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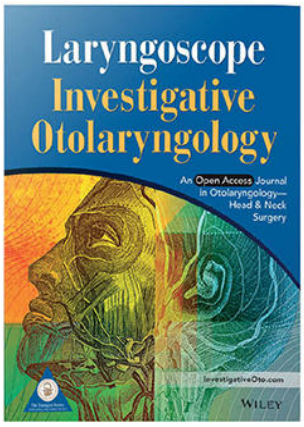

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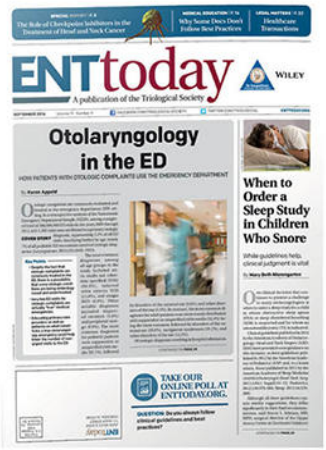

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Impact of Particulate Matter on the Clinical Characteristics of Rhinitis

Jin Youp Kim, MD; Dong Su Lee, MS; Hyun-Joon Woo, MD; Hyung Gu Kim, MD; Bu-Soon Son, PhD; Moo Kyun Park, MD, PhD; Seung-No Hong, MD

Objectives/Hypothesis: To investigate the association between PM_{10} concentration and the severity of rhinitis symptoms.

Study Design: Retrospective cohort study.

Methods: Retrospective analysis of the data of 590 participants prospectively enrolled in a regional population-based cohort study was performed. The ambient PM_{10} concentrations were measured at 12 different observatories located in three cities. All participants were screened for allergic sensitization by skin prick tests and asked to complete questionnaires regarding their rhinitis symptoms. The severity and duration of rhinitis were analyzed and compared at different levels of PM_{10} concentration.

Results: On multivariate analysis, the PM_{10} concentration significantly correlated with the severity of symptoms when adjusting for age, sex, presence of sensitized allergen, region, and the time of enrolment ($\beta = 0.102$, $P = .021$). Positive correlation was found between PM_{10} concentration and the duration of allergic rhinitis symptoms ($\beta = 0.082$, $P = .077$). In the stratified analysis on the atopic status, there was a significant correlation between PM_{10} concentration and the severity and duration of rhinitis symptoms in those without allergic sensitization ($\beta = 0.104$; $P = .032$ and $\beta = 0.104$; $P = .011$, respectively).

Conclusions: The significant correlation between the annual PM10 concentration and severity and duration of rhinitis symptoms suggests the necessity of intensive management of rhinitis patients exposed to elevated levels of ambient PM10 concentration.

Key Words: Air pollution, allergens, immunologic sensitization, particulate matter, rhinitis.

Level of Evidence: 3

***Laryngoscope*, 00:1–7, 2020**

INTRODUCTION

Rhinitis is a common inflammatory disease of the upper airways affecting approximately 20% to 50% of the population, depending on different regions and their definitions of rhinitis; however, its prevalence has increased in the past decades.[1–3] As this increase cannot be explained by genetic factors alone, other factors have been suggested. Air pollution, increased by industrialization and rapid urbanization, is considered one of the most influential factors. Various studies have investigated the correlation between air pollution and diseases of the respiratory tract.[4–7] Exposure to air pollutants has been demonstrated to be a risk factor for rhinitis in children. The prevalence of rhinitis increased when children were exposed to NO_2, SO_2, particulate matter (PM) of diameter < 10 um (PM_{10}), and particulate matter of diameter < 2.5 um ($PM_{2.5}$).[6]

PM was regarded as the most critical air pollutant for the healthy general population.[8] Consequently, many studies focused on the correlation between PM and chronic inflammatory diseases, including rhinitis.[9–11] In a cohort of French children, lifelong allergic rhinitis was associated with PM_{10}, while the sensitization against pollen was associated with benzene and PM_{10}.[12] Living in close proximity to PM sources, such as roads with high traffic density was also reported to be related with airway hyper-responsiveness, reduced lung function, and increased sensitization to common aeroallergens.[13] An animal study using a rat model of allergic rhinitis

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revealed that increased concentrations of $PM_{2.5}$ resulted in increased levels of adhesion molecules and inflammatory cytokine expression in a concentration-dependent manner.[14]

Nevertheless, the effect of PM on the clinical characteristics of allergic or non-allergic rhinitis has scarcely been studied.[8] In the present study, we aimed to investigate the association between the annual concentration of PM_{10} and the severity and duration of rhinitis symptoms, in relation to the status of allergic sensitization.

