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Research Paper

Individual ambient ozone exposure during pregnancy and adverse birth outcomes: Exploration of the potentially vulnerable windows

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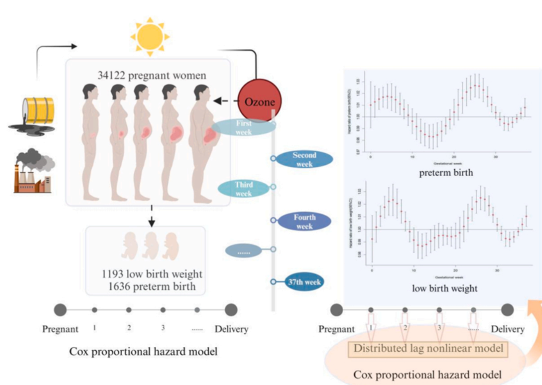
HIGHLIGHTS

- Ozone exposure during pregnancy is positively associated with a higher risk of PTB.
- Ozone exposure at earlier gestational weeks is positively associated with a higher risk of PTB or LBW.
- The exploration of weekly sensitive windows may be more helpful for pregnant women taking self-protection accurately.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: Ambient ozone (O_3) exposure during pregnancy might be associated with preterm birth (PTB) and low birth weight (LBW); however, existing evidence remains inconclusive. It is necessary to explore the relationships and potential susceptible periods further.
Methods: To explore the relationship between O_3 exposure and adverse birth outcomes, a study using records of 34,122 singleton live births in Beijing between 2016 and 2019 was conducted. The O_3 exposure in each gestational week of pregnant women was estimated, and Cox proportional hazard models were used to estimate the hazard ratios (HRs) and corresponding 95% confidence intervals (CIs). Distributed lag nonlinear model (DLNM) incorporated in Cox proportional hazard models were used to explore potential critical windows.

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Results: An increase of 10 μg/m^3 in O_3 exposure was associated with a 3.9% (95%CI: 0.6–7.3%) higher risk of PTB. Additionally, this increase in O_3 exposure was positively linked to PTB during the 2nd – 7th, 22nd – 29th, and 37th gestational weeks, and LBW during the 2nd – 7th, 24th – 29th, and 37th gestational weeks.
Conclusions: This study demonstrates a positive correlation between O_3 exposure and PTB, and identified specific sensitive periods during pregnancy when the risk was higher.

1. Introduction

Preterm birth (PTB) and low birth weight (LBW) are two primary adverse birth outcomes that could have profound lifetime implications for children's health. PTB was defined as live births less than 37 completed weeks, and LBW was defined as birth weight less than 2500 g [1]. The estimated global preterm prevalence in 2020 was 9.9% (95% CI: 9.1%–11.2%) [2], and LBW prevalence in 2015 was 14.6% worldwide [3]. Meanwhile, PTB was the leading cause of death in children younger than five years of age globally in 2016, accounting for 35% of deaths among newborn babies [4]. LBW has also become one of the main risk factors for global disease burden [5]. Various risk factors such as unhealthy lifestyles, genetic factors, and adverse environmental exposure, could induce or trigger PTB and LBW [5,6]. While certain factors, such as genetic factors, remain unmodifiable, and for hazardous environmental factors, we can take measures to reduce or prevent their harmful impacts.

There has been limited research examining the link between O_3 exposure during pregnancy and the risk of PTB or LBW, and the existing studies have produced inconsistent results. Most studies suggest that exposure to O_3 during pregnancy is linked to a higher risk of PTB or LBW [7–11], although relatively few studies have focused on LBW. At the same time, there are some studies that present inconsistent results, indicating no association between O_3 exposure and adverse birth outcomes [12,13] or even the opposite outcomes [14]. In addition to the regional heterogeneity, another potential explanation was that a pregnancy lasts for ten months, and pregnant women have different sensitivities to O_3 exposure at various stages during pregnancy. Previous researchers have explored associations between O_3 exposure during different trimesters and adverse birth outcomes, showing a higher risk of PTB and LBW associated with O_3 exposure during 1st trimester [15,16], or 2nd trimester [17] or both of 1st and 2nd trimesters of pregnancy [10, 18]. Therefore, exploring the potential sensitive windows of O_3 exposure during pregnancy is of great significance to determining the effect of O_3 on adverse birth outcomes.

