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## LETTER

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# Ambient air pollutant PM<sub>10</sub> and risk of pregnancy-induced hypertension in urban China

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## Abstract

**Background:** The relationship between air borne particulate matter  $\leq 10 \mu\text{m}$  (PM<sub>10</sub>) exposure and pregnancy-induced hypertension (PIH) is inconclusive. Few studies have been conducted, and fewer were conducted in areas with high levels of PM<sub>10</sub>. **Methods:** To examine the association between PM<sub>10</sub> and PIH by different exposure time windows during pregnancy, we analyzed data from a birth cohort study conducted in Lanzhou, China including 8 745 pregnant women with available information on air pollution during pregnancy. A total of 333 PIH cases (127 gestational hypertension (GH) and 206 preeclampsia (PE)) were identified. PM<sub>10</sub> daily average concentrations of each subject were calculated according to the distance between home/work addresses and monitor stations using an inverse-distance weighting approach. **Results:** Average PM<sub>10</sub> concentration over the duration of entire pregnancy was significantly associated with PIH (OR = 1.12, 95%CI: 1.02, 1.23 per  $10 \mu\text{g m}^{-3}$  increase), PE (OR = 1.16, 95%CI: 1.03, 1.30 per  $10 \mu\text{g m}^{-3}$  increase), late onset PE (OR = 1.17, 95% CI: 1.03, 1.32 per  $10 \mu\text{g m}^{-3}$  increase), and severe PE (OR = 1.25, 95% CI: 1.06, 1.48 per  $10 \mu\text{g m}^{-3}$  increase). Average PM<sub>10</sub> during the first 12 gestational weeks was associated with the risk of GH (OR = 1.10, 95% CI: 1.00, 1.21 per  $10 \mu\text{g m}^{-3}$  increase), and PM<sub>10</sub> exposure before 20 gestational weeks was associated with the risk of severe PE (OR = 1.14, 95% CI: 1.01, 1.30 per  $10 \mu\text{g m}^{-3}$  increase). **Conclusions:** We found that high level exposure to ambient PM<sub>10</sub> during pregnancy was associated with an increased risk of PIH, GH and PE and that the strength of the association varied by timing of exposure during pregnancy.

## Introduction

Ambient air contains a dynamic mixture of pollutants, including particulate matter (PM), nitrogen dioxide (NO<sub>2</sub>), ozone (O<sub>3</sub>), sulphur dioxide (SO<sub>2</sub>), and volatile organic compounds. PM poses the greatest global air pollution threat, and therefore has received more

attention [1]. According to the estimation of the 2010 Global Burden Disease [2], PM pollution causes more than 3.2 million deaths and 76 million disability adjusted life-years (DALYs) every year worldwide. Approximately one third of these deaths and DALYs occurred in China [3]. PM pollution has become a critical public health concern in China.

Pregnancy-induced hypertension (PIH), which includes gestational hypertension (GH) and pre-eclampsia (PE), is a major cause of maternal, fetal, and neonatal morbidity and mortality [4, 5]. Furthermore, PIH could increase the risk of long-term cardiovascular diseases of both mothers and their children [6, 7]. PIH became the second leading cause of maternal death in China, which accounted for 13.8% and 8.8% of total maternal deaths in urban and rural areas, respectively [8]. Several factors have been suggested to be associated with PIH risk, including maternal age older than 40 years, primiparity, diabetes, obesity and preexisting hypertension [9]. However, these factors cannot explain all PIH.

