BMJ Open

Ambient air pollutants in the first trimester of pregnancy and birth defects: an observational study

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To cite: Cheng Y, Yin J, Yang L, *et al*. Ambient air pollutants in the first trimester of pregnancy and birth defects: an observational study. *BMJ Open* 2023;**13**:e063712. doi:10.1136/bmjopen-2022-063712

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-063712).

Received 11 April 2022
Accepted 03 March 2023

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ABSTRACT

Objectives As current studies on the relationships between air pollutants exposure during the first trimester and birth defects were not fully elucidated, this study aimed to assess the association between selected air pollutants and birth defects.

Design An observational study.

Participants We obtained 70 854 singletons with gestational age <20 weeks who were delivered at a large maternal and child healthcare centre in Wuhan, China.

Outcome measures Birth defects data and daily average concentration of ambient particulate matter ≤10 μm diameter (PM_{10}), PM ≤2.5 μm diameter ($PM_{2.5}$), sulfur dioxide (SO_2) and nitrogen dioxide (NO_2) were obtained. Logistic regression analysis was applied to assess the association between maternal air pollutants exposure during first trimester and total birth defects, congenital heart defects (CHDs), limb defects and orofacial clefts with adjustments of potential covariates.

Results There were a total of 1352 birth defect cases included in this study, with a prevalence of 19.08‰. Maternal exposed to high concentrations of PM_{10}, $PM_{2.5}$, NO_2 and SO_2 in the first trimester were significantly associated with elevated ORs of birth defects (ORs ranged from 1.13 to 1.23). Additionally, for male fetuses, maternal exposed to high $PM_{2.5}$ concentration was associated with an elevated odd of CHDs (OR 1.27, 95% CI 1.06 to 1.52). In the cold season, the ORs of birth defects were significantly increased among women exposed to $PM_{2.5}$ (OR 1.64, 95% CI 1.41 to 1.91), NO_2 (OR 1.22, 95% CI 1.08 to 1.38) and SO_2 (OR 1.26, 95% CI 1.07 to 1.47).

Conclusions This study showed unfavourable effects of air pollutants exposure during the first trimester on birth defects. Especially, the association between maternal $PM_{2.5}$ exposure and CHDs was only observed among male fetuses, and stronger effects of $PM_{2.5}$, NO_2 and SO_2 exposure on birth defects were observed in the cold season.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study explored the associations between maternal air pollutants exposure during first trimester and fetal outcomes classified by total birth defects, heart defecs, limb defects and orofacial clefts based on a large population.
- ⇒ The stratification analysis by neonatal sex and season of conception indicated the specific high-risk population, which provided critical evidence of the air quality control policies.
- ⇒ The selected participants are located in a large tertiary maternal care centre in Wuhan and the representative of this study was undermined.
- ⇒ Maternal air pollutants exposure indoor or in other living residents including work, dining and shopping were not included, and other covariates including health behaviours and genetic factors were failed to obtain.

INTRODUCTION

Birth defects are structural or functional abnormalities occurred during embryonic development, most of them forming in the first trimester of pregnancy.[1] Birth defects are the leading cause of fetal death and are associated with the elevated risk of childhood mortality and reduced long-term survival.[2 3]

According to the Institute for Health Metrics and Evaluation, the prevalence of congenital birth defects increased from 6.08% in 2005 to 6.29% in 2019.[4] Although the upward trends were reported in severe congenital heart defects (CHDs), single ventricle, atrioventricular septal defects and tetralogy of Fallot in Europe during 1980–2012, the prevalence of birth defects is much lower (1.0‰–4.1‰).[5] In China, the overall prevalence of birth defects increased from 12.83‰ in 1986 to 15.70‰ in 2014.[6] There is a necessity to explore the potential hazard factors contributed to the high prevalence of birth defects in China based on current knowledge.

