



Associations between short-term exposure to fine particulate matter and acute exacerbation of asthma in Yancheng, China

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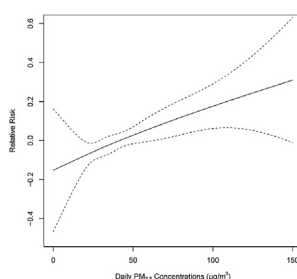
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HIGHLIGHTS

- PM_{2.5} was associated with increased risks of acute asthma exacerbation.
- Males and younger asthma patients were more susceptible to PM_{2.5}.
- Asthma patients were more sensitive to PM_{2.5} in cold season.

GRAPHICAL ABSTRACT



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ABSTRACT

Scarce evidence existed on the association between short-term exposure to fine particulate matter (PM_{2.5}) and asthma in China. In this study, we aimed to explore the relationship of PM_{2.5} with acute asthma exacerbation in a coastal city of China. Cases of acute asthma exacerbation were identified from hospital outpatient visits in Yancheng, China, from 2015 to 2018. We utilized the generalized additive model linked by a quasi-Poisson distribution to assess the association between PM_{2.5} and daily acute asthma exacerbation. Different lag structures were built, and we conducted stratification analyses by gender, age, and season. Two-pollutant models were fitted, and concentration-response (C-R) curves were pooled. A total of 3,520 cases of acute asthma exacerbation were recorded, with a daily average of 3. We observed positive and significant associations of PM_{2.5} on lag 1, 2, lag 02, and lag 03 day. For each 10-µg/m³ increase in PM_{2.5} (lag 02), the associated increment in asthma was 3.15% (95% CI: 0.99%, 5.31%). The association remained after adjusting for gaseous co-pollutants. We observed significant PM_{2.5}-asthma associations in males, patients ≤64 years, and during cold seasons. The C-R curves were positive and almost linear for total and strata-specific associations. In conclusion, this study provided robust evidence on the association of PM_{2.5} with acute asthma exacerbation, which may benefit future prevention strategy and policy making.

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1. Introduction

Asthma, a common chronic inflammatory disease of the

airways, is characterized by variable and recurring symptoms (i.e., wheezing, coughing, and breathlessness), reversible airflow obstruction, and easily triggered bronchospasms (Lin et al., 2014). In the Global Burden of Disease (GBD) report, the prevalence of asthma was 272.7 million in 2017, with an incidence of 43.1 million (GBD, 2018). The disease burden of asthma is also severe in China. According to an epidemiological survey in 2015, 17.4 million people (1.24% of the total population) were diagnosed with asthma (Su et al., 2014; Guan et al., 2016).

The hazardous impacts of air pollution on human health have been well documented (Jiang et al., 2016; Cox, 2017). Among air pollutants, fine particulate matter (PM_{2.5}, particles with aerodynamic diameters $\leq 2.5 \mu\text{m}$) is of greater public health concern because it is capable of penetrating into the lungs and reaching the pulmonary alveolar region (Harrison and Yin, 2000; Kim et al., 2015). It has been suggested that PM_{2.5} may exacerbate asthma symptoms and increase incidence risk of asthma (Bates et al., 2015; Deng et al., 2015; Matthews et al., 2016).

China is the largest developing country with high prevalence of asthma and some of the worst air quality levels. However, only a few epidemiological studies have examined the associations between PM_{2.5} and outpatient visits of asthma (Jung et al., 2017; Tian et al., 2017), and there is less evidence regarding the endpoint of acute asthma exacerbation. Therefore, we designed this time-series study in Yancheng, one of the coastal cities in East China, to investigate the relationship between short-term exposure to PM_{2.5} and acute asthma exacerbation.

2. Materials and methods

2.1. Data collection

Yancheng is an emerging industrial and commercial city on the east coast of Jiangsu Province. It is located between 32°34' to 34°28' N and 119°27' to 120°54' E. The current study was limited to the urban areas, which hosted a target population of 1.0 million. The Gross Domestic Product (GDP) per capita in Yancheng was 76,000 Chinese Yuan in 2018.

Data on outpatient visits for asthma from November 1, 2015 to October 31, 2018 were obtained from 3 major hospitals in the urban area of Yancheng, which serve more than 90% of total outpatient visits. Daily counts of acute asthma exacerbation were determined and extracted from the outpatient visits by experienced physicians. We used the diagnostic codes of the 10th International Classification of Diseases (ICD-10: J45 and J46). Information on the patient's name, gender, age, home address and treatment date were recorded. In the current study, we excluded patients who were younger than 18 years old as this study was initiated on adult asthma.

