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Relationship between exposure to air pollutants in the first trimester and spontaneous abortion in pregnant women in the river valley city

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Purpose The relationship between exposure doses of 2.5-micrometer Particulate Matter ($PM_{2.5}$), Inhalable particles (PM_{10}), Sulfur Dioxide (SO_2), Nitrogen Dioxide (NO_2) and Ozone (O_3) in the first trimester and spontaneous abortion of pregnant women was evaluated by global average method and nearest monitoring station method, respectively. Method Retrospective analysis of the clinical data of pregnant women with spontaneous abortion and full-term pregnant women in the Department of Obstetrics and Gynecology of two third-class hospitals in a valley city in Northwest China. According to the age factor, the eligible pregnant women were matched at a ratio of 1 : 4. The global average method and the nearest monitoring station method were used to evaluate the exposure of pollutants. The rank-sum test and conditional logistic regression were used to analyze the correlation between air pollutants and spontaneous abortion. Results Although the global average method and the nearest monitoring station method are slightly different in the assessment of exposure dose, they do not affect the correlation evaluation with spontaneous abortion. The exposure of pregnant women to $PM_{2.5}$($OR_1 = 1.156$, $OR_2 = 1.036$), SO_2 ($OR_1 = 1.432$, $OR_2 = 1.429$) and NO_2 ($OR_1 = 1.121$, $OR_2 = 1.159$) in the first trimester is related to the occurrence of spontaneous abortion.(OR_1: the global average method, OR_2: the nearest monitoring station method) Conclusion The exposure of $PM_{2.5}$, SO_2 and NO_2 in the first trimester in valley cities is associated with the occurrence of spontaneous abortion in pregnant women.

Keywords Spontaneous abortion, First trimester, Air pollution exposure

With the development of economy, air pollution has become an inseparable topic with people's health.Air pollution, especially fine particle pollutants, is considered to be one of the main causes of the global burden of disease, such as respiratory diseases[1,2],cardiovascular diseases[3,4],bowel disease[5]and adverse pregnancy outcomes[6,7], etc.Abortion, stillbirth and birth defects are the most common adverse pregnancy outcomes[8]. Pregnancy is the process of embryonic and fetal growth and development in the mother[9]. The commonly used diagnostic methods are pregnancy test and ultrasound examination. Spontaneous abortion accounts for 15-25% of all pregnancies[10].Spontaneous abortion has a great impact on the physical and mental health of women of childbearing age[11].Exploring the risk factors of spontaneous abortion is great significance to women 's health and fetus. There are many risk factors for spontaneous abortion, including age[12], history of spontaneous abortion[13], vaginal microbiome[14], genetic factors, environmental factors and immune factors[15,16].

Baoji City is located in the northwest of China. Its geological structure is complex, surrounded by mountains on three sides, and developed along the river valley with the Weihe River as the central axis. During winter, the consumption of coal for home heating time (From November 15 to March 15 of the following year) increases the concentraiotn of atmospheric pollutants. Through the analysis of five kinds of air pollutants and maternal data in Baoji City from 2018 to 2019, this study explores the relationship between the exposure of pregnant women to air pollutants in the first trimester(the first 14 weeks of gestation is called first trimester[17])and the occurrence of spontaneous abortion.

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Research methods
Collection of cases
The general data and pregnancy data of pregnant women admitted to the Department of Obstetrics and Gynecology of Baoji Central Hospital and Baoji People 's Hospital from 2018 to 2019 were collected. Demographic and clinical data of patients included: age, occupation, gravidity (number of pregnancies), parity (number of deliveries), previous caesarean section (number of cesarean sections), season of last mentruation, regular or irregular menses, pregnancy complications, pregnancy comorbidities, hypertensive disorders of pregnancy. The population was divided into two groups, the case group was the people of spontaneous abortion and the control group was the full-term birth population. Miscarriages cases were matched for maternal age with ongoing pregnancies to term in a one to four case-control study. Taking age as the matching factor, the interference of maternal age on the research results was removed.

Pregnancy complications are conditions in which a pregnant woman develops a series of diseases caused by pregnancy, including hyperemesis gravidarum, ectopic pregnancy, placenta previa, premature rupture of membranes, amniotic fluid embolism, fetal distress, and so on. Pregnancy comorbidities refer to the diseases existing before pregnancy or occurred during pregnancy due to non-pregnancy causes, which include combined heart disease, combined hematological disease, combined respiratory disease, combined gastrointestinal disease, combined urological disease, combined endocrine disease, combined infectious disease and combined tumor. Hypertensive disorders of pregnancy is a group of diseases in which pregnancy coexist with elevated blood pressure, including gestational hypertension, preeclampsia, eclampsia, chronic hypertension with superimposed preeclampsia as well as chronic hypertension in pregnancy, which seriously affects maternal and infant health.

