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# Ambient air pollutants exposure during gestation and incidence risk of hypertensive disorders of pregnancy or preeclampsia in China

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ABSTRACT

The relationships between the exposure to ambient air pollutants during gestation and the incidence of hypertensive disorders in pregnancy (HDPs) or preeclampsia are contradictory. This prospective cohort study enrolled the participants between January 2020 and December 2021 from the Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology. The exposure to ambient air pollutants and daily temperatures were obtained from the ChinaHighAirPollutants dataset and the Big Earth Data Platform for Three Poles, respectively. Logistic regression models were used as single- and two-pollutant models. Restricted cubic splines were applied to each ambient air pollutant exposure to further evaluate the exposure-response relationships. Quantile G-computation approaches were employed to evaluate the cumulative impact of mixed ambient air pollutants on the incidence risk HDPs and preeclampsia. Among 19,325 participants (median age: 30.2 years), 1669 (8.64%) were diagnosed with HDPs and 180 (0.94%) with preeclampsia. While mostly null risk estimates were observed, exposure to $PM_1$, $PM_{2.5}$, $PM_{10,}$ and $NO_2$ correlated with a decreased incidence risk for HDPs and preeclampsia during most gestational periods. Additionally, our multi-pollutant model presented that an increase by one quartile in the cumulative effect of ambient air pollutants was associated with a significantly decreased incidence risk for HDPs in the trimester before gestation and in the third trimester during gestation, as well as for preeclampsia in the third trimester during gestation. These findings warrant further investigation into the mechanisms underlying these associations.

## 1. Introduction

Hypertensive disorders of pregnancy (HDPs) and preeclampsia, significantly contribute to maternal morbidity and mortality. Recent data indicates the global prevalence of HDPs was 116.4 cases per 100,000 women of childbearing age in 2019 (Vos et al., 2020). Despite considerable advances in cardiovascular, obstetric and gynecological care, the HDPs incidence rate in some countries like the United State of America still showed a rising trend (Wen et al., 2022). The vast majority of HDPs and preeclampsia occur in the third half of pregnancy in cases with late placental lesions caused or associated with maternal cardiovascular and metabolic risk factors for endothelial dysfunction and oxidative stress (Burton et al., 2019). Additionally, these diseases are associated with the heightened risk of restricting fetal growth as well (Di Martino et al., 2022). This increasing trend highlights the urgent need to re-evaluate existing management approaches and intensify the call for more rigorous research and intervention efforts to combat these life-threatening conditions.

Extensive research has identified several risk factors for HDPs, including advanced maternal age (Abalos et al., 2014; Ye et al., 2014), overweight or obesity (Bilano et al., 2014; Shah et al., 2011), inadequate calcium and vitamin $D_3$ intake (Akbari et al., 2018; Kinshella et al., 2021). Alongside these well-documented risks, recent scholarly efforts have turned toward environmental determinants, specifically focusing

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on the mass of particles with an aerodynamic diameter smaller than 2.5 μm ($PM_{2.5}$) and their possible contribution to initiating HDPs. However, the results of these studies were inconsistent. Two cross-sectional studies presented that $PM_{2.5}$ exposure in pregnancy is associated with a higher incidence rate of HDPs (Su et al., 2020; Yuan et al., 2023). However, other studies reported no relationship (Nahidi et al., 2014; Savitz et al., 2015). Additionally, the relationships between HDPs and other atmospheric contaminants, such as particles smaller than 1 μm ($PM_1$) and 10 μm ($PM_{10}$) in aerodynamic diameter, as well as carbon monoxide (CO), nitrogen dioxide ($NO_2$), ozone($O_3$), and sulfur dioxide ($SO_2$), are characterized by either discrepancies or insufficient exploration (Cheng et al., 2023; Hu et al., 2014; Jiang et al., 2023; Johnson et al., 2016; Pedersen et al., 2014; Yan et al., 2022). Moreover, a shortcoming of existing research is its isolationist approach to pollutants, which fails to reflect the complexity of environmental pollution. Furthermore, the habitual categorization of preeclampsia under HDPs neglects to recognize distinct pathophysiological pathways (Burton et al., 2019).

Therefore, we conducted a cohort study using single-, two-, and multi-pollutant models to assess the association between exposure to ambient air pollutants during gestation and the incidence risk of HDPs or preeclampsia. Considering a broad spectrum of ambient air pollutants and their collective impact, this study comprehensively explains the environmental risk factors for HDPs and preeclampsia.

## 2. Methods

### 2.1. Study population

The participants of this study were enrolled between January 2020 and December 2021 from the Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology. The catchment area of this hospital covers Hubei Province, China, which has an estimated population of approximately 58.3 million in 2020. This study waived the requirement for written consent by the hospital's ethics committee and was conducted in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology reporting guideline (von Elm et al., 2007).

The flowchart of this study is depicted in Figure A.1. The inclusion criteria were maternal age over 18 years, having no serious infectious diseases or chronic noncommunicable diseases before gestation, singleton pregnancy, and planning to receive prenatal care and delivery in Hubei Province. To ensure accurate pollutant exposure estimates, the participants residing more than 5 km from their workplace (if employed) and those who changed their residential or work address during pregnancy were excluded. The participants' residential addresses were mainly located around Wuhan, the capital of Hubei Province, as illustrated in Figure A.2.