We derived data on ambient air pollutants during the study period from the database of the Environmental Monitoring Center of Yancheng, including PM_{2.5}, sulfur dioxide (SO₂), nitrogen dioxide (NO₂), carbon monoxide (CO), and ozone (O₃). We calculated city-level daily concentrations by averaging the 24-h hourly data from 5 monitoring stations in Yancheng as representative exposure levels for each individual, except for ozone (by averaging 8-h maximum values). We excluded approximately 5% of the total patients as they resided far from the nearest stations (>10 km). Locations of 3 hospitals and air quality monitoring stations are illustrated in Fig. S1. Measurements of weather conditions, including daily means of temperature (°C) and relative humidity (%), were obtained from the Yancheng Meteorological Bureau. The ethics committee of the First People's Hospital of Yancheng reviewed and approved the study protocol.

2.2. Statistical analyses

We first examined the Spearman correlation coefficients among air pollutants and meteorological factors. Generalized additive models (GAM) with *quasi*-Poisson regression were applied to analyze the associations between daily concentrations of air pollutants and acute asthma exacerbation. We introduced several covariates in the main model as a standardized protocol in time-series analyses (Tian et al., 2018; Sun et al., 2019), including 1) a natural spline function for time-trend with 7 degrees of freedom (*df*) per year; 2) a dummy variable indicating 7 days in a week to control for the day of week effect; 3) a natural spline function for daily mean temperature with 6 *dfs* and a natural spline function for relative humidity with 3 *dfs*; and 4) a dummy variable to account for holiday effect. The equations are as follows:

$$\begin{aligned} \text{Logit}[E(Y_t)] &= \alpha + \beta * X_{\text{pollutant}} + ns(\text{time}, df \\ &= 7 * \text{year}) + ns(\text{temp}, df = 6) + ns(\text{rh}, df = 3) + DOW \\ &+ \text{Holiday} \end{aligned}$$

where, *t* is the calendar time, *Y_t* is the daily counts of acute asthma exacerbation on day *t*, *E(Y_t)* is the expected number of asthma patients on day *t*, α is the intercept, *X_{pollutant}* indicates the pollutant of interest, and β is the regression coefficient, *ns* represents the natural spline function, *df* is the degree of freedom, *temp* is temperature, *rh* is relative humidity, and *DOW* is the variable for the day of week effect. We also conducted a sensitivity analysis that used alternative *dfs* from 3 to 6 in the natural cubic spline for daily mean temperature.

To determine the appropriate lag structure for the PM_{2.5}-asthma associations, we built several lags of PM_{2.5}, including lag 0, the present day; lag 1, the previous day; lag 2, the previous 2 day; lag 3, the previous 3 day; and the moving average of the present and previous day (lag 01), the previous 2-days (lag 02), and the previous 3-days (lag 03). Then, we determined the optimal lags for temperature and relative humidity by the minimum generalized cross-validation (GCV) statistics. The lag 03 of temperature and the lag 02 of relative humidity achieved the best model fitting and were then used in the main model.

We explored potential effect modification by gender and age

Table 1
Descriptive statistics on health outcomes, air pollutants, and environmental variables in Yancheng, China, from Nov.1, 2015 to Oct. 31, 2018.

Variables	N	Min	P25	P50	P75	Max	Mean	SD
Air pollutants ($\mu\text{g}/\text{m}^3$)								
PM _{2.5}	1,096	5.0	22.7	34.0	53.4	226.3	42.8	29.9
PM ₁₀	1,096	8.1	44.7	63.2	95.6	306.3	74.8	41.9
NO ₂	1,096	2.5	15.4	21.2	30.7	87.6	24.6	12.7
SO ₂	1,096	4.8	9.4	12.1	16.0	59.2	13.9	6.9
CO (mg/m^3)	1,096	0.3	0.6	0.7	0.9	2.2	0.8	0.2
O ₃	1,076	15.0	72.8	92.0	118.0	211.0	97.0	33.0
Meteorological factors								
Temperature (°C)	1,086	-9.9	6.5	15.7	23.3	33.0	15.1	9.5
Relative humidity (%)	1,086	33.0	71.0	82.0	89.0	100.0	79.4	12.3
Asthma patients								
Total	3,520	0	1	3	5	16	3	2
Gender								
Male	1,741	0	0	1	2	8	2	2
Female	1,779	0	0	1	2	11	2	2
Age group								
≤ 64 years	3,030	0	1	2	4	16	3	2
≥ 65 years	490	0	0	0	1	5	1	1

Abbreviations: SD, standard deviation; PM_{2.5}, particles with aerodynamic diameter < 2.5 μm ; PM₁₀, particles with aerodynamic diameter < 10 μm ; NO₂, nitrogen dioxide; SO₂, sulfur dioxide; CO, carbon monoxide; O₃, ozone.

Table 2
Spearman correlation coefficients of air pollutants and meteorological factors.