Cases with no communication disorder (including impairments in social cognition, the ability to recognize others' emotions and infer others' thoughts, which can have profound negative effects on communication functions[18]), local residence time more than one year and detailed address were collected. And those cases of assisted conception, non-spontaneous abortion and spontaneous abortion caused by genetic problems were excluded.

Approval to conduct this study was obtained from Medical ethics committee of Medical School of Yan'an University (NO.2018051).Informed consent was provided by all participants at enrollment. All of the methods were performed in accordance with the relevant guidelines and regulations. And in line with Declaration of Helsinki.

Exposure assessment of atmospheric pollutants
The air quality monitoring stations in the urban area of Baoji City are mainly distributed in the east-west downtown area along the Weihe River (Fig. 1).The daily average concentrations of five conventional air pollutants $PM_{2.5}$, PM_{10}, SO_2, NO_2 and O_3 in Baoji City from 2017 to 2019 were collected and sorted out (except that O_3 is an 8-hour moving average, the other four pollutants are 24-hour moving average).Taking the first trimester as the exposure window, the outdoor air pollutant exposure value of each pregnant woman during pregnancy was calculated. The global average method and the nearest monitoring station method were used to evaluate the exposure level of each pregnant woman in the first trimester. The global average method does not consider the distance between the maternal address and the monitoring site, adding the pollutant data during exposure window of all monitoring sites to calculate the mean value. The nearest monitoring station method bases on the address of the pregnant woman's place of residence during pregnancy, and then the latitude and longitude of her place of residence were obtained from Gaode Map. The distance from the latitude and longitude of the place of residence to the latitude and longitude of the monitoring station was calculated, and the pollutant mass concentration of the nearest monitoring station to the place of residence was selected as the individual's exposure mass concentration. After dividing exposure window according to the date of the last menstrual period of pregnant women, the mass concentration of pollutants in exposure window was calculated.

Statistical method
The case-control method of group design was used to analyze the risk factors of gravidity, parity, previous caesarean section, occupation, season of last mentruation, menstrual cycle, pregnancy complications, pregnancy comorbidities and hypertensive disorders of pregnancy by chi-square test. Excel was used for data collation, and IBM SPSS20 was used for data analysis. We performed the pollutant data for normality with K-S test, if the data met the normal distribution, the mean and standard deviation were used to describe, and difference within the group was tested by the t-test. If not, the median and upper and lower quartiles were chosen to describe the data, and difference between groups was judged using Mann-Whitney test. The difference of pollutant concentration between the case group and the control group in the exposure window was compared. The conditional logistic model was used to analyze each pollutant, and the OR value and its 95% confidence interval (95% CI) were used to represent the correlation strength between each pollutant and spontaneous abortion. Then the relevant risk factors were introduced to establish the model, and the data of each pollutant were substituted into the model to explore the relationship between each pollutant in the first trimester and spontaneous abortion.

Result
Maternal information
During the study period we collected 154 cases of spontaneous abortion and 616 cases of full-term birth in the control group, with a total of 770 cases, ranging from 19 to 44 years old. Table 1 reports the comparison between the main democrophic and clinical data of cases and controls. It was concluded that the differences in parity, previous caesarean section, occupation, last menstrual season, pregnancy complications, pregnancy comorbidities between the spontaneous abortion group and the full-term delivery group were significantly