In recent years, Beijing has implemented various measures to control ambient air pollution, leading to a significant reduction in the concentrations of particulate matter. However, the level of ozone (O_3) near the ground remains persistently high [19]. Based on the above, we aimed to investigate the association between O_3 exposure during pregnancy and PTB or LBW and further explore the potential sensitive windows based on data from birth records and weekly O_3 exposure during pregnancy in Beijing between 2016 and 2019. This study could provide solid evidence to prevent the potential harmful impacts of O_3 exposure on pregnant women and their fetuses.

2. Methods

2.1. Study population

This study was approved by the Medical Ethics Committee of Capital Medical University. We obtained the population data of 34, 852 pregnant women. The inclusion and exclusion criteria are as follows. The inclusion criteria: 1) The pregnant women delivered between 2016 and 2019. 2) Singleton live births. The exclusion criteria: 1) Stillbirth. 2) Ambiguous address information. We excluded 27 pregnant women finally. Birth records of 34,122 singleton live births in Beijing between January 1, 2016, and December 31, 2019 were included from the Maternal and Child Health Hospital in Tongzhou District, Beijing. We defined those term live births whose birthweight < 2500 g as LBW and live births before 37 weeks of pregnancy as PTB [1].

2.2. Covariates

We retrieved demographic characteristics, including 1) Maternal information: maternal age, marital status (married or unmarried), ethnicity (Han or minor nationality), the way of delivery (vaginal or cesarean delivery), the date of last menstrual period, and gestational week. 2) babies' information: babies' gender, date of birth, and birth weight. 3) Maternal residential address.

2.3. Exposure assessment

We collected daily average O_3 concentrations between January 1, 2015, and December 31, 2019. Data were publicly available from the ChinaHighO_3 dataset (https://weijing-rs.github.io/product.html), referring to the big data seamless 10 km Ground-level O_3 Dataset for China. The ground-level 8-hour maximum daily average O_3 concentration was forecasted by solar radiation intensity, surface temperature, remote sensing products, ground-based observations, etc., using an extended ensemble learning of the space-time extremely randomized trees (STET) model, which presented high performance. The 10-fold cross-validation showed an average out-of-sample coefficient of determination of 0.87 [20]. Daily ambient temperature and relative humidity were obtained from the China Meteorological Data Sharing System (http://www.nmic.cn). Each participant's weekly average exposure concentrations of O_3, ambient temperature, and relative humidity were calculated according to the end of each gestational week and the residential address.

2.4. Statistical analysis

Spearman correlation analysis was used to examine the correlation between O_3, ambient temperature, and relative humidity. In addition, a chi-square test for binary variables, an LSD test for multi-categorical variables, and a two-sample t-test for continuous variables were used to compare different groups (PTB and TB, LBW and non-LBW).

Firstly, we used the Cox proportional hazard models to evaluate the association between O_3 exposure during pregnancy and PTB or LBW. We fitted the following four models. (1) Model 1: single-variable model with only O_3 exposure included in the model. (2) Model 2: model 1 +covariates (maternal age, baby's gender, marital status, birth way and ethnicity). (3) Model 3: model 2 + ambient temperature. (4) Model 4: model 3 + relative humidity. Secondly, we conducted stratified analyses by delivery year and season to control for confounding effects such as yearly and seasonal variations. To explore the nonlinear relationship between O_3, temperature, relative humidity and adverse birth outcomes, we fitted the spline function in the model. Based on AIC (Akaike information criterion), the model with temperature splined was better fitted, degree of freedom for PTB was 8 and for LBW was 3. Thirdly, DLNM incorporated in Cox proportional hazard models was applied to explore the susceptible weeks of O_3 exposure for pregnant women. In this model, a cross-basis matrix for O_3 was created, in which the exposure-response dimension defaulted as linear, and natural cubic splines defined the lag-response dimension. Based on the AIC, the degree of freedom for the optimal model was set as 8. The ambient temperature and relative humidity were also included in the models by natural cubic splines, with degrees of freedom at 3 and 5 for the PTB model and LBW model, separately.

In addition, multiple sensitivity analyses were conducted to verify the model's robustness. The delivery season was further adjusted in the model due to the seasonal heterogeneity. The association between exposure to O_3 and PTB was analyzed only for those delivered before 42 gestational weeks. For LBW, only those delivered after 37 weeks and the babies' birthweight < 4000 g were included in the analysis. Finally, we only analyzed pregnant women delivered in 2016, 2017, and 2019 because the total number of births in 2018 was extremely different from the other years.

All statistical analyses were performed using SAS software 9.4 (SAS Inc., Cary, N.C., USA) and package "dlnm", "spline", "survival" in R software version 4.1.3 (R Core Team, 2022. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.).

