ARTICLE

Synergic effects of PM_1 and thermal inversion on the incidence of small for gestational age infants: a weekly-based assessment

Xupeng Zhang[1,8], Faxue Zhang[2,8], Yan Gao[3,8], Yuanyuan Zhong[4], Yan Zhang[4], Gaichan Zhao[1], Shijie Zhu[2], Xiaowei Zhang[2], Tianzhou Li[2], Bingbing Chen[5], Aojing Han[6], Jing Wei[7]✉, Wei Zhu[2]✉ and Dejia Li[1,2]✉

BACKGROUND: The synergic effects of thermal inversion (TI) and particulate matter with an aerodynamic diameter ≤1 μm (PM_1) exposure and incidence of small for gestational age (SGA) was not clear.
OBJECTIVE: We aimed to explore the independent effects of prenatal TI and PM_1 exposure on incidence of SGA and their potential interactive effects.
METHODS: A total of 27,990 pregnant women who delivered in Wuhan Children's Hospital from 2017 to 2020 were included. The daily mean concentration of PM_1 was obtained from ChinaHighAirPollutants (CHAP) and matched with the residential address of each woman. Data on TI was derived from National Aeronautics and Space Administration (NASA). The independent effects of PM_1 and TI exposures on SGA in each gestational week were estimated by the distributed lag model (DLM) nested in Cox regression model, and the potential interactive effects of PM_1 and TI on SGA were investigated by adapting the relative excess risk due to interaction (RERI) index.
RESULTS: Per 10 μg/m^3 increase in PM_1 was associated with an increase in the risk of SGA at 1–3 and 17–23 gestational weeks, with the strongest effect at the first gestational week (HR = 1.043, 95%CI: 1.008, 1.078). Significant links between one day increase of TI and SGA were found at the 1–4 and 13–23 gestational weeks and the largest effects were observed at the 17th gestational week (HR = 1.018, 95%CI: 1.009, 1.027). Synergistic effects of PM_1 and TI on SGA were detected in the 20th gestational week, with RERI of 0.208 (95%CI: 0.033,0.383).
IMPACT STATEMENT: Both prebirth PM_1 and TI exposure were significantly associated with SGA. Simultaneous exposure to PM_1 and TI might have synergistic effect on SGA. The second trimester seems to be a sensitive window of environmental and air pollution exposure.

Keywords: Particulate matters; PM_1; Thermal inversion; Synergistic effect; Small for gestational age

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INTRODUCTION

As a surrogate for abnormal fetal growth, small for gestational age (SGA) is defined as birthweight below the tenth percentile of a certain reference at a given gestational week [1]. SGA was found to be associated with adverse effects of both mother and baby. Evidences showed that mothers who had given birth to SGA infants were more easily to suffer from chronic kidney and cardiovascular diseases later in life [2, 3]. It has been suggested that SGA was related to neonatal morbidity and mortality [4], obesity and cognitive impairment in childhood [5, 6]. Furthermore, SGA may lead to poorer academic outcomes [7], type 2 diabetes mellitus, cardiovascular diseases and lower socioeconomic status (SES) in adulthood [8, 9]. In developed countries of North America and Europe, SGA occurs in approximately every 10 newborn births [10, 11]. For example, the prevalence of SGA was 9.1% in Denmark and 10.8% in Canada [12, 13]. Almost 32.4 million infants were born SGA in low-income and middle-income countries and China was the number five countries with the highest numbers of SGA infants born [1,072,100 (uncertainty range: 648,300–1,817,600)] in 2010 [14]. A study in France showed that the total maternal and infant hospital cost of SGA was estimated at 23% of the total cost of delivery, and the medical cost of SGA infants in the first year of life was 2783 euros higher than that of appropriate for gestational age (AGA) infants [15].

In addition to genetic and prenatal lifestyle factors, many studies focused on the relationships between environmental conditions and adverse birth outcomes [16, 17]. It was consistently showed that SGA was associated with air pollution exposure

[1]Department of Public Health, School of Public Health, Wuhan University, Wuhan 430071, China. [2]Department of Occupational and Environmental Health, School of Public Health, Wuhan University, Wuhan 430071, China. [3]Department of Neonatology, Lianyungang Maternal and Child Health Hospital, Lianyungang 222006, China. [4]Department of Obstetrics and Gynecology, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430014, China. [5]Department of Global Health, School of Public Health, Wuhan University, Wuhan 430071, China. [6]Department of Preventive Medicine, School of Public Health, Wuhan University, Wuhan 430071, China. [7]Department of Atmospheric and Oceanic Science, Earth System Science Interdisciplinary Center, University of Maryland, College Park, MD 20740, USA. [8]These authors contributed equally: Xupeng Zhang, Faxue Zhang and Yan Gao. ✉email: weijing@umd.edu; weizhu@whu.edu.cn; djli@whu.edu.cn

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during pregnancy [18–20]. However, the probable sensitive exposure windows of studies were different. A retrospective cohort study in China pointed out that negative associations between increases in ambient CO, O_3, $PM_{2.5}$ and PM_{10} and term birth weight were found during the entire pregnancy [18]. While statistically significant relationships of PM_{10} and SGA were only observed in the first and third trimesters in the UK [19]. Therefore, more recent studies subdivide the exposure window by gestational week to explore a more accurate sensitive period [6, 21]. Besides, smaller size of particulate matter (PM), such as PM_1, was found to be more harmful to human health with a larger surface area mass ratio than $PM_{2.5}$ and PM_{10} [22–24]. Researchers have lately followed the question of whether PM_1 could increase the risk of adverse birth outcomes, such as preterm birth (PTB), low birth weight (LBW), SGA and neurodevelopmental delay in children [25–27]. Although the study conducted in Beijing revealed an interesting impact of PM_1 on neonatal health, no significant correlation was found between PM_1 and SGA [26].

Thermal inversion (TI) is a meteorological phenomenon that occurs when a layer of hot air settles on top of a layer of cooler air near the ground [28]. It prevents air flow and hinders the diffusion of air pollutants, resulting in peaks of NO_2, SO_2, PM_{10} and $PM_{2.5}$ primarily occurring during TI [29–31]. Moreover, the Vietnam study assumed that TI was correlated with number of patients in 5 years [31]. And a survey developed in Brazil revealed that exposure to TI during the last three months of pregnancy caused sizable reductions in birth weight and an increase in the risk of PTB [32]. The relative excess risk due to interaction (RERI) index was usually applied to explore the potential synergistic effects of two risk factors on health [33, 34]. Recent studies announced the joint effects of heatwaves and air pollution on PTB by using RERI index [21, 35, 36].

In this study, the distributed lag model (DLM) was nested in Cox regression model to explore the independent effects of maternal exposure to PM_1 and TI on SGA in each gestational week. In addition, the possible interactive effects of PM_1 and TI were estimated by calculating RERI index. This would help fill the knowledge gap of the impacts of PM_1 and TI on pregnant women and better protect the health of next generations in the ear of climate change.

MATERIALS AND METHODS

Study area and population

Wuhan is located in the middle of China and the Yangtze River and its largest tributary converges in the city. As the capital of Hubei Province, Wuhan is an important transportation hub in China and known as the "thoroughfare to nine provinces", which has a northern subtropical monsoon climate with abundant rainfall and four distinct seasons. Wuhan Children's Hospital is the first specialized hospital to pass the Class A tertiary hospital in Wuhan, situated in the downtown area of Wuhan and undertakes numerous medical and health services for women and children.

Data collection

After screening and eliminating missing data according to inclusion and exclusion criteria, a total of 27,990 gravidas and their singleton live fetuses in Wuhan Children's Hospital from January 1, 2017 to December 31, 2020 were included in this study (Fig. 1). Except for participants with incomplete information, the characteristics of included and excluded participants were compared in Table S1. There was no significant difference in major individual characteristics, including maternal age, education level and infant sex. The distribution of their addresses can be seen as Fig. 2. Besides, we also retrieved variables of special interest from the hospital's delivery register, including maternal residential address and duration, age, gravidity and parity, education level, work status, high-risk factor during pregnancy (premature rupture of membranes, gestational diabetes, gestational hypertension, preeclampsia, eclampsia, oligohydramnios, placental abruption, placenta previa, cord entanglement and hepatitis B, etc.), gestational age, date of delivery, newborn sex and birth weight.

SGA refers to newborns whose birth weight is lower than the 10^{th} percentile of the average weight at the same gestational age [1]. And the weight of newborns was measured within an hour after delivery. The gestational age was determined by professional physicians combining ultrasound with the last self-reported menstrual period to represent the best clinical estimate for each mother. Similarly, AGA was defined as the fetus whose birth weight is between the 10th and 90th percentile of the average birth weight at the same gestational age [37]. SGA and AGA were both defined by a Chinese standard published in Chinese Journal of Pediatrics in 2020 [38].