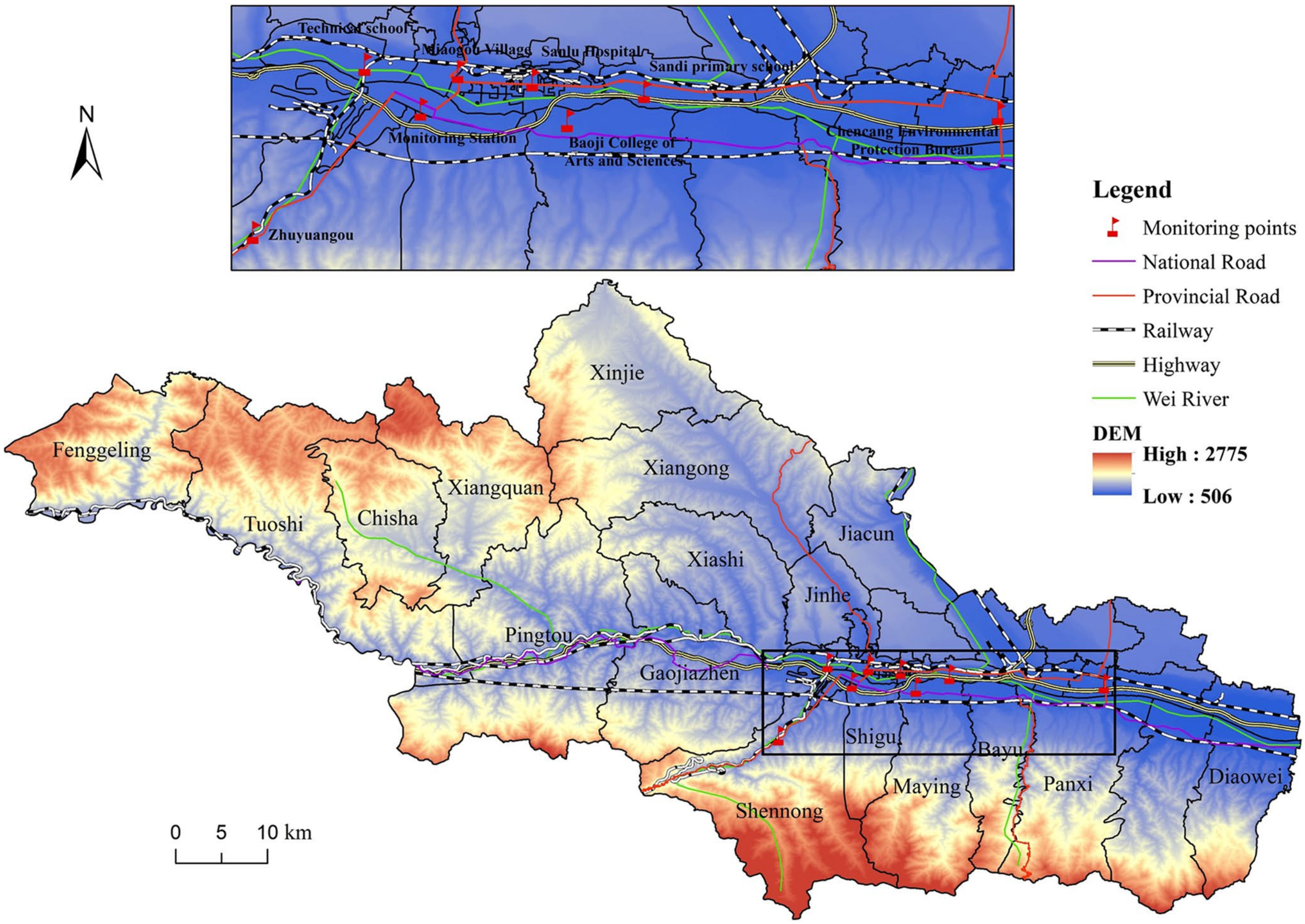

Figure 1. Distribution of air quality monitoring stations and topographic map of Baoji.

different between cases and controls ($P < 0.05$). These factors will be included in the model as risk factors. There was no significant difference in gravidity, menstrual cycle and hypertensive disorders of pregnancy between the two groups. It can also be found that people who are pregnant in spring and winter have a higher incidence of spontaneous abortion than those in summer and autumn (Table 1).

Atmospheric pollutant data

The daily average concentrations of outdoor $PM_{2.5}$, PM_{10}, SO_2, NO_2 and O_3 in Baoji City from 2017 to 2019 were collected and sorted out. It can be seen that the concentrations of these five pollutants in Baoji City showed obvious seasonal changes (Fig. 2). In terms of annual unit, the concentrations of $PM_{2.5}$, PM_{10}, SO_2 and NO_2 in Baoji City showed a trend of decreasing first and then increasing. The concentration of pollutants was higher in spring and winter, but lower in summer and autumn. The change of O_3 concentration is opposite, showing a trend of increasing first and then decreasing. The concentration is higher in spring and summer, with the highest value, and relatively low in autumn and winter.

Analysis results of global average method

The K-S test indicated that the data did not fit to the normal distribution, so the median and upper and lower quartiles were used to describe the contaminant data. We chose the rank sum test to judge the variability. The data were organized in Table 2: There was no significant difference in the exposure doses of the five pollutants between the groups ($P > 0.05$), and the median exposure doses of $PM_{2.5}$ and NO_2 in the case group(48.74ug/m^3,37.06ug/m^3) were higher than those in the control group(47.22ug/m^3,36.83ug/m^3).

Logistic regression analysis showed that (Table 3), before adjustment, $PM_{2.5}$ (OR = 1.016,95% CI = 1.005 ~ 1.027) and SO_2 (OR = 1.164,95% CI = 1.096 ~ 1.236) were statistically significant. In analyses after combining other risk factors, exposure to $PM_{2.5}$ (OR = 1.156,95% CI = 1.074 ~ 1.254), SO_2 (OR = 1.432,95% CI = 1.209 ~ 1.695) and NO_2 (OR = 1.121,95% CI = 1.004 ~ 1.204) in the first trimester was associated with the occurrence of spontaneous abortion, while PM_{10} ($P > 0.05$) and O_3 (OR = 0.93) were not significantly correlated.