3. Results

3.1. Descriptive results

Table 1 summarizes the demographic characteristics of the study population, including 34,122 singleton live births, in which 1193 (3.50%) were LBW and 1636 (4.79%) were PTB. More LBW babies were delivered among mothers of Han nationality or with cesarean delivery. The proportion of LBW and PTB gradually increased year by year. The incidences of LBW varied by season.

Table 2 depicts the average levels of O_3, ambient temperature, and relative humidity during 2015–2019. The median O_3 level was 102.28 μg/m^3, and IQR (Interquartile range) equals to 91.36 μg/m^3. The daily average levels of O_3 concentration were correlated with ambient temperature (correlation coefficient: 0.79, $P < 0.001$) and weakly associated with relative humidity (correlation coefficient: 0.08, $P < 0.001$) (Fig. S1).

Table 2
Characteristics of O_3 and meteorological factors.

	Min	P_{25}	Median	P_{75}	Max	IQR
O_3 (μg/m^3)	4.98	51.17	102.28	142.53	281.02	91.36
Temperature (°C)	-9.40	2.30	14.56	23.33	30.37	21.03
Relative humidity (%)	22.43	44.57	58.29	72.14	90.57	27.57

3.2. Association between O_3 exposure and PTB or LBW

Table 3 shows the effects of O_3 on PTB or LBW in different adjusted models. In model 4, we observed significantly positive associations between O_3 and PTB, with HRs of 1.039 (1.006, 1.073) for a 10 μg/m^3 increase of O_3.

Current studies have shown that ambient temperature was highly related to the occurrence of PTB or LBW [21], so we added ambient temperature to model 2, constructed model 3, and then added relative humidity, forming model 4. Significantly positive associations between exposure to O_3 during pregnancy and PTB could be observed in model 4, which showed that a per 10 μg/m^3 increase in O_3 was associated with 3.9% (95%CI: 0.6–7.3%) higher risk of PTB. However, these associations

Table 3
Risk of LBW and PTB with an increase of 10 μg/m^3 in O_3 concentration.

	PTB (HR (95%CI))	LBW (HR (95%CI))
Model1[a]	0.995 (0.983, 1.008)	0.996 (0.985, 1.008)
Model2[b]	0.996 (0.983, 1.008)	0.997 (0.986, 1.008)
Model3[c]	1.022 (0.995, 1.050)	1.012 (0.988, 1.036)
Model4[d]	1.039 (1.006, 1.073)*	1.017 (0.988, 1.046)

PTB: preterm birth; LBW: low birth weight. HR: hazard ratio, CI: confidence interval.
* : p value < 0.05; ** : p value < 0.01; *** : p value < 0.001.
a : Model 1: single-pollutant model for O_3;
b : Model 2: a single-pollutant model for O_3 adjusted by maternal age, baby's gender, marital status, birth way, and ethnicity;
c : Model 3: model 2 +temperature;
d : Model 4: model3 +relative humidity.

Table 1
Essential characteristics of pregnant women with different birth outcomes.

	LBW (n = 1193)	Non-LBW (n = 32929)	Proportion of LBW (%)	P value[a]	PTB (n = 1636)	TB (n = 32486)	Proportion of PTB (%)	P value[a]
Baby's gender								
Male	611	17 027	3.46	0.76	946	16 692	5.36	< 0.001 * **
Famale	582	15 902	3.53		690	15 794	4.19	
Age (Mean±*SD*)	30.41 ± 4.28	30.23 ± 4.00		0.13	30.77 ± 4.34	30.21 ± 3.96		< 0.001 * **
Marital status								
Married	1 179	32 678	3.48	0.16	1 612	32 245	4.76	< 0.01 * *
Unmarried	14	251	5.28		24	241	9.05	
Ethnic								
Han nationality	1 147	31 180	3.54	0.03 *	1 561	30 766	4.82	0.23
Minority nationality	46	1 749	2.56		75	1 720	4.17	
Delivery								
Vaginal delivery	525	19 008	2.69	< 0.001 * **	747	18 786	3.82	< 0.001 * **
Cesarean delivery	668	13 921	4.58		889	13 700	6.09	
Delivery year								
2016	348	10 518	3.20	0.02 *	454	10 412	4.18	< 0.001 * **
2017	337	9 700	3.36		478	9 559	4.76	
2018	76	2 165	3.39		105	2 136	4.69	
2019	432	10 546	3.94		599	10 379	5.46	
Delivery season								
Spring	287	7 809	3.54	0.04 *	383	7 713	4.73	0.14
Summer	305	8 131	3.62		420	8 016	4.98	
Autumn	285	9 035	3.06		411	8 909	4.41	
Winter	316	7 954	3.82		422	7 848	5.10	

LBW: low birth weight; PTB: preterm births; TB: term births; SD: standard deviation.
a: p values were calculated using the Chi-square test for binary variables, LSD-test for multi-categorical variables, and two-sample t-test for continuous variables. * : p value < 0.05; ** : p value < 0.01; *** : p value < 0.001.

were almost unobserved in models 1, 2, and 3. So, we'll adjust the model by covariates, temperature, and relative humidity in the subsequent analyses.

