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Weekly-specific ambient PM₁ before and during pregnancy and the risk of gestational diabetes mellitus

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ARTICLE INFO	ABSTRACT
Edited by Dr. Renjie Chen	Background: Exposure to fine or respirable particulate matter has been linked to an elevated risk of gestational diabetes mellitus (GDM). However, the association between exposure to particulate matter with an aerodynamic
Keywords: Gestational diabetes mellitus PM ₁ Exposure windows	→ the definition (GDM). However, the association between exposure to particulate matter with an aerodynamic diameter ≤ 1 µm (PM ₁) and GDM has not been explored. <i>Methods</i> : We conducted a cohort study involving 60,173 pregnant women from nine hospitals in Beijing, China, from February 2015 to April 2021. Daily concentrations of PM ₁ and ozone were obtained from a validated spatiotemporal artificial intelligence model. We used a modified Poisson regression combined with distributed lag models to estimate the association between weekly-specific PM ₁ exposure and the risk of GDM after adjusting for individual-level covariates. <i>Results</i> : Among the 51,299 pregnant women included in the final analysis, 4008 were diagnosed with GDM. Maternal exposure to PM ₁ during preconception and gestational periods was generally associated with an increased risk of GDM. The most pronounced associations were identified during the 12th week before pregnancy, the 5th-8th weeks of the first trimester, and the 23rd-24th weeks of the second trimester. Each 10 µg/m ³ increase in PM ₁ was associated with a relative risk of GDM of 1.65 (95 % CI: 1.59, 1.72) during the preconception period, 1.67 (95 % CI: 1.61, 1.73) in the first trimester, 1.52 (95 % CI: 1.47, 1.58) in the second trimester, and 2.54 (95 % CI: 2.45, 2.63) when considering the first and second trimester combined. <i>Conclusions</i> : Exposure to PM ₁ before and during pregnancy was associated with an increased risk of GDM, particularly during the 12 weeks before pregnancy and gestational trimester of the analysis of GDM, particularly during the 12 weeks before pregnancy was associated with an increased risk of GDM, particularly during the 12 weeks before pregnancy was associated with an increased risk of GDM, particularly during the 12 weeks before pregnancy was associated with an increased risk of GDM, particularly during the 12 weeks before pregnancy and gestational weeks 5–8 and 23–24.

1. Introduction

Gestational diabetes mellitus (GDM) is one of the most common complications of pregnancy and poses a significant global public health challenge (Wang et al., 2022). Recent estimates indicate that the prevalence of GDM ranges from 11.7 % to 30.2 % across different regions, with higher incidences observed in both low- and high-income countries (Wang et al., 2022). GDM not only increases the risk of various metabolic disorders but also adversely affects the short- and long-term health of both pregnant women and their unborn children, leading to potential adverse birth outcomes (Metzger et al., 2008; Mirghani Dirar and Doupis, 2017). For example, women with GDM are at an elevated risk of developing type 2 diabetes and macrovascular disease, such as cardiovascular and coronary artery disease, later in life (Retnakaran and Shah, 2016; Yu et al., 2019). In recent years, the prevalence of GDM has been on the rise in China, largely attributed to lifestyle changes and economic development, especially in regions experiencing rapid economic growth (Juan and Yang, 2020). Therefore, identifying modifying risk factors for GDM is critical for reducing disease burden and promoting the health of both mothers and their offspring.

Previous studies have explored the potential link between exposure to fine particulate matter (PM_{2.5}) or respirable particulate matter (PM₁₀) and the risk of GDM (Cheng et al., 2022; Choe et al., 2019; Liu et al., 2022b; Mai et al., 2022; Molitor et al., 2023; Yan et al., 2022; Zhang et al., 2020a; Zheng et al., 2022). However, no study has specifically examined particulate matter with an aerodynamic diameter $\leq 1 \ \mu m$ (PM₁). Due to its vast surface area and tiny molecule size, PM₁ can penetrate deep into the lungs, carrying more harmful chemicals, depositing them inside the alveoli, and entering the blood circulation. This process may have more pronounced adverse impacts on the blood

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glucose levels of pregnant women (Guo et al., 2023; Zajusz-Zubek et al., 2017). In addition, a study involving pregnant women with normal blood glucose levels found that exposure to PM_1 was associated with increased fasting blood glucose concentrations (Najafi et al., 2020).

Additionally, identifying critical exposure windows is essential for guiding targeted interventions. Most previous studies have assessed the relationship between exposure to air pollution and the risk of GDM using broad exposure window, often focusing on a single trimester, a combination of trimesters, or a specific gestational month without accounting for simultaneous exposure windows. This approach may result in the misidentification of critical exposure windows (Cheng et al., 2022; Liu et al., 2022b; Mai et al., 2022; Wilson et al., 2017a; Yan et al., 2022; Zheng et al., 2022). The distributed lag model (DLM) is a preferred approach for identifying unbiased exposure windows for the association between exposure to air pollution and the risk of GDM (Wilson et al., 2017b).

Accordingly, our study aimed to estimate the relationship between weekly-specific PM_1 exposure before and during pregnancy and the risk of GDM and to identify critical exposure windows using distributed lag models among 51,299 pregnant women from 9 hospitals in Beijing, China. We further examined whether this association varied by child sex, maternal age, pre-pregnancy body mass index (BMI), education, parity, and gestational age.

