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Fine particulate air pollution and hospitalization for pneumonia: a case-crossover study in Shijiazhuang, China

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Abstract Many epidemiological studies have shown that airborne particulate matter (PM) is a risk factor for multiple respiratory diseases and increased hospitalization rates. Fine PM ($PM_{2.5}$, diameter <2.5 μm) is considered to be a greater health hazard than coarse PM (PM_{10}, 2.5–10 μm) because it adsorbs more harmful substances and can enter deeper parts of the lungs. We investigated the correlation between hospitalization for pneumonia and $PM_{2.5}$ levels in Shijiazhuang, a city in northern China. Daily data on hospitalizations for community-acquired pneumonia and ambient air pollution levels in Shijiazhuang were obtained for 2013. A bidirectional case-crossover design was used to investigate the association between hospitalization for pneumonia and atmospheric $PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3 levels. The effects of pollutant levels from lag0 (day of hospitalization) to lag5 (five days before lag0) were investigated in both single and multi-pollutant models, adjusted for daily weather variables. For the single-pollutant model, hospitalization for pneumonia correlated positively with higher $PM_{2.5}$ levels, with an increase of 1.1 % in daily admissions per 10-μg/m^3 increase in the $PM_{2.5}$ level at lag0. In the multi-pollutant model, the observed effects of $PM_{2.5}$ remained significant. Stratified analysis of exposure based on sex, age, season, and comorbidities showed that the effect of $PM_{2.5}$ on hospitalization for pneumonia was stronger in males, people younger than 60 years, people without comorbidities, and on warm days. These results indicate that higher levels of $PM_{2.5}$ increase the risk of hospitalization for pneumonia in Shijiazhuang, China.

Keywords Fine particulate · Air pollution · Pneumonia · Case-crossover · Hospital admission

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Introduction

A large number of epidemiological studies have confirmed the hazards of airborne particulate matter (PM) on human health (Pope et al. 2004; Schwartz 2004; Analitis et al. 2006; Samet and Krewski 2007; Le Tertre et al. 2002). Inhalable PM (PM_{10}, measured as PM with an aerodynamic diameter <10 μm) can be divided into three categories: coarse PM ($PM_{2.5–10}$; aerodynamic diameter of 2.5–10 μm), fine PM ($PM_{2.5}$; aerodynamic diameter of 0.1–2.5 μm), and ultrafine PM ($PM_{0.1}$; aerodynamic diameter <0.1 μm). Fine PM has larger surface area, adsorbs more pathogenic microorganisms, aromatic hydrocarbons, and other harmful substances, and can enter the deep parts of the lungs, reaching various levels of bronchioles and depositing inside the alveoli. Thus, fine PM exhibits greater toxicity to humans than coarse PM (Wilson and Suh 1997; Pope and Dockery 2006). Many epidemiological studies have demonstrated that fine PM represents a greater health hazard than coarse PM (Cifuentes et al. 2000; Schwartz et al. 1996; Zanobetti et al. 2009; Liao et al. 2011). As a result, the World Health Organization has recommended that $PM_{2.5}$, rather than PM_{10}, be used as the major indicator for air quality monitoring (Samet et al. 2006).

Epidemiological studies have found that the rate of hospitalization for pneumonia is closely related to the ambient levels of PM (Chiu et al. 2009). Hospitalization for pneumonia has been reported to increase by 0.84 % per 10-μg/m^3 increase in the concentration of PM_{10} (Medina-Ramon et al. 2006), and by 4 % in the cold season and 12 % in the warm season per quartile increase in $PM_{2.5}$ (Tsai and Yang 2014). Emergency room admissions have been reported to increase by 3 % per 2-μg/m^3 increase in the concentration of $PM_{2.5}$ (Peel et al. 2005). However, most studies in this field have been carried out in Europe and the USA, while relatively few have been undertaken in Asia. China is a developing country with much more serious air pollution than Europe and other developed countries. Furthermore, it is highly likely that there is considerable heterogeneity in the levels and chemical composition of PM in different regions of China, and that this shows seasonal variation within each region. Since the research findings in Europe and other regions of the world may not apply to China, it is extremely important that the effects of $PM_{2.5}$ on the rate of hospitalization for pneumonia are studied in China.

Real-time monitoring of $PM_{2.5}$ levels in China started only recently, in January 2013. This monitoring is being undertaken in 74 cities, and the data are being published to facilitate epidemiological analysis. To date, however, no studies have been published regarding the impact of $PM_{2.5}$ levels on the rate of hospitalization for pneumonia in China. Therefore, the aim of the present study was to examine the association between the ambient levels of $PM_{2.5}$ and the rate of hospitalization for pneumonia in residents of Shijiazhuang in 2013, using a case-crossover design.

Materials and methods

City characteristics

This was an epidemiological study conducted in Shijiazhuang, a city located in north China, with a population of approximately 3 million inhabitants. Shijiazhuang has a warm, temperate, continental monsoon climate, with an annual mean temperature of 13 °C (range, −6.5 to 32.5 °C). Shijiazhuang is the second-most polluted city among the 74 cities for which $PM_{2.5}$ monitoring data has been published in China (Ministry of Environmental Protection of the People's Republic of China. The State of China's Environment 2013. http://jcs.mep.gov.cn/hjzl/zkgb/2013zkgb).

