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## Exposure to fine particulate matter during pregnancy and risk of term low birth weight in Jinan, China, 2014–2016

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## ABSTRACT

**Background:** Existing studies exploring the association between low birth weight (LBW) and maternal fine particulate matter (aerodynamic diameter < 2.5 μm, PM<sub>2.5</sub>) exposure have presented equivocal results, and one of the possible reasons for this finding might be due to relatively low maternal exposures. In addition, relatively narrow maternal exposure windows to PM<sub>2.5</sub> have not been well established for LBW.

**Methods:** We employed a nested matched case-control design among 43,855 term births in a large maternity and child care hospital in Jinan, China. A total of 369 cases were identified, and four controls per case matched by maternal age were randomly selected among those with normal birth weight (n = 1,476) from 2014 to 2016. Ambient air monitoring data on continuous measures of PM<sub>2.5</sub>, nitrogen dioxide (NO<sub>2</sub>), and sulfur dioxide (SO<sub>2</sub>) (24-h average concentrations) from 2013 to 2016 were collected from thirteen local monitoring stations. An inverse distance weighting method based on both home and work addresses was adopted to estimate the individual daily exposures to these air pollutants during pregnancy by weighting the average of the twelve nearest monitoring stations within 30 km of each 100 m × 100 m grid cell by an inverse squared distance, and then the average exposure concentrations for gestational months, trimesters and the entire pregnancy were calculated. Adjusted conditional logistic regression models were used to estimate the odds ratios (ORs) per 10 μg/m<sup>3</sup> increment in PM<sub>2.5</sub> and by PM<sub>2.5</sub> quartiles during different gestational periods.

**Results:** In this study, the estimated mean values of PM<sub>2.5</sub>, NO<sub>2</sub>, and SO<sub>2</sub> exposure during the entire pregnancy were 88.0, 54.6, and 63.1 μg/m<sup>3</sup>, respectively. Term low birth weight (TLBW) increased in association with per 10 μg/m<sup>3</sup> increment in PM<sub>2.5</sub> for the 8th month [OR = 1.13, 95% confidence interval (CI): 1.04, 1.22], the 9th month (OR = 1.06, 95% CI: 0.99, 1.15), the third trimester (OR = 1.17, 95% CI: 1.05, 1.29), and the entire pregnancy (OR = 1.38, 95% CI: 1.07, 1.77) in models adjusted for one pollutant (PM<sub>2.5</sub>). In models categorizing the PM<sub>2.5</sub> exposure by quartiles, comparing the second, third, and highest with the lowest PM<sub>2.5</sub> exposure quartile, the PM<sub>2.5</sub> was positively associated with TLBW during the 8th month (OR: 1.77, 95% CI: 1.09, 2.88; OR: 1.77, 95% CI: 1.03, 3.04; OR: 1.92, 95% CI: 1.04, 3.55, respectively) and for the 9th month, only association for exposure in the third versus the lowest quartile was significant (OR: 1.91, 95% CI: 1.02, 3.58).

**Conclusions:** The study provides evidence that exposure to PM<sub>2.5</sub> during pregnancy might be associated with the risk of TLBW in the context of very high pollution level of PM<sub>2.5</sub>, and the 8th and 9th months were identified as potentially relevant exposure windows.

### 1. Introduction

Low birth weight (birth weight less than 2500 g, LBW) is a common adverse birth outcome, and it is estimated that 15%–20% of all births are LBW globally, representing over 20 million births a year (WHO, 2014; Wu et al., 2017). Other than elevated neonatal morbidity and mortality, LBW also results in delayed effects into childhood and adulthood, such as chronic and metabolic diseases (e.g., obesity,

diabetes, and coronary heart disease) (WHO, 2014; Wu et al., 2017). Given the serious health burden of LBW, a number of studies exploring causation for LBW have been conducted, and some interrelated biological, physical, psychological, and social factors have been identified to play a significant role, but the etiology of LBW is still not well understood (Qian et al., 2016). More recently, developing fetuses have been considered to be subject to damage by air pollutant exposures that can trigger maternal systemic oxidative stress and inflammation, impair