### 2.2. Outcome and covariates assessment

The diagnosis of HDPs and preeclampsia adhered to the diagnostic standards established by the Chinese Society of Obstetrics and Gynecology in 2015 (Hypertensive Disorders in Pregnancy Subgroup, 2015). HDPs were characterized as increased blood pressure without proteinuria after the 20th week of gestation. Similarly, preeclampsia was characterized as increased blood pressure with proteinuria after the 20th week of gestation. The blood pressure and urine protein levels were retrieved from the patients' medical records. The diagnosis were independently conducted by two doctors from our team based on these records. In cases where the two doctors' diagnoses did not align, a third doctor was consulted to provide the final diagnosis.

The covariates included maternal age (years), pre-pregnancy body mass index (BMI) ($kg/m^2$), residential areas (categorized as rural or urban), educational attainment (classified as $< 13$, 13–16, and $\geq 17$ years), multiparous (categorized as yes or no), season of conception (categorized as spring, summer, autumn, or winter), gestation risk grade (categorized as green, yellow, orange or red). The gestation risk grade is a part of Five Strategies for Maternal and Newborn Safety, a risk management implemented by the Chinese government to reduce the maternal mortality ratio. Based on the gestation risk identified, pregnant women would have color-coded for classification and risk management: green for low risk, yellow for general risk, orange for high risk, red for the highest risk, and purple for infectious diseases. The specifics of these classifications and their implementation was described elsewhere (Liu et al., 2022). Furthermore, some studies presented that temperature was associated with HDPs and preeclampsia(Cheng et al., 2023; Xiong et al., 2020). Hence, temperature was included in the models as a covariate.

### 2.3. Ambient air pollutants exposure and daily temperature assessment

We utilized the ChinaHighAirPollutants (CHAP) dataset with a seamless 1 km × 1 km resolution (Li et al., 2021; Wei et al., 2019; Wei et al., 2022; Wei et al. 2021a; Wei et al. 2021b; Wei et al. 2023) to evaluate exposure to ambient air pollutants. These datasets represent comprehensive collections of long-term, high-resolution, high-quality data on ground-level air pollutants across China. And these meticulously compiled from vast data sources, including ground-based measurements, satellite remote sensing products, atmospheric reanalysis, and a machine-learning model called space-time extra trees. The observed ground data closely aligned with the predicted daily concentrations of $PM_1$, $PM_{2.5}$, $PM_{10}$, $O_3$, $SO_2$, $NO_2$, and CO. The analysis used the cross-validation coefficient of determination (CV-$R^2$ value), a robust statistical metric for evaluating model fit, which yielded values of 0.83, 0.92, 0.90, 0.87, 0.84, 0.84, and 0.80, respectively. Furthermore, the root mean square errors were determined as 9.50 $μg/m^3$ for $PM_1$, 10.76 $μg/m^3$ for $PM_{2.5}$, 21.12 $μg/m^3$ for $PM_{10}$, 17.10 $μg/m^3$ for $O_3$, 1.57 $μg/m^3$ for $SO_2$, 14.28 $μg/m^3$ for $NO_2$, and 0.29 $mg/m^3$ for CO.

The daily temperature dataset with a seamless 1 km × 1 km resolution was obtained from the Big Earth Data Platform for Three Poles (Tang et al., 2024). The mean bias deviation of the data set is 0.09 K and 0.03 K, and the standard deviation of bias is 1.45 K and 1.17 K for daytime and nighttime biases when land surface temperature from moderate-resolution imaging spectroradiometer was used as a reference.

The residential addresses of the enrolled participants were converted to latitude and longitude to collect daily ambient air pollutant and temperature data from 12 weeks before gestation to conception from the above dataset by point sampling using QGIS software (version 3.18) for each participant. The individual mean concentrations of air pollutant exposure and daily temperature were calculated for the following four periods: the trimester before gestation, first trimester during gestation (gestation weeks 1–12), second trimester during gestation (gestation weeks 13–28), and third trimester during gestation (gestation weeks 29 to conception).

### 2.4. Statistical analyses

The baseline characteristics of the participants were summarized using descriptive analysis, which included demographic characteristics, exposure to ambient air pollutants, and daily temperatures for each trimester of gestation. Pearson's correlation coefficient was employed to estimate the correlations among ambient air pollutants. Single-, two-, and multi-pollutant models were used to evaluate the association between various ambient air pollutants and the incidence risk of HDPs or preeclampsia during different trimesters of gestation.

Logistic regression models were used as single- and two-pollutant models, adjusted for maternal age, pre-pregnancy BMI, residential areas, educational attainment, multiparity, the season of conception, and gestation risk grade. Considering the differences in the magnitudes of various pollutants, we scaled down the initial concentrations of $PM_1$, $PM_{2.5}$, $PM_{10}$, $O_3$, and $NO_2$ by dividing by 10, whereas the CO initial concentrations were adjusted by dividing by 0.1. The $SO_2$ initial concentrations were maintained. Moreover, the restricted cubic splines with three to five knots, were implemented to investigate the exposure-response and potential nonlinear associations with HDPs or pre-eclampsia for each ambient air pollutant. Additionally, we performed stratified analyses according to maternal age, pre-pregnancy BMI, residential area, educational attainment, multiparity, and gestation risk grade to evaluate the robustness of the results.