Hospital admissions data

This study was approved by the Ethics Committee of The Second Hospital of Hebei Medical University. Written informed consent was obtained from all participants. This retrospective study was carried out in the respiratory departments of the seven main tertiary general hospitals in Shijiazhuang, China. These seven hospitals provide about 70 % of all the tertiary hospital beds for respiratory hospital admissions in Shijiazhuang. Patients were included in the study if they were urban residents of Shijiazhuang aged 18 years or more and had been admitted to hospital for community-acquired pneumonia (CAP) between January 1, 2013 and December 31, 2013. The criteria used for the diagnosis of CAP were those provided by the Chinese Medical Association of Respiratory Diseases (2006). Briefly, CAP was defined as chest X-ray evidence of lobar consolidation, cavitation or parenchymal involvement, with or without pleural effusion; plus at least one of the following: (1) new appearance of cough and/or sputum or aggravation of the symptoms of an existing respiratory disease, with production of a purulent sputum with or without chest pain; (2) fever; (3) signs of lung consolidation or wet rales on auscultation; or (4) white blood cell count $>10 \times 10^9$/L or $<4 \times 10^9$/L. In addition, the following diseases were excluded: pulmonary tuberculosis, lung tumor, noninfectious pulmonary interstitial disease, pulmonary edema, pulmonary atelectasis, pulmonary embolism, pulmonary infiltration with eosinophilia, and pulmonary vasculitis. Hospitalizations for both primary occurrence and recurrence of CAP were included. The exclusion criteria were the following: patients who were not urban residents of Shijiazhuang, patients with hospital-acquired pneumonia, patients with aspiration pneumonia, or patients with hypersensitivity pneumonitis.

The collection of data from the seven hospitals was carried out by six resident respiratory physicians, each of whom had at least two years of clinical experience in respiratory medicine and had received training in the collection of data for the study. For each patient, the following information was extracted from the medical records: admission date, age, sex, ethnicity, smoking history, and complications. The total number of patients newly admitted for CAP per day was determined; inpatients at the hospital who had not been newly admitted that day were not included in the figures.

Air pollution and meteorological data

Air pollution data were obtained from the website of the China Environmental Monitoring Center (http://www.cnemc.cn). The data were obtained from seven state-controlled, fully automated monitoring stations for environmental air quality, located in urban (but not rural) regions of Shijiazhuang city (Fig. 1). At each monitoring station, air samples were drawn by sampling pumps into collectors on the roof and transported by pipelines to the analytical devices. The ß-ray method was used to determine the concentrations of PM_{10} and $PM_{2.5}$, an ultraviolet fluorescence method was employed to obtain sulfur dioxide (SO_2) and ozone (O_3) levels, a chemiluminescence method was used to detect nitrogen dioxide (NO_2), and a gas filter-correlation infrared absorption method was used to detect carbon monoxide (CO). Each monitoring site provides data on an hourly basis. For each day, the hourly air pollution data from the seven monitoring stations were combined, and the mean hourly values were calculated for each of the pollutants. These mean hourly values were then used to calculate

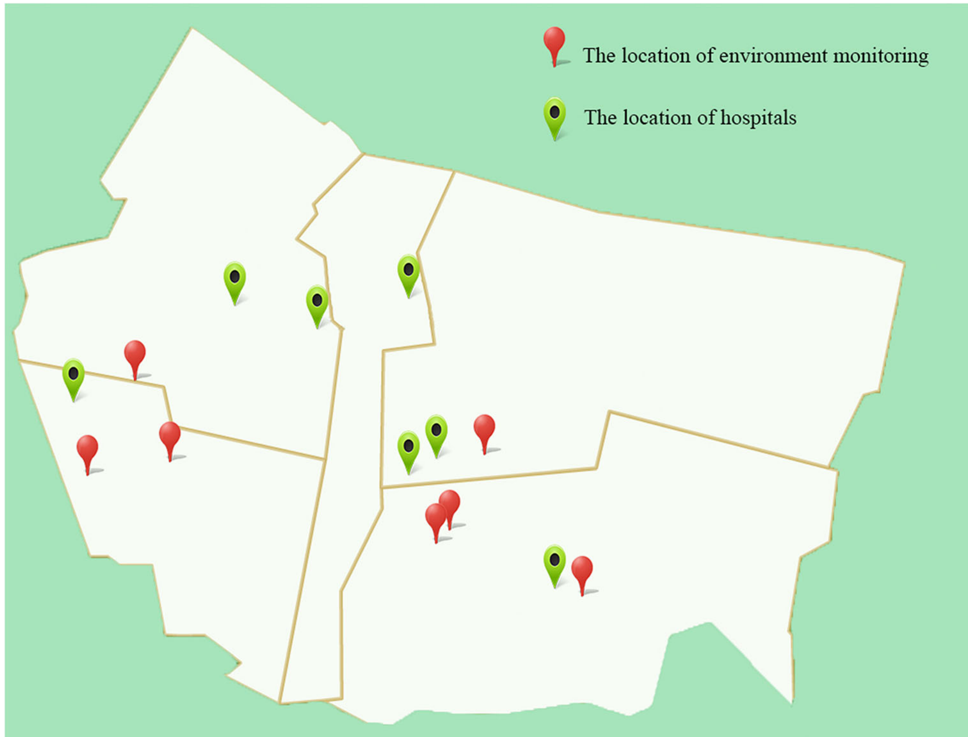

Fig. 1 Map of the monitoring stations and hospitals in Shijiazhuang, a city in northern China

mean daily values for each of the pollutants. Thus, the measurement of pollutant levels was not reliant on random sampling. Daily information on the mean temperature was provided by the Shijiazhuang Meteorological Bureau.

