



# Assessment of temporal variation for the risk of particulate matters on asthma hospitalization



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## ABSTRACT

Increased ambient concentration of particulate matters are considered as one of major causes for increased prevalence or exacerbation of asthma or asthma like symptoms. Recently, possible temporal variation in risks of PM on mortality has been suggested.

We investigated short-term effect of both PM<sub>10</sub> and PM<sub>2.5</sub> on asthma hospitalization, and assessed temporal variation of PM risks in Seoul, Korea, 2003–2011.

Generalized additive model was used to estimate PM risks on asthma hospitalization with consideration by long-term trend, influenza epidemic, day of week, meteorological factors. To assess temporal variation of PM risks, year-round PM risks were estimated. Stratified analysis by season and age-group were also conducted.

Estimated RRs of PM on asthma hospitalization by an increase of 10 $\mu$ g/m<sup>3</sup> were 1.0084 (95% CI: 1.0041–1.0127) and 1.0156 (95% CI: 1.0055–1.0259) respectively with 7-days lag periods (lag06). PM<sub>2.5</sub> had stronger effect than PM<sub>10</sub> for all age group. Elderly group was most affected by PM. For the analysis of temporal variation of PM risks, we found increasing trend in total population and the elderly group. In the season-specific analysis, we also found increasing trend in winter for PM<sub>10</sub>, and in spring for PM<sub>2.5</sub>.

PM<sub>10</sub> and PM<sub>2.5</sub> has adverse effect on asthma hospitalization with evidence suggesting temporal variation in PM risks. Further research will be needed to confirm the temporal variation of PM risk on asthma hospitalization, and to identify casual factors affecting this temporal variation. This study results could be evidentiary materials for establishing valid public health policies to reduce health burden or economic burden of asthma.

## 1. Introduction

The prevalence of allergic diseases such as asthma, allergic rhinitis, and allergic dermatitis has rapidly increased in the last decades in both developed countries and developing countries. As one of the allergic respiratory diseases, asthma has substantial economic burden and health burden. In Korea, according the Korea Health Statistics 2016 the prevalence of physician-diagnosed asthma increased from, 0.7% at 1998 to 3.1% at 2015 ("Korea Health Statistics 2015: Korean National Health and Nutrition Examination Survey (KNHANES VI-3)," 2016). And total expenditure of asthma hospitalization also increased from 29 billion Korean Won (1000 won approximate to 1 US dollar) at 2003 to 43 billion Korean Won at 2011 ("Health Insurance Statistical Yearbook," 2003; "Health Insurance Statistical Yearbook," 2011). In some developed countries, increasing asthma prevalence trends have plateaued or even reversed into a decreasing trend (Akinbami et al., 2012, 2016; De

Marco et al., 2012; Korte-de Boer et al., 2015; Sears, 2014; Wong et al., 2013). However, developing countries are still having an increasing pattern for the prevalence for these allergic diseases (Hansen et al., 2013; Sears, 2014; Wong et al., 2013).

Many studies were conducted in various countries to identify the causes of increasing prevalence of allergic diseases (Bowatte et al., 2015; Brauer et al., 2002; Gilmour et al., 2006; Ho et al., 2007; Tecer et al., 2008). In Korea, studies identifying the adverse effect of ambient particulate matters (PM) on asthma hospitalization have reported that PM has an adverse effect on asthma and asthma-related symptoms (Kim et al., 2007; Park et al., 2013; Park et al., 2016). The known mechanisms association between PM and asthma include oxidative stress, augmentation of inflammation, promotion of allergen sensitization, induction of airway hyper-responsiveness, aggravation of rhinitis, and DNA methylation (Nel et al., 2001; Shadie et al., 2014; Sofer et al., 2013). However, studies investigating the association between PM and

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hospitalization due to asthma have mainly focused on particles with diameter of  $10\mu\text{m}$  or less (also known as  $\text{PM}_{10}$ ). Particles with a diameter of  $2.5\mu\text{m}$  or less (also known as  $\text{PM}_{2.5}$ ) are known to have a more harmful effect on health due to its small size (Kim et al., 2015a, 2015b, 2015c). They can penetrate easily into the respiratory track (Brown et al., 2013). In addition, they are composed with relatively higher proportion of toxic components such as heavy metals than  $\text{PM}_{10}$  (Park et al., 2008). However, few studies have assessed the effect of  $\text{PM}_{2.5}$  on asthma hospitalization compare to studies on  $\text{PM}_{10}$ . Therefore, the one of the objects of this study was to determine the effect of PM (both  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$ ) on asthma in Seoul, Korea.

Many literatures have suggested that PM risk may change over time and space (Atkinson et al., 2001; Bell et al., 2009; Brook et al., 2010; Correia et al., 2013; Kim et al., 2015a, 2015b, 2015c). These studies mentioned that population characteristics including susceptible population, composition of PM, air pollution standards/policies might play role in variation of PM risk. Bell et al. (2009) have found that geographical and seasonal variations in the short-term effects of PM on cardiovascular and respiratory hospitalization between 106 counties in the United States could be explained by differences in PM chemical compositions (Bell et al., 2009). Correia et al. (2013) investigated the effect of  $\text{PM}_{2.5}$  on life expectancy in 545 US counties using regression model for the period 2000–2007, and they found the association between reduction in  $\text{PM}_{2.5}$  and changes in life expectancy and this association was stronger in urban and densely populated area (Correia et al., 2013). In that study, they conclude that reduction in  $\text{PM}_{2.5}$  through air pollution control were associated with improvement of life expectancy (Correia et al., 2013). Dominici et al. (2007) estimated the change of PM effects on mortality for the period 1987–2000 using National Morbidity Mortality Air Pollution Study data to evaluate the public health effect of air quality regulation, and found weak evidence of a declining trend in the short-term PM effects (Dominici et al., 2007).