To assess if the associations with ambient air pollutants were affected by other pollutants, logistic regression models that included the six air pollutants as potential confounders were employed as two-pollutant models. However, these models were not performed for air pollutants exhibiting strong correlations ($r > 0.95$). To assess the combined effects of various air pollutants, we utilized multi-pollutant models with the quantile G-computation model facilitated by the R package 'qgcomp.' This approach is particularly beneficial for analyzing the cumulative impact of air pollutant mixtures. It enables the simultaneous increment of one quantile across all pollutants, thereby accommodating the potential for diverse positive, negative, or neutral effects within the pollutant mixture without presupposing a linear relationship between exposure levels and health outcomes (Keil et al., 2020). The 95% confidence intervals (95% CI) for combined effects were determined using a bootstrap method involving 1000 replicates.

Statistical evaluations were conducted using R (version 4.23, provided by the Foundation for Statistical Computing). The significance threshold was set at $P < 0.05$, with all tests being bidirectional.

## 3. Results

### 3.1. Baseline characteristics of participants

This cohort study involved 19,325 pregnant women with a median age of 30.20 years. Table 1 shows the demographic characteristics of enrolled individuals. Of these, 1669 individuals (8.64%) were diagnosed with HDPs and 180 (0.94%) with preeclampsia. Notably, women with HDPs or preeclampsia had significantly higher pre-pregnancy BMI than those without these conditions. Nulliparous women were more likely to be diagnosed with HDPs or preeclampsia. Additionally, differences were observed in the season of conception and gestation risk grade between groups with and without HDPs or preeclampsia.

### 3.2. Distribution of ambient air pollutants and daily temperature

The median (interquartile range) exposure of pollutants and temperature during total and subdivided gestational periods are shown in Table 2. Figure A.3 presents strong correlations between different levels of exposure to ambient air pollutants ($r > 0.70$). A positive correlation was observed between exposure to all pollutants except $O_3$. The inverse correlations were observed between $O_3$ and other air pollutants.

### 3.3. Regression results in the single-pollutant models

The relationships between exposure to ambient air pollutants during gestation and the incidence risk of HDPs or preeclampsia were analyzed using multivariate logistic regression (Fig. 1). The analysis revealed that the incidence risk of HDPs decreased with every 10 $\mu g/m^3$ increase in $NO_2$ exposure in the trimester before gestation, the first trimester during gestation and the third trimester during gestation. Similarly, an inverse relationship was observed with a 10 $\mu g/m^3$ rise in $PM_1$, $PM_{2.5}$, and $PM_{10}$ exposure during the trimester before gestation. Regarding preeclampsia, the incidence risk was negatively associated with a 10 $\mu g/m^3$ increase in $PM_1$ exposure, $PM_{2.5}$ exposure and $PM_{10}$ exposure in the third trimester during gestation. Notably, a 10 $\mu g/m^3$ increase in $O_3$ exposure is associated with an increased preeclampsia incidence risk in the second trimester during gestation and the third trimester during gestation.

Nonlinear associations were detected between $PM_1$ exposure in the first trimester during gestation (Fig. 2), $O_3$ exposure in the second trimester, and incidence risk of HDPs ($P < 0.05$). However, the relationship did not reach statistical significance when considering the overall association across the full range of exposures ($P$ for overall $>$ 0.05). Furthermore, no nonlinear relationship was found between ambient air pollutants and incidence risk of preeclampsia (Fig. 3). Stratified analyses were presented in Table A.1-Tabl A.4.

### 3.4. Regression results in the two-pollutant and multi-pollutant models

In the two-pollutant models (TableA.5 and TableA.6), the associations between $NO_2$ exposure in the trimester before gestation, first trimester during gestation and third trimester during gestation and incidence risk of HDPs remained significantly negative. Similarly, significant negative associations were observed between HDPs and $PM_1$, $PM_{2.5}$, and $PM_{10}$ exposure in the trimester before gestation, except for