Daily mean concentrations of PM_1 from January 1, 2016 to December 31, 2020 in this study were obtained from ChinaHighAirPollutants (CHAP) [39–41]. CHAP is a series of long-term, high-quality and high-resolution (1 km × 1 km) air pollution datasets for China, and it was widely used in environmental epidemiology studies [42–44]. In brief, CHAP was obtained from satellite observation data based on Multi-source Satellite remote sensing technology by using artificial intelligence methods and considering natural and human factors (meteorological conditions, surface and topographic changes, human distribution, pollution emissions, etc.) as well as the Spatio-temporal characteristics of air pollution. The cross-validation coefficient of determination (CV-R^2) and root-mean-square error (RMSE) of PM_1 were 0.77 and 14.6 μg/m^3 on a daily basis, respectively.

Data on TI was derived from the product M2I6NPANA version 5.12.4, which was generated from Modern-Era Retrospective analysis for Research and Applications version 2 (MERRA-2) released by the National Aeronautics and Space Administration (NASA) of the U.S (http://disc.gsfc.nasa.gov/). This dataset provides 0.5° × 0.625° resolution (around 50 km × 60 km) and 6-h air temperature at 42 barometric layers ranging from 110 to 36,000 meters (https://disc.gsfc.nasa.gov/datasets/M2I6NPANA_V5.12.4/summary). Every 6 hours, we calculate the temperature difference between the second layer (320 meters) and the first layer (110 meters) of Wuhan. If the difference was positive, there existed TI. If the difference was negative, there was no TI [45, 46]. As long as there existed a TI in one of the four 6-h per day, we regarded that day as TI exposure.

Statistical analysis

Accounting for the different gestational weeks at birth and all live births in this study had a gestational age of 26 weeks or more, the first 26 gestational weeks of pregnant women in this study was chosen as the exposure period. The chi-squared test was used to compare SGA group and AGA group. Maternal exposure to PM_1 and TI in 1–26 gestational weeks between the two groups were compared by t-test. Potential confounders were selected a priori including maternal age (<35, 35+ years), gravidity (=1, >1), parity (=1, >1), education level (junior high school or below, high school and college degree or above), work status (employed, unemployed), whether there was high-risk factor during pregnancy (yes, no), newborn sex (male, female), average temperature and season become pregnant [Spring (Mar-May), Summer (Jun-Aug), Autumn (Sep-Nov) and Winter (Dec-Feb)]. After adjusting confounding factors, DLM nested in Cox regression model was used to investigate the associations between PM_1/TI and SGA. The basic risk model was as follow:

$$h[t, X_l, X_i(t)] = h_0(t)\exp[\beta_l X_l + \beta_d X_i(t)] \quad (1)$$

where SGA was treated as a time-to-event outcome and t represents the completed gestational week; h_0 is the baseline hazard function, indicating the hazard function for an individual with all variables equal to zero; X_l refers to the values of time-independent variables during pregnancy, including maternal age, gravidity, parity, education level, work status, whether there was high-risk factor, newborn sex, average temperature and season become pregnant. $X_i(t)$ are the values of time-varying variables during pregnancy like PM_1 and TI exposure.

Weekly mean concentration of PM_1 and days of TI were added in the model as a cross-basis matrix based on DLM, where the lag-outcome associations were modelled using a natural cubic spline with four degrees of freedom with knots equally spaced [21]. Independent effects of PM_1 and TI exposure on SGA were analyzed as the following model:

$$h[t, X_l, X_i(t)] = h_0(t)\exp\left[\beta_l X_l + \beta_{PM1/TI} cbX_{PM1/TI}\right] \quad (2)$$

where $cbX_{PM1/TI}$ refers to the cross-basis matrix of weekly concentration of PM_1 or days of TI during 1-26 gestational weeks. PM_1 and TI exposure were included as continuous variable, with the hazard ratios (HR) and 95% confidence interval (CI) calculated per 10 μg/m^3 increase in PM_1, and 1 day increase in TI.

In addition, the restricted cubic spline (RCS) was used to test the linearity of the associations between PM_1 and TI with SGA. We also analyzed the independent one-week effects of PM_1 and TI on SGA in different newborn genders (boys and girls), and gender was removed from covariates of the

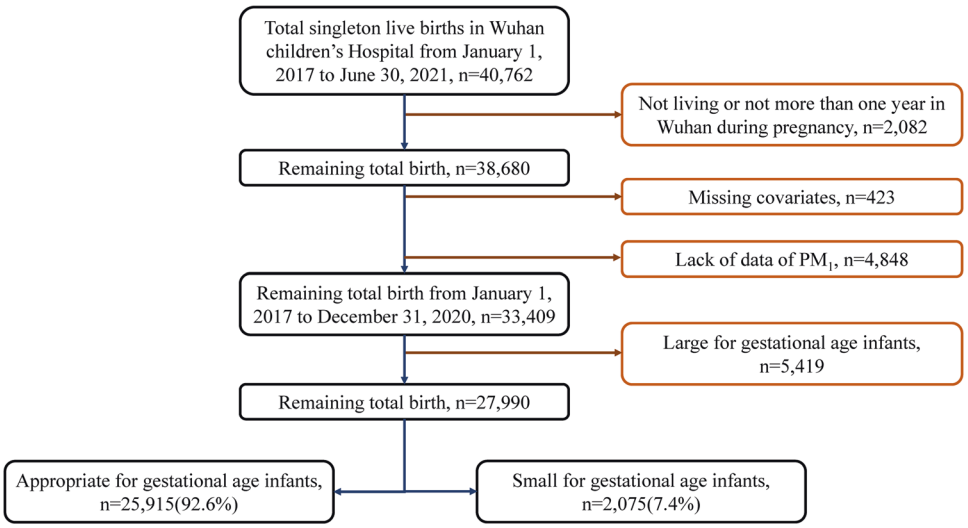

Fig. 1 Flow chart of the cohort study population selection. A total of 40,762 singleton live births were collected during the study, and 27,990 participants are presented in our analytic sample after exclusion according to specific requirements.

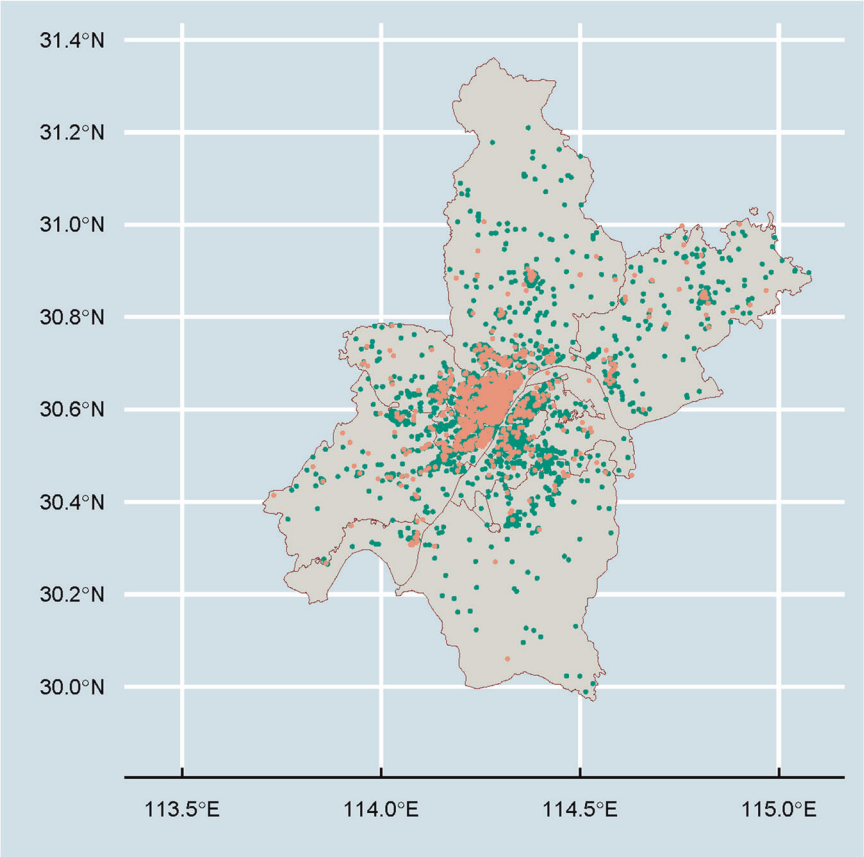

Fig. 2 The locations of residences of SGA gravidas and AGA gravidas. The distribution of SGA and AGA gravidas on the map is similar, with most of them living in the central area. Orange points: SGA infants; green points: AGA infants.

basic risk model in the stratification analysis. The correlations between PM_1 and TI in each gestational week were estimated by Spearman rank correlation coefficients. And Mediation effect analysis was used to detect the independence of PM_1 and TI exposure on the effect of SGA.

According to previous studies [21], we calculated the RERI to explore the potential interactive effects of maternal exposure to PM_1 and TI on SGA. The formula was shown as follow:

$$RERI = HR_{11} - HR_{10} - HR_{01} + 1 \quad (3)$$

We used the median of PM_1 and TI in each gestational week as a cut-off to divide the two exposures into binary variables (for example, in the first gestational week, TI was divided as ≥4 days and <4 days, PM_1 was divided as ≥ 26.2 μg/m^3 and < 26.2 μg/m^3). Where HR_{11} means the relative risk of high level of PM_1 (≥P50) and TI (≥P50); HR_{10} means the relative risk of high level of PM_1 (≥P50) and low level of TI (< P50); HR_{01} means the relative risk of low level of PM_1 and high level of TI; HR_{00} means the relative risk of low level of PM_1 and TI.