3.3. Critical sensitive windows

Fig. 1 shows the exposure-time-response three-dimensional associations between exposure to O_3 and HRs of PTB or LBW during different gestational weeks. We could find higher risks of PTB or LBW with higher exposure levels of O_3 in some gestational weeks. Subgroup analyses were conducted by delivery year and season, then we found a stronger association between exposure to O_3 and LBW or PTB among those women who delivered in spring, autumn, and winter (Table 4), which showed that a 10 μg/m^3 increase in O_3 was associated with 26.2% (15.8–37.5%), 25.4% (17.4–34.1%), 60.1% (48.3–72.8%) higher risk of PTB, respectively for women delivered in spring, autumn, and winter. In addition, a 10 μg/m^3 increase in O_3 was associated with 9.9% (2.0–18.3%), 13.3% (6.4–20.7%), 43.4% (32.7–54.9%) higher risk of LBW, respectively for women delivered in spring, autumn, and winter. However, no association was observed among women delivered in summer. In order to explore the sensitive windows, we observed the HR changes of the associations between a 10 μg/m^3 increase of O_3 and LBW or PTB in different gestational weeks. For a 10 μg/m^3 increase in O_3, exposure during the 2nd-7th, 22nd-29th, and 37th gestational weeks was associated with increased risk of PTB, with the strongest association at the 25th weeks. Exposure during the 2nd-7th, 24th-29th, and 37th gestational weeks was associated with an increased risk of LBW, with the strongest association at the 26th week (Fig. 2).

3.4. Sensitivity analysis

We conducted three sensitivity analyses, with the exposure effect shown in Fig. S2, which were consistent with the primary analyses. After adjusting by delivery season, we found similar results about the weekly associations between adverse birth outcomes and exposure to O_3 with the principal analysis (Fig. 3). Also, we excluded women delivered after 42 weeks of pregnancy to analyze the effect of O_3 exposure on PTB, and excluded women delivered before 37 weeks and babies' birthweight exceeded 4000 g in studying the impact of O_3 exposure on LBW; the associations keep consistent with the results mentioned above (Fig. 4). Results were likewise after excluding those who delivered in 2018 (Fig. 5).

4. Discussion

In the present study, we used Cox proportional hazard models to investigate the HRs of PTB and LBW associated with exposure to O_3 in different gestational weeks during pregnancy. Our results suggested that O_3 exposure during pregnancy was associated with the risk of PTB, which was partly consistent with the previous study [7,8]. The two studies illustrated that O_3 exposure could induce higher risk of PTB. However, we didn't find the association between O_3 and LBW. One study conducted in Guangdong province, China, has shown that term birth weight was negatively associated with per IQR increase of O_3 exposure (−3.52 g, 95%CI: −6.23 g, −0.81 g) [22]. Another also showed similar results that an interquartile range increase in O_3 during the entire pregnancy was associated with a − 2.9 g (−4.8 g, −1 g) decrease in birth weight [23]. However, one suggested no association exists between O_3 exposure and LBW [12]. The difference might be attributed to the following reasons. First, our results and the mentioned different results were based on different study areas; the significant effect may be attributed to severe pollution in the study period. In addition, different statistical models may explain the effect heterogeneity. Furthermore, we included ambient temperature into the models, because some studies showed that ambient temperature may be associated with risk of PTB or LBW, and temperature was positively correlated with O_3, so we should consider the synergy of ambient temperature and O_3.