**Table 1**
Characteristics of study participants (N = 19,329).

| Characteristic | HDPs | | | Preeclampsia | | |
|---|---|---|---|---|---|---|
| | No, N = 17,660 | Yes, N = 1669 | *P* | No, N = 19,149 | Yes, N = 180 | *P* |
| Maternal age, year | 30.20 (28.30, 32.00) | 30.30 (28.20, 32.20) | 0.5 | 30.50 (28.40, 33.70) | 30.30 (28.20, 34.40) | 0.025 |
| Pre-pregnancy BMI, kg/m$^2$ | 20.69 (19.10, 22.58) | 21.83 (19.95, 24.09) | <0.001 | 20.70 (19.13, 22.66) | 22.25 (20.49, 24.06) | <0.001 |
| Residential areas | | | >0.9 | | | 0.6 |
| Rural | 13,360 (76%) | 1264 (76%) | | 14,491 (76%) | 133 (74%) | |
| Urban | 4300 (24%) | 405 (24%) | | 4658 (24%) | 47 (26%) | |
| Educational attainment, year | | | 0.2 | | | 0.7 |
| <13 | 20 (0.1%) | 1 (<0.1%) | | 21 (0.1%) | 0 (0%) | |
| 13-16 | 13,003 (74%) | 1261 (76%) | | 14,134 (74%) | 130 (72%) | |
| ≥ 17 | 4637 (26%) | 407 (24%) | | 4994 (26%) | 50 (28%) | |
| Multiparous | 6464 (37%) | 428 (26%) | <0.001 | 6844 (36%) | 48 (27%) | 0.011 |
| Season of conception | | | <0.001 | | | 0.078 |
| Spring | 4060 (23%) | 480 (29%) | | 4486 (23%) | 54 (30%) | |
| Summer | 4160 (24%) | 421 (25%) | | 4541 (24%) | 40 (22%) | |
| Autumn | 4426 (25%) | 399 (24%) | | 4792 (25%) | 33 (18%) | |
| Winter | 5014 (28%) | 369 (22%) | | 5330 (28%) | 53 (29%) | |
| Gestation risk grade | | | <0.001 | | | <0.001 |
| Green | 7151 (40%) | 387 (23%) | | 7535 (39%) | 3 (1.7%) | |
| Yellow | 8599 (49%) | 1068 (64%) | | 9560 (50%) | 107 (59%) | |
| Orange or red | 1910 (11%) | 214 (13%) | | 2054 (11%) | 70 (39%) | |

Values are median (interquartile range) for continuous variables or numbers (%) for categorical variables. Wilcoxon rank-sum test was used for continuous variables, and chi-squared test with Rao and Scott's second-order correction was used for categorical variables.
Abbreviations: HDPs, Hypertensive disorders of pregnancy; BMI, body mass index

**Table 2**
Distribution of ambient air pollutants exposure and daily temperature during gestation.

| Gestational period | $PM_1$, μg/m$^3$ | $PM_{2.5}$, μg/m$^3$ | $PM_{10}$, μg/m$^3$ | $O_3$, μg/m$^3$ | $SO_2$, μg/m$^3$ | $NO_2$, μg/m$^3$ | CO, mg/m$^3$ | Temperature, °C |
|---|---|---|---|---|---|---|---|---|
| The trimester before gestation | 21.52 (16.08, 32.92) | 34.46 (26.04, 53.07) | 59.05 (46.52, 84.03) | 112.50 (72.95, 124.33) | 10.02 (8.70, 11.19) | 35.62 (29.67, 51.25) | 0.94 (0.85, 1.03) | 17.60 (10.34, 24.28) |
| First trimester during gestation | 21.88 (16.31, 32.11) | 35.04 (26.43, 52.04) | 66.08 (47.26, 82.71) | 98.48 (73.11, 121.50) | 9.29 (8.53, 10.89) | 40.29 (32.17, 50.41) | 0.92 (0.85, 1.02) | 16.61 (10.68, 23.95) |
| Second trimester during gestation | 20.71 (15.74, 31.75) | 33.62 (25.69, 50.99) | 62.82 (49.07, 81.57) | 106.53 (76.57, 122.93) | 9.13 (8.24, 10.69) | 39.05 (30.49, 49.19) | 0.90 (0.82, 1.01) | 17.93 (11.18, 24.98) |
| Third trimester during gestation | 19.59 (13.87, 29.72) | 32.10 (22.43, 47.76) | 61.08 (40.82, 76.76) | 117.39 (80.32, 129.92) | 8.86 (8.09, 10.25) | 37.34 (27.61, 46.25) | 0.88 (0.82, 0.98) | 17.38 (12.09, 20.29) |

Values are median (interquartile range).
Abbreviations: $PM_1$, fine particulate matter ≤1 μm; $PM_{2.5}$, fine particulate matter ≤2.5 μm; $PM_{10}$, particulate matter with diameter ≤10 μm; $NO_2$, nitrogen dioxide; $O_3$, ozone; $SO_2$, sulfur dioxide; CO, carbon monoxide.