Pollutants	PM _{2.5}	SO ₂	NO ₂	CO	O ₃	Temp
SO ₂	0.66*					
NO ₂	0.75*	0.72*				
CO	0.80*	0.57*	0.65*			
O ₃	0.13*	0.05	−0.03	0.09*		
Temp	−0.43*	−0.42*	−0.55*	−0.23*	0.37*	
RH	−0.22*	−0.45*	−0.33*	−0.10*	−0.20*	0.39*

Abbreviations as in Table 1. Temp, temperature; RH, relative humidity.

* P-value <0.05.

(less than or equal to 64, greater than or equal to 65). Season is divided into warm (May to October) and cold (November to April). To assess the independence of the PM_{2.5}-asthma association, we fitted two-pollutant models by introducing other gaseous air pollutants including NO₂, SO₂, O₃ and CO. Concentration-response (C-R) curves were pooled for the associations of total acute asthma exacerbation and each strata (Sun et al., 2019).

All statistical tests were conducted in R software (Version 3.5.1), and the “mgcv” and “spline” packages were used. We calculated the effect estimate and its 95% confidence intervals (95% CI) for the association between PM_{2.5} and acute asthma exacerbation. P-value < 0.05 was considered statistically significant.

3. Results

3.1. Descriptive results

A total of 3,520 cases (daily mean, 3 cases) of acute asthma exacerbation were included in this study. The male patients accounted for 49.5%, and 13.9% of participants were aged 65 or above. Descriptive statistics on acute asthma exacerbation, air pollutants, and meteorological factors during the study period are shown in Table 1. The average daily level of PM_{2.5} was 42.8 µg/m³ (5.0–226.3 µg/m³). On average, the mean (±standard deviation) concentrations of NO₂, SO₂, O₃, CO, temperature, and relative humidity were 24.6 ± 12.7 µg/m³, 13.9 ± 6.9 µg/m³, 97.0 ± 33.0 µg/m³, 0.8 ± 0.2 mg/m³, 15.1 ± 9.5 °C, and 79.4 ± 12.3% respectively.

As shown in Table 2, there were strong correlations between PM_{2.5} with SO₂, NO₂, and CO, with Spearman correlation coefficients of 0.66, 0.75, and 0.80, respectively. The correlation between PM_{2.5} with O₃ was very weak (Spearman $r = 0.13$), and the correlations with temperature and relative humidity were negative.

3.2. Regression results

Table 3 presents the lag patterns for the associations of PM_{2.5} with acute asthma exacerbation in single- and two-pollutant models. The PM_{2.5}-asthma associations were significant on lag 1,

2, lag 02, and lag 03 days in the single-pollutant models. Lag 02 generated the largest estimate with the minimum GCV statistics and best model fitting and was thus used as the main lag for analyzing the association. For a 10-µg/m³ increase in PM_{2.5} (lag 02), we observed a 3.15% (95% CI: 0.99%, 5.31%) increase in acute asthma exacerbation. In two-pollutant models, we observed a somewhat robust association on lag 1 day, in that the PM_{2.5}-asthma associations were insensitive to adjustment of each gaseous pollutant. In the main lag (lag 02), the associations remained after adjustment of SO₂ and O₃, but lost significance when adjusting for CO and NO₂. In addition, confidence intervals generally became larger when controlling for gaseous pollutants, indicating amplified uncertainty in the estimation of associations.

Fig. 1 illustrates the strata-specific association of acute asthma exacerbation associated with PM_{2.5} (lag 02). There were positive and significant associations in male patients, patients aged ≤64 years, and during the cold season. However, the confidence intervals overlapped between these groups (i.e., male and female groups), indicating that the between-group differences were not significant, and there was no evidence for significant effect modification.

Fig. 2 demonstrates the total and strata-specific C-R relationship curves of PM_{2.5} and acute asthma exacerbation on lag 02 day. The curves were positive and almost linear for total asthma cases, the age group of ≤64, and during the cold season. However, in the males, the curve turned flat with much wider confidence intervals at higher concentrations.

Results of the sensitivity analysis (Table S1) showed that there were no substantial changes in the estimates across different lags when using alternative *dfs* for adjustment of temperature.

4. Discussion

In this time-series study in Yancheng, we observed positive and significant associations of short-term PM_{2.5} exposure with acute asthma exacerbation. The associations were not insensitive to adjustment of co-pollutants in two-pollutant models. The overall C-R relationship curves were positive and almost linear in males, people in the ≤64 age group and during the cold season.

