are truly correlated, then prewhitening fails to make X 'perfect' white noise, and that prewhitened CCF will be significant.

RESULTS

To examine a possible relationship between psoriasis and PM, we investigated time series data regarding the number of psoriasis patients and the PM_{10} concentration collected by 7 major cities in South Korea.

First, we examined data from 7 major cities (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) to investigate correlation. In Fig. 1A, the sCCF values of the two data sets collected by these major cities are presented. The fluctuations in their sCCF values between cities showed a similar pattern. To test the dependence of the two data types, the sCCF values

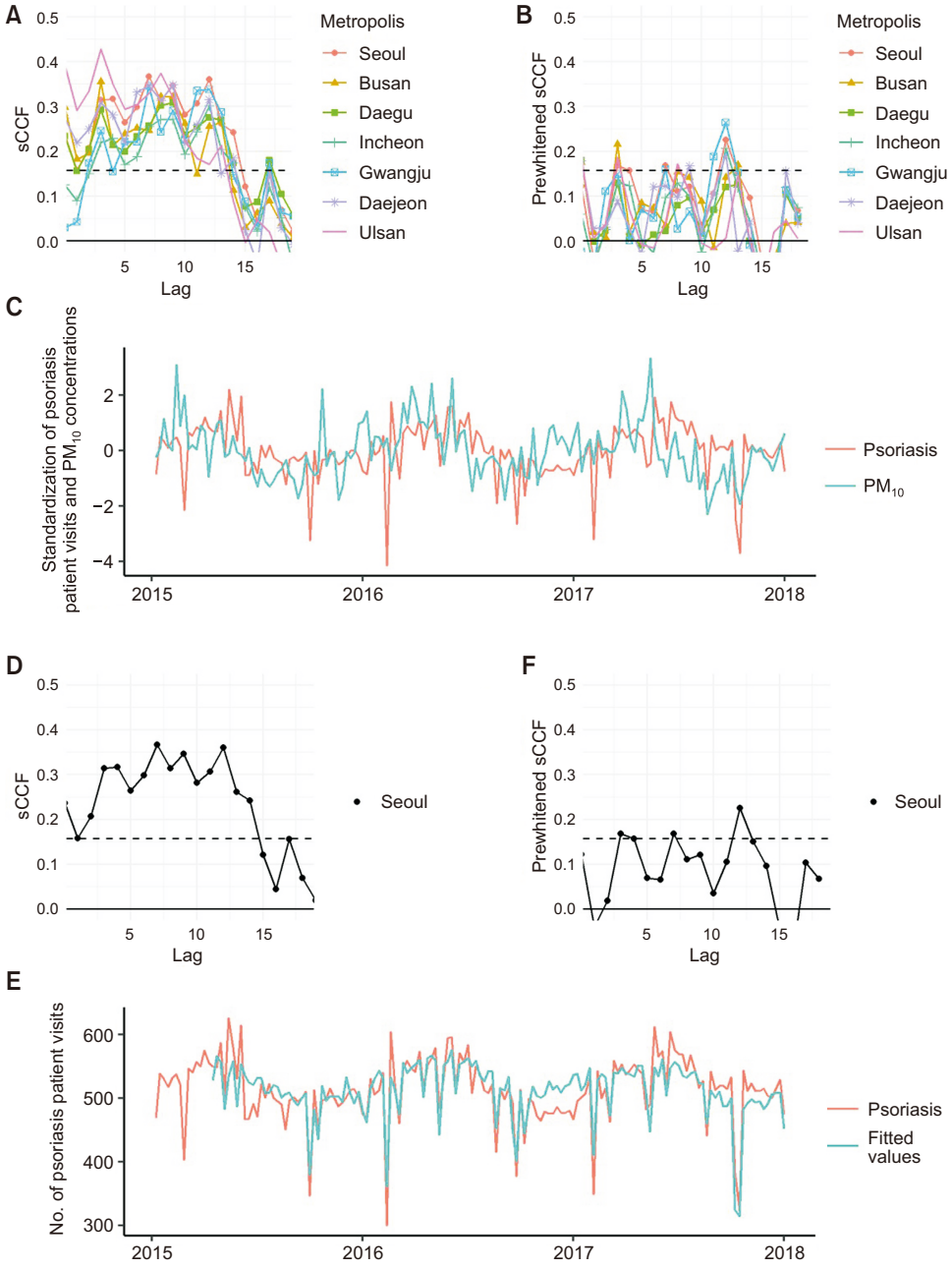

Fig. 1. The horizontal dashed line indicates the boundary of the rejection region (A, B, D, F). Plotted data are standardized in (C) to compare psoriasis and PM_{10} (n=156 and the overall maximum lag is k=18). The fitted values of E were generated by assuming the correlation is not spurious and the transfer-function model fits. (A) sCCF values from 7 major cities (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan), (B) prewhitened sCCF values from 7 major cities, (C) original psoriasis patient and PM_{10} data from Seoul, (D) sCCF values from Seoul, (E) time series regression model with spurious correlations, (F) prewhitened sCCF values from Seoul. PM: particulate matter, sCCF: sample cross-correlation function.

obtained by the prewhitening method (Fig. 1B). We found that most of the sCCF values shown in Fig. 1B are less than the critical value; however, at 1 or 2 lag points, the sCCF values exceeded the critical value.