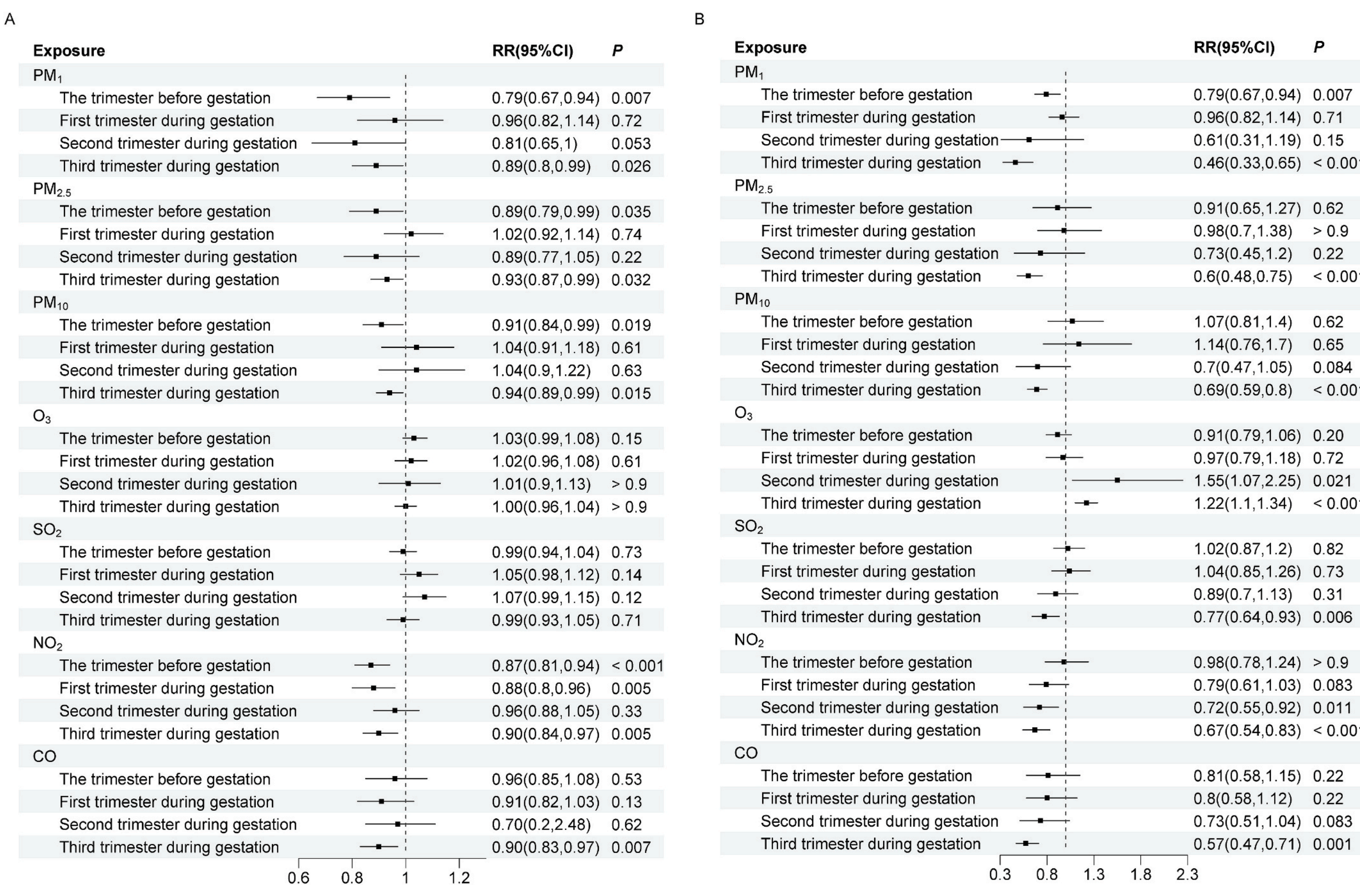


**Fig. 1.** Associations of ambient air pollutants exposure with incidence risk of HDPs (A) or preeclampsia (B). Models were adjusted for the maternal age (year), pre-pregnancy (BMI, kg/m$^2$), residential areas(rural or urban), educational attainment(< 13 year, 13–16 years, ≥ 17 years), multiparous(yes or no), season of conception (spring, summer, autumn or winter), pregnancy risk grade(green, yellow, orange or red).
Abbreviations: $PM_1$, fine particulate matter ≤1 μm; $PM_{2.5}$, fine particulate matter ≤2.5 μm; $PM_{10}$, particulate matter with diameter ≤10 μm; $NO_2$, nitrogen dioxide; $O_3$, ozone; $SO_2$, sulfur dioxide; CO, carbon monoxide; RR, relative risk; CI, confidence interval.

$NO_2$ exposure. Regarding preeclampsia, the association with $O_3$ exposure in the second trimester during gestation remained significantly positive. Conversely, $NO_2$ exposure during the same period was relevant to a significantly lower incidence risk. Moreover, exposure to $PM_1$, $PM_{2.5}$, and $PM_{10}$ in the third trimester during gestation was correlated with an elevated risk of preeclampsia, except for CO exposure.

The coefficient ψ of multi-pollutant models represented the combined impact on HDPs or preeclampsia when the levels of mixed ambient air pollutant were simultaneously elevated by one quartile (Table 3). Notably, an increase by one quartile in the cumulative effect of ambient air pollutants was associated with a significant decrease in the incidence risk of HDPs in the trimester before gestation (RR: 0.81, 95% CI: 0.72–0.91) and in the third trimester during gestation (RR: 0.88, 95% CI: 0.78–0.98). Furthermore, such a quartile increase in the cumulative effect of ambient air pollutants also significantly correlated with a reduced incidence risk of preeclampsia in the third trimester during gestation (RR: 0.50; 95% CI: 0.38–0.67). The details of the weight of each ambient air pollutants exposure are presented in Table A.7.