Air pollutants can have direct irritant and inflammatory effects on airway neuroreceptors and epithelium (Guarnieri and Balmes, 2014). It has been suggested that PM_{2.5} may induce asthma symptoms by causing airway inflammation (Delfino et al., 2006; Guarnieri and Balmes, 2014) and oxidative stress (Liu et al., 2009). A previous study found that PM_{2.5} caused asthma exacerbation by increasing apoptosis, the level of T-cell immunoglobulin, and the activation of mucin domain 1 (Zhao et al., 2018). Evidence from animal experiments also indicated that the pathological mechanisms of PM_{2.5} may be related to allergic/steroid-resistant airway inflammation, T-cell helper (Th) 1/Th 2 cytokine production, and

Table 3
Percent changes (means and 95% confidence intervals) in acute asthma exacerbation associated with a 10 µg/m³ increase in PM_{2.5} at different lag periods in the single- and two-pollutant models.

Models	PM _{2.5}	+SO ₂	+NO ₂	+CO	+O ₃
Lag 0	0.00 (−1.56, 1.56)	0.56 (−1.60, 2.71)	−1.26 (−3.61, 1.09)	−0.18 (−3.75, 3.40)	−0.36 (−2.02, 1.31)
Lag 1	2.54 (1.01, 4.06)	4.16 (2.11, 6.21)	3.02 (0.82, 5.22)	4.44 (1.08, 7.80)	2.13 (0.51, 3.75)
Lag 2	2.39 (0.82, 3.95)	2.98 (1.01, 4.94)	1.22 (−0.96, 3.40)	2.27 (−0.94, 5.48)	2.28 (0.65, 3.91)
Lag 3	−0.20 (−1.84, 1.45)	0.35 (−1.67, 2.36)	−0.57 (−2.76, 1.62)	−0.48 (−3.78, 2.82)	0.01 (−1.71, 1.73)
Lag 01	1.78 (−0.05, 3.61)	3.74 (1.10, 6.37)	1.47 (−1.39, 4.32)	3.34 (−0.88, 7.56)	1.27 (−0.71, 3.24)
Lag 02	3.15 (0.99, 5.31)	5.66 (2.59, 8.72)	2.40 (−0.98, 5.77)	4.32 (−0.32, 8.96)	2.56 (0.21, 4.90)
Lag 03	3.09 (0.56, 5.61)	5.61 (2.20, 9.02)	2.19 (−1.64, 6.02)	3.53 (−1.41, 8.47)	2.74 (−0.01, 5.48)

Notes: Associations with statistical significance are highlighted in bold. Abbreviations as in Table 1. Lag 0, the present day; Lag 1, the previous day; Lag 2, the previous 2 day; Lag 3, the previous 3 day; Lag 01, 2-day average of the present and previous day; Lag 02, 3-day average of the present and previous 2 days; Lag 03, 4-day average of the present and previous 3 days.

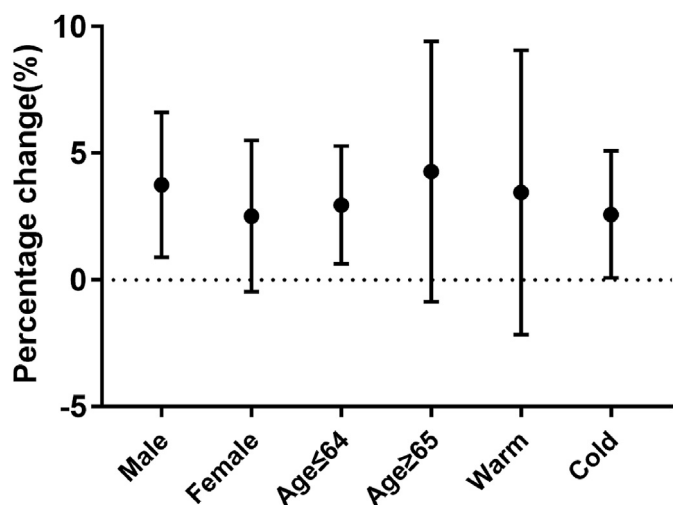


Fig. 1. Percent changes in acute asthma exacerbation (means and 95% confidence intervals) associated with a 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ (lag 02), stratified by gender, age, and season.

upregulation of thymic stromal lymphopoietin (TSLP) expression (Liu et al., 2017). Although the exact mechanism remains unclear,

epidemiological evidence supports the associations between $\text{PM}_{2.5}$ and asthma.

The present study provides information on the lag structure of $\text{PM}_{2.5}$ -asthma association. The most significant increment was observed on lag 02 day, which was consistent with existing evidence (Tian et al., 2017; Strosnider et al., 2019; Sun et al., 2019). For instance, one time-series study found the largest association of asthma outpatients with $\text{PM}_{2.5}$ on lag 02 day in Beijing (Tian et al., 2017). Another study with the same design reported a significant association between asthma and $\text{PM}_{2.5}$ on lag 03 day in Guangdong (Zhao et al., 2017), whereas, another study on chronic obstructive pulmonary disease observed a significant association on lag 0 day in Yancheng, China (Sun et al., 2019). Although these lag patterns demonstrated an acute effect of $\text{PM}_{2.5}$ air pollution on asthma exacerbation, the exact exposure window and potential region difference should be further investigated.