For a more detailed interpretation, we analyzed data collected in Seoul, the capital of South Korea and the largest number of patients. When a time series of the two data types (the number of patients with psoriasis and the PM_{10} concentration over 3 years) are plotted, they form a similar pattern, as shown in Fig. 1C. To further investigate this possible correlation, we tested the sCCF values between them, which showed that most exceeded critical values (Fig. 1D). That is, it appeared unimodal if it could be smoothed, which is a typical pattern of the transfer-function model. To do this, we used the multiple linear regression method with intervention analysis and generated the following statistical model for the number of patients with psoriasis: $Y_t=0.58X_t+0.48X_{t-4}+0.48X_{t-6}+0.48X_{t-10}+0.54X_{t-14}+530.86-400.85H$, where Y_t, X_{t-k}, and H indicate the number of psoriasis patients, PM_{10} concentration with a time lag of k, and an additive outlier term that reflects holiday

percentage over a week, respectively. Based on the time series regression, the time lag (k) of the PM_{10} concentration X_{t-k} was considered as 0, 4, 6, 10, and 14 (weeks). When a result obtained from the above statistical model was compared to the PM_{10} data, an agreement between them appeared (Fig. 1E). Thus, it seemed as if a correlation existed between psoriasis and PM.

We tried to confirm a clinical connection between the number of psoriasis patients and PM exposure (i.e. a dependence between the two data). We examined whether the result shown in Fig. 1E is from the numerical similarity between two data or not. To do this, we used the prewhitening method. Fig. 1F shows the sCCF values produced by the prewhitening method whose critical value is $0.1569 \approx 1.96/\sqrt{156}$. We found that most sCCF values were less than the critical value. This means that a correlation between psoriasis and PM_{10} cannot be found, especially among data collected in the Seoul area. Collectively, all data showed that a correlation between psoriasis and PM_{10} did not exist.

$PM_{2.5}$ is more likely to penetrate the skin barrier than PM_{10}.