We further used DLNM incorporated in Cox proportional hazard models to explore susceptible gestational weeks that pregnant women were affected by O_3 exposure. To our knowledge, no study examined the association between PTB and weekly specific O_3 exposure. Our results showed that exposure to O_3 during the 2nd-7th, 24th-29th, and 37th weeks was associated with higher risks of LBW, which was partly similar to the previous studies, and during the 2nd-7th, 22nd-29th, and 37th gestational weeks with PTB. Three studies have investigated the effect of weekly O_3 exposure on LBW, showing that exposure to O_3 during 20th-23rd weeks was associated with a higher risk of LBW [24], or O_3_1h average exposure during 15th-26th weeks and O_3_8h average exposure during 20th-26th weeks [25]. Also, one investigation showed no significant windows for O_3 exposure with birth weight [13]. However, we found that O_3 exposure during early pregnancy and the end of the prenatal period was also associated with LBW. Existing evidence showed that O_3 exposure during early pregnancy might restrict growth in offspring [26]. The results also showed that perinatal exposure to O_3 was associated with the occurrence of PTB or LBW, which was slightly different from the previous study.

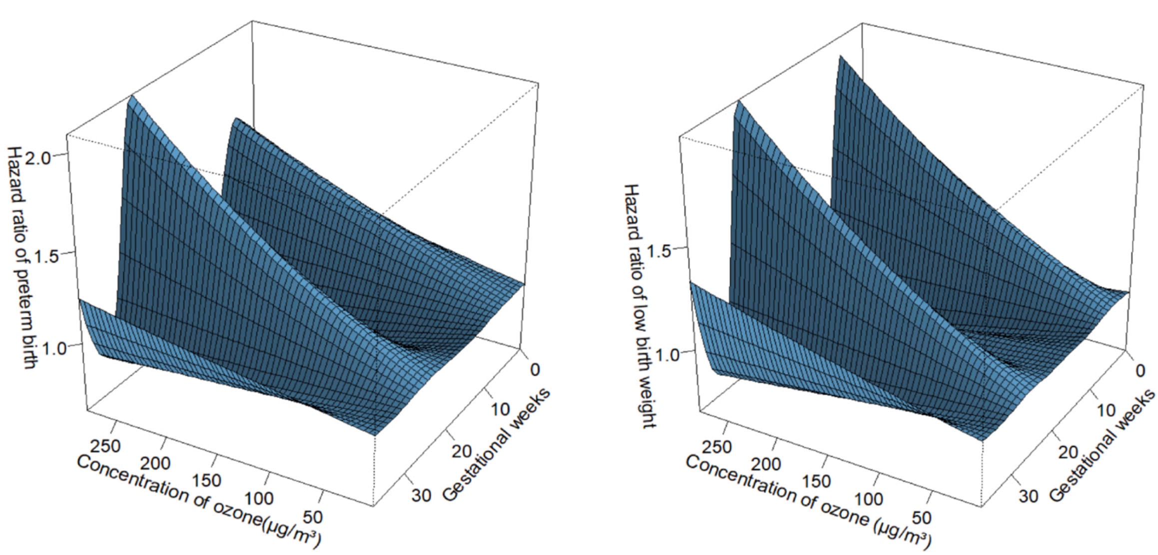

Fig. 1. The effects of O_3 exposure during pregnancy on PTB or LBW during different gestational weeks and under different exposure levels.

Table 4
HRs of LBW or PTB associated with 10 μg/m^3 O_3 exposure during pregnancy, stratified by delivery year and season.

Birth outcomes	Delivery year				Delivery season			
	2016	2017	2018	2019	spring	summer	autumn	winter
PTB HR (95% CI)	0.991 (0.927, 1.058)	0.984 (0.929, 1.043)	1.031 (0.878, 1.210)	1.046 (1.000, 1.094)*	1.262 (1.158, 1.375)*	0.865 (0.821, 0.912)	1.254 (1.174, 1.341)*	1.601 (1.483, 1.728)*
LBW HR (95% CI)	0.986 (0.930, 1.046)	0.981 (0.932, 1.033)	1.067 (0.929, 1.226)	1.029 (0.987, 1.073)	1.099 (1.020, 1.183)*	0.886 (0.845, 0.931)	1.133 (1.064, 1.207)*	1.434 (1.327, 1.549)*