Inhalable particles are generally defined as less than 10  $\mu\text{m}$  in aerodynamic diameter ( $\text{PM}_{10}$ ). Studies have reported that exposure to inhalable PM can damage vascular endothelium, impair vascular reactivity, and accelerate atherogenesis [1]. Although inhalable PM has the potential to increase the risk of PIH, the association between ambient  $\text{PM}_{10}$  pollution and PIH received inconsistent results. Some studies found a significantly positive association between  $\text{PM}_{10}$  exposure during entire pregnancy and GH [10], while others reported no association between GH or PE and  $\text{PM}_{10}$  during entire pregnancy [11] or  $\text{PM}_{10}$  during the first trimester [12, 13]. In addition, these studies were conducted in developed countries where the maximum  $\text{PM}_{10}$  levels were under 50  $\mu\text{g m}^{-3}$  [10–15]. Fifty eight percent of the urban population—concentrated in over 100 cities in China reported an annual average  $\text{PM}_{10}$  concentration exceeding 100  $\mu\text{g m}^{-3}$  in 2003 [16]. Given the inconsistent relationship between  $\text{PM}_{10}$  and PIH and the paucity of studies in areas with high levels of  $\text{PM}_{10}$ , we conducted a study in Lanzhou, China, where levels of  $\text{PM}_{10}$  were routinely above 140  $\mu\text{g m}^{-3}$ , to examine the association between  $\text{PM}_{10}$  and PIH.

## Methods

### Study population

The study population has been described previously [17–19]. In brief, pregnant women who came to the Gansu Provincial Maternity & Child Care Hospital (GPMCCCH) in Lanzhou, China for delivery in 2010–2012, who were 18 years or older with a gestational age of  $\geq 20$  weeks and without mental illness were eligible. A total of 10 542 (73.4%) women participated in the study. Subjects ( $N = 1344$ ) whose residence addresses during pregnancy were outside of Lanzhou city were excluded due to a lack of information on  $\text{PM}_{10}$  exposures. Furthermore, women who gave multiple births, still birth, and/or birth defects, or who had chronic hypertension or chronic cardiovascular diseases were also excluded, which yielded a final sample size of 8 745. All study procedures were approved by the Human Investigation Committees at

the GPMCCCH and Yale University. After obtaining written consent, an in-person interview was conducted at the hospital by trained study interviewers using a standardized and structured questionnaire to collect information on demographics, reproductive and medical history, lifestyle factors, occupation, and residential history. The majority of women (84%) were interviewed within one to three days after delivery, while others were interviewed within 2 days before delivery. Information on maternal complications and birth outcomes were abstracted from the medical records.

### Exposure assessment

Data on ambient air pollutants were obtained from the Gansu Provincial Environmental Monitoring Central Station, which collects 24 h average concentration for  $\text{PM}_{10}$ ,  $\text{SO}_2$ , and  $\text{NO}_2$  through an automated data reporting system from four monitoring stations in Lanzhou [20]. The 24 h average  $\text{PM}_{10}$  was measured for the period 1 April, 2009 to 31 December, 2012 for two stations (Huanghebei and Xigu stations), and 1 January, 2011 to 31 December, 2012 for the two additional stations (Xizhan and Tieluju stations). The monitors were located in the southern part of Lanzhou in the metropolitan area with high population density [20]. Though the distance from the participant's home and work addresses to the nearest monitors ranged from 0.1 to 88.5 km (mean: 5.0 km, median: 3.3 km), the majority (90%) of participants lived within 5.5 km from the nearest monitors. The coefficients of divergence between daily average observed  $\text{PM}_{10}$  levels versus distance between monitor locations for all monitor-pairs were lower than 0.20, indicating less spatial heterogeneity [18]. Values from these monitors were used to represent community-level exposure for Lanzhou, to investigate the association between outdoor air exposure and PIH.

The exposure measurement for each subject's residences throughout pregnancy was described previously [18]. In brief, we used the earth online sharing website provided by Google ([www.earthol.com](http://www.earthol.com)) to obtain longitude and latitude coordinates for each subject's home and work addresses. The move-in and move-out dates, and work addresses were collected. We calculated daily  $\text{PM}_{10}$  concentration at each subject's home and work addresses using (1) all four monitors with the inverse-distance weighting approach, (2) the two monitors in operation the full study period (April 2009 to December 2010) and inverse distance weighting, and (3) the nearest monitor.