Analysis results of nearest monitoring station method

The K-S test indicated that the data did not fit to the normal distribution, so the median and upper and lower quartiles were used to describe the contaminant data. We used the rank sum test to judge the variability. As shown

Sample characteristics		Spontaneous abortion ($N=154$) N(P)	Full-term birth ($N=616$) N(P)	χ^2	*P*
Age	<20	1(0.6)	4(0.6)	——	——
	20–29	70(45.4)	280(45.4)		
	30–39	74(48.0)	296(48.0)		
	40-	9(5.8)	36(5.8)		
Gravidity	1	34(22.7)	175(28.4)	2.005	0.157
	>1	116(77.3)	441(71.6)		
Parity	≤1	143(95.3)	276(44.8)	124.286	<0.001
	>1	7(4.7)	340(55.2)		
Previous caesarean section	≤1	148(98.7)	455(74.0)	42.547	<0.001
	>1	2(1.3)	160(26.0)		
Occupation	National Civil Servants	1(0.7)	54(8.9)	48.223	<0.001
	Professional and technical staff	14(9.3)	87(14.3)		
	Business and Services	22(14.6)	72(11.8)		
	Agriculture	22(14.6)	149(24.4)		
	Production and transport	2(1.3)	32(5.2)		
	Other special occupations	54(35.8)	141(23.1)		
	Unemployed	36(23.8)	75(12.3)		
Season of last menstruation	Spring	42(27.3)	271(44.0)	198.654	<0.001
	Summer	32(20.8)	2(0.3)		
	Autumn	31(20.1)	2(0.3)		
	Winter	49(31.8)	341(55.4)		
Menstrual cycle	Regularity	152(98.7)	607(98.7)	0	1.000
	Irregular	2(1.3)	8(1.3)		
Pregnancy complications	yes	43(33.1)	527(85.6)	163.976	<0.001
	no	87(66.9)	89(14.4)		
Pregnancy comorbidities	yes	61(49.2)	450(73.2)	27.809	<0.001
	no	63(50.8)	165(26.8)		
Hypertensive disorders of pregnancy	yes	1(0.9)	32(5.2)	2.878	0.090
	no	105(99.1)	579(94.8)		

Table 1. Comparison of demographic and clinical data of cases and controls (numbers and percentages in brakets).

in Table 4: There were significant differences in the exposure levels of NO_2($P=0.01<0.05$)and O_3($P=0.02<0.05$) between the case group and the control group. The median of PM_{10} and O_3 exposure concentration in the full-term group (105.08ug/m^3,101.16ug/m^3) was higher than that in the spontaneous abortion group (103.90ug/m^3,96.49ug/m^3),and the median of $PM_{2.5}$, SO_2 andNO_2 exposure doses in the case group (46.85ug/m^3,7.44ug/m^3,36.40ug/m^3)were higher than those in the control group(46.82ug/m^3,7.42ug/m^3,34.50ug/m^3).

Analysis concluded (Table 5), before adjustment, exposure to $PM_{2.5}$ (OR = 1.013, 95% CI = 1.004–1.022), SO_2 (OR = 1.117, 95% CI = 1.073–1.162) and NO_2 (OR = 1.056, 95% CI = 1.030–1.082) in the first trimester was associated with the occurrence of spontaneous abortion. After adjusting the relevant risk factors, It indicate that pregnant women exposure to $PM_{2.5}$ (OR = 1.036,95% CI = 1.009 ~ 1.064), SO_2 (OR = 1.429,95% CI = 1.189 ~ 1.718) and NO_2 (OR = 1.159,95% CI = 1.074 ~ 1.251) during first trimester may increase the risk of spontaneous abortion, while PM_{10} ($P>0.05$) and O_3 (OR = 0.924) did not show significant correlation.

Discussion

This study is a retrospective case-control study. Through the analysis of maternal data and five air pollutants in Baoji City from 2017 to 2019, it was found that parity, previous caesarean section, occupation, last menstrual season, pregnancy complications and pregnancy comorbidities were listed as other risk factors ($P<0.05$). Other studies have similar findings. As demonstrated by Magnus MC et al., the risk of miscarriage varies greatly with maternal age[19]. Moradinazar, M. et al. found that age and diabetes can increase the miscarriage rate in pregnant women[20].