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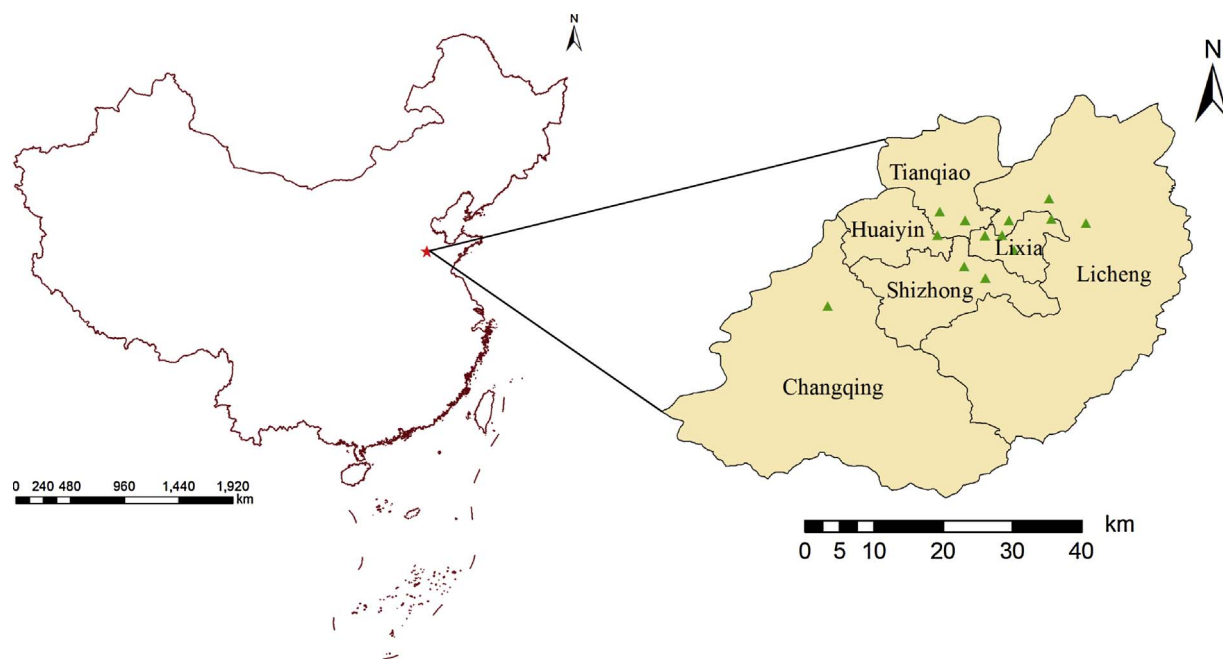


Fig. 1. Location of the study area (the six urban districts of Jinan) in China and the thirteen monitoring stations are indicated by green triangles. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

placenta, or cause endocrine disruption (Capobussi et al., 2016; Laurent et al., 2016; Nieuwenhuijsen et al., 2013). Among the various air pollutants, fine particulate matter (aerodynamic diameter < 2.5  $\mu\text{m}$ ,  $\text{PM}_{2.5}$ ) has become a research focus because of its unique characteristics such as smaller diameter, larger surface area, longer suspension time in air, and stronger toxic effects (Sun et al., 2015; Sun et al., 2016).