For each subject we calculated the daily exposure levels during pregnancy by considering exposure time at home and work. Since the regular working hours are about 8 h  $\text{d}^{-1}$ , we used a time-weighted approach to calculate daily  $\text{PM}_{10}$  on weekdays for each subject (i.e., two-thirds of exposure at home address and one-third

exposure at work address). Weekend exposures were based on home address. Residential mobility was considered as time-weighted averaging to account for changes in residence during pregnancy. Finally, the daily exposures were averaged over four exposure windows based on a priori decisions: 1–20 gestational weeks, <13 gestational weeks, 13–20 gestational weeks, and entire pregnancy. Exposures for each subject to NO<sub>2</sub> and SO<sub>2</sub> were generated in the same manner as PM<sub>10</sub>.

### Statistical Analysis

PIH cases included both GH and PE conditions. GH was diagnosed as hypertension (measured twice with 6 h apart,  $\geq 140/90$  mmHg) manifested after 20 weeks of gestation without proteinuria. PE was diagnosed as hypertension concurrent with proteinuria ( $\geq 1+$  on dipstick in two urine samples) after 20 weeks of gestation. PE was further classified as mild PE (raised blood pressure  $\geq 140/90$  mmHg and  $< 160/110$  mmHg, proteinuria  $\geq 1+$  and  $< 2+$  on dipstick in two urine samples, without symptoms of severity), severe PE (raised blood pressure  $\geq 160/110$  mmHg, proteinuria  $\geq 2+$  on dipstick in two urine samples, with symptoms of severity such as headache, blurred vision, epigastric burning pain, decreased urine output, decreased or absent fetal kick etc), early onset PE (EOPE, diagnosed before 34 weeks of gestation), or late onset PE (LOPE, diagnosed at or after 34 weeks of gestation). PIH was defined as a combination of GH and PE. Controls were those without GH or PE [19].

Chi-squared tests were used to compare the distributions of maternal characteristics between PIH and controls. Unconditional logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the associations between PM<sub>10</sub> exposure and risk of PIH, GH, PE, severe PE, mild PE, EOPE and LOPE by different exposure time windows. Average PM<sub>10</sub> levels in each exposure time window were treated as a continuous variable, and results were presented for the change in health outcome per  $10 \mu\text{g m}^{-3}$ . Potential confounding variables included maternal age (<25, 25–29, 30–34, and  $\geq 35$  years), education (<college,  $\geq$ college), family monthly income per capita (<2000, 2000–3999,  $\geq 4000$  RMB, and unknown), smoking during pregnancy (yes or no), pre-pregnancy BMI [21] (<18.5, 18.5–22.9, and  $\geq 23 \text{ kg m}^{-2}$ ), season of conception (spring (January–March), summer (April–June), fall (July–September), and winter (October–December)), nulliparous (yes or no), previous PIH (yes or no), vitamin supplement intake during pregnancy (yes or no), averaged temperatures and other pollutants (SO<sub>2</sub> and NO<sub>2</sub>) in the time windows corresponding to the time frame used for PM<sub>10</sub>. Additional adjustments for alcohol consumption, infant gender, weight gain during pregnancy did not result in material changes of the observed associations and thus were not included in

the final models (results not shown). All analyses were performed using SAS, version 9.2 (SAS Institute, Inc., Cary, NC).

## Results

Of the 8 745 study subjects, 333 (3.81%) were diagnosed with PIH (127(1.45%) GH and 206 (2.56%) PE) (table 1). Of the 206 PE cases, 110 (53.40%) were severe PE and 22 (10.68%) were EOPE. Compared to controls, women with PIH were more likely to be older, less educated, lower family income, higher pre-pregnancy BMI, having previous PIH, multipara, and less likely to take vitamin supplement during pregnancy. There were no significant differences in the distribution of conception season and exposure to smoking during pregnancy between the cases and controls. The results of the multivariate logistic analysis on the association between PIH and these risk factors were presented in supplementary table 2.

Table 2 presented average concentrations of PM<sub>10</sub> during different exposure time windows for the overall study population under different exposure estimation models. The different approaches yielded similar estimations of PM<sub>10</sub> exposure concentrations.