2. Methods

2.1. Study population

Our analysis included 60,173 pregnant women from 9 hospitals in Beijing, China, between February 1, 2015 and April 31, 2021. We collected demographic information using questionnaires that included maternal age, education, parity, child sex, pre-pregnancy BMI, last menstrual period, regular folic acid supplementation, and residential address. We excluded 121 women who did not provide a complete residential address, 721 women with a gestational age of more than 42 weeks, and 8032 women with incomplete information on child sex, prepregnancy BMI, or parity (Figure S1). Ultimately, 51,299 pregnant women were included in our analysis. The study was approved by the Ethics Committee of Capital Medical University (approval number Z2022SY052).

2.2. Outcome definition

All pregnant women underwent a 75-g oral glucose tolerance test (OGTT) between 24 and 28 weeks of gestation. Based on the criteria set by the International Association of Diabetes and Pregnancy Study Groups (IADPSG), GDM was diagnosed if any of the following thresholds were met or exceeded: fasting blood glucose of 5.10 mmol/L, 1 hour glucose of 10.00 mmol/L, or 2 hours glucose of 8.50 mmol/L (Metzger et al., 2010).

2.3. Environmental assessment

We obtained daily ambient PM_1 (Wei et al., 2019) and maximum 8-hour ozone (He et al., 2022; Wei et al., 2022) data from the China-HighAirPollutant (CHAP) dataset between 2014 and 2021. This dataset provides high-quality, near-surface air pollution data across China on a 1 km x 1 km grid. The CHAP data integrates satellite remote sensing technology coupled with various approaches, including ground observation, atmospheric reanalysis, and artificial intelligence analysis, allowing for a comprehensive consideration of the spatiotemporal heterogeneity of air pollutants. The accuracy of PM_1 and ozone predications at a 1 km spatial resolution was assessed using 10-fold cross-validation, with determination coefficients (R^2) of 0.83 and 0.92, respectively. Daily air pollutant levels were assigned to each participant based on his or her geocoded residential address. We gathered daily ambient temperatures (°C) from the China Meteorological Service Center (http://data.cma.cn/) and assigned each participant the measurement data from the nearest monitoring station.

Based on the last menstrual period, we calculated average weekly PM_1 concentrations for each participant, covering the period from 12 weeks before conception to 24 weeks of gestation. Similarly, we calculated the average ambient temperature and ozone levels for each participant over the same timeframe as PM_1 .

2.4. Statistical analyses

A descriptive analysis was employed to characterize the demographic variables of all pregnant women, presented by number and proportion. These characteristics included child sex (male, female), maternal age (\leq 24, 25–29, 30–34, \geq 35 years), pre-pregnancy BMI (<18.5, 18.5–24.9, 25.0–29.9, \geq 30 kg/m²), education (less than bachelor, bachelor or above), parity (nulliparous, multiparous), season of conception (spring [March to May], summer [June to August], autumn [September to November], and winter [December to February]), and gestational age (<37, 37–42 weeks).

We used modified Poisson regression to examine the association between PM_1 exposure and the risk of GDM, adjusting for child sex, maternal age, pre-pregnancy BMI, parity, education, season of conception, and regular folic acid supplementation (yes versus no). Results estimated from modified Poisson regressions provide unbiased relative risk with appropriate confidence intervals and are easier to interpret.

We used a distributed lag model to estimate the exposure-lagresponse relationship between exposure to weekly-specific PM_1 and the risk of GDM, as well as to identifying potential exposure windows. We used linear exposure-response functions and fitted lag-response functions using a natural cubic spline with 9 degrees of freedom, selected based on the minimum Akaike Information Criterion (AIC) (Table S1). Lag periods were set from 12 weeks before conception to 24 weeks of gestation.

In addition to estimating the weekly effects of PM₁ on GDM, we also calculated the cumulative effects of PM₁ during the preconception period (1–12 weeks before conception), the first trimester (1–12 weeks after conception), the second trimester (13–24 weeks after conception), the first and second trimesters combined (1–24 weeks after conception), and the entire period (12 weeks before conception to 24 weeks of gestation). We reported results as the relative risk (RR) and 95 % confidence intervals (CIs) for GDM associated with a 10 μ g/m³ increase in PM₁.

We conducted two main sensitivity analyses. First, we varied the number of knots in the natural cubic spline of PM_1 and modified the lag function using B-splines with 9 degrees of freedom. Second, to evaluate potential confounding effects of meteorological factors and other air pollutants, we additionally adjusted for ambient temperature using a natural cubic spline with 7 degrees of freedom and included ozone as a linear term in the models.

To identify potential susceptible subpopulations, we conducted subgroup analyses by child sex, maternal age, pre-pregnancy BMI, education, parity, and gestational age. We used *Z* test to examine whether the differences among subgroups were statistically significant using the following formula: $z = \frac{\beta_1 - \beta_2}{\sqrt{SE_1^2 + SE_2^2}}$ (Chen et al., 2022).

All statistical analyses were conducted using R software (version 4.2.2) with the "dlnm" package to fit a distributed lag model. *P*-values < 0.05 were regarded as statistically significant in two-sided tests.