Although existing studies have shown the relationship between air pollution and spontaneous abortion[21], studies in different regions have shown inconsistent results due to differences in research methods and research sites[22].In this study, the two exposure evaluation methods showed that the exposure of atmospheric pollutants $PM_{2.5}$, SO_2 and NO_2 in the first trimester had an effect on the occurrence of spontaneous abortion, but there was no significant correlation between spontaneous abortion and PM_{10} or O_3. A case-control study in China found that exposure to NO_2 during first trimester was associated with increased risk of spontaneous abortion[23],

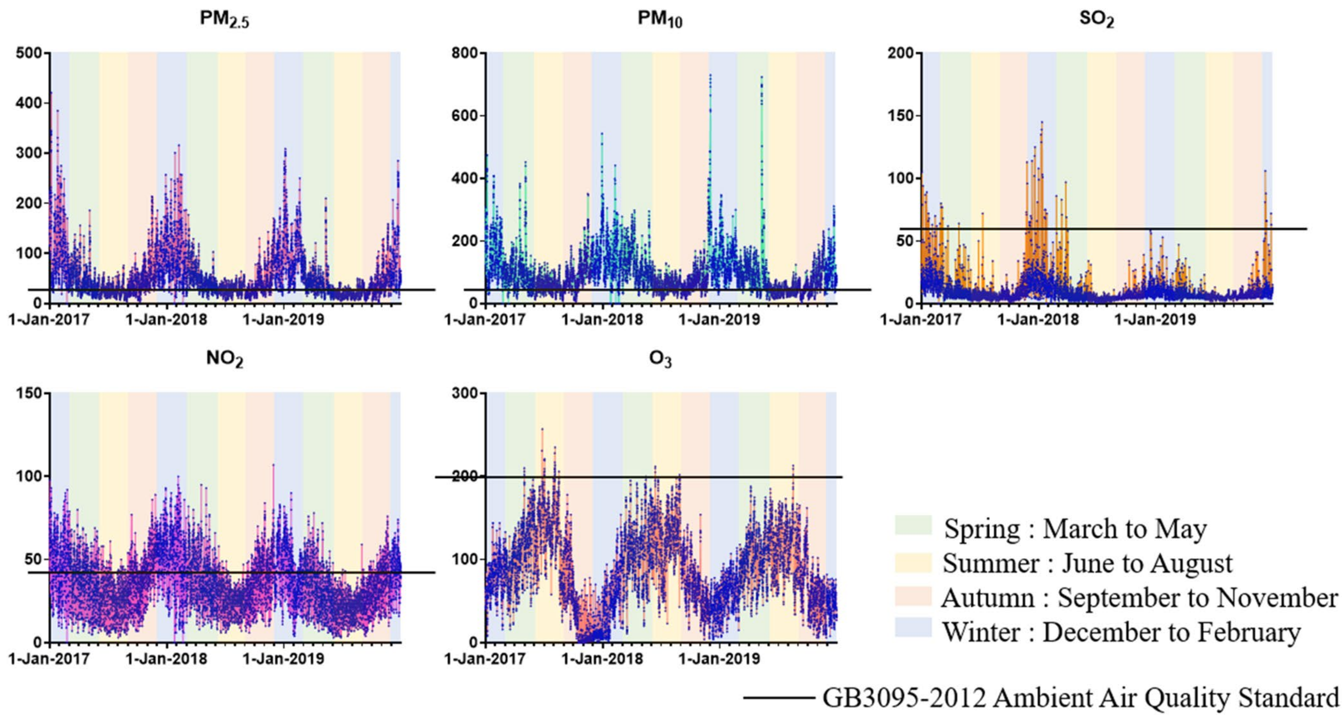

Figure 2. The daily average concentration changes of five air pollutants in Baoji City from 2017 to 2019. (The x axis represents date and the y axis represents pollutant concentration (ug/m 3)).

Pollutant	Spontaneous abortion			Full-term birth			z	p
	Median	P_{25}	P_{75}	Median	P_{25}	P_{75}		
$PM_{2.5}$	48.74	30.36	76.87	47.22	39.92	57.88	-0.75	0.46
PM_{10}	102.36	67.71	131.39	106.52	97.92	113.56	-1.18	0.24
SO_2	7.51	5.34	11.02	7.62	7.41	8.19	-1.35	0.18
NO_2	37.06	28.60	44.89	36.83	35.01	38.04	-0.58	0.56
O_3	98.16	59.56	98.16	102.94	93.57	106.81	-1.77	0.08

Table 2. Exposure levels of pollutants during first trimester in the study population (ug/m^3) (Differential testing of contaminant exposure).