Statistical analysis

A bidirectional case-crossover design (Maclure 1991) was used to assess the influence of exposure to various pollutants on the risk of hospitalization for pneumonia. A time-stratified approach was employed to select control days. Air pollution levels on each of the hospital admission dates were compared with air pollutant levels one week before and one week after the date of admission. The results of previous studies have indicated that an increased number of hospital admissions or emergency room admissions for pneumonia was associated with higher air pollutant levels on the same or previous days, suggesting a lag in the effect of the pollutant (Nascimento et al. 2006; Gouveia et al. 2006; Zanobetti and Schwartz 2006; Santus et al. 2012; Negrisoli and Nascimento 2013). In order to assess pollution exposure, same-day mean exposure and exposures at lagged intervals extending from 1 to 5 days before the case or control event were obtained. Lag0 was defined as the event day, lag1 as the day before the event day, lag2 as the day before lag1, and so forth.

All statistical analyses were performed using the SPSS 19.0 software package (IBM Corp., Armonk, NY, USA). Spearman's correlation coefficients were calculated to analyze cross-correlations between the various pollutants. The association between hospitalization for pneumonia and levels of $PM_{2.5}$ was estimated using the odds ratio (OR) and corresponding 95 % confidence intervals (95 % CI), which were calculated using conditional logistic regression with weights equal to the number of hospital admissions on that day. All models included daily temperature as a variable. A single-pollutant model was used initially, and multi-pollutant models were then fitted with different combinations of pollutants to assess the stability of the effect of $PM_{2.5}$. Stratified analyses of exposure based on age, sex, complications, and season were undertaken to evaluate effect modification. The results of the analyses were expressed as ORs to quantify the increase in risk based on a corresponding increase in exposure

Table 1 Distribution of the hospitalizations for community-acquired pneumonia according to patient characteristics and season

Characteristic		Number of events	Total (%)
Sex	Male	1204	53.44
Age	<60 years	1012	44.92
Season	Warm season	1207	53.57
Comorbidities	Present	1486	65.96
Chronic lung disease	Present	274	12.16
Total		2253	100.00

Comorbidities included heart disease, diabetes mellitus, and cerebrovascular disease. International Statistical Classification of Diseases and Related Health Problems (ICD) codes: heart disease, I10–I52; diabetes mellitus, E10–E14; cerebrovascular disease, I69; chronic pulmonary disease, J40–J47

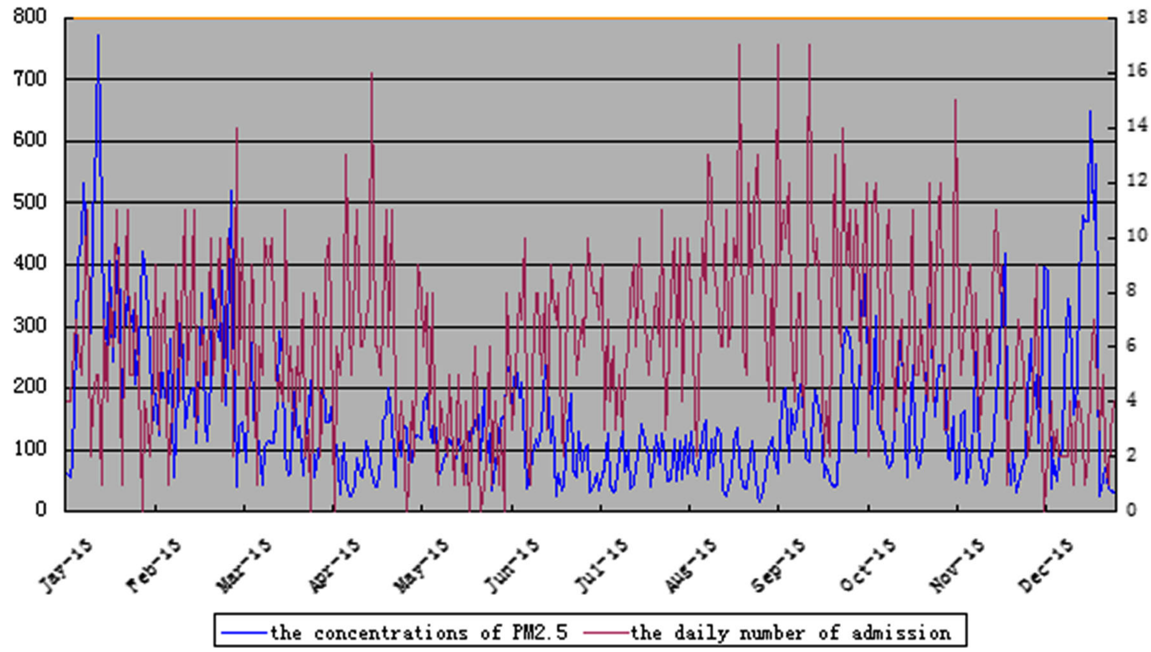

Fig. 2 Daily number of hospitalizations for pneumonia observed during the study period. The data show the total daily number of hospital admissions for community-acquired pneumonia at the seven hospitals involved in the study (study period: January 1, 2013 to December 31, 2013) together with the corresponding daily $PM_{2.5}$ levels

of 10 μg/m^3 of PM_{10}, 10 μg/m^3 of $PM_{2.5}$, 1 μg/m^3 of SO_2, 1 μg/m^3 of O_3, 1 μg/m^3 of NO_2, and 1 mg/m^3 of CO. The warm season was defined as being from April to September. $P < 0.05$ was considered to indicate statistical significance.

Results

During the study period, there were a total of 2253 hospital admissions for CAP. The distribution of these hospitalizations according to sex, age, season, the presence/absence of comorbidities (including heart disease, diabetes mellitus, and cerebrovascular disease), and the presence/absence of chronic lung disease (including chronic obstructive pulmonary disease, asthma, and bronchiectasis) is presented in Table 1. Among the 2253 patients hospitalized during the study period, 53 % were male, 55 % were aged 60 years or more, and 66 % had comorbidities. All patients were Han Chinese. Figure 2 displays the daily number of hospitalizations for pneumonia for the entire study period and shows that most hospitalizations occurred in August. Over the course of the study period, the mean number of hospital admissions for CAP was 6.17 per day.