Due to rapid urbanisation, China has experienced severe air pollution in recent years. The Report on China's implementation of the Millennium Development Goals (2000–2015) documented that particulate matter ≤10 μm diameter (PM_{10}), sulfur dioxide (SO_2) and nitrogen dioxide (NO_2) were major air pollutants in urban areas.[7] Moreover, ambient PM ≤2.5 μm diameter ($PM_{2.5}$), produced by coal combustion, industry sources and vehicular emissions, is also one of the main air pollutants of industrialisation.[8] The expanding coverage of ambient air pollutants surveillance has contributed to adverse pregnancy outcomes including small for gestational age, low birth weight, preterm birth, spontaneous abortion and stillbirth in recent years.[9–11] Moreover, there is a growing interest in the associations between ambient air pollutants and birth defects, but the results of previous studies are controversial. Most studies reported that ambient air pollutants were associated with increased risks of birth defects.[12–14] However, Parkes *et al* and Dolk *et al* pointed out that high concentrations of PM_{10} and NO_2 exposure were not related to birth defects.[15 16] A recent meta-analysis conducted by Ma *et al* even reported a protective effect of SO_2 on atrial septal defects.[17] These inconsistent results indicate that the effects of ambient air pollutants on birth defects could be varied by culture, ethnicity or geographical distribution. More evidence is needed to clarify the risk of birth defects derived from air pollutants during the rapid social-economical development worldwide.

As current studies on the relationships between air pollutants and birth defects were not fully elucidated, this study aimed to assess the association between selected air pollutants and birth defects. Furthermore, the first trimester of pregnancy is vital for fetal development because fetal major organs and systems are formed at this stage and the fetus is most susceptible to environmental hazards. As a result, we mainly focused on the associations between maternal exposure to air pollutants including PM_{10}, $PM_{2.5}$, SO_2 and NO_2 during the first trimester and birth defects in Wuhan, China.

METHODS

Patient and public involvement

Patients or the public were not involved in any part of the design, conduct, reporting or dissemination plans of this study.

Study design, site and population

This observational study was conducted in Wuhan city. Wuhan is the capital city of Hubei Province and a megacity in Central China. Its geographical location is 29° 58′ - 31° 22′ N and 113° 41′ - 115° 05′ E. The permanent resident population of Wuhan was over 10 million. Wuhan has four distinct seasons of hot summer and cold winter, with an annual average temperature of 15.8°C–17.5°C.[18]

There were a total of 130 186 perinatal women with detailed home addresses who delivered at the Maternal and Child Health Hospital of Hubei Province, and 98 877 of them lived in Wuhan City during the first trimester of pregnancy. Then we obtained 74 336 participants with distances less than 10 km from home to the nearest air surveillance station. After removing 3333 mothers of multiple pregnancies and 149 with gestational age <20 weeks, 70 854 participants were finally included in this study.

Birth defects

Birth defect cases with gestational age ≥20 weeks and 0–7 days after birth including elective termination of pregnancy. Based on the requirements of the Maternal and Child Health Monitoring Manual in China and the Implementation of National Hospital Birth Defects Surveillance of China, 23 types of common birth defects were categorised according to the 10th Revision of the International Classification of Diseases (Q00–Q99). The top three birth defects including CHDs (Q20–Q28), limb defects (Q69–Q72) and orofacial clefts (Q35–Q37) were further examined by trained obstetricians, paediatricians or paediatric cardiologists based on clinical observation, physical examination, biochemical index and image examination results. Strict quality control of the reported data was performed by the assigned county-level inspector every quarter year and further checked by the city-level inspector semiannually. Detailed descriptions of the 23 types of birth defects were provided in online supplemental table 1.

Exposure assessment

Data on the daily concentrations of air pollutants (PM_{10}, $PM_{2.5}$, NO_2 and SO_2) and the geographical locations (longitude and latitude) of the air surveillance stations were obtained from China's National Urban Air Quality Real-time Publishing Platform (https://air.cnemc.cn:18014/). Moreover, the geographical location data were converted from the detailed home address of participants by Baidu Map. The distance from each home address of participants to all of the air surveillance stations was calculated. Then the individual daily air pollutants data were obtained according to the nearest surveillance station from home, and we only keep participants who lived within 10 km from the nearest surveillance station, which was confirmed by other studies.[15 19] The median distance from home to the nearest station was 3.50 km in this study. Participants' average air pollutants exposure during the first trimester of pregnancy was estimated by mean levels of daily concentrations.