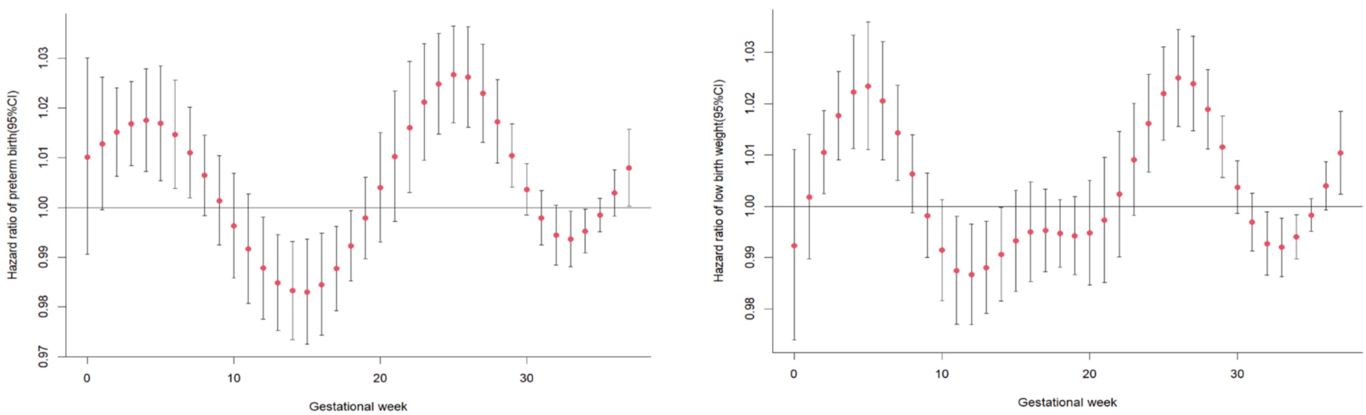

Fig. 2. HRs of LBW or PTB associated with weekly-specific O_3 exposure during the pregnancy.

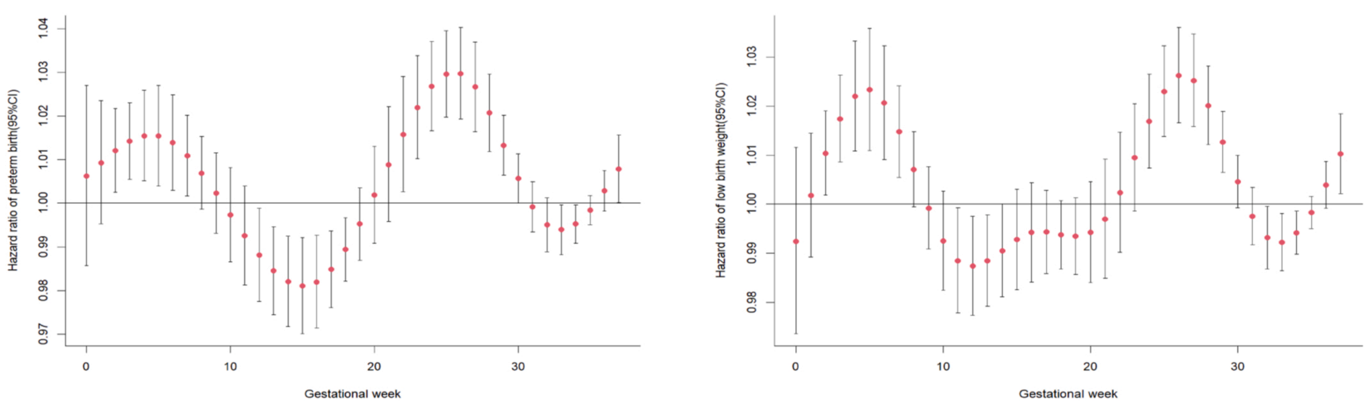

Fig. 3. Sensitivity analysis 1: HRs of LBW or PTB associated with weekly-specific O_3 exposure during pregnancy adjusted for delivery season.