An increasing number of studies have analyzed the association between  $\text{PM}_{2.5}$  and LBW. Although many published studies have reported that maternal  $\text{PM}_{2.5}$  exposure is associated with LBW, heterogeneous results including negative and null associations have also been observed. The majority of existing studies were conducted in the United States (Hao et al., 2016; Laurent et al., 2014; Tu et al., 2016), Canada (Stieb et al., 2016a,b), Japan (Yorifuji et al., 2015), and some European countries (Arroyo et al., 2016; Pedersen et al., 2013), where the mean  $\text{PM}_{2.5}$  exposure concentrations are generally low (no more than 25  $\mu\text{g}/\text{m}^3$ ). Apart from differences in study design, study location and population, exposure assessment method, and the constituent of  $\text{PM}_{2.5}$ , another possible reason for these equivocal results might be due to relatively low maternal exposures. Only one study (a global survey of 22 countries) provided results of China and India, where the mean exposure concentrations were up to 98 and 64  $\mu\text{g}/\text{m}^3$ , respectively, but the results were completely inconsistent (Fleischer et al., 2014). In this study, LBW in China was positively associated with an increment of 10  $\mu\text{g}/\text{m}^3$  in maternal  $\text{PM}_{2.5}$  exposure during the entire pregnancy [odds ratio (OR) = 1.07, 95% confidence interval (CI): 1.01, 1.14], whereas the association for India was negative (OR = 0.97, 95% CI: 0.95, 0.99) (Fleischer et al., 2014). Therefore, more evidence is needed to clarify the possible association, especially in areas with high pollution levels of  $\text{PM}_{2.5}$ .

In China, the unprecedented urbanization and industrialization during the last few decades have subsequently resulted in elevated industrial, automobile, and biomass combustion emissions, which are the primary sources of  $\text{PM}_{2.5}$  (Liu et al., 2016). The population-weighted mean of  $\text{PM}_{2.5}$  in China was over 60  $\mu\text{g}/\text{m}^3$  during the year of 2014–2015, which was six times as high as the WHO Air Quality Guidelines (AQG) for the annual average concentration (Krzyszowski and Cohen, 2008). It was reported that only one percent of the 500 largest cities of China could meet the WHO AQG, and seven cities,

including Jinan, were listed as the ten most polluted cities in the world (Zhang and Crooks, 2012; Zhang and Cao, 2015). Therefore, more research is required to clarify the possible influence of such high  $\text{PM}_{2.5}$  exposure level on health of the public, especially neonatal health.

The majority of the previous studies used a relatively broad range of time periods as exposure windows (i.e., trimesters or entire pregnancy) to present the associations between maternal  $\text{PM}_{2.5}$  exposure and LBW (Basu et al., 2014; Gray et al., 2014; Ha et al., 2014b; Hyder et al., 2014; Pedersen et al., 2016; Pedersen et al., 2013). A meta-analysis was conducted to summarize these inconsistent results and found non-significant but positive trimester-specific associations between LBW risk and per 10  $\mu\text{g}/\text{m}^3$  increment in  $\text{PM}_{2.5}$  exposure (for the first trimester: OR = 1.03, 95% CI: 0.93, 1.13; for the second: OR = 1.04, 95% CI: 0.95, 1.13; and for the third: OR = 1.23, 95% CI: 0.96, 1.59) (Sun et al., 2016). Only a few studies considered relatively narrow exposure windows (i.e., monthly or weekly) during pregnancy, but these studies also presented inconsistent results (Darrow et al., 2011; Stieb et al., 2016a; Symanski et al., 2014; Warren et al., 2013). Therefore, critical maternal exposure windows to  $\text{PM}_{2.5}$  have not been well established for LBW.

In this study, we aimed to examine if high pollution levels of  $\text{PM}_{2.5}$  were associated with an increased risk of term low birth weight (TLBW) in neonates born in urban areas of Jinan, China from 2014 to 2016. We selected only term births because prematurity is generally considered to be the leading cause of LBW as 60% of births presenting with LBW are preterm (Diaz et al., 2016). We focused on month-specific associations, aiming to identify a potentially relevant exposure window for maternal  $\text{PM}_{2.5}$  exposure on TLBW. We also examined if the associations were dependent on temperature and co-pollutants such as nitrogen dioxide ( $\text{NO}_2$ ) and sulfur dioxide ( $\text{SO}_2$ ).

## 2. Materials and methods

### 2.1. Study area

Jinan (36°10′–37°90′ N, 116°12′–117°35′ E), the capital of Shandong Province, is a typical second-tier city in eastern China. Its population is over 7.0 million people, and approximately 3.8 million of the people reside in its six urban districts (Lixia, Licheng, Shizhong, Tianqiao, Huaiyin, and Changqing, Fig. 1), whereas the remaining 3.2

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