Table 2 shows the descriptive statistics (percentiles, interquartile ranges, and means ± standard deviations) for the corresponding environmental data ($PM_{2.5}$, PM_{10}, SO_2, NO_2, CO, and O_3). $PM_{2.5}$ and PM_{10} were observed to be important air pollutants in Shijiazhuang, their mean levels exceeding those of SO_2, NO_2, and O_3. The mean concentration of PM_{10} was approximately double that of $PM_{2.5}$ (311 vs. 156 μg/m^3). Notably, there were significant variations in

Table 2 Descriptive analysis of the environmental variables measured daily during 2013 in Shijiazhuang, China

Variable	Unit	Percentiles				Total	
		25 %	50 %	75 %	IQR	Mean	SD
$PM_{2.5}$	μg/m^3	73.05	123.00	200.68	127.63	156.43	118.60
PM_{10}	μg/m^3	194.24	275.93	390.63	196.39	311.26	162.94
SO_2	μg/m^3	41.49	79.00	144.89	103.4	106.44	86.84
NO_2	μg/m^3	49.05	62.28	81.77	32.72	68.77	28.68
CO	mg/m^3	1.00	1.39	2.28	1.28	2.04	1.74
O_3	μg/m^3	42.55	81.43	137.42	94.87	96.25	67.99
Temperature	°C	5.00	14.50	24.50	19.50	14.33	11.14

IQR interquartile range, *$PM_{2.5}$* fine particulate matter, *PM_{10}* coarse particulate matter, *SD* standard deviation

Table 3 Spearman's correlation coefficients calculated for various pairings of the seven environmental variables

Variable	$PM_{2.5}$	PM_{10}	SO_2	NO_2	CO	O_3	T
$PM_{2.5}$	1.00	—	—	—	—	—	—
PM_{10}	0.89*	1.00	—	—	—	—	—
SO_2	0.55*	0.59*	1.00	—	—	—	—
NO_2	0.69*	0.74*	0.62*	1.00	—	—	—
CO	0.92*	0.83*	0.69*	0.75*	1.00	—	—
O_3	−0.39*	−0.30*	−0.59*	−0.47*	−0.53*	1.00	—
T	−0.41*	−0.31*	−0.75*	−0.40*	−0.54*	0.80*	1.00

*Significant correlation between variables ($P < 0.05$)

$PM_{2.5}$ fine particulate matter, PM_{10} coarse particulate matter, T temperature

the levels of all the pollutants, as shown by the interquartile range values (Table 2).

Calculation of Spearman's correlation coefficients (Table 3) revealed that there were significant cross-correlations between the various pollutants. $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO all showed significant positive correlations with each other (all $P < 0.05$), with the strongest associations between $PM_{2.5}$ and CO ($r = 0.92$), $PM_{2.5}$ and PM_{10} ($r = 0.89$), and PM_{10} and CO ($r = 0.83$). $PM_{2.5}$, PM_{10}, SO_2, NO_2, and CO all exhibited significant negative correlations with temperature (all $P < 0.05$). O_3 showed significant negative correlations with the other five pollutants, but was positively associated with temperature (all $P < 0.05$).

In order to estimate the effects of the individual environmental pollutants on hospitalization for CAP, a single-pollutant model was used to calculate the OR (and 95 % CI) of hospitalization for a 10-μg/m^3 increase in $PM_{2.5}$ or PM_{10}, a 1-μg/m^3 increase in SO_2, NO_2 or O_3, or a 1-mg/m^3 increase in CO. As shown in Table 4, a 10-μg/m^3 rise in $PM_{2.5}$ was associated with increased odds of hospitalization for pneumonia; the largest effect (OR, 1.011; 95 % CI, 1.005–1.017; $P < 0.05$) was observed for an increase in $PM_{2.5}$ on the day of hospitalization (lag0), although significant effects ($P < 0.05$) were also observed on lag1 to lag5 (Table 4). A 10-μg/m^3 rise in PM_{10} on any of the days from lag0 to lag5 was also associated with an enhanced OR for hospitalization, although the effect of increased PM_{10} appeared to be numerically smaller than that of $PM_{2.5}$. Significant effects of increased CO and NO_2 on hospitalization for pneumonia were also observed, whereas changes in SO_2 or O_3 had little or no effect on hospitalization (Table 4).

The stability of the effects of $PM_{2.5}$ and PM_{10} was assessed after adjustment for other air pollutants using a multi-pollutant model. As shown in Table 5 and Fig. 3, the effects of $PM_{2.5}$ on hospitalization for pneumonia remained significant even after accounting for all the other common air pollutants in the multiple-pollutant model. In contrast, in most cases, the effects of PM_{10} were no longer significant after adjustment for other air pollutants.

In order to adjust for possible effect modifiers, further analysis was undertaken with the data stratified for age, sex, the presence/absence of comorbidities, the presence/absence of chronic lung disease, and season. As illustrated in Fig. 4, the effect of a 10-μg/m^3 increase in $PM_{2.5}$ on hospitalization for pneumonia was stronger in males, younger people, people without comorbidities, and on warm days. The effects of a 10-μg/m^3 increase in PM_{10} (lower

Table 4 Odds ratios and corresponding 95 % confidence intervals of hospitalization for community-acquired pneumonia, calculated for a given increase in the level of each pollutant on different days (lag0 to lag5) using a single-pollutant model