MATERIALS AND METHODS

Study Participants

Retrospective analysis of the data of 590 participants (511 and 79 participants in 2007 and 2009, respectively), who were prospectively enrolled in a regional population-based cohort study, was performed. We excluded regions with lesser populations, high variance and outliers in relation to PM_{10} levels, and inaccurate matching of PM_{10} (Fig. 1). Participants lived in 12 distinct regions around Gwangyang bay (five in Hadong, four in Yeosu, and four in Gwang-Yang). There were several petrochemical corporations, and the regions within 5 kms from these were defined as industrial regions. Among the 590 participants, 286 lived in industrial regions, while the other 304 lived 15 km away from the industrial regions (defined as living in non-industrial regions). Written informed consent was obtained from all participants or their parents. This study was approved by the institutional review board of Seoul National University Hospital (IRB no.: 1608-138-787).

Symptom Evaluation and Skin Prick Test

All participants were asked to complete questionnaires regarding the severity and duration of their rhinitis symptoms. The severity of rhinitis symptoms was graded from 1 to 4 (1: no discomfort in daily life; 2: mild discomfort; 3: moderate discomfort; and 4: severe discomfort). Participants were asked to consider the months in which they suffered from rhinitis, and the duration of rhinitis symptoms was calculated as the sum of those months in a year. Skin prick tests (SPTs) with *Dermatophagoides pteronyssinus* (Dp), *Dermatophagoides farina* (Df), mugwort, and cockroach were conducted for all participants. Histamine (1% of