3. Results

A total of 51,299 pregnant women who attended 9 hospitals in Beijing between 2015 and 2021 were included in our analysis, of whom 4008 (7.8 %) were diagnosed with GDM. Most participants were aged 25–29 years (40.8 %), had a normal pre-pregnancy BMI (70.7 %), had less than a bachelor's level of education (57.4 %), and were nulliparous (59.6 %) (Table 1 & Table S2). Figure S1 shows the geographic distribution of participants in this study. The average levels of PM₁ exposure were 33.76 μ g/m³ during the preconception period, 31.02 μ g/m³ during the first trimester, 31.01 μ g/m³ during the second trimester, and 32.26 μ g/m³ during the first and second trimesters combined (Table 2). The average concentrations of PM₁ were higher in participants with GDM compared to those without GDM across multiple exposure windows.

Maternal exposure to PM_1 was associated with a higher risk of GDM using a distributed lag model with the period from 12 weeks before conception to 24 weeks of gestation (Figure S2). The strongest association between exposure to PM_1 and the risk of GDM was identified in 23–24 weeks of gestation, followed by 5–8 weeks of gestation, and the 12 week before pregnancy (Fig. 1). Sensitivity analyses including varying the number of knots of the fitted lag-response function or using B-splines yielded similar results (Figure S3).

We also calculated the cumulative effects of PM₁ on GDM. A 10 μ g/m³ increase in PM₁ was associated with a RR of 1.65 (95 % CI: 1.59, 1.72) during the preconception period, 1.67 (95 % CI: 1.61, 1.73) during the first trimester, 1.52 (95 % CI: 1.47, 1.58) during the second trimester, 2.54 (95 % CI: 2.45, 2.63) during the first and second trimesters combined, and 4.20 (95 % CI: 3.98, 4.43) across the entire period from the preconception to the second trimester (Table 3). In sensitivity analysis, additional adjustments for ambient temperature and ozone did not materially alter these results (Table 3).

To identify susceptible subpopulations, we conducted subgroup analyses by child sex, maternal age, pre-pregnancy BMI, parity, and gestational age. The association between PM_1 exposure and GDM was more pronounced among pregnant women aged 35 years or older, those with obesity, nulliparous women, and those with a gestational age between 37 and 42 weeks (Table 4).

Table 1	
Summary characteristics	of the study participants

Characteristics	GDM	Non GDM	Total
	(n=4008)	(n=47,291)	(n=51,299)
	n (%)	n (%)	n (%)
Child sex			
Male	2051 (51.2)	24,658 (52.1)	26,709 (52.1)
Female	1957 (48.8)	22,633 (47.9)	24,590 (47.9)
Maternal age, years			
<25	228 (5.7)	3708 (7.8)	3936 (7.7)
25–29	1564 (39.0)	19,387 (41.0)	20,951 (40.8)
30–34	1481 (37.0)	16,965 (35.9)	18,446 (36.0)
\geq 35	735 (18.3)	7231 (15.3)	7966 (15.5)
Pre-pregnancy BMI, kg/m ²			
<18.5	222 (5.5)	4713 (10.0)	4935 (9.6)
18.5–24.9	2543 (63.4)	33,714 (71.3)	36,257 (70.7)
25.0-29.9	1039 (25.9)	7261 (15.4)	8300 (16.2)
\geq 30.0	204 (5.1)	1603 (3.4)	1807 (3.5)
Education			
Less than bachelor	2426 (60.5)	27,011 (57.1)	29,437 (57.4)
Bachelor or above	1582 (39.5)	20,280 (42.9)	21,862 (42.6)
Parity			
Nulliparous	2273 (56.7)	28,308 (59.9)	30, 581 (59.6)
Multiparous	1735 (43.3)	18,983 (40.1)	20, 718 (40.4)
Season of conception			
Spring (March-May)	1341 (33.5)	11,405 (24.1)	12,746 (24.4)
Summer (June-August)	883 (22.0)	11,610 (24.6)	12,493 (26.2)
Autumn (September-November)	634 (15.8)	11,311 (23.9)	11,945 (24.2)
Winter (December-February)	1150 (28.7)	12,965 (27.4)	14,115 (25.2)
Gestational age, weeks			
<37	159 (4.0)	2127 (4.5)	2286 (4.3)
37–42	3849 (96.0)	45,164 (95.5)	49,013 (95.7)

Abbreviations: n, number of counts; Pre-pregnancy BMI, Pre-pregnancy body mass index.

4. Discussion

Among the 51,299 pregnant women who attended 9 hospitals in Beijing, China, we found that maternal exposure to PM_1 before and during pregnancy increased the risk of GDM, particularly during the 12 weeks before pregnancy and during gestational weeks 5–8 and 23–24. This association was most pronounced among pregnant women aged 35 years or older, those with obesity, nulliparous women, and those with a gestational age between 37 and 42 weeks.

To our knowledge, this study is the first to estimate the relationship between exposure to ambient PM_1 and the risk of GDM. We found that exposure to PM_1 was associated with an elevated risk of GDM, with the most pronounced associations observed during the 12 weeks before pregnancy and gestational weeks 5–8 and 23–24. Although direct comparisons with previous studies are challenging, findings from three studies generally support our findings (Gong et al., 2023; Liu et al., 2022a; Zheng et al., 2021). These studies found that the association between $PM_{2.5}$ exposure and GDM was most pronounced during the gestational weeks 21–24, 24–27, and 19–24 (Gong et al., 2023; Liu et al., 2022a; Zheng et al., 2021). Additionally, a study involving 11,639 pregnant women in Nanjing, China, reported a positive association between $PM_{2.5}$ exposure and the risk of GDM during the 3–10 weeks before conception, with a peak in the 8th week before conception (Zhang et al., 2020b).