Table 1. Summary statistic of small for gestational age infants (SGA) in study sample compared with appropriate for gestational age infants (AGA), Wuhan (January 1, 2017 to December 31, 2020).

	AGA ($n = 25,915$)	SGA ($n = 2075$)	*P*-value
Age (years), *n* (%)			**<0.001**
<35	16589 (64.0%)	1452 (70.0%)	
35+	9326 (36.0%)	623 (30.0%)	
Gravidity, *n* (%)			**<0.001**
=1	12254 (47.3%)	1154 (55.6%)	
>1	13661 (52.7%)	921 (44.4%)	
Parity, *n* (%)			**<0.001**
Primiparous	16957 (65.4%)	1596 (76.9%)	
Multiparous	8958 (34.6%)	479 (23.1%)	
Maternal education, *n* (%)			0.639
Junior high school or below	5432 (21.0%)	448 (21.6%)	
High school	2010 (7.8%)	156 (7.5%)	
College degree or above	18473 (71.3%)	1471 (70.9%)	
Work status, *n* (%)			0.093
Yes	14469 (55.8%)	1119 (53.9%)	
No	11446 (44.2%)	956 (46.1%)	
Highrisk, *n* (%)			0.836
Yes	18153 (70.0%)	1458 (70.3%)	
No	7762 (30.0%)	617 (29.7%)	
Infant sex, *n* (%)			**0.019**
Male	13796 (53.2%)	1160 (55.9%)	
Female	12119 (46.8%)	915 (44.1%)	
Season, *n* (%)			
Spring (Mar-May)	6202(23.9%)	413(19.9%)	**<0.001**
Summer (Jun-Aug)	6511(25.1%)	589(28.4%)	
Autumn (Sep-Nov)	6916(26.7%)	591(28.5%)	
Winter (Dec-Feb)	6286(24.3%)	482(23.2%)	
Temperature (°C), $\overline{X} \pm s$	24.0 ± 2.2	24.1 ± 2.3	**0.001**
PM_1 (μg/m^3), $\overline{X} \pm s$	30.1 ± 8.3	30.9 ± 8.3	**<0.001**
TI (days), $\overline{X} \pm s$	102.3 ± 12.5	103.5 ± 12.3	**<0.001**

Bolds represent statistically significant.
TI thermal inversion.

The RERI = 0 means the absence of an additive interaction, RERI > 0 represents that the joint effects of PM_1 and TI is greater than the sum of each exposure alone, and RERI < 0 indicates less than combined effects. And the attributable proportion of interaction (AP) was also calculated to verify the robustness of the results [47]. The confidence interval of RERI and AP contained 0 suggesting that there was no interaction between PM_1 and TI. Further, sensitivity analyses were conducted: all models were changed the control group from AGA to non-SGA to test the robustness of the results in the current study.

The effects of PM_1, TI and interactive effects were reported as HR and 95% CI. We performed all statistical analyses by R software (version 4.0.5), packages dlnm, splines, survival, mediation and Rinteratction in R software were used. The results were two-side, and *P*-values <0.05 was considered statistically significant.

RESULTS

A total of 25,915 cases of AGA and 2075 cases of SGA infants were eligible for the analysis (Fig. 1). Table 1 presented overall specific maternal and infant characteristics as well as average concentration of PM_1 and total days of TI during 1-26 gestational weeks. Most Mothers in SGA group were younger than 35 years old (70.0%, $P < 0.001$). Women who delivered AGA infants were more likely to have more gravidities and parities (52.7%, $P < 0.001$ and 34.6%, $P < 0.001$ respectively). No significant differences were observed in education level, work status and whether there were high risk factors during pregnancy between AGA and SGA group ($P = 0.639$, $P = 0.093$ and $P = 0.836$, separately). Compared with AGA infants, the proportion of male in SGA infants were larger (55.9%, $P = 0.019$). The season of pregnancy in two group were also appeared different pattern ($P < 0.001$). During 1-26 gestational weeks, the average mean temperature, concentration of PM_1 and total TI days in case group was 24.0 °C, 30.9 μg/m^3 and 103.5 days, significantly higher than that in control group [24.1 °C ($P = 0.001$), 30.1 μg/m^3 ($P < 0.001$) and 102.3 days ($P < 0.001$), separately].

Figure 3 showed HR of SGA infants associated with per 10 μg/m^3 increase of maternal PM_1 exposure in 1–26 gestational weeks. For one week model, statistically significant positive effects of PM_1 on SGA were found at 1–3 and 17–23 gestational weeks, with the strongest estimated value at first gestational week (HR = 1.043, 95%CI: 1.008, 1.078) (Table S2). In the cumulative model, significant adverse effect of maternal PM_1 exposure for SGA births during 1–4 gestational weeks were observed, and the largest HR values was found at 4th gestational week (HR = 1.098, 95%CI: 1.013, 1.190).

Figure 4 illustrated the impacts of maternal exposure to TI on SGA during 1–26 gestational weeks. The statistical associations of exposure to TI increasing the risks of SGA were only detected at the 1–4 and 13–23 gestational weeks in one week analysis, and the largest and statistically significant effects of TI on SGA were observed at the 19th gestational week (HR = 1.018, 95%CI: 1.009, 1.027) (Table S3). And the significant adverse cumulative effects of TI on SGA were found at 2–26 weeks, with the strongest values appeared at 24th gestational week (HR = 1.260, 95%CI: 1.119, 1.419).

Furthermore, PM_1 and TI at the gestational weeks with strongest adverse effects on SGA were added in RSC model to test the linearity of the associations, seen in Fig. S1. There was a significant nonlinear association was observed between PM_1 and SGA ($P = 0.034$), but a strong linear relationship between PM_1 (at first gestational week) and SGA was evidenced when PM_1 concentration ≥40 μg/m^3. Therefore, PM_1 was included in the model as categorical variable (PM_1 concentration <40 μg/m^3 and ≥40 μg/m^3). Table S4 showed that the results had little change when PM_1 was treated as categorical variable, suggesting the models were robust. No significant nonlinear association in TI and SGA was found ($P = 0.866$).

Figure 5 showed the one-week effects of per 10 μg/m^3 increase of PM_1 concentration or per 1 day increase of TI maternal exposure on SGA in different newborn genders. For PM_1 exposure, significant adverse effects in boys were detected at 1–3 and 17–22 gestational weeks, and the most positive association was observed at first gestational week (HR = 1.059, 95%CI: 1.013, 1.108). While there was no statistically significant relationship between PM_1 and SGA in girls. In boy group, per 1 day increase of TI was found to be associated with SGA at 1–4 and 12–22 gestational weeks, with the highest HR value appeared at first gestational week (HR = 1.032, 95%CI: 1.012, 1.053). And significant adverse effects of TI on SGA were presented in 17–23 gestational weeks in girls. The strongest positive association was witnessed at 20th gestational week (HR = 1.020, 95%CI: 1.006, 1.034) (Table S5).

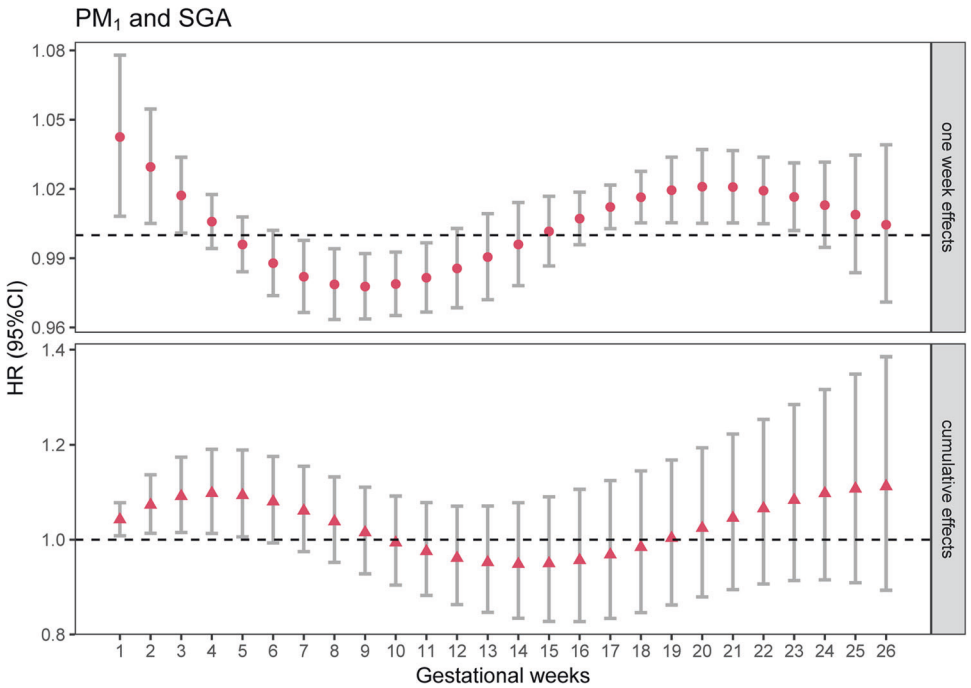

Fig. 3 Hazard ratios (95% CI) for SGA with per 1 μg/m^3 increase of PM_1 during 1–26 gestational weeks in Wuhan, 2017–2020. All models control for maternal age, gravidity, parity, education level, work status, whether there was high-risk factor,newborn sex, average temperature and season become pregnant. 95% CI, 95% Confidence Interval. Full model results are avaliable in Supplementary Table S2.