Pollutant	Before adjustment			After adjustment		
	P	Exp(B)	95%CI	*P*	Exp(B)	95%CI
$PM_{2.5}$	0.004	1.016	1.005 ~ 1.027	<0.001	1.156	1.074 ~ 1.245
PM_{10}	0.002	0.986	0.977 ~ 0.995	0.523	1.005	0.989 ~ 1.022
SO_2	<0.001	1.164	1.096 ~ 1.236	<0.001	1.432	1.209 ~ 1.695
NO_2	0.177	1.024	0.989 ~ 1.059	0.020	1.121	1.004 ~ 1.204
O_3	<0.001	0.961	0.950 ~ 0.972	<0.001	0.930	0.897 ~ 0.963

Table 3. Logistic regression analysis of risk factors related to first trimester pollutants (associations between pollutants and spontaneous abortion). Adjustment factors: parity, previous caesarean section, occupation, last menstrual season, pregnancy complications, pregnancy comorbidities.

which is similar to the results of this study. Nevertheless, as a result of the selection of exposure window period, research methods and regional differences, a study in Mongolia shows that seasonal environmental air pollution is closely related to spontaneous abortion in Mongolia, which is reflected in the strong dose-response correlation of SO_2, $PM_{2.5}$, PM_{10} and NO_2, but the correlation of O_3 has not been studied[24].Also a study in Chongqing showed that high levels of exposure to $PM_{2.5}$, PM_{10}, NO_2 and SO_2 during pregnancy increased the risk of spontaneous abortion[25]. The difference is that this study did not find the correlation between PM_{10} and spontaneous abortion.

Pollutant	Spontaneous abortion			Full-term birth			z	*P*
	Median	P_{25}	P_{75}	Median	P_{25}	P_{75}		
$PM_{2.5}$	46.85	30.44	78.26	46.82	39.45	58.51	-0.54	0.59
PM_{10}	103.90	67.82	132.46	105.08	97,17	112.32	-0.42	0.67
SO_2	7.44	5.38	10.67	7.42	7.16	7.89	-0.37	0.71
NO_2	36.40	28.90	44.72	34.50	32.63	35.70	-2.80	0.01
O_3	96.49	58.99	112.93	101.16	92.90	107.00	-2.04	0.02

Table 4. Exposure levels of pollutants during first trimester in the study population (ug/m^3) (Differential testing of contaminant exposure)

Pollutant	Before adjustment			After adjustment		
	P	Exp(B)	95%CI	*P*	Exp(B)	95%CI
$PM_{2.5}$	0.004	1.013	1.004 ~ 1.022	0.008	1.036	1.009 ~ 1.064
PM_{10}	0.067	0.933	0.985 ~ 1.001	0.812	1.002	0.985 ~ 1.019
SO_2	<0.001	1.117	1.073 ~ 1.162	<0.001	1.429	1.189 ~ 1.718
NO_2	<0.001	1.056	1.030 ~ 1.082	<0.001	1.159	1.074 ~ 1.251
O_3	<0.001	0.978	0.973 ~ 0.983	<0.001	0.924	0.893 ~ 0.957

Table 5. Logistic regression analysis of risk factors related to first trimester (associations between pollutants and spontaneous abortion). Adjustment factors: parity, previous caesarean section, occupation, last menstrual season, pregnancy complications, pregnancy comorbidities.

Other researchers have found that exposure to SO_2 and PM_{10} during pregnancy in Ahwas, Iran, is significantly directly related to the occurrence of spontaneous abortion[26], which is different from the results of this study.

Through the analysis of pollutants from 2017 to 2019 (Fig. 2), it is concluded that the concentrations of $PM_{2.5}$, SO_2 and NO_2 are higher in spring and winter and the analysis of maternal data found that the incidence of spontaneous abortion in spring and winter is also relatively high, which could be a good evidence of the association between $PM_{2.5}$, SO_2, NO_2 and spontaneous abortion. Further comparison of the maternal pollutant exposure data estimated by global average method and the nearest monitoring station method (Tables 2 and 4) found that there was difference. Obviously, the first trimester pollutant exposure values are different between the two methods. Contaminants in the case group with a median exposure higher than that in the control group may increase the risk of spontaneous abortion in the first trimester: $PM_{2.5}$, NO_2 in the global average method and $PM_{2.5}$, SO_2, NO_2 in the nearest monitoring station method. What's more, there was no significant difference in the exposure level of any pollutant in the global average method, but a significant difference in the exposure level of NO_2 ($P = 0.01 < 0.05$) and O_3 ($P = 0.02 < 0.05$) in the nearest monitoring station method. The reason for this difference still needs further study, probably because the data obtained by the global average method are susceptible to extreme values, while the nearest monitoring station method does not take into account the influence of space when the pregnant women are out or at work.

As for the mechanism of air pollution on spontaneous abortion, Xu Q et al. proposed that air pollution exposure affects spontaneous abortion by affecting pregnancy hormones[27].Some pointed out that contamants affect embryo normality by affecting oxidative stress[28].Others considered that exposure to ambient air pollution leads to abnormal placental development that leads to adverse pregnancy outcomes[29].Studies have also found that air pollution may lead to spontaneous abortion by affecting the methylation level of the IGF2BP1 promoter[30] and $PM_{2.5}$ may cause spontaneous abortion by causing inflammation in women[31].