In Korea, air quality standard of  $\text{PM}_{10}$  has been strengthened from ‘interim target-I ( $70\mu\text{g}/\text{m}^3$  24-annual mean,  $150\mu\text{g}/\text{m}^3$  24-h mean)’ of WHO guideline in 2001 to ‘interim target-II ( $50\mu\text{g}/\text{m}^3$  annual mean  $100\mu\text{g}/\text{m}^3$  24-h mean)’ in 2007. For  $\text{PM}_{2.5}$ , the standard was established as ‘interim target-II ( $25\mu\text{g}/\text{m}^3$  annual mean  $50\mu\text{g}/\text{m}^3$  24-h mean)’ in 2011. Although these efforts resulted in decreasing mass concentration of PM concentration, Kim et al. (2015a), (2015b), (2015c) showed that PM risk in respiratory mortality increased over time (H. Kim, H. Kim et al., 2015a, 2015b, 2015c). In light of both the increase in prevalence of asthma and the of PM risk on respiratory mortality, this research should be undertaken in order to properly understand this temporal variation.

Thus, the objective of this study was to determine the effect of  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  on asthma hospitalization, and to examine the annual temporal variations of estimated risks of PM, in Seoul, Korea.

## 2. Material and methods

### 2.1. Study population

In this study, we targeted people who are residing in Seoul, Korea. Seoul is the capital city of Korea. It is located at the center of the Korean Peninsula, with an area coverage of  $605\text{ km}^2$ . According the Statistics Korea 2013, approximately 10,195,000 people (approximately 1/5 of Korean population) were living in Seoul in January of 2013.

Visiting records of asthma hospitalization were obtained from National Health Insurance Corporation between January 1st, 2003 and December 31st, 2011. Individuals who were diagnosed with asthma (ICD-10 J45, predominantly allergic asthma) as primary or secondary diagnosis were included as study subjects. The visiting records does not provide whether they hospitalized by emergency room visit. Therefore, we could not possible to differentiate individual admission route. Nonetheless, most of asthma hospitalization was occurred by acute severe asthma attack, subject in our study could have high chance to

hospitalize through emergency room visit.

Daily counts of hospitalization due to asthma were calculated for the entire subjects. Age group (0–18, 19–64, and 65+ years) counts were also calculated.

### 2.2. Air pollution and meteorological data

Hourly measured ambient concentration of  $\text{PM}_{10}$  in a single day and daily averaged ambient concentration of  $\text{PM}_{2.5}$  were obtained from the National Institute of Environmental Research in the same period (i.e., between January 1st, 2003 and December 31st, 2011).  $\text{PM}_{10}$  was measured routinely in Korea after 1998. At present, 25 monitoring stations are measuring air pollutants including both  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  in Seoul. To calculate daily mean concentration of PM from hourly-based measurements, the hourly mean value of measurements from the 25 monitoring stations were calculated. Daily mean concentration was then calculated from the 24 hourly averaged values of  $\text{PM}_{10}$ . For  $\text{PM}_{2.5}$ , it was measured routinely after 2003 with fewer monitoring stations than  $\text{PM}_{10}$  and 25 monitoring stations are settle down at 2007. Missing values in measurements of PM are imputed with the mean value of each year of each monitoring station.

Hourly measured daily temperature and humidity in Seoul were obtained from the Meteorological Administration. We calculated the daily mean temperature and humidity using hourly measured data.

### 2.3. Statistical analysis

In this study, we assumed homogeneous distribution of particulate matters across in Seoul because we could not possible to obtain the address of subject by institutional privacy policy. To support this homogeneity assumption of PM concentration in Seoul, we compared the distribution of  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  in 25 monitoring stations by each year. In addition, we calculated correlation coefficients between 25 monitoring stations. Distribution of ambient PM concentration measured in 25 monitoring stations showed relatively similar distribution (Supplemental Figure A, Figure B) and measured values are highly correlated across the 25 monitoring stations (Supplemental Table A-C). Therefore, the hypothesis that homogeneous distribution of PM concentration in Seoul is plausible.

Generalized additive model (GAM) with log link and Poisson error was used to estimate the relative risks (RR) of  $\text{PM}_{10}$  and  $\text{PM}_{2.5}$  on asthma hospitalization after adjusting for long-term trend, day of week, holiday, influenza epidemic, temperature, and humidity. Meteorological conditions such as temperature and humidity were considered as confounding factors. They not only might exacerbate the existing disease status, but also might cause formation or dispersion of PM. Regression spline were used to consider non-linear association between long-term trend (*Time*), temperature, and humidity with asthma hospitalization (degree of freedom: 7 per year for long-term trend, 4 for temperature, and 4 for humidity). Degree of freedom of long-term trend was chosen through sensitivity analysis by varying the degree of freedom from 3 to 9 per year, and showed stabilized estimated coefficient of PM risks at 7 per year. The basic model that we considered was:

$$\begin{aligned} \text{Log}(E(\text{Counts of hospitalization})) &= \beta_0 + \beta_1(\text{PM}_{10} \text{ or } \text{PM}_{2.5}) + s(\text{Temperature}, df=4) \\ &+ s(\text{Humidity}, df=4) + s(\text{Time}, df=7 \text{ per year}) \\ &+ D(\text{Day of week}) + D(\text{Holiday}) \\ &+ D(\text{Influenza Epidemic}) \end{aligned}$$

To consider the delayed effect of PM, we calculated the RRs for the day of hospitalization (lag0) and for average concentration of PM up to nine days before hospitalization (average concentration of ten days PM concentration, lag09). As the estimated risks were higher at lag06 with stabilized values, we set the lag effect at lag06 for the analysis of

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