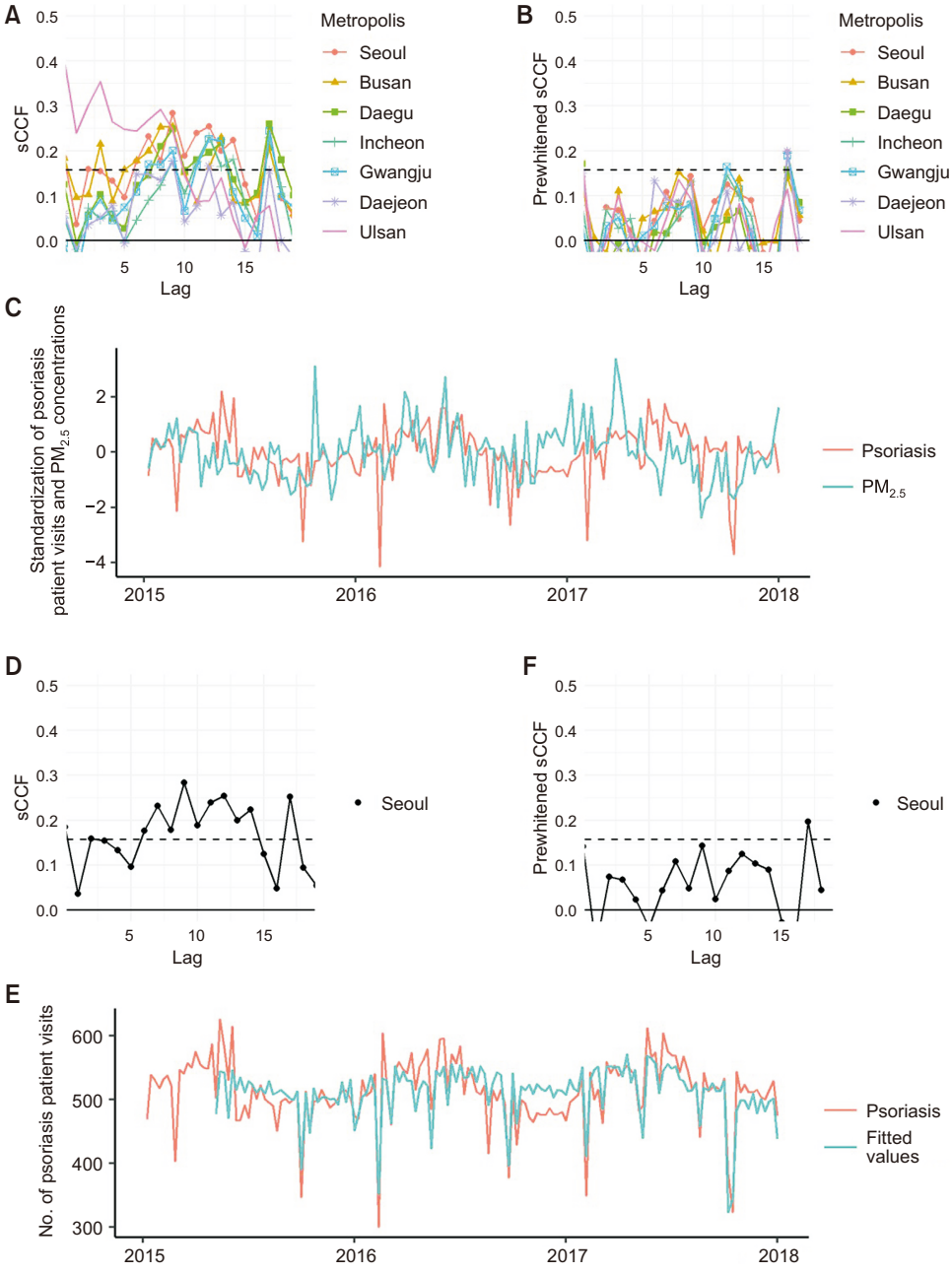

Fig. 2. The horizontal dashed line indicates the boundary of the rejection region in (A, B, D, F). Plotted data are standardized in (C) to compare psoriasis and $PM_{2.5}$ (n=156 and the overall maximum of lag is k=18). The fitted values of E were generated by assuming the correlation is not spurious and the transfer-function model fits. (A) sCCF values from 7 major cities (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan), (B) prewhitened sCCF values from 7 major cities, (C) original psoriasis patient and $PM_{2.5}$ data from Seoul, (D) sCCF values from Seoul, (E) time series regression model with spurious correlations, (F) prewhitened sCCF values from Seoul. PM: particulate matter, sCCF: sample cross-correlation function.