We found that exposure to PM1 was associated with increased risk of GDM across the preconception period, the first trimester, the second trimester, and the first and second trimester combined. These findings are consistent with a recent systematic review and meta-analysis that integrated 13 studies with 2826,544 pregnant women and investigated the relationship between PM2.5 exposure and the risk of GDM (Nazarpour et al., 2023). The pooled odds ratio associated with a $10 \ \mu\text{g/m}^3$ increase in PM_{2.5} was 1.10 (95 % CI: 1.07, 1.13) for the preconception period, 1.09 (95 % CI: 1.07, 1.12) for the first trimester, 1.13 (95 % CI: 1.10, 1.16) for the second trimester, and 1.10 (95 % CI: 1.04, 1.16) for the first and second trimesters combined. Compared to the pooled risk estimates, our findings showed stronger associations, which may be attributed to differences in particulate matter sizes, individual exposure assessment approaches, statistical analysis techniques, and GDM diagnostic criteria. The preconception and pregnancy periods are critical times characterized by increased nutrient intake and fat accumulation, which can heighten susceptibility to insulin resistance and, consequently, GDM due to particulate matter exposure (Xu et al., 2011).

Despite the precise biological mechanism linking maternal PM₁ exposure to an increased risk of GDM remaining unclear, inflammation, oxidative stress, and insulin resistance are likely significant contributors (Brook et al., 2013; Chen et al., 2018; Guan et al., 2019, 2018; Kelishadi et al., 2009; Velali et al., 2019). During pregnancy, there is a physiological decrease in insulin sensitivity, which indicates an inadequate cellular response to insulin and can lead to GDM (Szlapinski and Hill, 2020). In vitro studies have shown that exposure to particulate matter induces oxidative stress in cells, resulting in elevated levels of reactive oxygen species, malondialdehyde, and DNA damage, as evidenced by decreased expression of β-galactosidase (Velali et al., 2019). Furthermore, animal studies have demonstrated that particulate matter exposure impairs glucose tolerance and induces both local and systemic insulin resistance (Xu et al., 2011). Additionally, research using a rat model of GDM has found that particulate matter exposure causes pancreatic oxidative stress and inflammation, leading to reduced expression of pancreatic glucose transporter 2 (GLUT2) and higher blood glucose levels (Yi et al., 2017).

We found that the association between PM_1 exposure and GDM was more pronounced among pregnant women aged 35 or older, those who were obese, nulliparous women, and those with a gestational age 37–42 weeks. This heightened association may be due to the aggravation of insulin resistance in these groups, potentially exacerbated by synergistic PM_1 exposure (Jackson et al., 2017; Lain and Catalano, 2007; Liang

Table 2

The average air pollutants levels among the included pregnant women across multiple exposure windows.

Pollutants	Exposure windows	Total (n=51,299)		GDM (n=4008)		Non GDM (n=47, 291)	
		Mean (SD)	IQR	Mean (SD)	IQR	Mean (SD)	IQR
PM_1	Preconception	33.76 (13.79)	13.93	43.44 (15.49)	25.73	32.94 (13.31)	13.8
	First trimester	32.02 (11.96)	12.26	38.06 (14.38)	18.33	31.51 (11.58)	12.56
	Second trimester	31.01 (12.21)	12.37	36.39 (14.00)	9.29	30.55 (11.94)	13.22
	First and second trimesters combined	32.26 (8.12)	8.90	39.31 (7.29)	13.45	31.67 (7.90)	7.20
Ozone	Preconception	101.05 (45.09)	84.56	89.62 (43.22)	79.33	102.02 (45.11)	84.86
	First trimester	104.13 (44.07)	82.15	107.14 (45.70)	83.57	103.87 (43.92)	81.92
	Second trimester	106.23 (43.74)	80.48	108.59 (43.97)	75.11	106.03 (43.72)	80.65
	First and second trimesters combined	103.80 (19.19)	33.89	101.75 (19.77)	37.34	103.97 (19.13)	33.87
Ambient temperature	Preconception	12.85 (9.99)	19.65	11.23 (9.45)	17.49	12.99 (10.02)	19.85
	First trimester	13.22 (10.11)	20.03	14.55 (10.03)	19.42	13.10 (10.11)	19.97
	Second trimester	13.89 (9.86)	19.06	16.04 (9.25)	16.44	13.71 (9.89)	19.19
	First and second trimesters combined	13.03 (7.60)	15.46	12.89 (7.46)	14.93	13.05 (7.62)	15.49

Abbreviations: GDM, gestational diabetes mellitus; IQR, interquartile range; SD, standard deviation; n, number of counts.

We defined the preconception period as 1–12 weeks before conception, the first trimester as 1–12 weeks after conception, the second trimester as 13–24 weeks after conception, the first and second trimesters combined as 1–24 weeks after conception.



Fig. 1. The relative risks of gestational diabetes mellitus associated with weekly-specific particulate matter with aerodynamic diameter $\leq 1 \ \mu m$ (PM₁) before and during pregnancy. Results were presented as relative risks associated with 10 $\mu g/m^3$ increase in PM₁.

et al., 2023; Park et al., 2014). For example, nulliparous women might be more likely to weight gain and fat accumulation due to a lack of awareness about fertility, which could lead to higher body weight (Liang et al., 2023). Evidence suggests that adipose tissue can accumulate environmental pollutants like PM₁, contributing to chronic inflammation that facilitates insulin resistance (Jackson et al., 2017). Additionally, studies have shown that several key inflammatory genes are upregulated with aging, and elevated levels of pro-inflammatory cytokines further exacerbate insulin resistance (Park et al., 2014). Insulin resistance naturally increases during late pregnancy to ensure adequate nourishment for the fetus (Lain and Catalano, 2007). However, merely 4.5 % of the participants in our analysis had a gestational age of less than 37 weeks, interpretations of findings in this subgroup should be made with caution, and further studies with larger populations are needed to confirm these findings.