Pollutant	Lag0	Lag1	Lag2	Lag3	Lag4	Lag5
$PM_{2.5}$	1.011* (1.005–1.017)	1.009* (1.003–1.015)	1.008* (1.003–1.014)	1.008* (1.003–1.014)	1.008* (1.002–1.014)	1.009* (1.003–1.015)
PM_{10}	1.004 (1.000–1.008)	1.004* (1.000–1.008)	1.004* (1.001–1.008)	1.005* (1.001–1.009)	1.004* (1.000–1.008)	1.005* (1.001–1.009)
CO	1.071* (1.019–1.126)	1.052 (0.999–1.109)	1.063* (1.010–1.119)	1.087* (1.030–1.148)	1.084* (1.029–1.143)	1.058* (1.003–1.116)
SO_2	1.001 (0.999–1.002)	1.001 (1.000–1.002)	1.001 (0.999–1.002)	1.001 (1.000–1.002)	1.001 (1.000–1.002)	1.001* (1.000–1.003)
NO_2	1.003* (1.001–1.006)	1.003* (1.000–1.006)	1.003* (1.000–1.006)	1.004* (1.001–1.007)	1.004* (1.001–1.007)	1.005* (1.002–1.008)
O_3	1.000 (0.999–1.001)	0.999 (0.998–1.000)	1.001* (1.000–1.003)	1.000 (0.999–1.002)	1.000 (0.999–1.001)	1.000 (0.999–1.001)

Data are shown as the odds ratio (95 % confidence interval) for hospitalization, calculated for a 10-μg/m^3 increase in $PM_{2.5}$ or PM_{10}, a 1-μg/m^3 increase in SO_2, NO_2, or O_3, or a 1-mg/m^3 increase in CO. Lag0 represents the day of hospitalization for community-acquired pneumonia, lag1 the day preceding lag0, lag2 the day preceding lag1, and so forth

*$P < 0.05$ (i.e., significant increase in risk of hospitalization for the given rise in pollutant level)

Table 5 Odds ratios and corresponding 95 % confidence intervals of hospitalization for community-acquired pneumonia calculated for a given increase in the level of fine or coarse particulate matter, after adjustment for other air pollutants using a multi-pollutant model

Pollutant(s) adjusted for	$PM_{2.5}$		PM_{10}	
	OR	95 % CI	OR	95 % CI
CO	1.011*	1.003–1.018	1.004	0.999–1.009
NO_2	1.011*	1.004–1.018	1.007*	1.000–1.013
SO_2	1.010*	1.003–1.016	1.004	0.999–1.009
O_3	1.010*	1.005–1.016	1.005*	1.001–1.009
$CO + NO_2$	1.011*	1.003–1.018	1.005	0.999–1.012
$CO + SO_2$	1.010*	1.003–1.018	1.003	0.997–1.008
$CO + O_3$	1.009*	1.002–1.017	1.003	0.998–1.008
$NO_2 + SO_2$	1.011*	1.004–1.018	1.006	1.000–1.012
$NO_2 + O_3$	1.010*	1.004–1.017	1.006	1.000–1.012
$SO_2 + O_3$	1.009*	1.003–1.015	1.004	0.998–1.009
$CO + NO_2 + SO_2$	1.011*	1.004–1.019	1.005	0.999–1.012
$CO + NO_2 + O_3$	1.010*	1.002–1.017	1.005	0.998–1.011
$CO + SO_2 + O_3$	1.009*	1.002–1.017	1.002	0.997–1.008
$NO_2 + SO_2 + O_3$	1.010*	1.004–1.017	1.005	0.999–1.012
$CO + NO_2 + SO_2 + O_3$	1.010*	1.002–1.018	1.004	0.998–1.011

The odds ratio (OR) and 95 % confidence interval (95 % CI) for hospitalization, calculated for a 10-μg/m^3 increase in $PM_{2.5}$ or PM_{10}, after adjustment for a 1-μg/m^3 increase in SO_2, NO_2, or O_3, or a 1-mg/m^3 increase in CO

*$P < 0.05$ (i.e., significant increase in risk of hospitalization for a 10-μg/m^3 rise in $PM_{2.5}$ or PM_{10}, after adjustment for other pollutants)

panel) were significant only in males, older people, people without chronic lung disease, and during the cold season.

Discussion

The present study was designed to investigate the possible association between environmental $PM_{2.5}$ levels and hospitalization for CAP, during 2013, in urban residents of Shijiazhuang, China. The main findings were that $PM_{2.5}$ levels were associated with a significant increase in the rate of hospitalization for CAP, with the strongest effect being a 1.1 % increase in the number of daily hospitalizations for a 10-μg/m^3 rise in the $PM_{2.5}$ levels on the day of hospitalization. Furthermore, this effect of $PM_{2.5}$ remained even after adjustment for other air pollutants (SO_2, NO_2, CO, and O_3). In addition, PM_{10} was also associated with a higher rate of hospitalization, although the effects were smaller than those of $PM_{2.5}$ and not as stable after adjustment for other pollutants. Due to the lack of $PM_{2.5}$ monitoring data before 2013, there is a paucity of epidemiological data specifically addressing the health effects of $PM_{2.5}$ in China. To the best of our knowledge, the present study is the first to investigate the association between the level of $PM_{2.5}$ and hospitalization for pneumonia in China. The data in this study reveal that $PM_{2.5}$ and PM_{10} were the primary atmospheric pollutants in Shijiazhuang in 2013 and hence, represented the major health hazards. This information may help policy makers to take steps to reduce $PM_{2.5}$ and PM_{10} levels in the atmosphere, through appropriate policy interventions and legislations.