Therefore, we also investigated whether a correlation exists between $PM_{2.5}$ and the number of psoriasis patients (Fig. 2). However, the same analysis used for PM_{10} showed that $PM_{2.5}$ did not associate with the number of psoriasis patient hospital visits. Thus, we concluded that there is no correlation between the two.

DISCUSSION

This 3-year longitudinal study investigated the correlation between PM concentration and the number of psoriasis patients in Korea. The present study evaluated the daily average concentrations of PM_{10} in Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan. When we plotted a time series of the number of psoriasis patients and PM concentrations for 3 years, they displayed similar patterns. However, in a time series model using prewhitening for accurate analysis, the effect estimates of PM_{10} and $PM_{2.5}$ were not statistically significant.

According to a systematic review and meta-analysis of human skin disease due to PM, PM is closely associated with atopic dermatitis, eczema, and skin allergies[9,10]. Air pollutants could aggravate the dermatological symptoms and signs of inflammatory skin disease or weaken skin protection[11-13]. According to recent studies using animal and cell models, air pollutants such as PM are involved in the pathogenesis of inflammatory skin diseases because they enhance oxidative stress and pro-inflammatory cytokines[14]. In particular, particles can directly induce the production of reactive oxygen species and consequently result in oxidative stress-induced damage and inflammation reactions to the immune system[15]. Also, exposure to air pollutants, including chemicals such as toxic metals with oxidant-generating capacities, may induce neutrophilic inflammation, decreased pH, elevated eosinophil and cytokine levels, and immunoglobulin E generation[16,17].

Atopic dermatitis and psoriasis are the most common inflammatory skin diseases. Many studies have investigated the association between atopic dermatitis and PM[18,19], but few have studied direct associations between psoriasis and PM. And previous studies have indicated a biologically plausible positive association between PM and psoriasis, but the exact principle of this association has not been uncovered. Therefore, we investigated the clinical connection between psoriasis and PM based on a large database from Korea. High PM levels and distinct seasons in Korea provided a sufficient number of opportunities to investigate the effects of environmental risk factors on skin conditions. However, we did not confirm a link between the two, which may mean that high PM concentrations do not aggravate the disease seriously enough to cause patients to visit the hospital.

This study has several limitations. First, it did not adjust for individual confounding factors that we did not consider such as gender, age, smoking, socioeconomic status, medication, and comorbidities. As a retrospective study, information such as gender and age were difficult to study due to limited data accessibility and availability; therefore, we obtained the daily total number of psoriasis patients instead of detailed information on each patient. Second, our data include uncertainty about the assessment of an individual, which can lead to errors in assessing the effects of PM on psoriasis symptoms. The most common symptoms of psoriasis are red, raised, and inflamed patches and whitish-silver scales or plaques on the red patches. It is necessary to evaluate the skin lesions of an individual to determine whether and how their symptoms have changed. Third, due to the nature of the hospital care systems in Korea, outpatient visits are often scheduled for doctor's appointments and regular follow-ups. Therefore, the number of outpatient visits may not reflect the number of visits to the hospital caused by worsening psoriasis symptoms due to PM.

In conclusion, this study provides evidence that high PM concentrations do not increase the number of hospital visits by psoriasis patients in Korea. However, according to previous studies, the hypothesis that PM can affect psoriasis warranted consideration. Further studies are needed to better establish the relationship between air pollution, including PM, and psoriasis in individual patients.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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DATA SHARING STATEMENT

Research data are not shared.