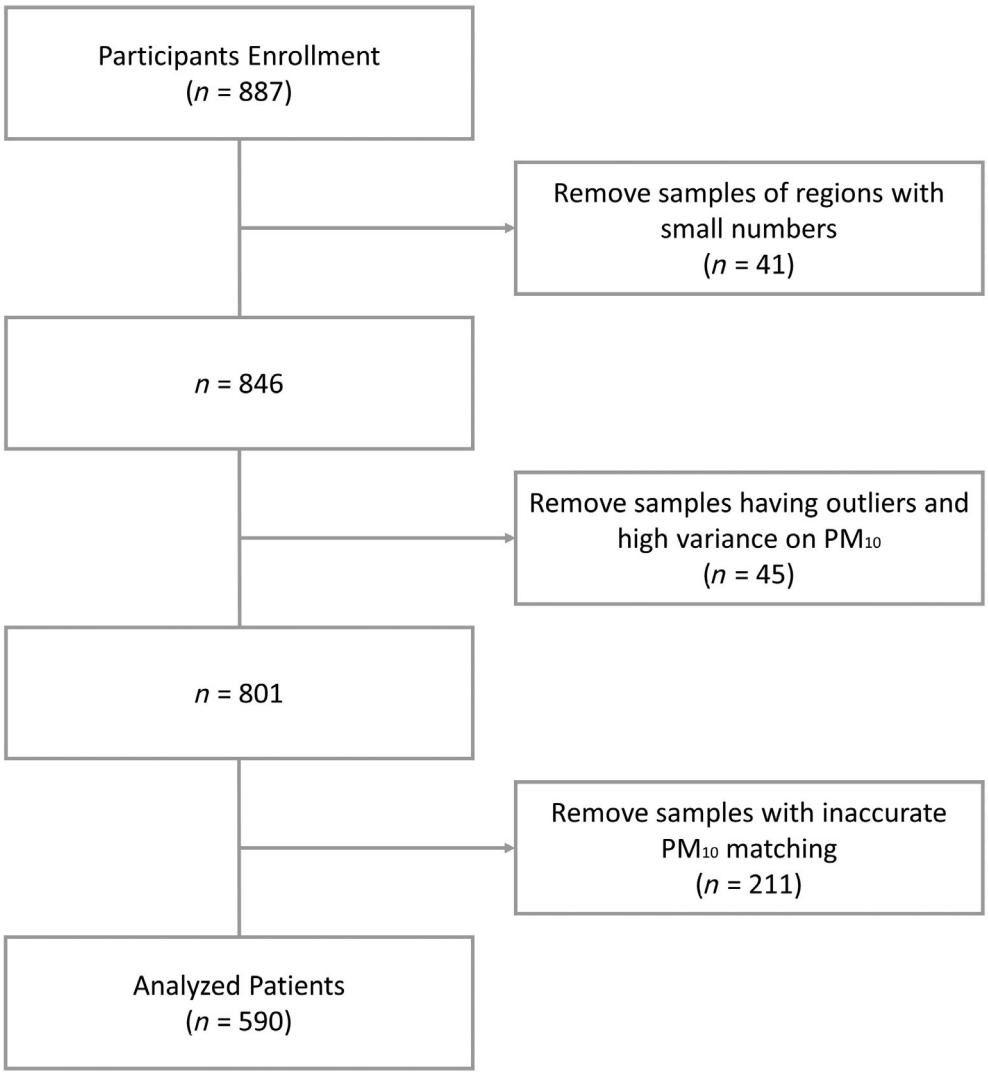

Fig. 1. Enrolment and selection of the participants.