For the magnitude of association, we observed a 3.15% increment in acute asthma exacerbation for a 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$, which was slightly larger than that found in previous studies in China. For instance, Tian et al. reported a 0.65% in asthma outpatients for the same increase in $\text{PM}_{2.5}$ (Tian et al., 2017). A meta-analysis pooled a 2.3% increase in asthma hospital visits per 10- $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ (Zheng et al., 2015). In developed areas like Europe and North America, outpatient visits require an

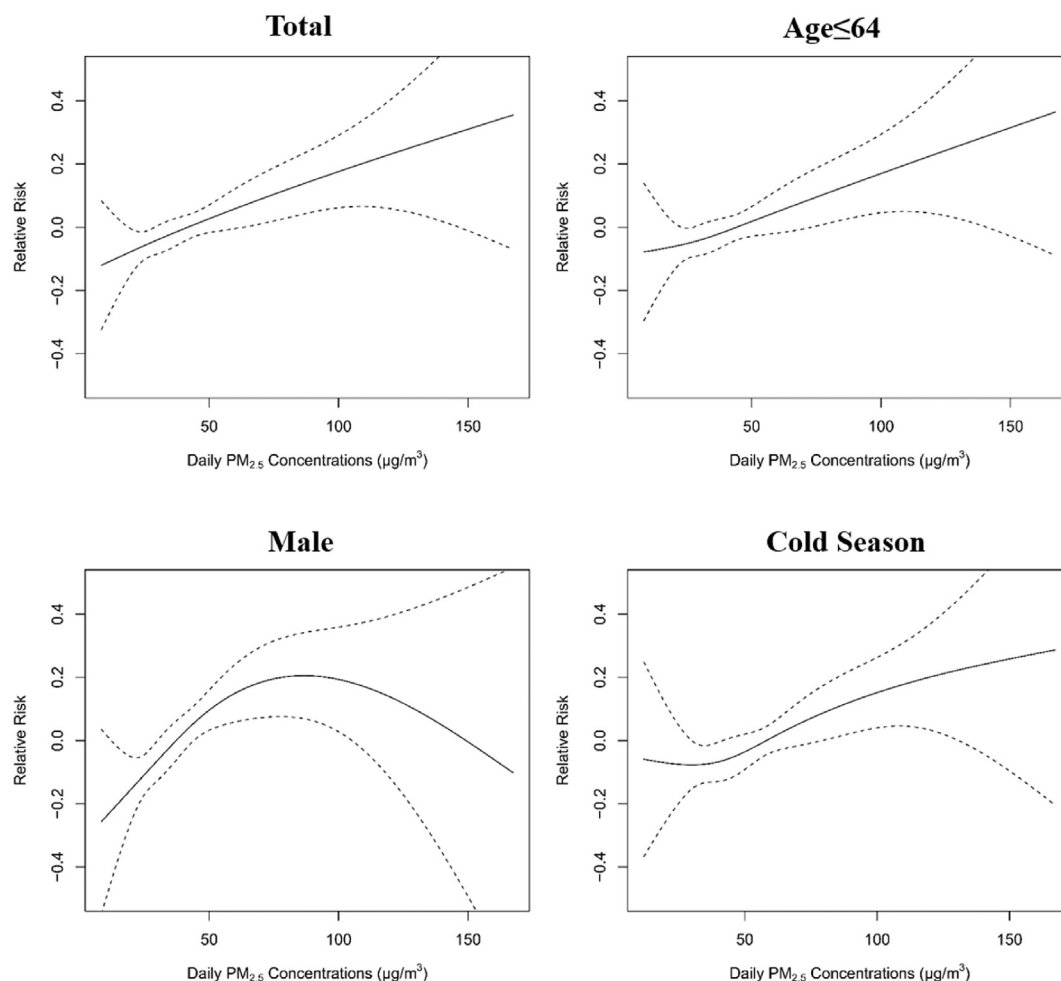


Fig. 2. The concentration–response relationship curves between $\text{PM}_{2.5}$ (lag 02 day) and acute asthma exacerbation. X-axis: $\text{PM}_{2.5}$ concentrations at lag 02 day; Y-axis: the vertical scale can be interpreted as the log-relative change from the mean effect of $\text{PM}_{2.5}$ on acute asthma exacerbation. The solid line represents the mean estimate, and the dashed lines represent the 95% confidence intervals.

appointment, thus the relationship of emergency room (ER) visits with PM_{2.5} receives more interest. For instance, a study in the US found a 3.8% increase in asthma associated with a 10-μg/m³ increase in PM_{2.5} (Strosnider et al., 2019). A meta-analysis pooled an increased risk of 1.5% for asthma ER visits (Fan et al., 2016). The discrepancies in estimates may be related to different endpoints of interest, different visiting habits, and air pollution characteristics in different places.