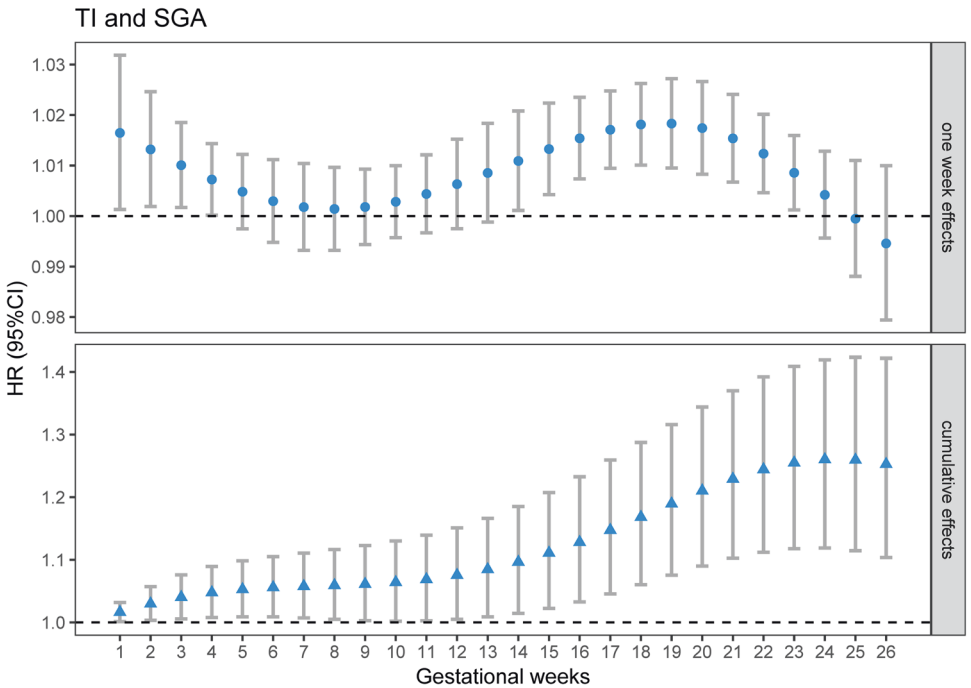

Fig. 4 Hazard ratios (95% CI) for SGA with per one day increased in thermal inversion (TI) during 1–26 gestational weeks in Wuhan, 2017–2020. All models control for maternal age, gravidity, parity, education level, work status, whether there was high-risk factor, newborn sex, average temperature and season become pregnant. 95% CI, 95% Confidence Interval. Full model results are avaliable in Supplementary Table S3.

Spearman correlation coefficients, the average concentration of PM_1 and days of TI in 1–26 gestational weeks were shown in Table S6. The relationships between PM_1 and TI in 1–26 gestational weeks were relatively low. Similarly, PM_1 and TI in the two gestational weeks with PM_1 and TI each strongest adverse effects on SGA were added in Casual Mediation Analysis to test their independence on the effect of SGA. As presented in Table S7, no significant average casual mediation effect (ACME) was observed both at first and 19th gestational weeks, and the significant average direct effects (ADE) were appeared both at first and 19th gestational weeks [0.0023 (0.0011, 0.0036) and 0.0018 (0.0003, 0.0033) respectively]. It suggested that TI had adverse

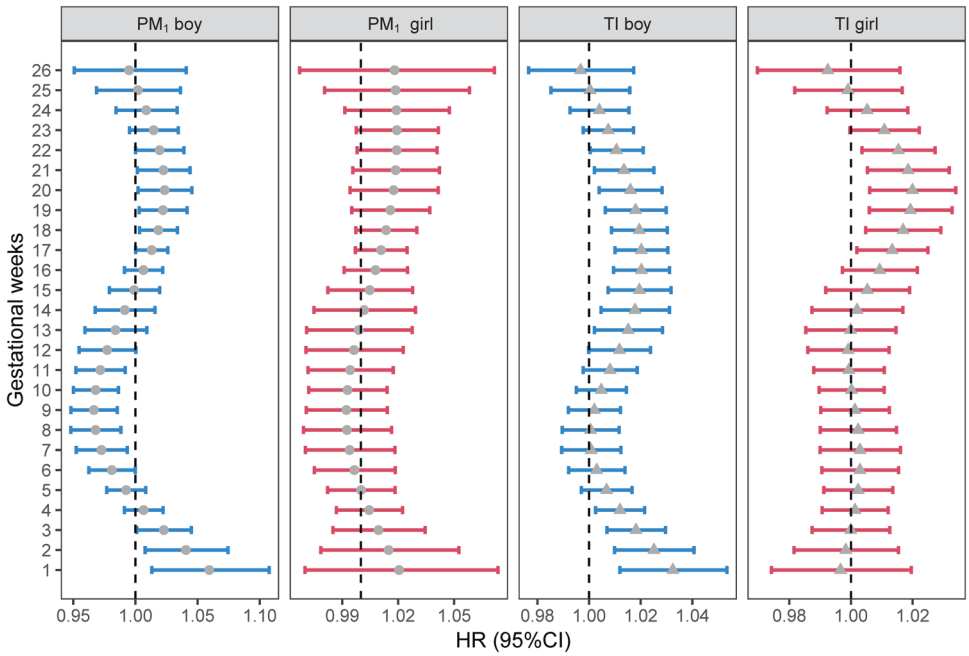

Fig. 5 Hazard ratios (95% CI) of one-week effects for SGA with per 10 μg/m^3 increase of PM_1 concentration or per 1day increase of TI in different newborn gender. All models control for maternal age, gravidity, parity, education level, work status, whether there was high-risk factor,newborn sex, average temperature and season become pregnant. 95% CI, 95% Confidence Interval. Full model results are avaliable in Supplementary Table S5.

effects on SGA mainly through direct effects instead of the mediation of PM_1 on SGA. And the non-significant proportion of mediation effects were relatively small, accounting for a tenth around. Therefore, we assumed PM_1 and TI were independent in their influence on SGA.

When PM_1 and TI exposure to mothers in 1–26 gestational weeks were treated as binary variables (cut off by median of each gestational week), we found evidence of greater than additive risks for high PM_1 and long TI at 6th, 13th and 20th gestational weeks (Table 2). Both RERIs and APs for additive interactions statistically were significant. In gestational weeks where both PM1 and TI were statistically significant (1–3 and 17–23 gestational weeks), synergistic effects for higher PM_1 (≥25.7 μg/m^3) and longer TI (≥4 days) exposure was found in 20th gestational week, with RERIs from the adjusted model of 0.208 (95%CI: 0.033,0.383), suggesting that 20.8% excess risks relative to expectations of the combined effects. And AP from the adjusted model was also significant in 20th gestational week [0.198 (95%CI: 0.028, 0.368)], which showed that our results were robust.

In sensitive analyses, correlations between maternal exposure to PM_1 and SGA newborns were almost consistent when we replaced the control group with non-SGA group instead of AGA group (Table 3). After changing the control group for SGA group, all of the HRs between TI exposure to mothers and SGA births in the 1–4 and 14–22 gestational weeks remained statistically significant, suggesting that our results and models were robust.

DISCUSSION

To the best of our knowledge, the present study was the first study to estimate both independent effects of maternal TI exposure during the first and second trimesters of pregnancy on SGA and its potential interaction effects with PM_1 exposure. We observed statistically significant impacts of exposure to PM_1 on SGA at the 1–3 and 17–23 gestational weeks and evident associations between mothers' exposure to TI and SGA births at the 1–4 and 14–23 gestational weeks in one-week model. For cumulative models, significant associations between PM_1 and SGA were found at 1–5 gestational weeks, the relationships between TI and SGA were found at 1–26 weeks. PM_1 was only related with SGA in boy group while TI was correlated SGA in both gender groups. In addition, the interactive analyses suggested synergistic effects on SGA of PM_1 exposure combined with TI exposure at 20th gestational week.