Table 3 presented the results using exposure data obtained from all four monitors with the inverse-distance weighting approach. Average PM<sub>10</sub> exposure during the entire pregnancy was significantly associated with an increased risk of PE, LOPE, and severe PE (OR = 1.15, 95%CI: 1.03, 1.28; OR = 1.15, 95%CI: 1.03, 1.28; OR = 1.18, 95%CI: 1.02, 1.36 per  $10 \mu\text{g m}^{-3}$  increase, respectively), but not with PIH, GH, EOPE and mild PE (OR = 1.08, 95%CI: 0.99, 1.18; OR = 0.96, 95%CI: 0.84, 1.11; OR = 1.16, 95%CI: 0.84, 1.59; OR = 1.12, 95%CI: 0.97, 1.31 per  $10 \mu\text{g m}^{-3}$  increase, respectively). Average PM<sub>10</sub> exposures in other time windows were not significantly associated with the risk of PIH GH, PE and PE subtypes. After additional adjustment for SO<sub>2</sub> and NO<sub>2</sub>, the association between average PM<sub>10</sub> concentration during the entire pregnancy and PIH changed from borderline significance (OR = 1.08, 95%CI: 0.99, 1.18 per  $10 \mu\text{g m}^{-3}$  increase) to statistical significance (OR = 1.12, 95%CI: 1.02, 1.23 per  $10 \mu\text{g m}^{-3}$  increase). The associations with average PM<sub>10</sub> concentration during the entire pregnancy and PE, LOPE, and severe PE were also strengthened (OR and 95%CI were 1.16 (1.03, 1.30), 1.17 (1.03, 1.32), and 1.25 (1.06, 1.48) per  $10 \mu\text{g m}^{-3}$  increase, respectively). Moreover, during the first 12 gestational weeks, a  $10 \mu\text{g m}^{-3}$  increase in PM<sub>10</sub> was borderline significantly associated with the risk of GH (OR = 1.10, 95%CI: 1.00, 1.21). Severe PE during the first 20 gestational weeks was also significantly associated with PM<sub>10</sub> (OR = 1.14, 95%CI: 1.01, 1.30 per  $10 \mu\text{g m}^{-3}$  increase). The correlations of PM<sub>10</sub> with SO<sub>2</sub> and NO<sub>2</sub> were weak (correlation coefficient = 0.30 and 0.23 respectively), therefore no

**Table 1.** Distributions of selected characteristics between PIH and controls.

Characteristics	Control		GH/PE		<i>p</i>	
	<i>N</i> = 8412	%	<i>N</i> = 333	%		
Maternal age						
	<25 years	1217	14.47	44	13.21	<0.000
	25–29	4193	49.85	115	34.53	
	30–34	2302	27.37	108	32.43	
	35–	700	8.32	66	19.82	
Education						
	<College	2953	35.10	143	42.94	0.007
	≥College	5311	63.14	182	54.65	
	Unknown	148	1.76	8	2.40	
Family income per capita ( ¥ )						
	<2000	1719	20.44	100	30.03	<0.000
	2000–3999	4053	48.18	135	40.54	
	≥4000	1843	21.91	60	18.02	
	Unknown	797	9.47	38	11.41	
Nulliparous						
	Yes	6342	75.39	232	69.67	0.018
	No	2070	24.61	101	30.33	
Pre-pregnancy BMI (kg m <sup>−2</sup> )						
	<18.5	1762	20.95	41	12.31	<0.000
	18.5–22.9	5079	60.38	166	49.85	
	23–	1340	15.93	114	34.23	
	Unknown	231	2.75	12	3.60	
Previous PIH						
	Yes	8379	99.61	314	94.29	<0.000
	No	33	0.39	19	5.71	
Vitamin intake during pregnancy						
	Yes	1881	22.36	92	27.63	0.021
	No	6531	77.64	241	72.37	
Season of conception						
	Spring	1822	21.66	70	21.02	0.173
	Summer	2001	23.79	86	25.83	
	Fall	2356	28.01	105	31.53	
	Winter	2233	26.55	72	21.62	
Smoking during pregnancy						
	Yes	2953	35.10	143	42.94	0.855
	No	5311	63.14	182		