This study also has shortcomings: First of all, not taking into account the exposure of air pollutants in the indoor environment of pregnant women. Secondly, only one exposure window in the first trimester was explored and the sample size was relatively small, which made the research results less supported by some data. In addition, contaminant data derived from the global average method and the nearest monitoring station method used the same analysis method, and the retrospective nature of the study does not allow to distinguish between association and causal relationship. Subsequently, different methods can be used to analyze the data. Inverse distance weighting method, land regression utilization model and linear diffusion model can also be used to evaluate pollutant exposure concentration.

Data availability

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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References

1. Andersen, Z. J., Vicedo-Cabrera, A. M., Hoffmann, B. & Melén, E. Climate change and respiratory disease: clinical guidance for healthcare professionals. *Breathe (Sheff)*. **19** (2), 220222. https://doi.org/10.1183/20734735.0222-2022 (2023).
2. Zhang, W. et al. Short-term effects of air pollution on hospitalization for acute lower respiratory infections in children: a time-series analysis study from Lanzhou, China. *BMC Public. Health*. **23** (1), 1629. https://doi.org/10.1186/s12889-023-16533-7 (2023). Published 2023 Aug 25.
3. Wang, K. et al. Incident risk and burden of cardiovascular diseases attributable to long-term NO2 exposure in Chinese adults [published online ahead of print, 2023 Jun 23]. *Environ. Int.* **178**, 108060. https://doi.org/10.1016/j.envint.2023.108060 (2023).
4. Henning, R. J. Particulate matter air pollution is a significant risk factor for cardiovascular disease [published online ahead of print, 2023 Sep 19]. *Curr. Probl. Cardiol.* 102094. https://doi.org/10.1016/j.cpcardiol.2023.102094 (2023).
5. Vignal, C., Guilloteau, E., Gower-Rousseau, C. & Body-Malapel, M. Review article: epidemiological and animal evidence for the role of air pollution in intestinal diseases. *Sci. Total Environ.* **757**, 143718. https://doi.org/10.1016/j.scitotenv.2020.143718 (2021).
6. Lin, L. Z., Chen, J. H., Yu, Y. J. & Dong, G. H. Ambient air pollution and infant health: a narrative review. *EBioMedicine*. **93**, 104609. https://doi.org/10.1016/j.ebiom.2023.104609 (2023).
7. Qian, Z. et al. Ambient Air Pollution and Adverse Pregnancy Outcomes in Wuhan, China. *Res. Rep. Health Eff. Inst.* **189**, 1–65 (2016).
8. Grippo, A. et al. Air pollution exposure during pregnancy and spontaneous abortion and stillbirth. *Rev. Environ. Health*. **33** (3), 247–264. https://doi.org/10.1515/reveh-2017-0033 (2018).
9. Kong, B. Ma,D,Duan,T.Obstetrics and gynecology. 36 (People's medical publishing house,2024).ISBN: 978-7-117-36436-2.
10. Kong, B. Ma,D,Duan,T.Obstetrics and gynecology. 75 (People's medical publishing house,2024).ISBN: 978-7-117-36436-2.
11. Kwesiga, D. et al. Psychosocial effects of adverse pregnancy outcomes and their influence on reporting pregnancy loss during surveys and surveillance: narratives from Uganda. *BMC Public. Health*. **23** (1), 1581. https://doi.org/10.1186/s12889-023-16519-5 (2023). Published 2023 Aug 18.
12. Zhang, M. et al. Development and validation of a visualized prediction model for early miscarriage risk in patients undergoing IVF/ICSI procedures: a real-world multi-center study. *Front. Endocrinol. (Lausanne)*. **14**, 1280145. https://doi.org/10.3389/fendo.2023.1280145 (2024). Published 2024 Feb 14.
13. Saavedra-Avendano, B., Schiavon, R. & Darney, B. G. Relationship between abortion at first pregnancy and live births by Young Adulthood: a Population-based study among Mexican Women. *J. Pediatr. Adolesc. Gynecol.* **34** (4), 552–557. https://doi.org/10.1016/j.jpag.2021.01.007 (2021).
14. Shahid, M., Quinlivan, J. A., Peek, M., Castaño-Rodríguez, N. & Mendz, G. L. Is there an association between the vaginal microbiome and first trimester miscarriage? A prospective observational study. *J. Obstet. Gynaecol. Res.* **48** (1), 119–128. https://doi.org/10.1111/jog.15086 (2022).
15. Nyadanu, S. D. et al. Prenatal exposure to ambient air pollution and adverse birth outcomes: an umbrella review of 36 systematic reviews and meta-analyses. *Environ. Pollut*. **306**, 119465. https://doi.org/10.1016/j.envpol.2022.119465 (2022).