Statistically significant effects of PM_1 exposure on SGA were detected during the second trimesters of pregnancy in this study. The relationships between air pollution and SGA had been widely assessed in recent years, especially particulate matter (such as $PM_{2.5}$ and PM_{10}) [18–20]. A study conducted in Lima, Peru reported that higher exposure to $PM_{2.5}$ was associated with increased risk of SGA [48]. In a national Canadian study, a 10-μg/m^3 increase in $PM_{2.5}$ over the entire pregnancy was associated with SGA (odds ratio = 1.04; 95% CI 1.01, 1.07) and reduced term birth weight (−20.5 g; 95% CI −24.7, −16.4) [49]. Such correlations were also evidenced in the US, showing associations between $PM_{2.5}$ exposure and adverse birth outcomes particularly for SGA [50]. Avon Longitudinal Study of Parents and Children (ALSPAC) reported that odds of TLBW increased by 40% (OR: 1.40, 95%CI: 1.12, 1.75) and odds of SGA increased by 18% (OR: 1.18, 95%CI: 1.05, 1.32) per IQR (6.54 μg/m^3) increase of total PM_{10} exposure. Hao et al. also observed that the increase of PM_{10} concentration during the whole pregnancy was related with a higher risk of SGA in Huangshi, China[37].

Although there have been few studies working on the relationships between PM_1 and SGA, similar results to our related findings were still showed in the available studies. A study in Beijing suggested that reducing PM_1 exposure can prevent early-life health problems as PM_1 was negatively correlated with fetal growth in utero [26]. And another study that involved the impacts of PM_1 on adverse pregnancy outcomes estimated that the critical window of air pollution impacts might be early-to-mid pregnancy, consistent with our results [27]. However, there had not been studies working on the effects of PM_1 on SGA in the level of every gestational week. Referring to previous studies on the weekly impact of PM on adverse birth outcomes, the results also showed similar sensitive exposure window [51–53]. A case-control study in

Table 2. Relative excess risk due to interaction of TI and PM_1 exposure on SGA (binary variable) in Wuhan, China, 2017–2020.

Gestational Weeks	Cut-off for PM_1 (μg/m^3)	Cut-off for TI (days)	RERI (95% CI)	AP (95% CI)
1	26.2	4	−0.223 (−0.438, −0.008)	−0.211 (−0.411, −0.011)
2	26.3	4	−0.062 (−0.251, 0.127)	−0.067 (−0.272, 0.137)
3	26.3	4	−0.022 (−0.213, 0.169)	−0.022 (−0.217, 0.172)
4	26.3	4	0.086 (−0.093, 0.265)	0.089 (−0.097, 0.275)
5	26.2	4	0.004 (−0.179, 0.186)	0.004 (−0.191, 0.198)
6	26.0	4	**0.188 (0.015, 0.360)**	**0.188 (0.014, 0.361)**
7	26.1	4	0.158 (−0.025, 0.341)	0.146 (−0.024, 0.317)
8	26.0	4	0.079 (−0.092, 0.251)	0.088 (−0.103, 0.279)
9	25.9	4	0.028 (−0.152, 0.208)	0.031 (−0.164, 0.226)
10	26.0	4	−0.040 (−0.221, 0.141)	−0.047 (−0.254, 0.161)
11	25.9	4	0.051 (−0.132, 0.234)	0.051 (−0.135, 0.237)
12	25.7	4	0.154 (−0.015, 0.323)	0.168 (−0.022, 0.358)
13	25.6	4	**0.194 (0.034, 0.354)**	**0.219 (0.032, 0.406)**
14	25.7	4	0.067 (−0.121, 0.254)	0.064 (−0.118, 0.245)
15	25.8	4	0.172 (−0.004, 0.349)	0.168 (−0.008, 0.344)
16	25.7	4	−0.013 (−0.210, 0.184)	−0.012 (−0.199, 0.174)
17	25.7	4	0.070 (−0.131, 0.271)	0.058 (−0.109, 0.225)
18	25.6	4	−0.093 (−0.304, 0.118)	−0.080 (−0.261, 0.101)
19	25.7	4	0.178 (−0.002, 0.358)	0.163 (−0.004, 0.330)
20	25.7	4	**0.208 (0.033, 0.383)**	**0.198 (0.028, 0.368)**
21	25.6	4	0.030 (−0.166, 0.226)	0.027 (−0.151, 0.205)
22	25.5	4	−0.011 (−0.215, 0.193)	−0.010 (−0.186, 0.166)
23	25.4	4	0.098 (−0.091, 0.286)	0.089 (−0.086, 0.265)
24	25.3	4	0.050 (−0.146, 0.247)	0.045 (−0.132, 0.222)
25	25.3	4	−0.081 (−0.296, 0.135)	−0.070 (−0.255, 0.115)
26	25.1	4	−0.004 (−0.196, 0.189)	−0.004 (−0.197, 0.189)

Bolds represent statistically significant.
PM_1 and TI were cut by median in each gestational week.
TI thermal inversion.

Tianjin found that clinically recognized early pregnancy loss (CREPL) was significantly associated with a 10 μg/ m^3 increase in $PM_{2.5}$ exposure during second gestational week (OR = 1.15; 95% CI: 1.04, 1.27) [51]. Results from project Environmental and LifEstyle FActors iN metabolic health throughout life-course Trajectories (ELEFANT) also showed positive significant relationships between $PM_{2.5}$ and SGA at the first to second gestational weeks ($P < 0.05$) [52]. These evidences hinted that the first few weeks after conception possibly were the exposure window of most vulnerability. In addition, an Italian birth cohort study suggested that PM_{10} exposure between 15–20 gestational week seemed to be associated with shorter telomeres at birth, which might influence later disease susceptibility [53]. Future studies need focus on replicating these findings with specifical vulnerable exposure windows and on pathogenic mechanisms.

The specific biological mechanism of the relationships between PM and SGA was not fully elucidated. There were some possible theories: (1) Many previous studies speculated that air pollution like particulate matter might trigger oxidative stress and inflammatory response, impairing placental oxygen and nutrient transport function [25, 54]. (2) Growing evidence hinted that the increase of hemoglobin concentration played a mediating role in the relationship between $PM_{2.5}$ and SGA [20, 55]. (3) A study conducted in 16 counties across China during 2014–2018 also found that hypertension could mediate $PM_{2.5}$ and SGA relationship [55]. Maternal oxidative stress and inflammatory reaction caused by air pollution can cause blood pressure to rise and interfere the development of placental villus trees, resulting in the decline of placental function and intrauterine growth restriction [56, 57]. It was reported that PM_1 was the main component of $PM_{2.5}$ and contributed to nearly four-fifth of $PM_{2.5}$ in China [58]. In this study, PM_1 might play a similar role to $PM_{2.5}$ in theories mentioned above. Moreover, an experiment on rats showed that the surface area of particles inhaled into lungs was proportional to the intensity of the inflammatory response [59]. PM_1 may cause more deleterious health outcomes than $PM_{2.5}$ or PM_{10} because it has greater surface area. On the other hand, Therefore, it is necessary to explore and prevent the harm of particulate matter of smaller size to human health.

Antenatal exposure to TI was significant correlated with the increasing risks of SGA during most gestational weeks in the second trimester, which was the first time to be reported. On the scarcity of relevant studies, we have made some conjectures about the association. TI could prevent air convection and give rise to a windless environment, resulting in urban microclimate being affected and pavement surface temperature 3–10 °C hotter than those in windy weather [60, 61]. Furthermore, TI was elucidated to be related with a significant decrease in birth weight and an increase in the incidence of PTB in Brazil [32]. On the other hand, it was universally acknowledged that TI could inhibit the diffusion of air pollutants and increase the concentrations of pollutants [62, 63]. Except for the aggravation of air pollution, other meteorological factors associated with TI (e.g., relative humidity and weather) may directly impact health and affect the lifestyle of pregnant women [32]. Based on the

Table 3. Sensitive analyze of the effects of maternal exposure to PM_1 and TI on SGA after replacing the control group with non-SGA group instead of AGA group.

