



Acute and chronic effects of ambient fine particulate matter on preterm births in Beijing, China: A time-series model

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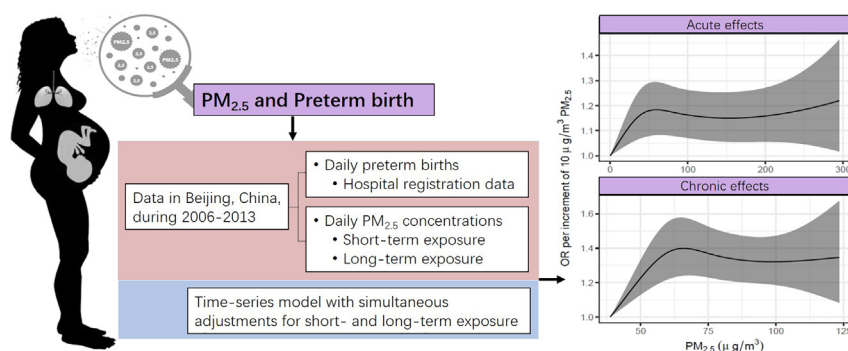
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HIGHLIGHTS

- 7-year daily data from Beijing, China were used in this study.
- Preterm birth was found associated with both short- and long-term PM_{2.5} exposure.
- The exposure-response curves were linear at low exposures without a threshold.
- The exposure-response curves flattened out at higher PM_{2.5} concentrations.
- The chronic effect was found much larger than the acute effect.

GRAPHICAL ABSTRACT



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ABSTRACT

Accumulating evidence suggests that short- and long-term exposure to ambient fine particulate matter $\leq 2.5 \mu\text{m}$ (PM_{2.5}) during pregnancy is associated with preterm births, yet the results are inconsistent, and the shape of the exposure-response curve is unclear, partially due to the limited studies conducted in areas with high air pollution. Our study evaluated the association between ambient PM_{2.5} concentration and preterm births in Beijing, China.

Daily preterm birth data were collected from a hospital in Beijing during 2006 to 2013; a time-series of daily PM_{2.5} concentrations during the same period is assembled with measured data at three monitoring sites in Beijing. An extension of the Poisson regression and a time-series model were applied to simultaneously estimate the acute and chronic effects of exposure to PM_{2.5}, with mutual adjustment for short- and long-term exposure as well as for confounders.

During the study period, the PM_{2.5} concentration was $70.4 \pm 60.6 \mu\text{g}/\text{m}^3$ and was found to be associated with an increased risk of preterm birth. In the study cohort, a 0.52% (95% confidence interval, CI: 0.09%, 0.96%) and 3.13% (95%CI: 1.92%, 4.35%) increase in preterm births was estimated for each 10- $\mu\text{g}/\text{m}^3$ increase in short- and long-term exposure, respectively. This association was significantly modified by

Abbreviations: PM, particulate matter; PM_{2.5}, particulate matter with an aerodynamic diameter $< 2.5 \mu\text{m}$; HMCHH, Beijing Haidian Maternal and Child Health Hospital; SD, standard deviation; PKUERS, Peking University Urban Atmosphere Environment Monitoring Station; AIC, Akaike information criterion; OR, odds ratio; 95% CI, confidence interval; PAHs, polycyclic aromatic hydrocarbons.

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season ($p < 0.05$). With mutual adjustments for short- and long-term exposure, a more robust association (3.16%, 95% CI: 1.95%, 4.39%; per $10\text{-}\mu\text{g}/\text{m}^3$ increment in $\text{PM}_{2.5}$) was observed for chronic effects. The exposure–response relationships for both short- and long-term exposure were linear, without a threshold, over the relatively low exposure range and flattened out at higher concentration levels. The maximum effect for long-term exposure to $\text{PM}_{2.5}$ (33.6%) was much greater than that for short-term exposure (19.9%). These findings indicate that air quality improvements over a long period could yield significant health benefits.

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1. Introduction

Preterm birth, defined as any live birth prior to 37 completed weeks of gestation, is the most significant determinant of adverse infant outcomes in terms of survival and quality of life (World Health Organization, 2015). Preterm birth is an important global health issue, as an estimated 15 million babies are born preterm annually, and the rate has been consistently increasing worldwide (Blencowe et al., 2012). Preterm birth complications are the leading cause of death for children under 5 years of age, accounting for approximately 1 million deaths worldwide in 2015 (Liu et al., 2016).

Spontaneous preterm birth is a multifactorial process. Common conditions associated with preterm birth include multiple pregnancies; infection; chronic conditions, such as diabetes and high blood pressure; and genetic, behavioral, socioeconomic, and environmental factors (Braillon and Bewley, 2010; Liang et al., 2016). However, no cause has been identified, and the etiology remains unclear. A better understanding of the causes and mechanisms of this phenomenon will promote the development of new approaches to prevention.