Abbreviation: PIH, pregnancy induced hypertension; GH, gestational hypertension; PE, preeclampsia; BMI, body mass index.

collinear effects were observed with adjustments for SO<sub>2</sub> and NO<sub>2</sub>. Average SO<sub>2</sub> and NO<sub>2</sub> exposure during the entire pregnancy were not significantly associated with an increased risk of PIH (OR = 1.01, 95%CI: 0.89, 1.15; OR = 0.82, 95%CI: 0.65, 1.03 per 10 µg m<sup>-3</sup> increase, respectively). Sensitivity analyses based on two monitors or on nearest monitors yielded similar results (supplementary table 1) to what we

expected due to less spatial heterogeneity of PM<sub>10</sub> in our study region.

## Discussion

Our study is the first to examine the effects of exposures to very high level of ambient PM<sub>10</sub> and the

**Table 2.** Estimation of average PM<sub>10</sub> exposure concentration ( $\mu\text{g m}^{-3}$ ) of overall subjects ( $N = 8745$ ) by using different models.

Gestational Week	PM <sub>10</sub> <sup>a</sup>	PM <sub>10</sub> <sup>b</sup>	PM <sub>10</sub> <sup>c</sup>
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
1–20 week	141.76 $\pm$ 34.3	139.71 $\pm$ 35.2	140.94 $\pm$ 34.1
<13 week	140.23 $\pm$ 42.3	138.21 $\pm$ 43.2	139.69 $\pm$ 40.7
13–20 week	144.24 $\pm$ 44.9	142.12 $\pm$ 46.0	141.18 $\pm$ 44.6
Entire pregnancy	142.27 $\pm$ 17.4	140.00 $\pm$ 19.2	140.48 $\pm$ 21.6

Abbreviations: PM, particulate matter; SD: standard deviation

<sup>a</sup> Calculated by using exposure data obtained from all four monitors.<sup>b</sup> Calculated by using exposure data obtained from two monitors in operation the full study period.<sup>c</sup> Calculated by using the nearest monitor.

risk of PIH, GH and PE. Our results support the hypothesis that exposure to high levels of PM<sub>10</sub> increases the risk of GH and PE and that the risk may vary by exposure time windows.

The results of previous studies assessing PM<sub>10</sub> and risk of PIH have been inconsistent. Vinikoor-Imler *et al* [10] conducted a study in North Carolina that included more than 222 000 women (12 085 PIH) and reported a 7% increased risk of PIH per 3.92  $\mu\text{g m}^{-3}$  increase in daily concentration of PM<sub>10</sub> during entire pregnancy. Van den Hooven *et al* in Netherlands [14] including 7006 (250 PIH and 141 PE) study subjects found that per 10  $\mu\text{g m}^{-3}$  increase in daily concentration of PM<sub>10</sub> during entire pregnancy was associated with a 72% increased risk of PIH but not PE. Consistent with these two studies, we also observed an increased risk of PIH associated with per 10  $\mu\text{g m}^{-3}$  increase in PM<sub>10</sub> levels during entire pregnancy. Dadvand *et al* [11] conducted a study in Spain involving 8398 (103 PE) women and found no statistically significant association between PE and PM<sub>10</sub> exposure during entire pregnancy and different trimesters. Mobasher *et al* [12] conducted a case-control study among Hispanic women with 136 PIH cases and found no association between PIH and PM<sub>10</sub> exposure in any trimester. However, Lee *et al* conducted a cohort study in Pittsburgh including 1684 women (110 GH and 32 PE) and found that exposure to PM<sub>10</sub> during the first 20 weeks of gestation significantly increased systolic and diastolic blood pressures [15]. In Lee's later research in Pittsburgh, which enrolled another 34 705 women with 2078 GH, they found that PM<sub>10</sub> during the first 12 weeks of gestation marginally increased the risk of GH (OR = 1.08, 95%CI: 0.98, 1.20 per 7.7  $\mu\text{g m}^{-3}$  increase in PM<sub>10</sub>) [13], which was comparable to our study finding that per 10  $\mu\text{g m}^{-3}$  increase in PM<sub>10</sub> during the first 12 weeks of gestation significantly increased the risk of GH.