Gestational weeks	PM_1 [HR (95%CI)]		TI [HR (95%CI)]	
	AGA	non-SGA	AGA	non-SGA
1	**1.043 (1.008, 1.078)**	**1.049 (1.016, 1.084)**	**1.016 (1.001, 1.032)**	**1.019 (1.004, 1.035)**
2	**1.030 (1.005, 1.055)**	**1.034 (1.011, 1.058)**	**1.013 (1.002, 1.025)**	**1.016 (1.004, 1.027)**
3	**1.017 (1.001, 1.034)**	**1.020 (1.005, 1.035)**	**1.010 (1.002, 1.019)**	**1.012 (1.004, 1.021)**
4	1.006 (0.994, 1.018)	**1.007 (0.997, 1.016)**	**1.007 (1.000, 1.014)**	**1.009 (1.002, 1.016)**
14	0.996 (0.978, 1.014)	0.991 (0.975, 1.008)	**1.011 (1.001, 1.021)**	**1.010 (1.000, 1.020)**
15	1.002 (0.987, 1.017)	0.997 (0.983, 1.010)	**1.013 (1.004, 1.022)**	**1.012 (1.003, 1.021)**
16	1.007 (0.996, 1.019)	1.002 (0.992, 1.012)	**1.015 (1.007, 1.024)**	**1.014 (1.005, 1.022)**
17	**1.012 (1.003, 1.022)**	1.007 (0.997, 1.016)	**1.017 (1.009, 1.025)**	**1.015 (1.007, 1.022)**
18	**1.016 (1.005, 1.028)**	1.010 (0.999, 1.022)	**1.018 (1.010, 1.026)**	**1.015 (1.007, 1.023)**
19	**1.019 (1.005, 1.034)**	1.013 (0.998, 1.028)	**1.018 (1.009, 1.027)**	**1.015 (1.006, 1.024)**
20	**1.021 (1.005, 1.037)**	1.014 (0.997, 1.031)	**1.017 (1.008, 1.027)**	**1.014 (1.005, 1.023)**
21	**1.021 (1.005, 1.037)**	1.013 (0.997, 1.029)	**1.015 (1.007, 1.024)**	**1.012 (1.003, 1.021)**
22	**1.019 (1.005, 1.034)**	1.011 (0.997, 1.025)	**1.012 (1.005, 1.020)**	**1.009 (1.002, 1.017)**
23	**1.017 (1.002, 1.031)**	1.007 (0.995, 1.020)	**1.009 (1.001, 1.016)**	1.006 (0.999, 1.014)

Bolds represent statistically significant.
TI thermal inversion.

similarity of the sensitive exposure window of the impact of TI and PM_1 on SGA, we assumed that the critical exposure windows of the associations between TI on SGA could be explained as the effects of PM_1 on SGA. However, the specific mechanism of the relationships between TI and adverse birth outcomes still needs further study.

Male fetus was found to be more vulnerable to PM_1 and TI exposure in the current study. The impact of air pollution on birth outcomes had gender differences, which have been discussed in previous studies. It was suggested that prenatal exposure to bisphenol A played a different role in birth weights between infants of different sex in a multicenter birth cohort study from Korea [64]. A study in Shanghai found that maternal exposure to household air pollution could contribute to more adverse birth outcomes in boys, which was consistent with this study [65]. Similarly, the result that boys are more sensitive to prenatal air pollution was also presented in a time series study in Hefei [66]. Based on vitro study, male fetuses were assumed to be more susceptible to pro-inflammatory environment during pregnancy, which may be a reasonable explanation for our results [67]. However, more mechanism that sexual differences may alter the effects of the external environment should be further studied.

After PM_1 and TI were treated as binary variables, 20.8% excess risks for SGA exposure to higher PM_1 with longer TI based on the independent effects of each exposure alone was found in 20th gestational week. It was possible that abnormal temperatures would function interactively with air pollution to damage health and even mortality [34, 68, 69]. In addition to inhibition of pollutants diffusion, TI had potential influences on ambient temperature variation. On the basis of the original environment, temperature rise might accelerate the intake of air pollutants through pulmonary ventilation and elevation in skin blood flow [36]. While a decrease in temperature may reduce mucociliary clearance and increase human susceptibility to pollutants [70]. These deductions might explain the interaction effect between environmental exposures to some extent, but the specific theories have not been fully understood. It could be an interesting work in the future to evaluate the interaction effects of environmental exposure mixtures in the status of related mechanisms not entirely clear.

There were several strengths in this study. Firstly, this might be the first study to focus on the impacts of prenatal exposure to TI on SGA and explore the interaction effects with PM_1 in China. Secondly, the high-resolution (1 km × 1 km) air pollution datasets, detailed addresses and the geographic information system technique applied in the present study allowed us to enhance the accuracy of exposure assessment and the authenticity of the result prediction [71–73]. Thirdly, taking advantage of detailed individual adjustments, we calculated the interactive effects of PM_1 and TI on SGA, which strengthened the chance to obtain effect estimates close to reality. Finally, with gestational weeks as the exposure period, more detailed potential susceptible exposure windows were detected, which might provide more elaborate references for the health management of pregnant women.

Some limitations in this study should be acknowledged. Firstly, data on individual diet and lifestyles such as drinking, smoking, and physical activity are not available, which might be potentially correlated with SGA. Second, the change in mothers' activity areas may cause exposure bias. Third, since not every pregnant woman has more than 26 gestational weeks, we did not consider the risk of PM_1 and TI exposure to SGA after 26th gestational week to ensure the sample size as large as possible. And due to the limitation of sample size, the number of SGA in different types of infants varies greatly, which may lead to some random errors. Furthermore, some participants had to be excluded before the analysis due to the incompleteness of the data, and there were significant differences in some personal characteristics between them and the finally included population. Lastly, the present study was conducted in Wuhan, the limited region could result in lacking representativeness to other areas.

CONCLUSIONS

In conclusion, we found the independent and interactive effects of PM_1 and TI on SGA from 2017 to 2020 in Wuhan. Results in this study showed that maternal exposure to PM_1 at the 1–3 and 17–23 gestational weeks, and TI at the 1–4 and 14–23

gestational weeks were linked with a higher risk of SGA in one-week model. For cumulative models, significant associations between PM_1 and SGA were found at 1–5 gestational weeks, the relationships between TI and SGA were found at 1–26 weeks. Furthermore, a synergistic effect of PM_1 exposure and TI to SGA was observed during 20th gestational week. In the context of climate change, the interactive effect of meteorological factors and air pollutants were worthy of attention to protect the health of next generations.

DATA AVAILABILITY

The datasets generated during and/or analysed during the current study are not publicly available but are available from the corresponding author on reasonable request.