Our study has three potential limitations. First, we were unable to

capture the local spatial variations in PM₁ caused by motorized traffic and other emission sources, which could lead to exposure misclassification. Additionally, the assignment of ambient PM1 levels to each participant based on residential addresses did not account for mobile and indoor exposures during pregnancy, further contributing to potential exposure misclassification. However, any nondifferential misclassification of exposure would likely bias the relative risk towards the null (Copeland et al., 1977). Second, although we adjusted for a wide range of potential confounders, including maternal characteristics, season of conception, child sex, and ambient temperatures, there might be potential confounding factors that was not accounted for, such as exposure to metals, light pollution, greenspace, dietary habits, and physical activity (Liao et al., 2019). Third, since the pregnant women in our analysis were recruited from hospitals in Beijing, the results may not be generalizable to other cities and countries in China. Despite of these limitations, this is the first study to estimate the association between

Table 3

Relative risk of gestational diabetes mellitus associated with each $10~\mu\text{g/m}^3$ increase in particulate matter with aerodynamic diameter $\leq 1~\mu\text{m}$ (PM₁) exposure by exposure windows.

Models	Exposure windows	Relative risk (95 % CI)
Main model ^a	Preconception	1.65 (1.59, 1.72)
	First trimester	1.67 (1.61, 1.73)
	Second trimester	1.52 (1.47, 1.58)
	First and second trimesters combined	2.54 (2.45, 2.63)
	Entire period	4.20 (3.98, 4.43)
Main model + ambient temperature ^b	Preconception	1.96 (1.81, 2.13)
-	First trimester	1.83 (1.75, 1.92)
	Second trimester	1.56 (1.50, 1.63)
	First and second trimesters combined	2.87 (2.74, 3.00)
	Entire period	5.63 (5.04, 6.28)
Main model + ozone ^c	Preconception	1.69 (1.62, 1.75)
	First trimester	1.79 (1.72, 1.86)
	Second trimester	1.61 (1.55, 1.67)
	First and second trimesters combined	2.87 (2.74, 3.02)
	Entire period	4.84 (4.56, 5.14)

Abbreviations: CI, confidence interval.

We defined the preconception period as 1-12 weeks before conception, the first trimester as 1-12 weeks after conception, the second trimester as 13-24 weeks after conception, the first and second trimesters combined as 1-24 weeks after conception, and the entire period as 12 weeks before conception to 24 weeks of gestation.

^a Models were adjusted for child sex, maternal age, pre-pregnancy body mass index, parity, education, season of conception, and regular folic acid supplementation.

^b Models were additionally adjusted for average ambient temperature from 12 weeks before conception to 24 weeks of gestation using natural cubic splines with 7 degrees of freedom.

^c Models were additionally adjusted for ozone from 12 weeks before conception to 24 weeks of gestation.

Table 4

Relative risk of gestational diabetes mellitus associated with each $10 \ \mu g/m^3$ increase in particulate matter with aerodynamic diameter $\leq 1 \ \mu m$ (PM₁) stratified by child sex, maternal age, pre-pregnancy body mass index (BMI), education, parity, and gestational age.

Characteristics	Relative risk (95 % CI)	P for heterogeneity
Child sex		
Male	4.28 (4.04, 4.54)	[Reference]
Female	4.14 (3.82, 4.50)	0.521
Maternal age, years		
≤ 24	4.09 (3.54, 4.72)	0.865
25–29	4.03 (3.78, 4.30)	[Reference]
30–34	4.24 (3.86, 4.66)	0.673
\geq 35	4.72 (4.35, 5.13)	0.085
Pre-pregnancy BMI, kg/m ²		
Underweight (<18.5)	3.42 (2.98, 3.94)	0.005
Normal (18.5–24.9)	4.28 (3.99, 4.59)	[Reference]
Overweight (25.0-29.9)	4.05 (3.79, 4.32)	0.266
Obese (≥30.0)	5.25 (4.47, 6.17)	0.022
Education		
Less than bachelor	4.08 (3.79, 4.39)	[Reference]
Bachelor or above	4.42 (4.16, 4.69)	0.100
Parity		
Nulliparous	4.51 (4.29, 4.75)	[Reference]
Multiparous	3.88 (3.58, 4.21)	0.002
Gestational age, weeks		
<37	3.56 (3.04, 4.17)	[Reference]
37–42	4.24 (4.01, 4.47)	0.041

Abbreviations: CI, confidence interval; Pre-pregnancy BMI, Pre-pregnancy body mass index.

exposure to ambient PM_1 and the risk of GDM.

5. Conclusion

Among 51,299 pregnant women in Beijing, China, we found that weekly-specific ambient PM_1 exposure before and during pregnancy was linked to an elevated risk of GDM. Our results suggest that PM_1 is a potentially risk factor for GDM, indicating that pregnant women should minimize their exposure to PM_1 to reduce the risk of developing GDM.