Identifying potential susceptible populations is of great public health importance in terms of intervention strategy and policy making. In the subgroup analysis, we found a slightly larger but not significant association during the warm season. This result was consistent with a study by Tian et al. that reported a larger estimate during the warm (1.21%) compared to the cold (1.12%) season (Tian et al., 2017). Another meta-analysis also reported a 3.7% increase in the risk of asthma in warm season (cold season, 2.6%) (Fan et al., 2016). The marginally significant results in this study may be due to the relatively smaller sample size. In addition, we found significant associations in male patients (also with a larger estimate), which was consistent with previous studies (Tian et al., 2017; Wang et al., 2018). This may be because males spend more time outdoors in China and are more exposed to outdoor air pollutants. Potential genetic susceptibility to respiratory diseases may also be underlying this observation (Clougherty, 2010). Notably, we observed a significant association in younger age groups, but not in older patients. Similarly, a study in the US found a larger estimate in the younger patients (3.4%) compared with older patients (3.2%) (Strosnider et al., 2019). This may be related to the fact that young patients tend to have more outdoor activities and work and subsequently are more likely to be exposed to PM_{2.5}.

The independence of the PM_{2.5}-asthma association has been well debated. In the two-pollutant models, the associations remained after adjustment of SO₂ and O₃, but not for NO₂ and CO. As PM_{2.5}, NO₂, and CO are all typical traffic-related air pollutants, this observation may be largely due to the stronger correlations between PM_{2.5} and NO₂ (Spearman $r = 0.75$) and CO (Spearman $r = 0.80$). A previous study in Taiwan reported similar results (Cheng et al., 2014). However, some studies did find a significant association after inclusion of NO₂ and CO, although the estimates of association became smaller (Hwang et al., 2017). Nevertheless, more studies are needed to validate this finding.

The current study was subject to several limitations. First, as a time-series analysis, exposure misclassification was inevitable as we used aggregated levels of air pollutants for each individual (Goldman et al., 2011). Second, we cannot rule out potential diagnostic error as some allergic patients with cough or wheezing might be recorded as asthma by the outpatient system. Third, the study sample of this single-city analysis was small, which limited the statistical power to find robust estimates, especially in subgroup analyses. Future multi-city studies with larger time-series are required to verify these findings. Fourth, the strong correlations between PM_{2.5} and gaseous pollutants (i.e., NO₂ and CO) may produce complicated impacts on the results of two-pollutant models, and the results should be interpreted with caution.

5. Conclusions

To sum up, this study suggested a link of short-term exposure to PM_{2.5} with acute asthma exacerbations in Yancheng, China. Novel evidence was provided on the different lag structures of the PM_{2.5}-asthma association and susceptible subgroups that may be more sensitive to PM_{2.5} exposure. The association was generally robust to adjustment of co-pollutants. These findings indicated potential health benefits on reducing acute asthma exacerbations from lowering ambient PM_{2.5} air pollution levels.

Conflicts of interest

The authors declared no conflicts of interests.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.chemosphere.2019.124497>.