REFERENCES

1. Ding G, Tian Y, Zhang Y, Pang Y, Zhang JS, Zhang J. Application of a global reference for fetal-weight and birthweight percentiles in predicting infant mortality. BJOG. 2013;120:1613–21. https://doi.org/10.1111/1471-0528.12381.
2. Bonamy AK, Parikh NI, Cnattingius S, Ludvigsson JF, Ingelsson E. Birth characteristics and subsequent risks of maternal cardiovascular disease: effects of gestational age and fetal growth. Circulation. 2011;124:2839–46. https://doi.org/10.1161/CIRCULATIONAHA.111.034884.
3. Pariente G, Shoham Vardi I, Kessous R, Sheiner E. 800: Delivery of an SGA neonate as an independent risk factor for long-term maternal chronic kidney disease. Am J Obstet Gynecol. 2015;212:S387 https://doi.org/10.1016/j.ajog.2014.10.1006.
4. McIntire DD, Bloom SL, Casey BM, Leveno KJ. Birth weight in relation to morbidity and mortality among newborn infants. N. Engl J Med. 1999;340:1234–8. https://doi.org/10.1056/nejm199904223401603.
5. Meas T, Deghmoun S, Armoogum P, Alberti C, Levy-Marchal C. Consequences of being born small for gestational age on body composition: an 8-year follow-up study. J Clin Endocrinol Metab. 2008;93:3804–9. https://doi.org/10.1210/jc.2008-0488.
6. Sacchi C, Marino C, Nosarti C, Vieno A, Visentin S, Simonelli A. Association of Intrauterine Growth Restriction and Small for Gestational Age Status With Childhood Cognitive Outcomes: A Systematic Review and Meta-analysis. JAMA Pediatr. 2020;174:772–81. https://doi.org/10.1001/jamapediatrics.2020.1097.
7. Hollo O, Rautava P, Korhonen T, Helenius H, Kero P, Sillanpää M. Academic achievement of small-for-gestational-age children at age 10 years. Arch pediatrics Adolesc Med. 2002;156:179–87. https://doi.org/10.1001/archpedi.156.2.179.
8. Mericq V, Martinez-Aguayo A, Uauy R, Iñiguez G, Van der Steen M, Hokken-Koelega A. Long-term metabolic risk among children born premature or small for gestational age. Nat Rev Endocrinol. 2017;13:50–62. https://doi.org/10.1038/nrendo.2016.127.
9. Strauss RS. Adult functional outcome of those born small for gestational age: twenty-six-year follow-up of the 1970 British Birth Cohort. Jama. 2000;283:625–32. https://doi.org/10.1001/jama.283.5.625.
10. Francis A, Hugh O, Gardosi J. Customized vs INTERGROWTH-21(st) standards for the assessment of birthweight and stillbirth risk at term. Am J Obstet Gynecol. 2018;218:S692–s699. https://doi.org/10.1016/j.ajog.2017.12.013.
11. Behboudi-Gandevani S, Bidhendi-Yarandi R, Panahi MH, Mardani A, Paal P, Prinds C, et al. Adverse Pregnancy Outcomes and International Immigration Status: A Systematic Review and Meta-analysis. Ann Glob Health. 2022;88:44. https://doi.org/10.5334/aogh.3591.
12. Pedersen GS, Mortensen LH, Gerster M, Rich-Edwards J, Andersen AM. Preterm birth and birthweight-for-gestational age among immigrant women in Denmark 1978-2007: a nationwide registry study. Paediatr Perinat Epidemiol. 2012;26:534–42. https://doi.org/10.1111/ppe.12010.
13. Urquia ML, Berger H, Ray JG. Risk of adverse outcomes among infants of immigrant women according to birth-weight curves tailored to maternal world region of origin. CMAJ. 2015;187:E32–e40. https://doi.org/10.1503/cmaj.140748.
14. Lee AC, Katz J, Blencowe H, Cousens S, Kozuki N, Vogel JP, et al. National and regional estimates of term and preterm babies born small for gestational age in 138 low-income and middle-income countries in 2010. Lancet Glob Health. 2013;1:e26–36. https://doi.org/10.1016/S2214-109X(13)70006-8.
15. Marzouk A, Filipovic-Pierucci A, Baud O, Tsatsaris V, Ego A, Charles MA, et al. Prenatal and post-natal cost of small for gestational age infants: a national study. BMC Health Serv Res. 2017;17:221. https://doi.org/10.1186/s12913-017-2155-x.
16. Diabelková J, Rimárová K, Urdzík P, Dorko E, Houžvičková A, Andraščíková Š, et al. Risk factors associated with low birth weight. Cent Eur J Public Health. 2022;30:S43–s49. https://doi.org/10.21101/cejph.a6883.
17. Parra-Saavedra M, Simeone S, Triunfo S, Crovetto F, Botet F, Nadal A, et al. Correlation between histological signs of placental underperfusion and perinatal morbidity in late-onset small-for-gestational-age fetuses. Ultrasound Obstet Gynecol. 2015;45:149–55. https://doi.org/10.1002/uog.13415.
18. Guo P, Chen Y, Wu H, Zeng J, Zeng Z, Li W, et al. Ambient air pollution and markers of fetal growth: A retrospective population-based cohort study of 2.57 million term singleton births in China. Environ Int. 2020;135:105410. https://doi.org/10.1016/j.envint.2019.105410.
19. Hannam K, McNamee R, Baker P, Sibley C, Agius R. Air pollution exposure and adverse pregnancy outcomes in a large UK birth cohort: use of a novel spatio-temporal modelling technique. Scand J Work, Environ Health. 2014;40:518–30. https://doi.org/10.5271/sjweh.3423.
20. Liao J, Li Y, Wang X, Zhang B, Xia W, Peng Y, et al. Prenatal exposure to fine particulate matter, maternal hemoglobin concentration, and fetal growth during early pregnancy: associations and mediation effects analysis. Environ Res. 2019;173:366–72. https://doi.org/10.1016/j.envres.2019.03.056.
21. Wang Q, Li B, Benmarhnia T, Hajat S, Ren M, Liu T, et al. Independent and Combined Effects of Heatwaves and PM2.5 on Preterm Birth in Guangzhou, China: A Survival Analysis. Environ Health Perspect. 2020;128:17006 https://doi.org/10.1289/EHP5117.
22. Yang BY, Guo Y, Markevych I, Qian ZM, Bloom MS, Heinrich J, et al. Association of Long-term Exposure to Ambient Air Pollutants With Risk Factors for Cardiovascular Disease in China. JAMA Netw Open. 2019;2:e190318 https://doi.org/10.1001/jamanetworkopen.2019.0318.
23. Chuang KJ, Chan CC, Chen NT, Su TC, Lin LY. Effects of particle size fractions on reducing heart rate variability in cardiac and hypertensive patients. Environ Health Perspect. 2005;113:1693–7. https://doi.org/10.1289/ehp.8145
24. Hu K, Guo Y, Hu D, Du R, Yang X, Zhong J, et al. Mortality burden attributable to PM(1) in Zhejiang province, China. Environ Int. 2018;121:515–22. https://doi.org/10.1016/j.envint.2018.09.033.
25. Zhou S, Lin L, Bao Z, Meng T, Wang S, Chen G, et al. The association of prenatal exposure to particulate matter with infant growth: A birth cohort study in Beijing, China. Environ Pollut. 2021;277:116792. https://doi.org/10.1016/j.envpol.2021.116792.
26. Lin L, Guo Y, Han N, Su T, Jin C, Chen G, et al. Prenatal exposure to airborne particulate matter of 1 μm or less and fetal growth: A birth cohort study in Beijing, China. Environ Res. 2021;194:110729. https://doi.org/10.1016/j.envres.2021.110729.
27. Su X, Zhang S, Lin Q, Wu Y, Yang Y, Yu H, et al. Prenatal exposure to air pollution and neurodevelopmental delay in children: A birth cohort study in Foshan, China. Sci Total Environ. 2022;816:151658. https://doi.org/10.1016/j.scitotenv.2021.151658.
28. Liu YM, Ao CK. Effect of air pollution on health care expenditure: Evidence from respiratory diseases. Health Econ. 2021;30:858–75. https://doi.org/10.1002/hec.4221.
29. Dejchanchaiwong R, Tekasakul P, Tekasakul S, Phairuang W, Nim N, Sresawasd C, et al. Impact of transport of fine and ultrafine particles from open biomass burning on air quality during 2019 Bangkok haze episode. J Environ Sci. 2020;97:149–61. https://doi.org/10.1016/j.jes.2020.04.009.
30. Rohrer M, Flahault A, Stoffel M. Peaks of Fine Particulate Matter May Modulate the Spreading and Virulence of COVID-19. Earth Syst Environ. 2020;4:789–96. https://doi.org/10.1007/s41748-020-00184-4.
31. Trinh TT, Trinh TT, Le TT, Nguyen TDH, Tu BM. Temperature inversion and air pollution relationship, and its effects on human health in Hanoi City, Vietnam. Environ Geochem Health. 2019;41:929–37. https://doi.org/10.1007/s10653-018-0190-0.
32. Rangel MA, Tome R. Health and the Megacity: Urban Congestion, Air Pollution, and Birth Outcomes in Brazil. Int J Environ Res Public Health. 2022;19. https://doi.org/10.3390/ijerph19031151.
33. Knol MJ, VanderWeele TJ. Recommendations for presenting analyses of effect modification and interaction. Int J Epidemiol. 2012;41:514–20. https://doi.org/10.1093/ije/dyr218.
34. Lee W, Choi HM, Kim D, Honda Y, Leon Guo YL, Kim H. Synergic effect between high temperature and air pollution on mortality in Northeast Asia. Environ Res. 2019;178:108735. https://doi.org/10.1016/j.envres.2019.108735.
35. Richards M, Huang M, Strickland MJ, Newman AJ, Warren JL, D'Souza R, et al. Acute association between heatwaves and stillbirth in six US states. Environ Health. 2022;21:59. https://doi.org/10.1186/s12940-022-00870-y.
36. Sun Y, Ilango SD, Schwarz L, Wang Q, Chen JC, Lawrence JM, et al. Examining the joint effects of heatwaves, air pollution, and green space on the risk of preterm birth in California. Environ Res Lett 2020;15. https://doi.org/10.1088/1748-9326/abb8a3.
37. Hao J, Zhang F, Chen D, Liu Y, Liao L, Shen C, et al. Association between ambient air pollution exposure and infants small for gestational age in Huangshi, China: a cross-sectional study. Environ Sci Pollut Res Int. 2019;26:32029–39. https://doi.org/10.1007/s11356-019-06268-7.