An emerging body of evidence suggests that exposure to fine particulate matter (PM) $\leq 2.5\ \mu\text{m}$ ($\text{PM}_{2.5}$) may play an important role in the incidence of preterm birth (Stieb et al., 2012; Sun et al., 2015; X. Li et al., 2017), and the estimated number of $\text{PM}_{2.5}$ -associated preterm births was 2.7 million worldwide in 2010 (Malley et al., 2017). Several hypotheses have been suggested for the possible pathways by which PM contributes to the onset of preterm birth (Chang et al., 2012; Ghosh et al., 2007; Shah and Balkhair, 2011). Inflammatory cytokines and reactive oxygen species, directly or indirectly generated by inhaled PM, may cause vasoconstriction, maternal hypertension, uterine contractions, DNA damage, and placental dysfunction, potentially leading to preterm birth. Alternatively, the toxic components in maternal circulation and the ultrafine PM that penetrates the placental barrier may directly affect the fetus and initiate preterm labor (Shah and Balkhair, 2011; Buerki-Thurnherr et al., 2012).

Previous reviews suggest that epidemiological evidence supports the association between $\text{PM}_{2.5}$ and preterm birth (Stieb et al., 2012; Sun et al., 2015; X. Li et al., 2017; Malley et al., 2017; Chang et al., 2012; Ghosh et al., 2007; Shah and Balkhair, 2011; Sagiv et al., 2005); however, the weight of the evidence is insufficient to establish causality (Fleischer et al., 2014). Indeed, the underlying mechanisms remain unclear, and current epidemiological results are mixed and controversial (Fleischer et al., 2014; Johnson et al., 2016; Giorgis-Allemand et al., 2017; Schifano et al., 2016). Additionally, the majority of studies have been conducted in high-income countries with relatively low levels of exposure. Few studies have been conducted in low- and middle-income countries, such as India and China, where the levels of both PM and preterm births are very high (Sun et al., 2015). The association between $\text{PM}_{2.5}$ and preterm birth at high $\text{PM}_{2.5}$ levels remains unclear. Global estimates of air pollution and preterm birth reflected significant differences between China and Western countries (Malley et al., 2017; Fleischer et al., 2014), and results from studies conducted in Western countries may not generalize to areas with higher $\text{PM}_{2.5}$ concentrations.

Previous studies indicate that PM exposure may not have a short-term effect on preterm birth; rather, there may be cumulative long-term effects as a result of short-term impacts (Li et al., 2016; Hansen

et al., 2006). However, a conclusive determination has not been possible due to lack of evidence. Either the long-term or the short-term effects of air pollution have been generally focused on, and cohort studies have not controlled for the acute effects of air pollution when estimating chronic effects. Previous studies assessing $\text{PM}_{2.5}$ -related mortality revealed independent chronic effects, which represented more than the cumulative effects of acute responses (Shi et al., 2016; Kloog et al., 2012). This hypothesis has not been tested in previous investigations of preterm births.

In this study, we simultaneously estimated the acute and chronic effects of $\text{PM}_{2.5}$ exposure on preterm births in Beijing, China, where the air pollution level is high, with mutual adjustment for short- and long-term exposure. The exposure–response relationship was estimated, and potential modifying factors were examined.

2. Methods

2.1. Study population

Beijing is the capital of China and has a total population of 20 million. Data on preterm births were provided by the Beijing Haidian Maternal and Child Health Hospital (HMCHH), which provides maternal and child healthcare primarily to residents in the Haidian district in Beijing. HMCHH performs medical exams on approximately 10,000 newborns annually, accounting for 18.8% of deliveries in Beijing. Maternal demography and medical history information was collected at admission. Gestational age was determined from the date of the mother's last menstrual period and confirmed by a sonographic examination prior to 20 weeks of gestation. Written informed consent was obtained from the participants at the time of their usual hospital care during the birth. The quality of the data is considered high-standard and has been discussed elsewhere (Zhang et al., 2012; Huang et al., 2015).

Preterm birth was defined as a gestational age of <37 weeks. From the period of September 1, 2006 to July 11, 2013, daily anonymous records were collected on preterm infants, including date of birth, gestational age at birth, infant sex, maternal age, gravidity, and parity. Induced preterm births were included in the primary analysis because medically indicated preterm births and spontaneous preterm births share many risk factors (Darrow et al., 2009). A sensitivity analyses was conducted excluding inductions, the results of which were found to be similar.

2.2. Meteorological and air pollution exposure

Because continuous historical $\text{PM}_{2.5}$ data are not available from any single source, the daily values for ambient $\text{PM}_{2.5}$ concentrations were assembled using an approach based on structural equation modeling of the measured data from the three monitoring sites (Bilonick et al., 2015a, b): the Peking University Urban Atmosphere Environment Monitoring Station (PKUERS; data from 2006 to 2013; located 3.1 km from HMCHH); Haidian Monitoring Station (data from 2006 to 2010; located 4.4 km from HMCHH); and the United States Embassy monitoring data (data from 2008 to 2013; located 17 km from HMCHH). The assembled concentrations of $\text{PM}_{2.5}$ could be interpreted as optimally weighted averages based on the correlations between the three time-series data,

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