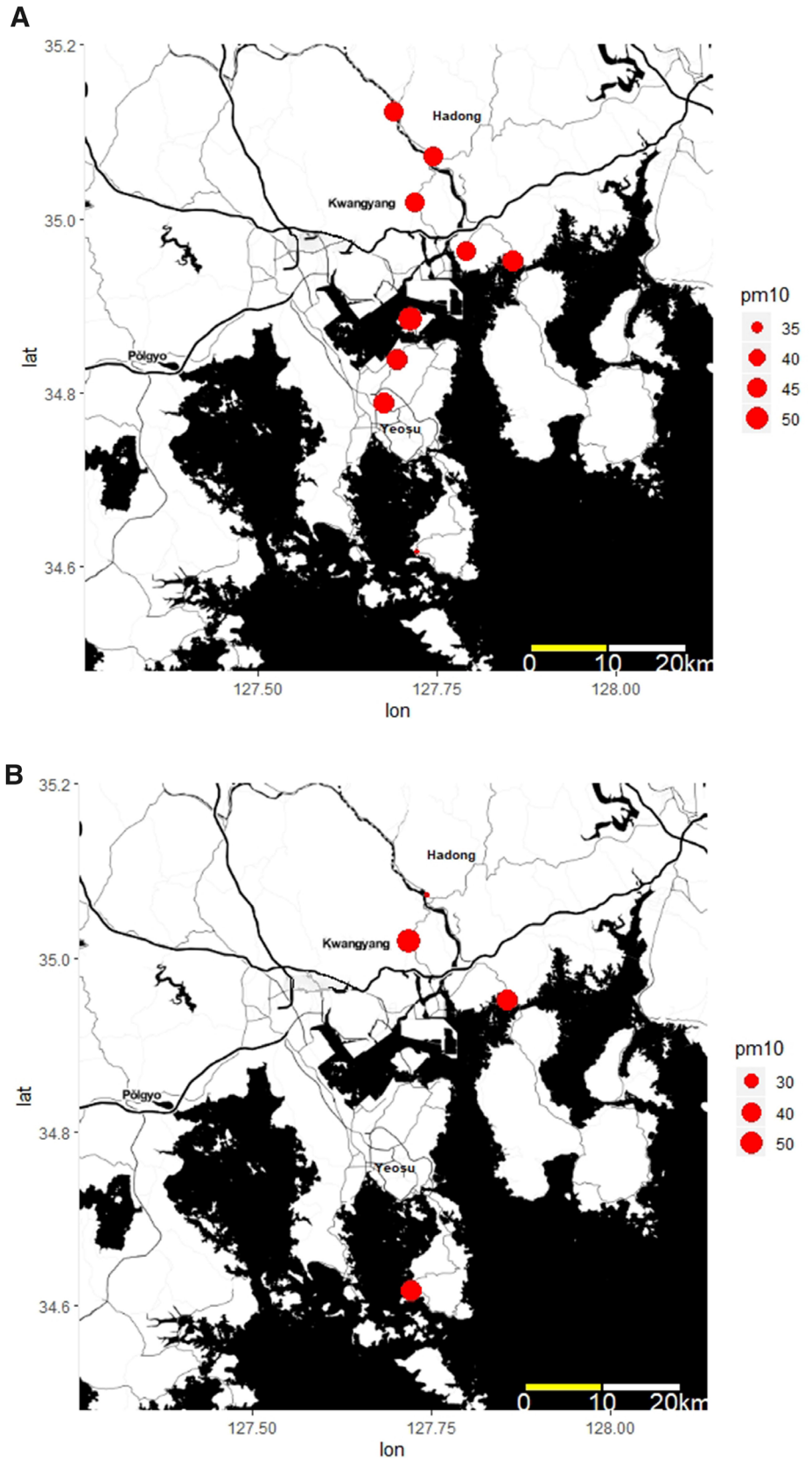

Fig. 2. The annual concentration of PM_{10} for each observatory detected in (A) 2007 and (B) 2009. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

histamine phosphate) and 50% glycerol were used as positive and negative controls, respectively. The results of SPT were evaluated 15 minutes after the allergens were applied. A result was considered positive when the mean wheal diameter for that allergen was larger than or equal to that of the positive control. Patients who were sensitized for at least one or more allergens were considered to be atopic.

Evaluation and Matching of PM_{10}

The ambient PM_{10} concentration was measured at 12 different observatories located in Gwangyang, Yeosu, and Hadong. Air quality was automatically monitored, and the level of PM_{10} was calculated using the air quality dispersion model - ISCST-3.[15] Each participant's region of residence was matched with the closest PM_{10} observatory with the Haversine formula. Thereafter, the annual mean value of PM_{10} concentration for each participant was calculated, and was assumed to be proportional to the individual's level of exposure to PM_{10}.

Statistical Analyses

Continuous variables, such as age and PM_{10} concentration, were presented as the mean ± SD, and were analyzed using the independent sample t-test. Independent group proportion t-test was carried out to evaluate categorical variables. We conducted multiple linear regression analysis to evaluate the correlation between PM_{10} concentrations and the severity and duration of allergic rhinitis symptoms while adjusting for age, sex, atopic status, region, and the time of enrolment. Stratified analysis was performed according to the atopic status of the patients. *P* value <.05 was considered significant, and all analyses were conducted with the R software v.3.6 (R Development Core Team, Vienna, Austria).

RESULTS

Demographics and Clinical Features of the Participants

The 590 participants consisted of 278 men and 312 women. The mean age was 46.4 years, and the mean concentration of PM_{10} was 43.7 ug/m^3. The PM_{10} concentration of each observatory is illustrated in Figure 2. Participants were divided into the industrial and non-industrial groups, based on the location of their region of residence. Demographic features and clinical parameters are shown in Table I. The mean age of the industrial group participants was higher than that of the non-industrial group participants (*P* = .001). There was no significant difference between the groups in terms of allergic sensitization. Figure 3A shows the concentration of PM_{10} in both groups; it was significantly higher in the industrial group than that in the non-industrial group (*P* < .001). The severity and duration of allergic rhinitis symptoms are shown in Figure 3B,C. The mean values of severity of symptoms were 1.35 and 1.33 for participants in the industrial and non-industrial groups, respectively (*P* = .718). The ratio of participants with symptom severity of two or three was slightly higher in the industrial group (29.4%) than in the non-industrial group (27.2%); however, this was not statistically significant (*P* = .641, Fig. 3B). The duration of symptoms was not different between both groups (1.04 vs. 1.02 months in the industrial and non-industrial groups, respectively, *P* = .922, Fig. 3C).