References

- Bates, J.T., Weber, R.J., Abrams, J., et al., 2015. Reactive oxygen species generation linked to sources of atmospheric particulate matter and cardiorespiratory effects. *Environ Sci Technol* 49, 13605–13612.
- Cheng, M.H., Chen, C.C., Chiu, H.F., et al., 2014. Fine particulate air pollution and hospital admissions for asthma: a case-crossover study in Taipei. *J Toxicol Environ Health A* 77, 1075–1083.
- Clougherty, J.E., 2010. A growing role for gender analysis in air pollution epidemiology. *Environ Health Perspect* 118, 167–176.
- Cox Jr., L.A.T., 2017. Socioeconomic and air pollution correlates of adult asthma, heart attack, and stroke risks in the United States, 2010–2013. *Environ Res* 155, 92–107.
- Delfino, R.J., Staimer, N., Gillen, D., et al., 2006. Personal and ambient air pollution is associated with increased exhaled nitric oxide in children with asthma. *Environ Health Perspect* 114, 1736–1743.
- Deng, Q., Lu, C., Norback, D., et al., 2015. Early life exposure to ambient air pollution and childhood asthma in China. *Environ Res* 143, 83–92.
- Fan, J., Li, S., Fan, C., et al., 2016. The impact of PM_{2.5} on asthma emergency department visits: a systematic review and meta-analysis. *Environ Sci Pollut Res Int* 23, 843–850.
- GBD, 2018. Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 392, 1789–1858.
- Goldman, G.T., Mulholland, J.A., Russell, A.G., et al., 2011. Impact of exposure measurement error in air pollution epidemiology: effect of error type in time-series studies. *Environ Health* 10, 61.
- Guan, W.J., Zheng, X.Y., Chung, K.F., et al., 2016. Impact of air pollution on the burden of chronic respiratory diseases in China: time for urgent action. *Lancet* 388, 1939–1951.
- Guarnieri, M., Balmes, J.R., 2014. Outdoor air pollution and asthma. *Lancet* 383, 1581–1592.
- Harrison, R.M., Yin, J., 2000. Particulate matter in the atmosphere: which particle properties are important for its effects on health? *Sci Total Environ* 249, 85–101.
- Hwang, S.L., Lin, Y.C., Lin, C.M., et al., 2017. Effects of fine particulate matter and its constituents on emergency room visits for asthma in southern Taiwan during 2008–2010: a population-based study. *Environ Sci Pollut Res Int* 24, 15012–15021.
- Jiang, X.Q., Mei, X.D., Feng, D., 2016. Air pollution and chronic airway diseases: what should people know and do? *J Thorac Dis* 8, E31–E40.
- Jung, C.R., Young, L.H., Hsu, H.T., et al., 2017. PM_{2.5} components and outpatient visits for asthma: a time-stratified case-crossover study in a suburban area. *Environ Pollut* 231, 1085–1092.
- Kim, K.H., Kabir, E., Kabir, S., 2015. A review on the human health impact of airborne particulate matter. *Environ Int* 74, 136–143.
- Lin, C.C., Lin, L.J., Wang, S.D., et al., 2014. The effect of serine protease inhibitors on airway inflammation in a chronic allergen-induced asthma mouse model. *Mediators Inflamm* 2014, 879326.
- Liu, L., Poon, R., Chen, L., et al., 2009. Acute effects of air pollution on pulmonary function, airway inflammation, and oxidative stress in asthmatic children. *Environ Health Perspect* 117, 668–674.
- Liu, Y., Feng, G.Z., Du, Q., et al., 2017. Fine particulate matter aggravates allergic airway inflammation through thymic stromal lymphopoietin activation in mice. *Mol Med Rep* 16, 4201–4207.
- Matthews, N.C., Pfeffer, P.E., Mann, E.H., et al., 2016. Urban particulate matter-activated human dendritic cells induce the expansion of potent inflammatory Th1, Th2, and Th17 effector cells. *Am J Respir Cell Mol Biol* 54, 250–262.
- Strosnider, H.M., Chang, H.H., Darrow, L.A., et al., 2019. Age-specific associations of ozone and fine particulate matter with respiratory emergency department visits in the United States. *Am J Respir Crit Care Med* 199, 882–890.
- Su, N., Lin, J., Liu, G., et al., 2014. [An epidemiological survey of current asthma control status in China]. *Zhonghua Nei Ke Za Zhi* 53, 601–606.
- Sun, Q., Liu, C., Chen, R., et al., 2019. Association of fine particulate matter on acute exacerbation of chronic obstructive pulmonary disease in Yancheng, China. *Sci Total Environ* 650, 1665–1670.
- Tian, Y., Xiang, X., Juan, J., et al., 2018. Short-term effects of ambient fine particulate

- matter pollution on hospital visits for chronic obstructive pulmonary disease in Beijing, China. *Environ Health* 17, 21.
- Tian, Y., Xiang, X., Juan, J., et al., 2017. Fine particulate air pollution and hospital visits for asthma in Beijing, China. *Environ Pollut* 230, 227–233.
- Wang, A.X., Chen, X., Song, C.B., et al., 2018. Association between fine particulate matter and asthma hospital outpatient visits in Hangzhou. *Huan Jing Ke Xue* 39, 4457–4462.
- Zhao, Y., Wang, S., Lang, L., et al., 2017. Ambient fine and coarse particulate matter pollution and respiratory morbidity in Dongguan, China. *Environ Pollut* 222, 126–131.
- Zhao, Y.X., Zhang, H.R., Yang, X.N., et al., 2018. Fine particulate matter-induced exacerbation of allergic asthma via activation of T-cell immunoglobulin and mucin domain 1. *Chin Med J (Engl)* 131, 2461–2473.
- Zheng, X.Y., Ding, H., Jiang, L.N., et al., 2015. Association between air pollutants and asthma emergency room visits and hospital admissions in time series studies: a systematic review and meta-analysis. *PLoS One* 10, e0138146.