The data in this study demonstrate that the levels of $PM_{2.5}$ and PM_{10} were positively associated with the daily number of hospitalizations for pneumonia. The observed effects of $PM_{2.5}$ remained significant even after accounting for other common air pollutants and were strongest at lag0. Investigations of the effects of $PM_{2.5}$ on hospitalization for pneumonia are rare, and the results have varied between studies. A study in Boston by Zanobetti et al. (Zanobetti and Schwartz 2006) found that the effect of $PM_{2.5}$ on emergency department admissions for pneumonia was particularly evident at lag0, with a 6.5 % increase in the risk of hospitalization for pneumonia per 17.1-μg/m^3 increase in the levels of $PM_{2.5}$. Another study in the USA determined that emergency department visits for pneumonia increased by 3 % per 2-μg/m^3 increase in the levels of $PM_{2.5}$ (Peel et al. 2005). Santus et al. (Santus et al. 2012) conducted a study in Milan, and their stratified analysis for days lag0–lag2 showed a 10 % risk increase for emergency room admissions due to pneumonia per 10-μg/m^3 increase in the levels of $PM_{2.5}$ during the warm season. In a study in Brazil, a 10-μg/m^3 increase in the concentration of PM_{10} was associated with an increase of nearly 9 % in the risk of pediatric hospitalization due to pneumonia, and the effects of PM_{10} were strongest at lag4 (Negrisoli and Nascimento 2013). In general, the present study is consistent with the above studies in that it demonstrated significant associations between exposure to $PM_{2.5}$ and hospital admissions for pneumonia. However, our results differ from those of these previous studies in terms of the magnitude of the effect of $PM_{2.5}$ and the lag periods. The reasons for these inconsistencies remain unclear but might be related to several factors such as differences between countries in the national healthcare system or in the criteria used for deciding whether or not to admit a patient. Another potentially key factor is the chemical composition of $PM_{2.5}$ which varies with season and region. Thus, the toxicity of $PM_{2.5}$ may vary between studies because of differences in its chemical composition (Suh et al. 2011).

The mechanisms through which $PM_{2.5}$ increases the risk of pneumonia are not fully understood, although hypotheses have been proposed to explain the contribution of $PM_{2.5}$ to pulmonary pathophysiology. First, PM could impair microbial clearance and pulmonary host defense mechanisms (Clarke et al. 2000; Leonardi et al. 2000) by damaging the mucociliary system of the respiratory tract (Duan et al. 2013; Ferreira-Ceccato et al. 2011), hindering macrophage

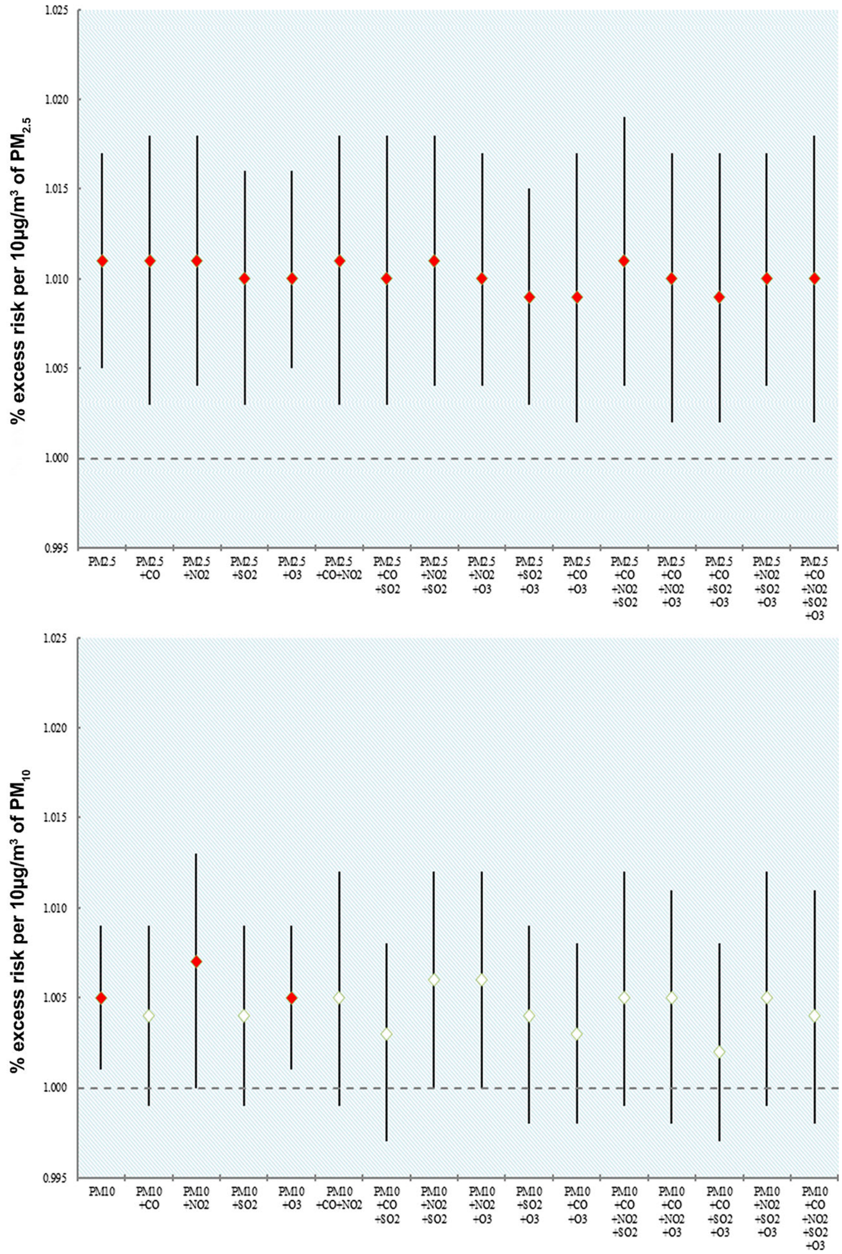

Fig. 3 Estimates of the effects of fine ($PM_{2.5}$) and coarse (PM_{10}) particulate matter on hospitalization for community-acquired pneumonia after adjustment for other air pollutants in a multi-pollutant model. Data are plotted as odds ratios and 95 % confidence intervals. *Red symbols* indicate significant effect, and *white symbols* non-significant effect. A 10-μg/m^3 increase in $PM_{2.5}$ (upper panel) was associated with a significant effect even after adjustment for other pollutants, whereas a 10-μg/m^3 increase in PM_{10} (lower panel) was in most cases not associated with a significant effect after adjustment for other air pollutants