Multivariate Analysis

On multivariate analysis, the concentration of PM_{10} significantly correlated with the severity of symptoms when adjusting for age, sex, presence of sensitized allergen, region, and the time of enrolment (β = 0.102, *P* = .021) (Table II). Under the same circumstances, permutation tests in multivariate linear regression were conducted to prove PM_{10} correlation in randomly shuffled dataset, and PM_{10} was significantly correlated with the severity of symptoms (*P* = .046, Table S1). We also evaluated the association between the concentration of PM_{10} and the duration of allergic rhinitis symptoms, when adjusting for the confounding factors mentioned above. Although not significant, there was a positive correlation between PM_{10} concentration and duration of allergic rhinitis symptoms (β = 0.082, *P* = .077) (Table II).

TABLE I.
Demographic and Clinical Features of Participants in Industrial and Non-Industrial Groups.

	Industrial Group (n = 286)	Non-Industrial Group (n = 304)	*P* Value
Demographics			
Age, years	49.6 ± 23.84	43.4 ±22.02	**.001**
Sex (male: female)	124: 162	154: 150	.090
Region (Gwangyang/Yeosu/Hadong)	1/116/169	147/89/68	
Allergic sensitization			
Atopic status	46/286 (16.1%)	57/304 (18.8)	.457
Dp	41/286 (14.3%)	42/304 (13.8%)	.950
Df	32/286 (11.2%)	31/304 (10.2%)	.798
Cockroach	5/286 (1.7%)	12/304 (3.9%)	.177
Mugwort	11/286 (3.8%)	16/304 (5.2%)	.531

Bold text indicates statistical significance (*P* < .05).
Dp = *Dermatophagoides pteronyssinus*; Df = *Dermatophagoides farina*.