Our study found that LOPE, not EOPE, was associated with average PM<sub>10</sub> exposure during entire pregnancy. While no study examined LOPE and EOPE separately in relation to PM<sub>10</sub> exposure, Dadvand *et al* [11] found that PM<sub>2.5</sub> exposure in the third trimester

was associated with LOPE. Previous studies have also demonstrated that EOPE and LOPE might have different pathogenesis [22, 23]. EOPE appears to be more related to placental disorder. However, LOPE seems to be more linked to maternal constitutional factors [22, 23]. We speculated that high PM<sub>10</sub> exposure during entire pregnancy might do harm to maternal cardiovascular constitution. We also found that PM<sub>10</sub> exposure during the first 20 gestational weeks or entire pregnancy could increase the risk of severe PE but not mild PE. While its mechanism needs further research, it might suggest that PM<sub>10</sub> plays a major role in PE progression not PE initiation.

All previous studies were conducted in areas with relatively low concentrations of PM<sub>10</sub>. The mean PM<sub>10</sub> exposure concentrations in previous studies [10, 11, 13–15] ranged from 22.4 to 39.0  $\mu\text{g m}^{-3}$ , which were below the hazard level recommended by the World Health Organization (WHO) air quality guidelines for 24 h concentrations (50  $\mu\text{g m}^{-3}$ ) [24]. A large percent of the world's population is exposed to high levels of air pollution and relatively few studies have been conducted in such areas. Our study is a timely effort to address this understudied issue.

Air pollution is a complex mixture of several pollutants. Other pollutants such as PM<sub>2.5</sub>, CO, O<sub>3</sub>, NO<sub>2</sub>, and SO<sub>2</sub> could also increase the risk of PIH. Given the available data in our study, we included SO<sub>2</sub>, NO<sub>2</sub>, and PM<sub>10</sub> into the multivariate models simultaneously and found that the associations with PM<sub>10</sub> were strengthened. We observed stronger associations with average PM<sub>10</sub> exposure in an entire pregnancy than in a specific trimester. A different time window of exposure during pregnancy yields different effects on PIH that are likely through different mechanisms [15]. Previous studies have demonstrated that long term exposure to air pollutants, such as high exposure during an entire pregnancy, may be related to the harmful effects on cardiovascular constitution [14]. Short term exposure to harmful pollutants, such as brief exposure during a specific trimester, may trigger harmful effects [11].

Strengths and limitations should be considered when interpreting the study findings. Diagnosis of