phagocytosis (Zhou and Kobzik 2007; Lundborg et al. 2001). and causing intense capillary engorgement and loss of epithelium (Knox 2008). Animal studies have supported a role for PM in the impairment of microbial clearance (Phipps et al. 2010). For example, animals infected with *Streptococcus pneumoniae* and subsequently exposed to concentrated air particles had double the bacterial burden in the lungs 48 h later, compared with animals infected with the bacterium but exposed to filtered air (Zelikoff et al. 1999). Second, PM could induce and sustain alveolar inflammation and thereby aggravate lung diseases via inflammatory mediators and oxidative stress (Samet et al. 2006; Tsai et al. 2013; Ghio et al. 2012). The responses seem to depend on the material adsorbed in the particles, such as metals, organic carbon, ions (sulfates and nitrates), and other biogenic components (Samet et al. 2006).

Stratified analysis of exposure based on sex showed that the effect of $PM_{2.5}$ on pneumonia admissions was evident both in males and in females, but was stronger in males. The effect of PM_{10} on hospitalization for pneumonia was statistically significant only in males. Our data appear to be in line with those of previous studies. For example, Zanobetti et al. (Zanobetti et al. 2000) showed that the effect of PM_{10} on pneumonia admissions tended to be higher for males, while Santus et al. (Santus et al. 2012) reported larger effects of $PM_{2.5}$ on hospitalization for pneumonia in males. The reasons for the higher risk of $PM_{2.5}$-associated hospitalization for pneumonia in males may be related to higher