## 4. Discussion

The body of research investigating the environmental determinants of HDPs and preeclampsia has recently expanded. However, these

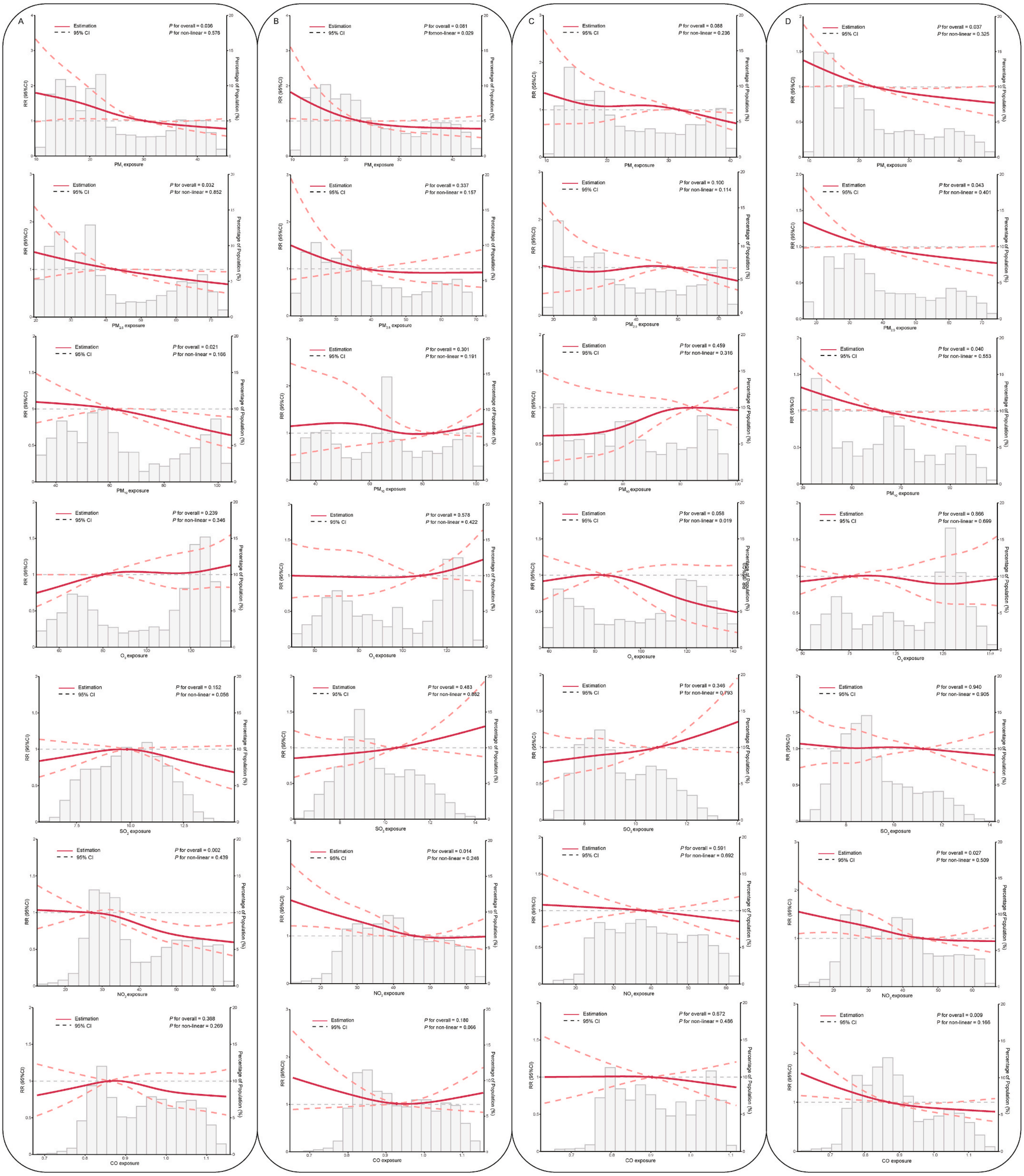

**Fig. 2.** Exposure-response associations between ambient air pollutants and incidence risk of HDPs in the trimester before gestation (A), first trimester during gestation (B), second trimester during gestation (C) and third trimester during gestation (D).
Abbreviations: $PM_1$, fine particulate matter ≤1 μm; $PM_{2.5}$, fine particulate matter ≤2.5 μm; $PM_{10}$, particulate matter with diameter ≤10 μm; $NO_2$, nitrogen dioxide; $O_3$, ozone; $SO_2$, sulfur dioxide; CO, carbon monoxide; RR, relative risk; CI, confidence interval.