CRediT authorship contribution statement

Kun Yuan: Writing – review & editing. Yangchang Zhang: Writing – review & editing. Ruiyi Liu: Writing – review & editing. Tian Liang: Writing – review & editing. Guiyin Lin: Writing – review & editing, Data curation. Xin Lv: Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis. Huanling Yu: Writing – review & editing, Supervision. Ying Du: Writing – review & editing. Supervision, Project administration, Funding acquisition, 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

Data will be made available on request.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ecoenv.2024.117006.

References

Brook, R.D., Xu, X., Bard, R.L., Dvonch, J.T., Morishita, M., Kaciroti, N., Sun, Q.,	
Harkema, J., Rajagopalan, S., 2013. Reduced metabolic insulin sensitivity following	ng
sub-acute exposures to low levels of ambient fine particulate matter air pollution	
Sci. Total Environ. 448, 66–71. https://doi.org/10.1016/j.scitotenv.2012.07.034.	

- Chen, R., Jiang, Y., Hu, J., Chen, H., Li, H., Meng, X., Ji, J.S., Gao, Y., Wang, W., Liu, C., Fang, W., Yan, H., Chen, J., Wang, W., Xiang, D., Su, X., Yu, B., Wang, Y., Xu, Y., Wang, L., Li, C., Chen, Y., Bell, M.L., Cohen, A.J., Ge, J., Huo, Y., Kan, H., 2022. Hourly air pollutants and acute coronary syndrome onset in 1.29 million patients. Circulation 145, 1749–1760. https://doi.org/10.1161/ CIRCULATIONAHA.121.057179.
- Chen, R., Li, H., Cai, J., Wang, C., Lin, Z., Liu, C., Niu, Y., Zhao, Z., Li, W., Kan, H., 2018. Fine particulate air pollution and the expression of micrornas and circulating cytokines relevant to inflammation, coagulation, and vasoconstriction. Environ. Health Perspect. 126 (1), 017007 https://doi.org/10.1289/EHP1447.
- Cheng, X., Ji, X., Yang, D., Zhang, C., Chen, L., Liu, C., Meng, X., Wang, W., Li, H., Kan, H., Huang, H., 2022. Associations of PM_{2.5} exposure with blood glucose impairment in early pregnancy and gestational diabetes mellitus. Ecotoxicol. Environ. Saf. 232, 113278 https://doi.org/10.1016/j.ecoenv.2022.113278.
- Choe, S.-A., Eliot, M.N., Savitz, D.A., Wellenius, G.A., 2019. Ambient air pollution during pregnancy and risk of gestational diabetes in New York City. Environ. Res. 175, 414–420. https://doi.org/10.1016/j.envres.2019.04.030.
- Copeland, K.T., Checkoway, H., McMichael, A.J., Holbrook, R.H., 1977. Bias due to misclassification in the estimation of relative risk. Am. J. Epidemiol. 105, 488–495. https://doi.org/10.1093/oxfordjournals.aje.a112408.
- Gong, Z., Yue, H., Li, Z., Bai, S., Cheng, Z., He, J., Wang, H., Li, G., Sang, N., 2023. Association between maternal exposure to air pollution and gestational diabetes mellitus in Taiyuan, North China. Sci. Total Environ. 875, 162515 https://doi.org/ 10.1016/j.scitotenv.2023.162515.
- Guan, L., Geng, X., Stone, C., Cosky, E.E.P., Ji, Y., Du, H., Zhang, K., Sun, Q., Ding, Y., 2019. PM_{2.5} exposure induces systemic inflammation and oxidative stress in an intracranial atherosclerosis rat model. Environ. Toxicol. 34, 530–538. https://doi. org/10.1002/tox.22707.

Guan, T., Hu, S., Han, Y., Wang, R., Zhu, Q., Hu, Y., Fan, H., Zhu, T., 2018. The effects of facemasks on airway inflammation and endothelial dysfunction in healthy young X. Lv et al.

adults: a double-blind, randomized, controlled crossover study. Part. Fibre Toxicol. 15 (1), 30. https://doi.org/10.1186/s12989-018-0266-0.