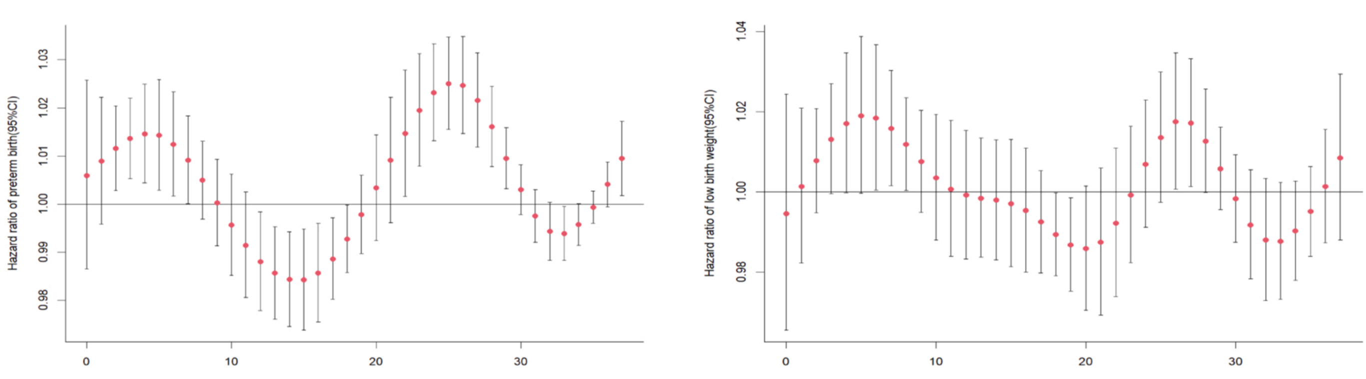

Fig. 4. Sensitivity analysis 2: HRs of LBW or PTB associated with weekly-specific O_3 exposure during the pregnancy. excluded women delivered after 42 weeks for analyses of PTB, and excluded women delivered before 37 weeks and babies' birthweight exceeding 4000 g for analyses of LBW.

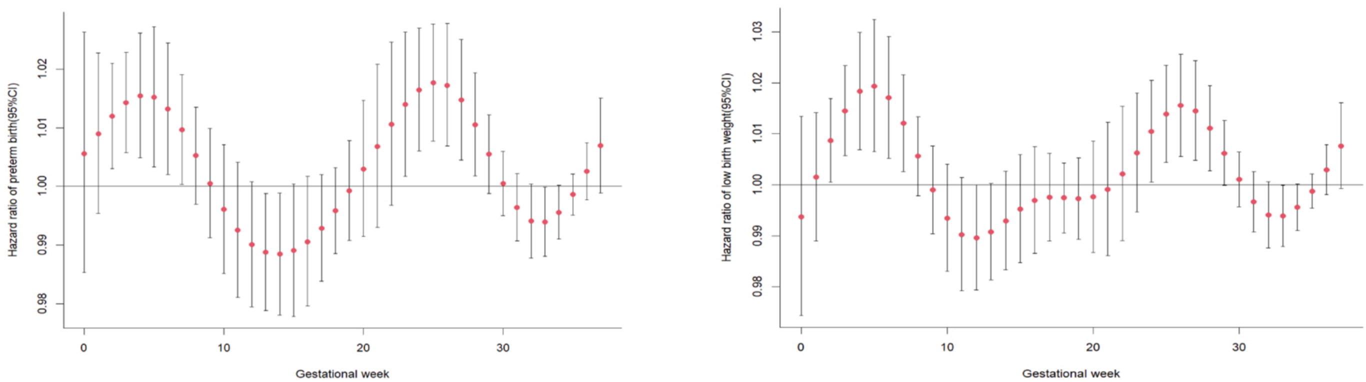

Fig. 5. Sensitivity analysis 3: HRs of LBW or PTB associated with weekly-specific O_3 exposure during the pregnancy when excluding individuals delivered in 2018.

From the results of stratified analysis, we found significantly positive associations only for those delivered in spring, autumn, or winter but not in summer. We assume that the phenomenon was due to that pregnant women delivered in spring, autumn, or winter experienced a higher level of ozone exposure during the sensitive windows, such as the 2nd - 9th weeks and 22nd - 29th weeks. Those delivered in summer might not experience the higher ozone exposure at susceptible windows but only during the perinatal periods, which might have no strong impact on the delivery and birth weight. However, the scale of data after stratification would be smaller to a certain extent, and the above illustration should be further verified in the future based on larger-scale data.

To evaluate the robustness of our results, we conducted three sensitivity analyses, showing similar results to the primary analyses. To avoid the confounding impact of the delivery season, we further adjusted it in the models, the sensitive windows were similar to the primary results, though the exposure effect throughout the pregnancy was different. Secondly, it's worth noting that after excluding pregnant women delivered before 37 weeks and birthweight exceeded 4000 g in analyzing the association between O_3 exposure and LBW, there were narrower sensitive windows than the primary analyses. Lastly, because an unusual situation occurred during 2018, not only did the incidence of PTB and LBW decrease but also did the overall number of births, so we excluded the women delivered in 2018 and analyzed; the sensitive windows were also similar with primary results. In summary, our study was relatively robust and credible.

Although the mechanism for PTB and LBW caused by O_3 exposure is unclear, existing evidence shows that O_3 exposure could induce oxidative stress [27], which could influence vascular dysfunction [28] and impact the transport of nutrients and oxygen. Our results may provide some clues for further study into the mechanism. The second and third trimesters are critical periods for fetal growth and development [29], which depend on the maternal-fetal exchange of nutrients and oxygen [30].