16. Daumová, M., Hadravská, Š. & Putzová, M. Spontaneous abortion in the first trimester of pregnancy. Spontánní Potrat v prvním trimestru gravidity. *Cesk. Patol.* **59** (2), 60–63 (2023).
17. Kong, B. Ma,D,Duan,T.Obstetrics and gynecology.49 (People's medical publishing house,2024).ISBN: 978-7-117-36436-2.
18. Togher, L. et al. INCOG 2.0 guidelines for Cognitive Rehabilitation following traumatic Brain Injury, Part IV: cognitive-communication and Social Cognition disorders. *J. Head Trauma Rehabil.* **38** (1), 65–82. https://doi.org/10.1097/HTR.0000000000000835 (2023).
19. Magnus, M. C., Wilcox, A. J., Morken, N. H., Weinberg, C. R. & Håberg, S. E. Role of maternal age and pregnancy history in risk of miscarriage: prospective register based study. *BMJ*. **364**, l869. https://doi.org/10.1136/bmj.l869 (2019). PMID: 30894356; PMCID: PMC6425455.
20. Moradinazar, M. et al. Lifetime Prevalence of Abortion and Risk Factors in Women: Evidence from a Cohort Study. *J Pregnancy* 4871494. https://doi.org/10.1155/2020/4871494 (2020).
21. Zhu, W. et al. The correlation between chronic exposure to particulate matter and spontaneous abortion: a meta-analysis. *Chemosphere*. **286** (Pt 2), 131802. https://doi.org/10.1016/j.chemosphere.2021.131802 (2022).
22. Wang, J., Han, J., Li, T., Wu, T. & Fang, C. Impact analysis of meteorological variables on PM2.5 pollution in the most polluted cities in China. *Heliyon*. **9** (7), e17609. https://doi.org/10.1016/j.heliyon.2023.e17609 (2023). Published 2023 Jun 24.
23. Wang, B. et al. Nitrogen dioxide exposure during pregnancy and risk of spontaneous abortion: a case-control study in China. *J. Maternal-Fetal Neonatal Med.***35** (19), 3700–3706. https://doi.org/10.1080/14767058.2020.1837772 (2020).
24. Enkhmaa, D. et al. Seasonal ambient air pollution correlates strongly with spontaneous abortion in Mongolia. *BMC Pregnancy Childbirth.* **14**, 146. https://doi.org/10.1186/1471-2393-14-146 (2014) (Published 2014 Apr 23).
25. Zhou, W., Ming, X., Chen, Q., Liu, X. & Yin, P. The acute effect and lag effect analysis between exposures to ambient air pollutants and spontaneous abortion: a case-crossover study in China, 2017–2019. *Environ. Sci. Pollut Res. Int.* **29** (44), 67380–67389. https://doi.org/10.1007/s11356-022-20379-8 (2022).
26. Dastoorpoor, M. et al. Prenatal exposure to ambient air pollution and adverse pregnancy outcomes in Ahvaz, Iran: a generalized additive model [published correction appears in Int Arch Occup Environ Health. 2022;95(8):1805]. *Int. Arch. Occup. Environ. Health*. **94** (2), 309–324. https://doi.org/10.1007/s00420-020-01577-8 (2021).
27. Xu, Q. et al. Effect of short-term ambient air pollution exposure on early miscarriage and pregnancy hormones with critical window identification. *J. Hazard. Mater.* **460**, 132328. https://doi.org/10.1016/j.jhazmat.2023.132328 (2023).
28. Aitken, R. J. Impact of oxidative stress on male and female germ cells: implications for fertility. Reproduction, 159(4), R189-R201. Retrieved Sep 7, 2024, from (2020). https://doi.org/10.1530/REP-19-0452.
29. Tosevska, A. et al. Integrated analysis of an in vivo model of intra-nasal exposure to instilled air pollutants reveals cell-type specific responses in the placenta. *Sci. Rep.* **12** (1), 8438. https://doi.org/10.1038/s41598-022-12340-z (2022).
30. Zhu, W. et al. Integrated single-cell RNA-seq and DNA methylation reveal the effects of air pollution in patients with recurrent spontaneous abortion. *Clin Epigenetics.* **14**(1), 105. https://doi.org/10.1186/s13148-022-01327-2 (2022) (Published 2022 Aug 23).
31. Zhang, B. et al. Ambient $PM_{2.5}$ exposures and systemic inflammation in women with first trimester. *Sci. Total Environ.* **829**, 154564. https://doi.org/10.1016/j.scitotenv.2022.154564 (2022).

Author contributions

Meiying Cao collected, analyzed, and visualized the data, and wrote and reviewed the paper. Ying Kang collected, analyzed and visualized the data. Jimin Li guided us in the data analysis process. Jiajia Gu and Lang Liu collected and organized the data. Jinwei He, Jing wang provided direction and methodology, modified and approved the submitted version.

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Declarations

Competing interests
The authors declare no competing interests.

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