- Guo, Q., Zhao, Y., Zhao, J., Bian, M., Qian, L., Xue, T., Zhang, J., Duan, X., 2023. Acute change of lung function to short-term exposure to ambient air pollutants with and without physical activity: a real-world crossover study. Environ. Pollut. 316, 120481 https://doi.org/10.1016/j.envpol.2022.120481.
- He, L., Wei, J., Wang, Y., Shang, Q., Liu, J., Yin, Y., Frankenberg, C., Jiang, J.H., Li, Z., Yung, Y.L., 2022. Marked impacts of pollution mitigation on crop yields in China. Earth'S. Future 10, e2022EF002936. https://doi.org/10.1029/2022EF002936.
- Jackson, E., Shoemaker, R., Larian, N., Cassis, L., 2017. Adipose tissue as a site of toxin accumulation. Compr. Physiol. 8 (3), 1251. https://doi.org/10.1002/cphy.c160038.
- Juan, J., Yang, H., 2020. Prevalence, prevention, and lifestyle intervention of gestational diabetes mellitus in China. Int. J. Res. Pub. He. 17 (24), 9517. https://doi.org/ 10.3390/ijerph17249517.
- Kelishadi, R., Mirghaffari, N., Poursafa, P., Gidding, S.S., 2009. Lifestyle and environmental factors associated with inflammation, oxidative stress and insulin resistance in children. Atherosclerosis 203, 311–319. https://doi.org/10.1016/j. atherosclerosis.2008.06.022.
- Lain, K.Y., Catalano, P.M., 2007. Metabolic Changes in Pregnancy. Clin. Obstet. Gynecol. 50 (4), 938–948. https://doi.org/10.1097/GRF.0b013e31815a5494.
- Liang, W., Zhu, H., Xu, J., Zhao, Z., Zhou, L., Zhu, Q., Cai, J., Ji, L., 2023. Ambient air pollution and gestational diabetes mellitus: an updated systematic review and metaanalysis. Ecotoxicol. Environ. Saf. 255, 114802 https://doi.org/10.1016/j. ecoenv.2023.114802.
- Liao, J., Chen, X., Xu, S., Li, Y., Zhang, B., Cao, Z., Zhang, Y., Liang, S., Hu, K., Xia, W., 2019. Effect of residential exposure to green space on maternal blood glucose levels, impaired glucose tolerance, and gestational diabetes mellitus. Environ. Res. 176, 108526 https://doi.org/10.1016/j.envres.2019.108526.
- Liu, R., Zhang, J., Chu, L., Zhang, J., Guo, Y., Qiao, L., Niu, Z., Wang, M., Farhat, Z., Grippo, A., Zhang, Y., Ma, C., Zhang, Y., Zhu, K., Mu, L., Lei, L., 2022a. Association of ambient fine particulate matter exposure with gestational diabetes mellitus and blood glucose levels during pregnancy. Environ. Res. 214, 114008 https://doi.org/ 10.1016/j.envres.2022.114008.
- Liu, W.-Y., Lu, J.-H., He, J.-R., Zhang, L.-F., Wei, D.-M., Wang, C.-R., Xiao, X., Xia, H.-M., Qiu, X., 2022b. Combined effects of air pollutants on gestational diabetes mellitus: A prospective cohort study. Environ. Res. 204, 112393 https://doi.org/10.1016/j. envres.2021.112393.
- Mai, D., Xu, C., Lin, W., Yue, D., Fu, S., Lin, J., Yuan, L., Zhao, Y., Zhai, Y., Mai, H., Zeng, X., Jiang, T., Li, X., Dai, J., You, B., Xiao, Q., Wei, Q., Hu, Q., 2022. Association of abnormal-glucose tolerance during pregnancy with exposure to PM_{2.5} components and sources. Environ. Pollut. 292, 118468 https://doi.org/10.1016/j. envpol.2021.118468.
- Metzger, B.E., Gabbe, S.G., Persson, B., Buchanan, T.A., Catalano, P.A., Damm, P., Dyer, A.R., Leiva, A., Hod, M., Kitzmiler, J.L., Lowe, L.P., McIntyre, H.D., Oats, J.J., Omori, Y., Schmidt, M.I., 2010. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 33 (3), 676–682. https://doi.org/10.2337/dc09-1848.
- Metzger, B.E., Lowe, L.P., Dyer, A.R., Trimble, E.R., Chaovarindr, U., Coustan, D.R., Hadden, D.R., McCance, D.R., Hod, M., McIntyre, H.D., Oats, J.J., Persson, B., Rogers, M.S., Sacks, D.A., 2008. Hyperglycemia and adverse pregnancy outcomes. N. Engl. J. Med 358, 1991–2002. https://doi.org/10.1056/NEJMoa0707943.
- Mirghani Dirar, A., Doupis, J., 2017. Gestational diabetes from A to Z. World J. Diabetes 8, 489–511. https://doi.org/10.4239/wjd.v8.i12.489.
- Molitor, J., Sun, Y., Rubio, V.G., Benmarhnia, T., Chen, J.-C., Avila, C., Sacks, D.A., Chiu, V., Slezak, J., Getahun, D., Wu, J., 2023. Modeling spatially varying compliance effects of PM_{2.5} exposure reductions on gestational diabetes mellitus in southern California: results from electronic health record data of a large pregnancy cohort. Environ. Res. 231, 116091 https://doi.org/10.1016/j.envres.2023.116091.
- Najafi, M.L., Zarei, M., Gohari, A., Haghighi, L., Heydari, H., Miri, M., 2020. Preconception air pollution exposure and glucose tolerance in healthy pregnant women in a middle-income country. Environ. Health 19, 131. https://doi.org/ 10.1186/s12940-020-00682-y.
- Nazarpour, S., Ramezani Tehrani, F., Valizadeh, R., Amiri, M., 2023. The relationship between air pollutants and gestational diabetes: an updated systematic review and meta-analysis. J. Endocrinol. Invest. 46, 1317–1332. https://doi.org/10.1007/ s40618-023-02037-z.