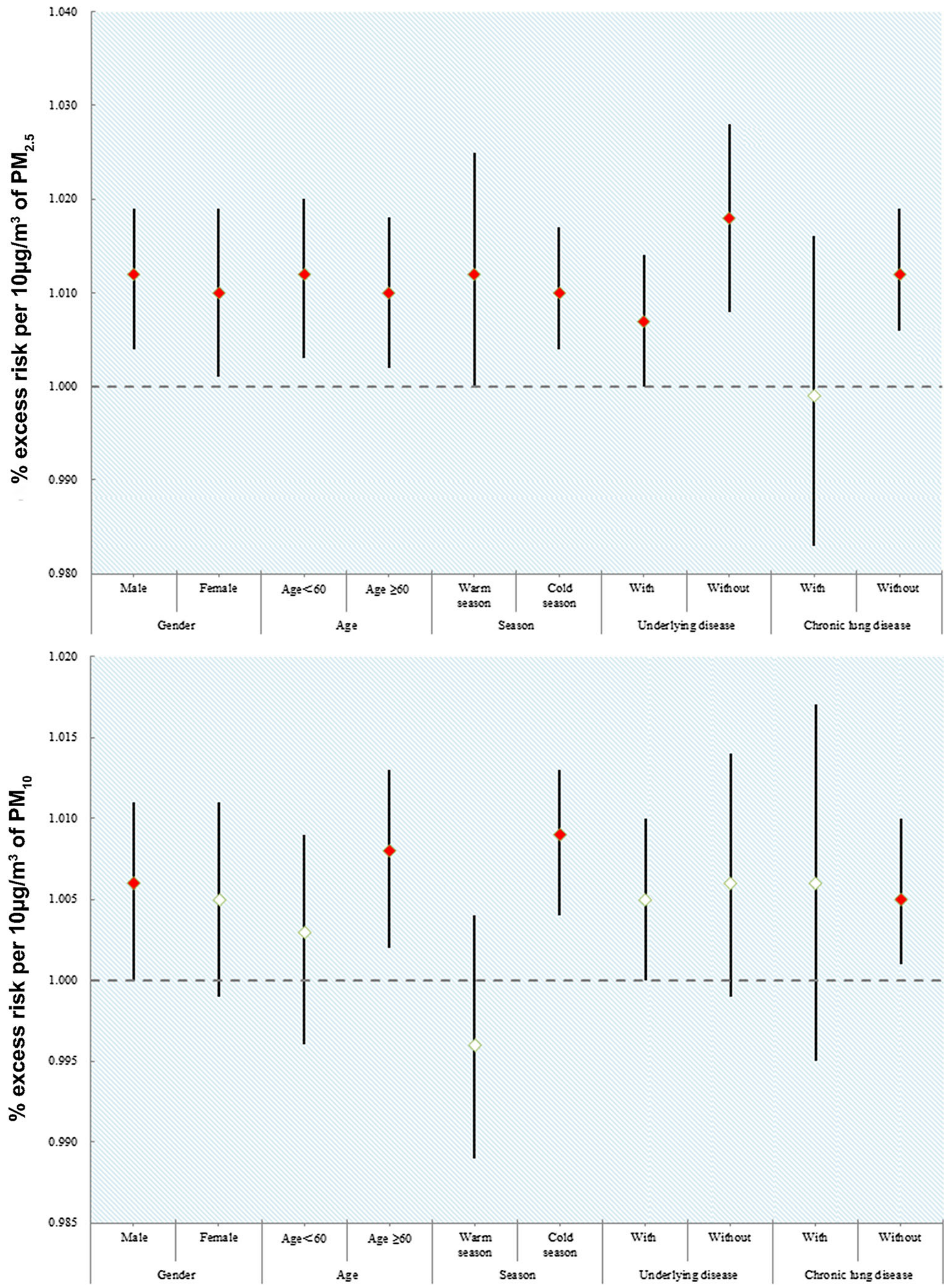

Fig. 4 Estimates of the effects of fine ($PM_{2.5}$) and coarse (PM_{10}) particulate matter on hospitalization for community-acquired pneumonia after stratification of data based on possible effect modifiers. Data are plotted as odds ratios and 95 % confidence intervals. *Red symbols* indicate significant effect, and *white symbols* non-significant effect. The effect of a 10-µg/m^3 increase in $PM_{2.5}$ (upper panel) appeared to be stronger in males, younger patients, patients without comorbidities or chronic lung disease, and during the warm season. The effects of a 10-µg/m^3 increase in PM_{10} (lower panel) were significant only in males, older patients, patients without chronic lung disease, and during the cold season

smoking rates in males, although the mechanisms are not yet fully understood.

In the present study, stratified analysis based on age showed that the effects of $PM_{2.5}$ on hospitalization for pneumonia were more important for people younger than 60 years. This finding differs from those of Zanobetti et al. (Santus et al. 2012; Zanobetti et al. 2000). who reported a stronger association between $PM_{2.5}$ and hospital admission for pneumonia in an elderly population. The elderly may be more susceptible to pollution (Neupane et al. 2010). although our data appears contradictory to this. One possible explanation for our finding is that the elderly population may have a tendency to spend more time indoors at home, thereby reducing outdoor exposure. Indeed, a recent study in China showed that indoor PM levels were lower during the cold season compared with outdoor PM levels, but that the levels were similar during the warm season, probably because people open their windows (Zhang et al. 2015). If so, the actual level of exposure of the elderly to $PM_{2.5}$ would have been below the monitored concentrations of $PM_{2.5}$, leading to bias in the results (Katsouyanni et al. 1997; Zeger et al. 2000).

When the data were analyzed by season, effects of $PM_{2.5}$ on hospitalization for pneumonia were evident on both warm and cold days, but were stronger on warm days. These findings appear to be in agreement with those of previous studies (Santus et al. 2012; Medina-Ramon et al. 2006). The concentrations of PM_{10} and $PM_{2.5}$ during the warm season (243.6 ± 96.1 μmol/l and 104.2 ± 56.1 μmol/l, respectively) tended to be lower than those during the cold season (376.2 ± 184.1 μmol/l and 209.0 ± 140.0 μmol/l, respectively). Thus, the stronger effect during the warm season may be related to an increase in individual exposure rather than to an overall increase in the outdoor ambient concentration of pollutant, since people are more likely to go outdoors and open windows in the warm season than in the cold season. Thus, the monitored $PM_{2.5}$ concentrations may be closer to the actual levels of personal exposure in the warm season than in the cold season (Tsai et al. 2013; Xu et al. 2011).

The stratified analysis also examined whether the effect of $PM_{2.5}$ on the risk of hospitalization for pneumonia differed depending on the presence of comorbidities (such as heart disease, diabetes mellitus, asthma, and chronic obstructive pulmonary disease). We found that the effects of $PM_{2.5}$ on hospital admissions for pneumonia were more important for people without comorbidities. Our results differ from the study by Zanobetti et al. (Zanobetti et al. 2000) which showed that people with heart diseases appeared to be at higher risk of a PM_{10}-associated admission for pneumonia, and that people with asthma had twice the risk of hospitalization for PM_{10}-induced pneumonia as people without asthma. Animal studies (Costa and Dreher 1997) have demonstrated that animals with cardiopulmonary diseases have an increased vulnerability to PM_{10}. There are several possible explanations for the apparent difference between our study and that of Zanobetti et al. One relevant factor may be variation in exposure patterns, since people with comorbidities tend to adopt a more indoor lifestyle because of poor cardiorespiratory functions. In addition, the level of exposure to a pollutant is dependent not only on the environmental concentration of $PM_{2.5}$ and the exposure time but also on the pulmonary ventilation of the individual. People with chronic lung disease often have ventilation defects that could reduce the total load of $PM_{2.5}$, resulting in the level of exposure of a patient with lung disease being lower than that expected from the monitored $PM_{2.5}$ concentration. Differences in healthcare systems between countries might also be responsible for the differences in the impact of comorbidities on the effects of PM.

One limitation of the present study is exposure measurement error, which is a common concern in environmental epidemiology. $PM_{2.5}$ levels were determined from fixed, outdoor monitoring stations, and these values were extrapolated to estimate exposure in individuals. The $PM_{2.5}$ concentrations were treated as homogenous throughout the city, and variations between locations were not considered. Furthermore, an individual's exposure to $PM_{2.5}$ is influenced by a variety of factors including the time he/she spends outdoors and his/her pulmonary ventilation. These types of exposure measurement error would likely lead to underestimation of pollutant effects (Zeger et al. 2000). Another limitation may result from cases of pneumonia treated in outpatient clinics, which did not lead to hospitalization and were not included in the study. Such under-reporting of the occurrence of the disease would also be expected to result in an underestimation of pollutant effects. Finally, the exact composition of the PM was not analyzed. It is possible that the chemicals adsorbed onto PM might have a greater influence on CAP than PM levels. However, further studies are necessary to address this issue.

In conclusion, this study provided evidence that short-term exposure to $PM_{2.5}$ is associated with increased hospitalization for pneumonia in Shijiazhuang, China.

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Compliance with ethical standards This study was approved by the Ethics Committee of The Second Hospital of Hebei Medical University. Written informed consent was obtained from all participants.

Conflict of interest The authors declare that they have no competing interests.

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