**Table 3.** Associations between PIH and average ambient PM<sub>10</sub> expose during pregnancy.

		Per 10 $\mu\text{g m}^{-3}$ increase in PM <sub>10</sub>					
PIH type	Time periods	OR <sub>adj</sub> <sup>a</sup>			95%CI		
		OR <sub>adj</sub> <sup>b</sup>	95%CI				
GH/PE							
	1–20 weeks	1.03	0.96	1.10	1.05	0.98	1.13
	<13weeks	1.03	0.98	1.09	1.06	0.99	1.12
	13–20 weeks	1.01	0.96	1.05	1.01	0.96	1.06
	Entire pregnancy	1.08	0.99	1.18	1.12	1.02	1.23
GH							
	1–20 weeks	0.99	0.89	1.10	1.05	0.93	1.18
	<13weeks	1.04	0.95	1.13	1.10	1.00	1.21
	13–20 weeks	0.95	0.87	1.02	0.96	0.88	1.04
	Entire pregnancy	0.96	0.84	1.11	1.04	0.89	1.22
PE							
	1–20 weeks	1.05	0.97	1.15	1.06	0.97	1.16
	<13weeks	1.03	0.96	1.11	1.03	0.95	1.12
	13–20 weeks	1.04	0.98	1.10	1.03	0.97	1.10
	Entire pregnancy	1.15	1.03	1.28	1.16	1.03	1.30
EOPE							
	1–20 weeks	1.08	0.82	1.41	1.05	0.79	1.38
	<13weeks	1.02	0.81	1.28	1.02	0.79	1.33
	13–20 weeks	1.07	0.90	1.27	1.01	0.85	1.20
	Entire pregnancy	1.16	0.84	1.59	1.06	0.76	1.49
LOPE							
	1–20 weeks	1.05	0.96	1.15	1.06	0.96	1.17
	<13weeks	1.03	0.95	1.11	1.03	0.95	1.12
	13–20 weeks	1.04	0.98	1.10	1.04	0.97	1.11
	Entire pregnancy	1.15	1.03	1.28	1.17	1.03	1.32
Mild PE							
	1–20 weeks	1.01	0.89	1.14	0.98	0.86	1.12
	<13weeks	0.99	0.89	1.10	0.96	0.86	1.08
	13–20 weeks	1.03	0.95	1.12	1.01	0.93	1.10
	Entire pregnancy	1.12	0.97	1.31	1.07	0.91	1.26
Severe PE							
	1–20 weeks	1.10	0.98	1.25	1.14	1.01	1.30
	<13weeks	1.07	0.97	1.18	1.11	0.99	1.23
	13–20 weeks	1.05	0.97	1.14	1.06	0.97	1.15
	Entire pregnancy	1.18	1.02	1.36	1.25	1.06	1.48

Abbreviation: PIH, pregnancy induced hypertension; GH, gestational hypertension; PE, preeclampsia; EOPE, early onset preeclampsia; LOPE, late onset preeclampsia; OR, odds ratio; CI: confident interval.

<sup>a</sup> Adjusted for maternal age, education, income per capita, prenatal BMI, parity, folic acid intakes, previous PIH, conception season, and average temperature in corresponding time periods.

<sup>b</sup> Additional adjustment for average SO<sub>2</sub> and NO<sub>2</sub> exposure in corresponding time periods.

GH/PE in our study was based on medical records not self-report, which minimized potential disease misclassification. Our study collected detailed information on demographic factors, smoking, occupation and medical histories, which allowed us to control for these important potential confounding factors. We considered both residential and work addresses as well as mobility during pregnancy when we calculated daily

exposure levels of each pollutant. Information on work address and on residences throughout pregnancy is often not available in studies of air pollution and pregnancy outcomes. Individual exposures to ambient air pollutants in our study were based on monitoring stations rather than direct measurement (i.e., personal monitoring) for each subject due to feasibility concerns in such a large population-based

study. PM<sub>10</sub> exposure in our study was much higher than in other published studies, and the findings from our study might not be generalizable to populations who live in the areas with low air pollution levels, although the results could be applicable to other regions of the developing world with similarly high levels of ambient air pollution. Previous studies have also reported a positive relationship between PM<sub>2.5</sub> and PE [12, 14, 15, 25] which we were unable to investigate due to the lack of PM<sub>2.5</sub> monitoring. Therefore, our observed association between PM<sub>10</sub> and PIH may involve the effects of PM<sub>2.5</sub> on PIH.

## Conclusion

The results of our study support the notion that increasing exposure to ambient PM<sub>10</sub> during pregnancy is associated with an increased risk of PIH, GH and PE, and the positive linear relationship sustains in high level exposures of PM<sub>10</sub>. These findings have important public health implications and warrant further investigation in other regions of the world.

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JQ, QL, and YZ designed the research; WQ, XH, YW, QS, HC, SL, ZT, YC, LY, ZD, LL, XL, CZ, HZ, RX, DZ, XX, YD, XH conducted the birth cohort study; XH, NZ, RL, TY, JS, HZ, HB, WW, YW, XL, BM, HH, JL, MJ performed exposure assessment and statistical analysis; XH, JQ, YZ, NZ, SM, MB, CK, QL, YZ wrote the first draft and all authors contributed to the final draft and approved the manuscript. The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. Yawei Zhang and Qin Liu had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors had final responsibility for the decision to submit for publication.

## Conflict of interest

The authors declares that they have no conflicting interests.

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