- Park, M.H., Kim, D.H., Lee, E.K., Kim, N.D., Im, D.S., Lee, J., Yu, B.P., Chung, H.Y., 2014. Age-related inflammation and insulin resistance: a review of their intricate interdependency. Arch. Pharm. Res. 37, 1507–1514. https://doi.org/10.1007/ s12272-014-0474-6.
- Retnakaran, R., Shah, B.R., 2016. Role of type 2 diabetes in determining retinal, renal, and cardiovascular outcomes in women with previous gestational diabetes mellitus. Diabetes Care 40, 101–108. https://doi.org/10.2337/dc16-1400.
- Szlapinski, S.K., Hill, D.J., 2020. Metabolic adaptations to pregnancy in healthy and gestational diabetic pregnancies: the pancreas - placenta axis. Curr. Vasc. Pharmacol. 19, 141–153. https://doi.org/10.2174/1570161118666200320111209.
- Velali, E., Pantazaki, A., Besis, A., Choli-Papadopoulou, T., Samara, C., 2019. Oxidative stress, DNA damage, and mutagenicity induced by the extractable organic matter of airborne particulates on bacterial models. Regul. Toxicol. Pharm. 104, 59–73. https://doi.org/10.1016/j.yrtph.2019.03.004.
- Wang, H., Li, N., Chivese, T., Werfalli, M., Sun, H., Yuen, L., Hoegfeldt, C.A., Elise Powe, C., Immanuel, J., Karuranga, S., Divakar, H., Levitt, N., Li, C., Simmons, D., Yang, X., 2022. IDF diabetes atlas: estimation of global and regional gestational diabetes mellitus prevalence for 2021 by international association of diabetes in pregnancy study group's criteria. Diabetes Res. Clin. Pract. 183, 109050 https://doi. org/10.1016/j.diabres.2021.109050.
- Wei, J., Li, Z., Guo, J., Sun, L., Huang, W., Xue, W., Fan, T., Cribb, M., 2019. Satellite-Derived 1-km-Resolution PM(1) Concentrations from 2014 to 2018 across China. Environ. Sci. Technol. 53, 13265–13274. https://doi.org/10.1021/acs.est.9b03258.
- Wei, J., Li, Z., Li, K., Dickerson, R.R., Pinker, R.T., Wang, J., Liu, X., Sun, L., Xue, W., Cribb, M., 2022. Full-coverage mapping and spatiotemporal variations of groundlevel ozone (O₃) pollution from 2013 to 2020 across China. Remote Sen. Environ. 270, 112775 https://doi.org/10.1016/j.rse.2021.112775.
- Wilson, A., Chiu, Y.-H.M., Hsu, H.-H.L., Wright, R.O., Wright, R.J., Coull, B.A., 2017a. Potential for bias when estimating critical windows for air pollution in children's health. Am. J. Epidemiol. 186, 1281–1289. https://doi.org/10.1093/aje/kwx184.
- Xu, X., Liu, C., Xu, Z., Tzan, K., Zhong, M., Wang, A., Lippmann, M., Chen, L.-C., Rajagopalan, S., Sun, Q., 2011. Long-term exposure to ambient fine particulate pollution induces insulin resistance and mitochondrial alteration in adipose tissue. Toxicol. Sci. 124, 88–98. https://doi.org/10.1093/toxsci/kfr211.
- Yan, M., Liu, N., Fan, Y., Ma, L., Guan, T., 2022. Associations of pregnancy complications with ambient air pollution in China. Ecotoxicol. Environ. Saf. 241, 113727 https:// doi.org/10.1016/j.ecoenv.2022.113727.
- Yi, L., Wei, C., Fan, W., 2017. Fine-particulate matter (PM_{2.5}), a risk factor for rat gestational diabetes with altered blood glucose and pancreatic GLUT2 expression. Gynecol. Endocrinol. 33, 611–616. https://doi.org/10.1080/ 09513590.2017.1301923.
- Yu, Y., Arah, O.A., Liew, Z., Cnattingius, S., Olsen, J., Sørensen, H.T., Qin, G., Li, J., 2019. Maternal diabetes during pregnancy and early onset of cardiovascular disease in offspring: population based cohort study with 40 years of follow-up. BMJ 367, 16398. https://doi.org/10.1136/bmj.16398.
- Zajusz-Zubek, E., Radko, T., Mainka, A., 2017. Fractionation of trace elements and human health risk of submicron particulate matter (PM₁) collected in the surroundings of coking plants. Environ. Monit. Assess. 189, 389. https://doi.org/ 10.1007/s10661-017-6117-x.
- Zhang, H., Dong, H., Ren, M., Liang, Q., Shen, X., Wang, Q., Yu, L., Lin, H., Luo, Q., Chen, W., Knibbs, L.D., Jalaludin, B., Wang, Q., Huang, C., 2020a. Ambient air pollution exposure and gestational diabetes mellitus in Guangzhou, China: a prospective cohort study. Sci. Total Environ. 699, 134390 https://doi.org/10.1016/ j.scitotenv.2019.134390.
- Zhang, M., Wang, X., Yang, X., Dong, T., Hu, W., Guan, Q., Tun, H.M., Chen, Y., Chen, R., Sun, Z., Chen, T., Xia, Y., 2020b. Increased risk of gestational diabetes mellitus in women with higher prepregnancy ambient PM_{2.5} exposure. Sci. Total Environ. 730, 138982 https://doi.org/10.1016/j.scitotenv.2020.138982.
- Zheng, Y., Bian, J., Hart, J., Laden, F., Wen, T.S.-T., Zhao, J., Qin, H., Hu, H., 2022. PM_{2.5} constituents and onset of gestational diabetes mellitus: identifying susceptible exposure windows. Atmos. Environ. 291, 119409 https://doi.org/10.1016/j. atmosenv.2022.119409.
- Zheng, Y., Wen, X., Bian, J., Lipkind, H., Hu, H., 2021. Associations between the chemical composition of PM_{2.5} and gestational diabetes mellitus. Environ. Res. 198, 110470 https://doi.org/10.1016/j.envres.2020.110470.