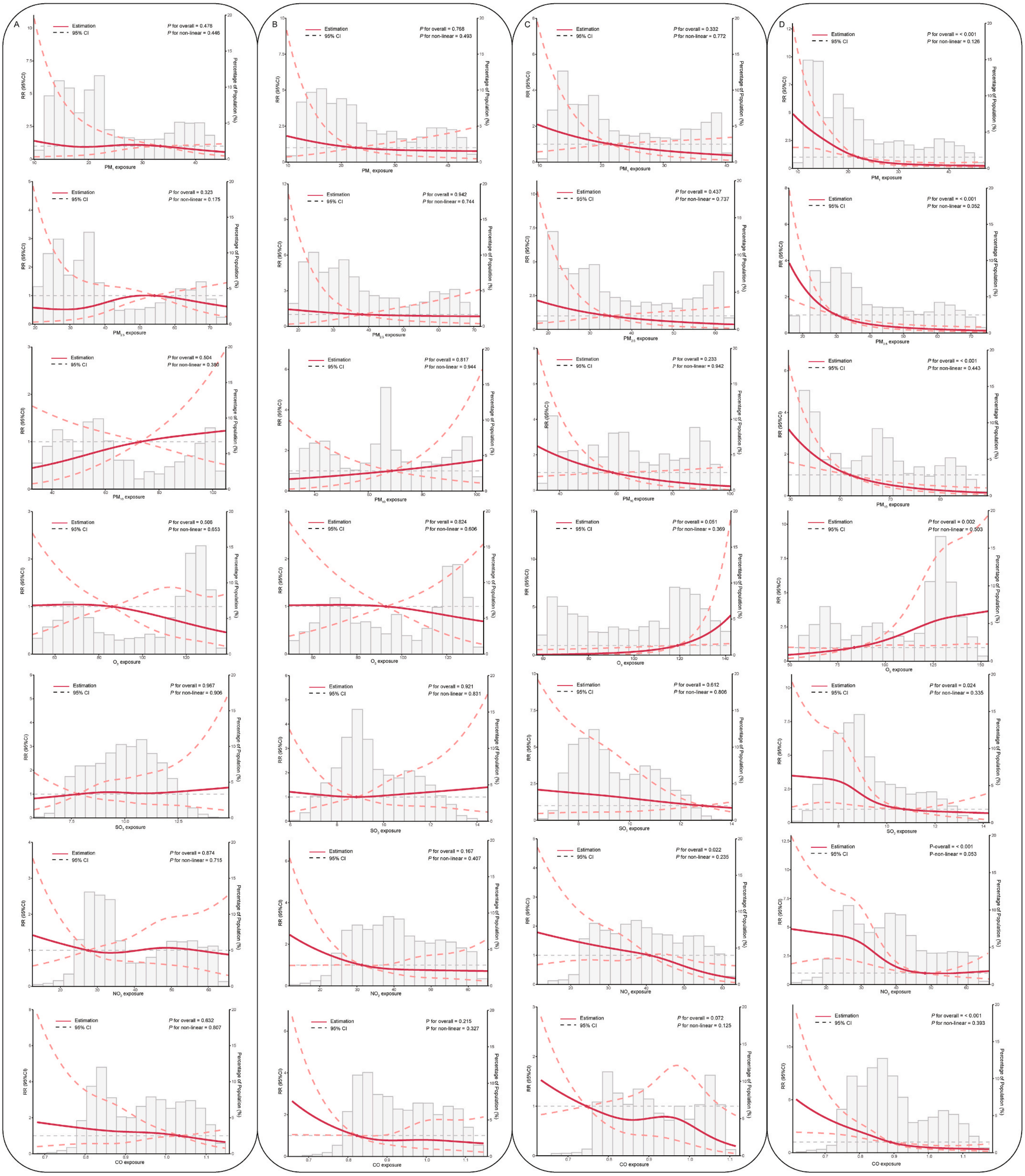


**Fig. 3.** Exposure-response associations between ambient air pollutants and incidence risk of preeclampsia in the trimester before gestation (A), first trimester during gestation (B), second trimester during gestation (C) and third trimester during gestation (D).
Abbreviations: $PM_1$, fine particulate matter ≤1 μm; $PM_{2.5}$, fine particulate matter ≤2.5 μm; $PM_{10}$, particulate matter with diameter ≤10 μm; $NO_2$, nitrogen dioxide; $O_3$, ozone; $SO_2$, sulfur dioxide; CO, carbon monoxide; RR, relative risk; CI, confidence interval.

**Table 3**
Adjusted RRs (95% CIs) of incidence risk of HDPs and preeclampsia associated with ambient air pollution in multi-pollutant models from 1000 bootstrap replicates.

| Gestational time | HDPs | | Preeclampsia | |
|---|---|---|---|---|
| | RR (95% CI) | P | RR (95% CI) | P |
| The trimester before gestation | 0.81(0.72, 0.91) | < 0.001 | 0.92(0.67, 1.24) | 0.59 |
| First trimester during gestation | 0.91(0.76, 1.08) | 0.31 | 0.91(0.77, 1.07) | 0.28 |
| Second trimester during gestation | 0.97(0.86, 1.07) | 0.54 | 1.09(0.28, 2.88) | 0.87 |
| The third trimester during gestation | 0.88(0.78, 0.98) | 0.045 | 0.50(0.38, 0.67) | < 0.001 |

Models were adjusted for the maternal age (year), pre-pregnancy (BMI, kg/m$^2$), residential areas(rural or urban), educational attainment(< 13 year, 13–16 years, ≥ 17 years), Multiparous(yes or no),season of conception(spring, summer, autumn or winter), gestation risk grade(green, yellow, orange or red).
Abbreviations: RR, relative risk; CI, confidence interval; HDPs, hypertensive disorders of pregnancy.

studies are still contradictory and focused on single pollutant. A Shanghai study reported a 1.14-fold increased incidence risk for HDPs with every 10 μg/m$^3$ rise in $PM_{2.5}$ concentration, particularly for those who became pregnant in the winter season (Su et al., 2020). Conversely, Wu P et al. investigated the $PM_{2.5}$ exposure during gestation was not associated with the risk of developing HDPs in Monroe County (Savitz et al., 2015). Our multi-pollutant model presented an increase by one quartile in the cumulative effect of ambient air pollutants, associated with a significantly decreased incidence risk for HDPs in the trimester before gestation and third trimester during gestation, as well as for preeclampsia in the third trimester during gestation.