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REFERENCES

1. Saikawa E, Kim H, Zhong M, Avramov A, Zhao Y, Janssens-Maenhout G, et al. Comparison of emissions inventories of anthropogenic air pollutants and greenhouse gases in China. Atmos Chem Phys 2017;17:6393-6421.
2. Carlsten C, Melén E. Air pollution, genetics, and allergy: an update. Curr Opin Allergy Clin Immunol 2012;12:455-460.
3. Noh J, Sohn J, Cho J, Cho SK, Choi YJ, Kim C, et al. Short-term effects of ambient air pollution on emergency department visits for asthma: an assessment of effect modification by prior allergic disease history. J Prev Med Public Health 2016;49:329-341.
4. Pope CA 3rd, Dockery DW, Spengler JD, Raizenne ME. Respiratory health and PM10 pollution. A daily time series analysis. Am Rev Respir Dis 1991;144(3 Pt 1):668-674.
5. Gold DR, Mittleman MA. New insights into pollution and the cardiovascular system: 2010 to 2012. Circulation 2013;127:1903-1913.
6. Sano S. Psoriasis as a barrier disease. Dermatol Sin 2015;33:64-69.
7. Wilhelm KP, Zhai H, Maibach HI. Dermatotoxicology. 8th ed. London: Informa Healthcare; 2012.
8. Son JS, Choi S, Kim K, Kim SM, Choi D, Lee G, et al. Association of blood pressure classification in Korean young adults according to the 2017 American College of Cardiology/American Heart Association Guidelines with subsequent cardiovascular disease events. JAMA 2018;320:1783-1792.
9. Ngoc LTN, Park D, Lee Y, Lee YC. Systematic review and meta-analysis of human skin diseases due to particulate matter. Int J Environ Res Public Health 2017;14:1458.
10. Li Q, Yang Y, Chen R, Kan H, Song W, Tan J, et al. Ambient air pollution, meteorological factors and outpatient visits for eczema in Shanghai, China: a time-series analysis. Int J Environ Res Public Health 2016;13:1106.
11. Song S, Lee K, Lee YM, Lee JH, Lee SI, Yu SD, et al. Acute health effects of urban fine and ultrafine particles on children with atopic dermatitis. Environ Res 2011;111:394-399.
12. Eberlein-König B, Przybilla B, Kühnl P, Pechak J, Gebefügi I, Kleinschmidt J, et al. Influence of airborne nitrogen dioxide or formaldehyde on parameters of skin function and cellular activation in patients with atopic eczema and control subjects. J Allergy Clin Immunol 1998;101(1 Pt 1):141-143.
13. Huss-Marp J, Eberlein-König B, Breuer K, Mair S, Ansel A, Darsow U, et al. Influence of short-term exposure to airborne Der p 1 and volatile organic compounds on skin barrier function and dermal blood flow in patients with atopic eczema and healthy individuals. Clin Exp Allergy 2006;36:338-345.
14. Kim KE, Cho D, Park HJ. Air pollution and skin diseases: adverse effects of airborne particulate matter on various skin diseases. Life Sci 2016;152:126-134.
15. Huang SK, Zhang Q, Qiu Z, Chung KF. Mechanistic impact of outdoor air pollution on asthma and allergic diseases. J Thorac Dis 2015;7:23-33.
16. Diaz-Sanchez D. The role of diesel exhaust particles and their associated polyaromatic hydrocarbons in the induction of allergic airway disease. Allergy 1997;52(38 Suppl):52-56; discussion 57-58.
17. Nikasinovic L, Just J, Sahraoui F, Seta N, Grimfeld A, Momas I. Nasal inflammation and personal exposure to fine particles PM2.5 in asthmatic children. J Allergy Clin Immunol 2006;117:1382-1388.
18. Oh I, Lee J, Ahn K, Kim J, Kim YM, Sun Sim C, et al. Association between particulate matter concentration and symptoms of atopic dermatitis in children living in an industrial urban area of South Korea. Environ Res 2018;160:462-468.
19. Kim YM, Kim J, Jung K, Eo S, Ahn K. The effects of particulate matter on atopic dermatitis symptoms are influenced by weather type: application of spatial synoptic classification (SSC). Int J Hyg Environ Health 2018;221:823-829.