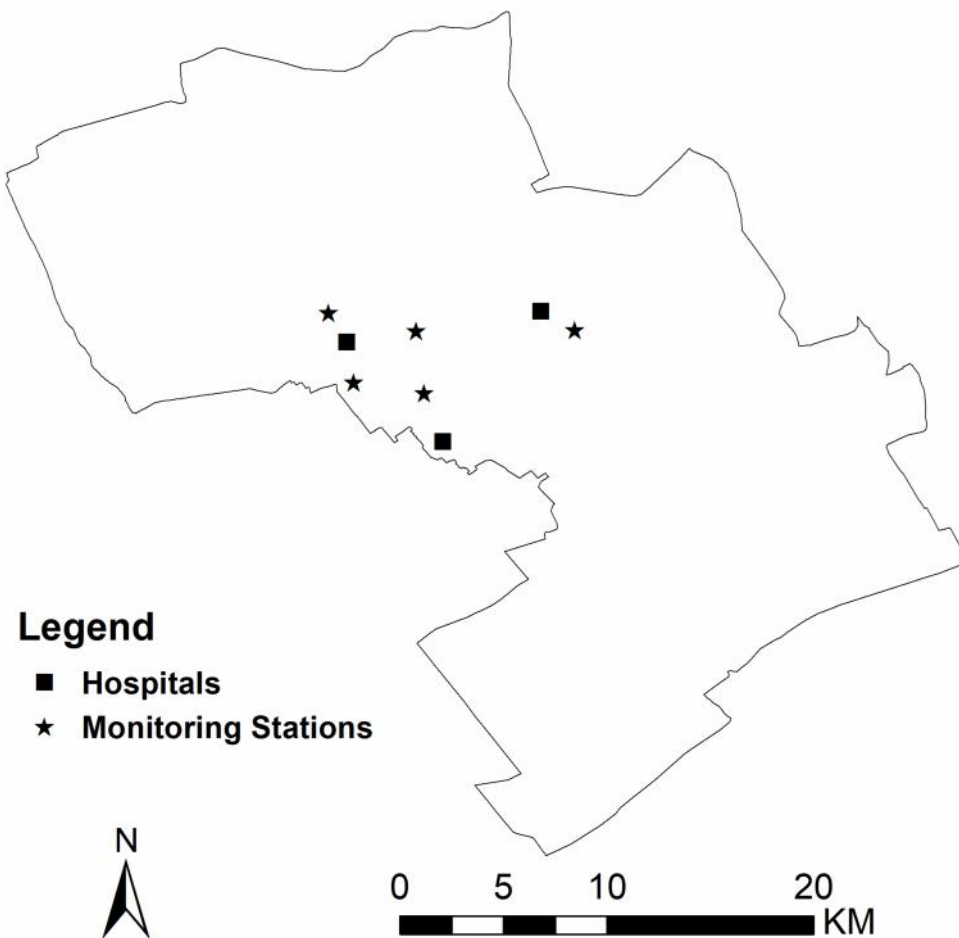


Figure S1. Air quality monitoring stations and three major hospitals in central urban district of Yancheng, China

Table S1. Percent changes (means and 95% confidence intervals) in acute asthma exacerbation associated with a 10 $\mu\text{g}/\text{m}^3$ increase in $\text{PM}_{2.5}$ at different lag periods by different degrees of freedoms for the temperature cubic splines.

<i>Dfs</i>	3	4	5	6
Lag 0	-0.02 (-1.58, 1.54)	-0.04 (-1.60, 1.52)	0.01 (-1.56, 1.57)	0.00 (-1.56, 1.56)
Lag 1	2.48 (0.96, 3.99)	2.45 (0.93, 3.97)	2.50 (0.98, 4.02)	2.54 (1.01, 4.06)
Lag 2	2.33 (0.77, 3.89)	2.32 (0.75, 3.88)	2.36 (0.80, 3.92)	2.39 (0.82, 3.95)
Lag 3	-0.27 (-1.91, 1.38)	-0.28 (-1.92, 1.37)	-0.19 (-1.83, 1.45)	-0.20 (-1.84, 1.45)
Lag 01	1.72 (-0.10, 3.54)	1.69 (-0.13, 3.51)	1.76 (-0.06, 3.58)	1.78 (-0.05, 3.61)
Lag 02	3.04 (0.90, 5.18)	3.01 (0.86, 5.15)	3.11 (0.96, 5.26)	3.15 (0.99, 5.31)
Lag 03	2.92 (0.41, 5.42)	2.88 (0.37, 5.39)	3.05 (0.53, 5.57)	3.09 (0.56, 5.61)

Notes: Associations with statistical significance are highlighted in bold.

Abbreviations: df, degree of freedom. Lag 0, the present day; Lag 1, the previous day; Lag 2, the previous 2 day; Lag 3, the previous 3 day; Lag 01, 2-day average of the present and previous day; Lag 02, 3-day average of the present and previous 2 days; Lag 03, 4-day average of the present and previous 3 days.