The balance of pro-inflammatory and anti-inflammatory factors in pregnant women, and the imbalance of this balance promotes the occurrence of HDPs and preeclampsia (Murthi et al., 2020). Exposure to $PM_{2.5}$ can activate macrophages via the TLR4/COX-2/NF-κB pathway, leading to a significant inflammatory response (Fu et al., 2020). However, it may also trigger anti-inflammatory and protective pathways by activating the ACE2/Ang (1–7)/MAS axis (Botto et al., 2023). Our results indicated that $PM_{2.5}$ exposure was associated with a decreased incidence risk in some periods of pregnancy. The complex physiological changes during pregnancy and the dual effects of $PM_{2.5}$ may lead to inconsistencies in different gestation time.

Several investigations have documented an association between exposure to $NO_2$ and increased prevalence and mortality rates associated with cardiovascular diseases (Chen et al., 2022; Wen et al., 2023; Zhang et al., 2023). However, our findings revealed the negative association between $NO_2$ exposure in the trimester before gestation, first trimester during gestation, and third trimester during gestation and HDPs incidence, inconsistent with previous studies. Unlike general hypertension, HDPs are specifically associated with pregnancy and typically develop after 20th weeks during gestation (Jiang et al., 2022; Wu et al., 2023). The changes during gestational volume expansion stress the maternal cardiovascular system, potentially leading to HDPs (Gyselaers, 2022). Under sunlight and certain meteorological conditions, $NO_2$ can be converted into the vasodilator NO (Kimbrough et al., 2017; Signori et al., 2022). Then, NO can be converted into nitrate (Lundberg et al., 2008). Dietary nitrate supplementation could improv vascular flow (Burleigh et al., 2019; Walker et al., 2019). Environmental conditions in different regions and genetic variations among different populations may significantly affect the conversion rates of these matters and their ultimate impact on health. This explains why similar studies might yield different results in different regions. Further investigation is warranted to confirm and elucidate the underlying mechanisms.

In this study, exposure to $O_3$ during the second trimester of gestation was not associated with an increased incidence of HDPs. However, it was associated with a higher incidence of preeclampsia. A cohort study from Shanghai, China (n = 7841) showed an association between gestational hypertension incidence risk and $O_3$ exposure but failed to support an association between $O_3$ exposure and preeclampsia risk (Cheng et al., 2023). Differences in sample size and urban-rural differences within the sample can explain these inconsistent results. Furthermore, participants residing more than 5 km from their workplace and those whose residential or work addresses changed during gestation were excluded from this study. This exclusion criterion reduces possible bias owing to inaccurate address information. Additionally, compared to other studies on preeclampsia in China, our incidence rate of preeclampsia is relatively low. This may be due to admission bias and differences in population baseline characteristics.

This study has a few limitations to consider when interpreting its results. First, we assessed ambient air pollutant exposure using a high-precision and high-resolution model. However, given data availability, we solely conducted outdoor exposure assessments without considering indoor ambient air pollutants and humidity. Second, we lacked access to the diagnosis time of HDPs and preeclampsia. Thirdly, the diagnosis of HDPs and preeclampsia may vary across different countries. In China, the diagnosis of these diseases is primarily based on the presence of hypertension and proteinuria. Consequently, the initial design of our study did not account for fetal outcomes such as gestational age at delivery and birth weight. Last, although numerous confounding factors were accounted for, uncontrolled variables such as environmental noise, psychosocial stress, and smoking may influence the results (Chen et al., 2021; Morisaki et al., 2023; Wilson et al., 2024)

## 5. Conclusion

Exposures to $PM_1$, $PM_{2.5}$, $PM_{10}$, and $NO_2$ across different trimesters of gestation were inversely associated with the incidence risk of HDPs. Additionally, our multi-pollutant model presented that an increase by one quartile in the cumulative effect of ambient air pollutants was associated with a significantly decreased incidence risk for HDPs in the trimester before gestation and the third trimester during gestation, as well as for preeclampsia in the third trimester during gestation. These findings underscore the importance of further investigating the mechanisms underlying these associations.

## Conflict of interest and financial disclosure

None.

## Funding

None.

## Data sharing statement

Data cannot be shared due to patient privacy concerns.

## CRediT authorship contribution statement

**Wenkai Zhang:** Writing – original draft, Visualization, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Minghao Kong:** Writing – review & editing, Validation, Supervision, Resources, Conceptualization. **Yuan Jiang:** Writing – original draft, Resources, Methodology, Formal analysis, Data curation, Conceptualization. **Quan Gan:** Validation, Software, Resources, Methodology, Formal analysis. **Jing Wei:** Software, Resources, Methodology, Investigation. **Qing Zhang:** Validation, Software, Resources. **Jiayi Wang:** Software, Resources, Methodology. **Jun Shen:** Visualization, Software, Methodology. **Shijie Wu:** Writing – review & editing, Validation, Supervision, Software, Methodology, Data curation, Conceptualization.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

The data that has been used is confidential.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envpol.2024.124722.

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