There are some strengths in our study. First, we used satellite retrieval data to assess the daily average O_3 concentration for every person, which could reduce exposure misclassification to a certain extent, and then assess the effect of exposure to O_3 on PTB and LBW more precisely. Second, we used the Cox proportional hazard model to analyze, which applies to the time-dependent variable in our data, and utilized DLNM incorporated in the Cox proportional hazard models to evaluate the effect of weekly-specific O_3 exposure on birth outcomes. Most current studies investigated sensitive periods using monthly, trimester, or even broader time frames. We believe that using narrower time frames to estimate pollutant exposure levels is more conducive to identifying accurate sensitive periods and also provides more detailed theoretical support for anticipated protection measures and related mechanistic studies. Furthermore, as we all know, when we use Logistic regression, it is just like a cross-section concept, only taking the O_3 exposure during one specific period as the variable of interest, without considering the actual O_3 exposure during the whole pregnancy period. Incorporating DLNM into the Cox model allows us to consider the entire pregnancy, such as the continuous exposure to pollutants in other stages besides the tested sensitive period, while discussing the exposure to pollutants during the sensitive period. This approach is more in line with the actual exposure situation of pregnant women and makes our results more objective. Third, our study is the first to investigate the association between weekly-specific O_3 exposure and PTB; we studied PTB and LBW together and got similar results. Fourth, we conducted a stratified analysis by delivery season, giving us new insights. Fifth, we adjusted the ambient temperature in the model to avoid its confounding effects on the association between exposure to O_3 and PTB or LBW.

There are also some limitations. The ambient temperature level was only derived from the Tongzhou district in Beijing, matched with population data and O_3 concentration by date, which may induce misclassification and inevitably assess the biased impact of ambient temperature. Also, based on the results of adjusted Cox models, we found positive associations between O_3 and PTB only when the temperature was put into the models, which might be attributable to the area limitation. So, a more extensive research scope might be needed. In addition, we only included some covariates, including babies' gender, maternal age, etc. In fact, some other basic characteristics may have confounding effects on the association, such as the smoking or drinking status of the mother and some basic information about the father. More information may be needed in future studies.

The cause of PTB and LBW is various, whereas the adverse impact of air pollutants could be modified by action to some extent; since it's not practical to keep pregnant women away from O_3 pollution throughout their pregnancy, the exploration of narrow sensitive periods of our study has its own actual significance. This study found that O_3 exposure during the 2nd-7th, 22nd-29th, and 37th gestational weeks was more highly related to PTB increases. An accurate estimation of the sensitive period is the primary foundation and theoretical basis for establishing a comprehensive protection system. Based on our results, and combined with more relevant previous studies and studies in the future, pregnant women should take measures to protect themselves on specific periods according to relevant guidelines.

5. Conclusion

We found that the higher risk of PTB was associated with a 10 $\mu g/m^3$ increment in O_3 exposure during the entire pregnancy. In addition, the results showed that O_3 exposure during the 2nd-7th, 24th-29th, and 37th weeks was associated with a higher risk of LBW and during the 2nd-7th, 22nd-29th, and 37th gestational weeks with PTB. This study illustrated that exposure to O_3 during pregnancy might increase the risk of PTB or LBW; pregnant women should take precautions in specific gestational weeks and avoid adverse impacts of O_3.

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CRediT authorship contribution statement

All authors contributed to the research article and approved the final version. **C.Q. Zhang:** Formal analysis, Visualization, Writing – original draft. **J. Yang**: Data curation, Formal analysis, Writing – review & editing. **Y.S. Liu**: Methodology. **H.P. Zhu:** Methodology, Writing – review & editing. **X.B. Li**: Methodology, Investigation, Writing – review & editing. **J.J. Wang:** Conceptualization, Investigation, Methodology, Data curation, Funding acquisition. **R. Chen:** Writing – review & editing, Funding acquisition.

Environmental Implication

The ground-level ozone exposure poses significant health hazards to the human body. Pregnant women and their fetuses, being sensitive and vulnerable groups, are particularly susceptible to the detrimental effects of ozone, which can result in adverse birth outcomes such as preterm birth. Despite the implementation of control measures in recent years, the environmental ozone levels remain high. Therefore, it is important to investigate the relationship between ozone exposure during pregnancy and adverse birth outcomes and identify the key sensitive periods of exposure. This study can assist pregnant women in taking appropriate self-protective measures during specific periods.

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. The de-identified individual participant data will be available based on reasonable request.

Acknowledgments

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jhazmat.2023.132945.

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