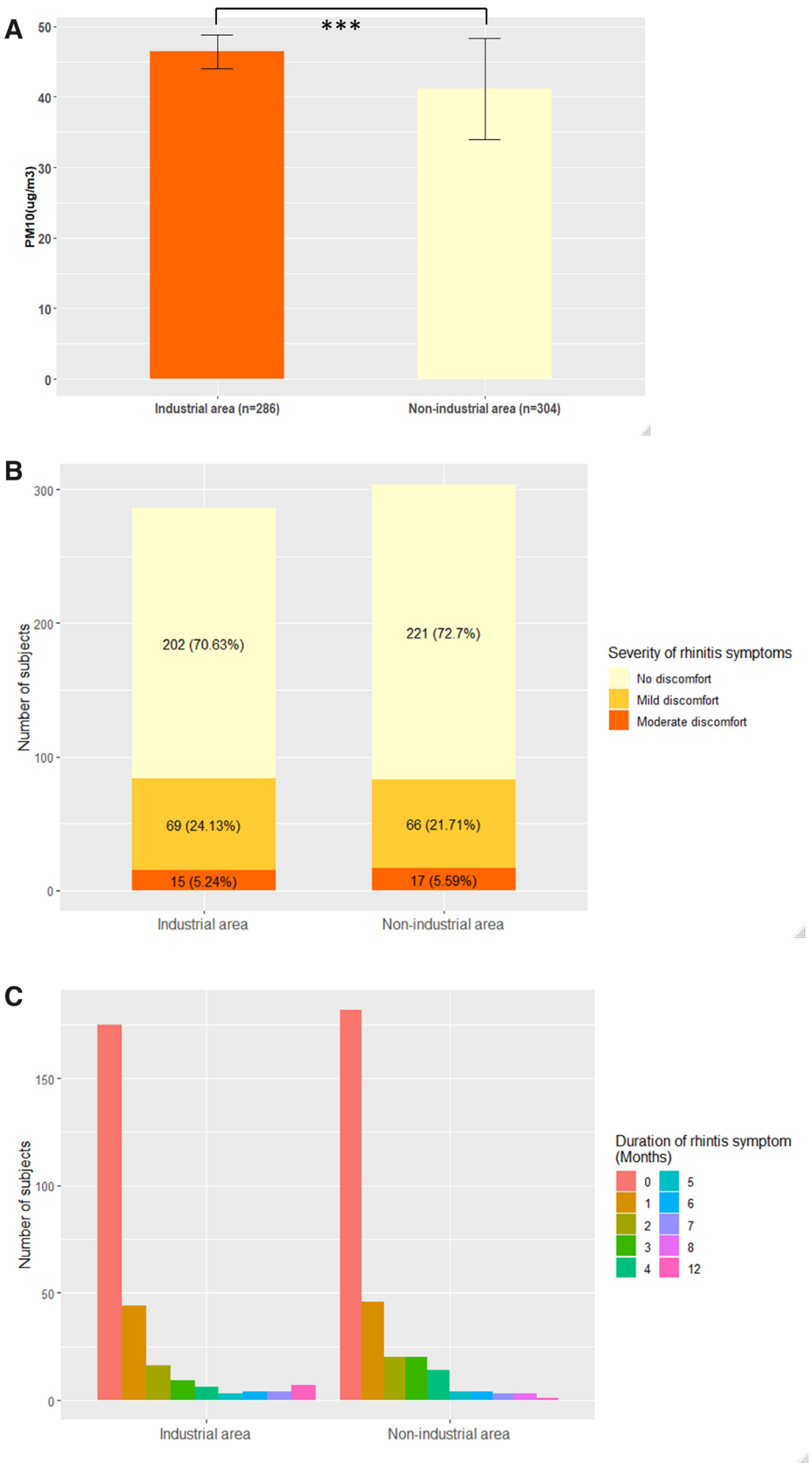

Fig. 3. Comparison between industrial and non-industrial groups. (A) Comparison of the annual concentration of PM_{10} between two groups (***: $P < .001$). (B) Comparison of the severity of rhinitis symptoms between two groups. (C) Comparison of the duration of rhinitis symptoms between two groups. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE II.
Multivariate Analysis for Association Between PM_{10} Concentration and Symptoms of Allergic Rhinitis.

	Standardized β	Standard Error	*P* Value
Severity of symptoms	0.102	0.004	**.021**
Duration of symptoms	0.082	0.017	.077

Bold text indicates statistical significance ($P < .05$). Confounding factors (sex, age, atopic status, the time of enrolment, and region) were adjusted.

TABLE III.
Stratified Multivariate Analysis on the Atopic Status for Association Between Concentration of PM10 and Symptoms of Allergic Rhinitis.

(A) Patients with Allergic Sensitization (n = 103)			
	Standardized β	Standard Error	*P* Value
Severity of symptoms	0.048	0.010	.678
Duration of symptoms	−0.101	0.048	.406
(B) Patients without Allergic Sensitization (n = 487)			
	Standardized β	Standard Error	P Value
Severity of symptoms	0.104	0.005	**.032**
Duration of symptoms	0.127	0.018	**.011**

Bold text indicates statistical significance ($P < .05$). Confounding factors (sex, age, the time of enrolment, and area) were adjusted.

Stratified Analysis on the Atopic Status

Stratified multivariate analysis on the atopic status was performed. One hundred and three among 590 participants were atopic (17.5%). Multivariate analysis of the data of participants with allergic sensitization showed that the concentration of PM_{10} did not correlate with the severity or duration of symptoms, after adjusting for age, sex, region, and the time of enrolment (Table IIIA). However, multivariate analysis of the data of participants without atopy revealed that the concentration of PM_{10} correlated with both, severity and duration of symptoms, after adjusting for the confounding factors mentioned above ($\beta = 0.104$; $P = .032$ and $\beta = 0.104$; $P = .011$, respectively) (Table IIIB).