38. [Growth standard curves of birth weight, length and head circumference of Chinese newborns of different gestation]. Zhonghua er ke za zhi = Chin J pediatrics. 2020;58:738–46. 10.3760/cma.j.cn112140-20200316-00242.
39. Wei J, Li Z, Guo J, Sun L, Huang W, Xue W, et al. Satellite-Derived 1-km-Resolution PM1 Concentrations from 2014 to 2018 across China. Environ Sci Technol. 2019;53:13265–74. https://doi.org/10.1021/acs.est.9b03258.
40. Wei J, Li Z, Lyapustin A, Sun L, Peng Y, Xue W, et al. Reconstructing 1-km-resolution high-quality PM2.5 data records from 2000 to 2018 in China: spatiotemporal variations and policy implications. Remote Sens Environ. 2021;252:112136. https://doi.org/10.1016/j.rse.2020.112136.
41. Wei J, Li Z, Xue W, Sun L, Fan T, Liu L, et al. The ChinaHighPM10 dataset: generation, validation, and spatiotemporal variations from 2015 to 2019 across China. Environ Int. 2021;146:106290. https://doi.org/10.1016/j.envint.2020.106290.
42. Song J, Ding Z, Zheng H, Xu Z, Cheng J, Pan R, et al. Short-term PM(1) and PM(2.5) exposure and asthma mortality in Jiangsu Province, China: What's the role of neighborhood characteristics?. Ecotoxicol Environ Saf. 2022;241:113765. https://doi.org/10.1016/j.ecoenv.2022.113765.
43. Wu H, Zhang B, Wei J, Lu Z, Zhao M, Liu W, et al. Short-term effects of exposure to ambient PM(1), PM(2.5), and PM(10) on ischemic and hemorrhagic stroke incidence in Shandong Province, China. Environ Res. 2022;212:113350. https://doi.org/10.1016/j.envres.2022.113350.
44. Zhang Y, Wei J, Shi Y, Quan C, Ho HC, Song Y, et al. Early-life exposure to submicron particulate air pollution in relation to asthma development in Chinese preschool children. J Allergy Clin Immunol. 2021;148:771–782.e712. https://doi.org/10.1016/j.jaci.2021.02.030.
45. Chen S, Oliva P, Zhang P. The effect of air pollution on migration: Evidence from China. J Dev Econom. 2022;156. https://doi.org/10.1016/j.jdeveco.2022.102833.
46. Deschenes O, Wang HX, Wang S, Zhang P. The effect of air pollution on body weight and obesity: Evidence from China. J Dev Econom. 2020;145. https://doi.org/10.1016/j.jdeveco.2020.102461.
47. Andersson T, Alfredsson L, Källberg H, Zdravkovic S, Ahlbom A. Calculating measures of biological interaction. Eur J Epidemiol. 2005;20:575–9. https://doi.org/10.1007/s10654-005-7835-x.
48. Tapia VL, Vasquez BV, Vu B, Liu Y, Steenland K, Gonzales GF. Association between maternal exposure to particulate matter (PM(2.5)) and adverse pregnancy outcomes in Lima, Peru. J Expo Sci Environ Epidemiol. 2020;30:689–97. https://doi.org/10.1038/s41370-020-0223-5.
49. Stieb DM, Chen L, Beckerman BS, Jerrett M, Crouse DL, Omariba DW, et al. Associations of Pregnancy Outcomes and PM2.5 in a National Canadian Study. Environ Health Perspect. 2016;124:243–9. https://doi.org/10.1289/ehp.1408995.
50. Hyder A, Lee HJ, Ebisu K, Koutrakis P, Belanger K, Bell ML. PM2.5 exposure and birth outcomes: use of satellite- and monitor-based data. Epidemiology. 2014;25:58–67. https://doi.org/10.1097/ede.0000000000000027.
51. Zhang Y, Wang J, Chen L, Yang H, Zhang B, Wang Q, et al. Ambient PM(2.5) and clinically recognized early pregnancy loss: A case-control study with spatiotemporal exposure predictions. Environ Int. 2019;126:422–9. https://doi.org/10.1016/j.envint.2019.02.062.
52. Chen J, Li PH, Fan H, Li C, Zhang Y, Ju D, et al. Weekly-specific ambient fine particular matter exposures before and during pregnancy were associated with risks of small for gestational age and large for gestational age: results from Project ELEFANT. Int J Epidemiol. 2022;51:202–12. https://doi.org/10.1093/ije/dyab166.
53. Isaevska E, Fiano V, Asta F, Stafoggia M, Moirano G, Popovic M, et al. Prenatal exposure to PM(10) and changes in DNA methylation and telomere length in cord blood. Environ Res. 2022;209:112717. https://doi.org/10.1016/j.envres.2022.112717.
54. Kannan S, Misra DP, Dvonch JT, Krishnakumar A. Exposures to airborne particulate matter and adverse perinatal outcomes: a biologically plausible mechanistic framework for exploring potential effect modification by nutrition. Environ Health Perspect. 2006;114:1636–42. https://doi.org/10.1289/ehp.9081.
55. Zhu Z, Hu H, Benmarhnia T, Ren Z, Luo J, Zhao W, et al. Gestational PM(2.5) exposure may increase the risk of small for gestational age through maternal blood pressure and hemoglobin: A mediation analysis based on a prospective cohort in China, 2014-2018. Ecotoxicol Environ Saf. 2022;242:113836. https://doi.org/10.1016/j.ecoenv.2022.113836.
56. Macdonald-Wallis C, Tilling K, Fraser A, Nelson SM, Lawlor DA. Associations of blood pressure change in pregnancy with fetal growth and gestational age at delivery: findings from a prospective cohort. Hypertension (Dallas, Tex: 1979). 2014;64:36–44. https://doi.org/10.1161/hypertensionaha.113.02766.
57. Kingdom JC, Kaufmann P. Oxygen and placental villous development: origins of fetal hypoxia. Placenta. 1997;18:613–21. https://doi.org/10.1016/s0143-4004(97)90000-x.
58. Wang YY, Li Q, Guo Y, Zhou H, Wang X, Wang Q, et al. Association of Long-term Exposure to Airborne Particulate Matter of 1 mum or Less With Preterm Birth in China. JAMA Pediatr. 2018;172:e174872. https://doi.org/10.1001/jamapediatrics.2017.4872.
59. Brown DM, Wilson MR, MacNee W, Stone V, Donaldson K. Size-Dependent Proinflammatory Effects of Ultrafine Polystyrene Particles: A Role for Surface Area and Oxidative Stress in the Enhanced Activity of Ultrafines. Toxicol Appl Pharmacol. 2001;175:191–9. https://doi.org/10.1006/taap.2001.9240.
60. Zhu W, Xu X, Zheng J, Yan P, Wang Y, Cai W. The characteristics of abnormal wintertime pollution events in the Jing-Jin-Ji region and its relationships with meteorological factors. Sci Total Environ. 2018;626:887–98. https://doi.org/10.1016/j.scitotenv.2018.01.083.
61. Qin Y, Zhang X, Tan K, Wang J. A review on the influencing factors of pavement surface temperature. Environ Sci Pollut Res Int. 2022;29:67659–74. https://doi.org/10.1007/s11356-022-22295-3.
62. Wagner DR, Brandley DC. Exercise in Thermal Inversions: PM(2.5) Air Pollution Effects on Pulmonary Function and Aerobic Performance. Wilderness Environ Med. 2020;31:16–22. https://doi.org/10.1016/j.wem.2019.10.005.
63. Wagner DR, Clark NW. Effects of ambient particulate matter on aerobic exercise performance. J Exerc Sci Fit. 2018;16:12–15. https://doi.org/10.1016/j.jesf.2018.01.002.
64. Lee B-E, Park H, Hong Y-C, Ha M, Kim Y, Chang N, et al. Prenatal bisphenol A and birth outcomes: MOCEH (Mothers and Children's Environmental Health) study. Int J Hyg Environ health. 2014;217:328–34. https://doi.org/10.1016/j.ijheh.2013.07.005.
65. Liu W, Huang C, Cai J, Wang X, Zou Z, Sun C. Household environmental exposures during gestation and birth outcomes: A cross-sectional study in Shanghai, China. Sci Total Environ. 2018;615:1110–8. https://doi.org/10.1016/j.scitotenv.2017.10.015.
66. Zhang Q, Sun S, Sui X, Ding L, Yang M, Li C, et al. Associations between weekly air pollution exposure and congenital heart disease. Sci total Environ. 2021;757:143821. https://doi.org/10.1016/j.scitotenv.2020.143821.
67. Challis J, Newnham J, Petraglia F, Yeganegi M, Bocking A. Fetal sex and preterm birth. Placenta. 2013;34:95–99. https://doi.org/10.1016/j.placenta.2012.11.007.
68. Mokoena KK, Ethan CJ, Yu Y, Quachie AT. Interaction Effects of Air Pollution and Climatic Factors on Circulatory and Respiratory Mortality in Xi'an, China between 2014 and 2016. Int J Environ Res Public Health. 2020;17. https://doi.org/10.3390/ijerph17239027.
69. Li H, Li M, Zhang S, Qian ZM, Zhang Z, Zhang K, et al. Interactive effects of cold spell and air pollution on outpatient visits for anxiety in three subtropical Chinese cities. Sci Total Environ. 2022;817:152789. https://doi.org/10.1016/j.scitotenv.2021.152789.
70. Eccles R. An explanation for the seasonality of acute upper respiratory tract viral infections. Acta Otolaryngol. 2002;122:183–91. https://doi.org/10.1080/00016480252814207.
71. Wang YY, Li Q, Guo Y, Zhou H, Wang QM, Shen HP, et al. Ambient temperature and the risk of preterm birth: A national birth cohort study in the mainland China. Environ Int. 2020;142:105851. https://doi.org/10.1016/j.envint.2020.105851.
72. He JR, Liu Y, Xia XY, Ma WJ, Lin HL, Kan HD, et al. Ambient Temperature and the Risk of Preterm Birth in Guangzhou, China (2001-2011). Environ Health Perspect. 2016;124:1100–6. https://doi.org/10.1289/ehp.1509778.
73. Wei Y, Qiu X, Yazdi MD, Shtein A, Shi L, Yang J, et al. The Impact of Exposure Measurement Error on the Estimated Concentration-Response Relationship between Long-Term Exposure to PM2.5 and Mortality. Environ Health Perspect. 2022;130:77006. https://doi.org/10.1289/ehp10389.

AUTHOR CONTRIBUTIONS

JW, WZ and DL conceived and designed the study; YZhang, YZhong, GZ, SZ, Xiaowei Zhang, TL, BC and AH collected and cleaned the data; Xupeng Zhang and FZ performed the data analysis and drafted the manuscript. YG helped revise the manuscript. All authors read and approved the final manuscript.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICAL APPROVAL

This study was approved by the Ethics Committee of Wuhan Children's Hospital (2021R139-F01).

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Correspondence and requests for materials should be addressed to Jing Wei, Wei Zhu or Dejia Li.