DISCUSSION

We found that there was a positive correlation between the air pollution level, represented by the annual PM concentration, and the severity and duration of rhinitis symptoms based on a regional population-based cohort study. Air pollution has increased due to global industrialization and urbanization and a relationship between the level of air pollution and diseases of the respiratory tract have been suggested.[4–7] The nasal airway is the entrance of the respiratory tract that comes into contact with air pollutants; thus, patients with inflammatory diseases of the nasal airway, such as rhinitis, are susceptible to these pollutants. While particles larger than 10 μm can be filtered by the filtration capability of the nasal airway, particles smaller than 2.5 μm cannot be filtered and enter the lower airway.[16] Persistent exposure of the nasal airway toward PM can irritate the nasal mucosa and lead to inflammation and disruption of epithelial barrier functions that in turn result in the initiation and/or aggravation of inflammatory diseases such as, allergic rhinitis and rhinosinusitis.[16] A recent multicenter study revealed a significant association between the severity of rhinitis symptoms and PM concentration, including that of $PM_{2.5}$ and PM_{10} (adjusted odds ratio for a 10 mg/m^3 increase in PM_{10} was 1.20, 1.53, and 1.72 for those with mild, moderate, and high severity of symptoms, respectively).[17] Unlike our study, the participants of this study were from different European countries and the duration of symptoms was not evaluated.

We measured the PM_{10} concentration using regional air quality monitors. Although, the 12 observatories were present in three adjacent cities, the presence of petrochemical corporations in the industrial regions, led to varying concentrations of PM_{10}. Accordingly, there was a significant difference in the PM_{10} concentrations between the industrial and non-industrial regions. Participants in the industrial group were older than those in the non-industrial group, and the proportion of the elderly (age > 60 years) in the industrial group was higher than that in the non-industrial group (49.0% vs. 27.3%, respectively, $P < .001$, data not shown). Although, rhinitis symptoms tend to become milder with aging,[18] the industrial group comprised a higher proportion of older participants, and the severity of their rhinitis symptoms was slightly higher than or comparable with that of those in the non-industrial group.

With regard to allergic sensitization, there was no significant difference between the industrial and non-industrial groups, although, one study revealed a positive association between $PM_{2.5}$ exposure and allergic sensitization in children.[19] Meta-analyses of birth cohorts did not show a statistically significant association between allergic sensitization and air pollutants such as $PM_{2.5}$, PM_{10}, and NO_2.[20] In the stratified analysis on the atopic status, contradictory to the multivariate analysis of patients with allergic sensitization, there was a significant correlation between PM_{10} concentration and the severity and duration of rhinitis symptoms in those without allergic sensitization. This result was consistent with that of a previous study,[17] and suggested that PM_{10} may exert a greater influence on rhinitis symptoms in non-allergic rhinitis patients. This may be attributed to the fact that allergic sensitization is already a risk factor for the relatively higher severity of rhinitis symptoms. A greater proportion of patients with allergic sensitization suffered from the discomfort of rhinitis in their daily life than those without it (40.8% vs. 25.7%, respectively, $P = .003$, data not shown). Therefore, the impact of PM_{10} may have been lower in patients with allergic sensitization who suffered from rhinitis. In addition, these patients were possibly affected by the sensitized allergen rather than the ambient air pollutants.

The strength of our study was that all participants who completed the SPT and questionnaire for allergic rhinitis symptoms were evaluated according to the regional concentration of PM_{10} monitored at 12 different

observatories, in three cities. In contrast to the previous studies that used the mean value of concentration of air pollutants in each city,[12, 21] we assessed the correlation between allergic rhinitis symptoms and PM_{10} concentration according to the different regions within three cities that reflected an individual's ambient concentration of PM more appropriately. In addition, the stratified analysis on the atopic status was performed to validate the different effects of PM_{10} on allergic and non-allergic rhinitis. However, our study also had some limitations. Although, a detailed regional analysis was performed, the exact individual PM_{10} levels were not assessed. As the amount of air pollution exposure is rarely constant and individual behavioral components are also complex and variable, an accurate assessment is usually not possible. Conversely, as people generally receive the information of air pollution from the regional air quality monitors, our study results could be applied to real life scenarios.

CONCLUSION

In conclusion, our regional analysis demonstrated a significant correlation between the annual exposure of PM_{10} and the severity and duration of rhinitis symptoms. This result suggests that intensive management of rhinitis patients exposed to high levels of ambient PM_{10}, especially those with non-allergic rhinitis, is necessary.

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