Statistical analysis

Observed outcomes were classified as total birth defects, CHDs, limb defects and orofacial clefts. Maternal exposure variables including PM_{10}, $PM_{2.5}$, NO_2 and SO_2 were divided by IQR based on the daily average concentration during the first trimester. Covariates including the year of conception (2013–2018), maternal age (<25, 25–29, 30–34 and >34 years), gravidity (1, 2–3 and >3) and urban/rural were obtained. Moreover, other covariates including per capita of cars, unemployment, per capita area of roads, per capita of medication beds were retrieved from the official website of Wuhan Bureau of Statistics (http://tjj.wuhan.gov.cn/). Logistic regression analysis was applied to assess the association between maternal air pollutants exposure during first trimester and birth defects adjusted for potential covariates. Stratified analyses by neonatal sex (male and female fetus) and season of conception by

Table 1 Prevalence of birth defects among the subgroups of enrolled participants in Wuhan, China

Variables	Birth defect cases	Total cases	Prevalence (%)
Year of conception			
2013	272	12 856	21.16
2014	203	11 236	18.07
2015	174	11 274	15.43
2016	227	12 261	18.51
2017	226	12 844	17.60
2018	250	10 383	24.08
Season of conception			
Spring	321	18 312	17.53
Summer	295	18 853	15.65
Autumn	287	17 045	16.84
Winter	449	16 644	26.98
Age (years)			
<25	122	4341	28.10
25–29	632	34 412	18.37
30–34	401	23 783	16.86
>34	197	8318	23.68
Gravidity			
1	604	35 590	16.97
2–3	372	19 552	19.03
>3	376	15 712	23.93
Neonatal sex			
Male	771	37 488	20.57
Female	560	33 337	16.80
Total	1352	70 854	19.08

last menstrual period (March to August and September to February) were applied to further explore the associations between air pollutants exposure in the first trimester of pregnancy and birth defects. The adjusted OR and 95% CI were provided in each model. Statistical analyses were performed by using SAS V.9.4 (SAS Institute).

RESULTS

There were a total of 1352 birth defect cases among 70 854 singletons, with a prevalence of 19.08‰ (table 1). The prevalence of birth defects increased from 21.16‰ in 2013 to 24.08‰ in 2018. Subpopulations who conceived in winter (26.98‰), aged <25 years (28.10‰) or with gravidity >3 times (23.93‰) rank the first place among corresponding categories. In addition, the male fetuses had a higher prevalence of birth defects than female fetuses (20.57‰ vs 16.80‰).

Table 2 shows the distributions of daily average ambient air pollutants concentrations in the first trimester among the five groups including non-defects, birth defects, CHDs, limb defects and orofacial clefts. The median exposures of PM_{10}, $PM_{2.5}$, NO_2 and SO_2 during the first trimester were 101.78 µg/m^3, 61.98 µg/m^3, 53.64 µg/m^3 and 13.97 µg/m^3, respectively, among the birth defects groups.

Table 3 presents the associations between ambient air pollutants exposure in the first trimester of pregnancy and birth defects. We also provided the ORs of birth defects in the second and third trimesters, as well as the entire pregnancy in online supplemental tables S2–S4. High concentrate exposure to air pollutants was significantly associated with increased odds of total birth defects, yielding adjusted ORs of 1.13, 1.23, 1.18 and 1.19 for PM_{10}, $PM_{2.5}$, NO_2 and SO_2, respectively. Moreover, similar elevated odds of CHDs were observed for maternal exposure of $PM_{2.5}$ (OR 1.21, 95% CI 1.06 to 1.38), NO_2 (OR 1.13, 95% CI 1.01 to 1.27) and SO_2 (OR 1.24, 95% CI 1.03 to 1.48), but not PM_{10} (1.08, 95% CI 0.95 to 1.24).

For male fetuses, there were significantly increased odds of total birth defects among mothers exposed to PM_{10}, $PM_{2.5}$, NO_2 and SO_2 by interquartile increased concentrations during the first trimester (OR=1.13–1.23). Moreover, a positive association between $PM_{2.5}$ exposure during the first trimester and CHDs was detected (OR 1.27, 95% CI 1.06 to 1.52). For female fetuses, elevated odds of total birth defects (OR=1.14–1.22) were also observed among maternal exposed to heavy concentrated PM_{10}, $PM_{2.5}$, NO_2 and SO_2.

After stratified by season, the results show that the odds of total birth defects were significantly increased among women who conceived in autumn/winter and were exposed to $PM_{2.5}$ (OR 1.64, 95% CI 1.41 to 1.91), NO_2 (OR 1.22, 95% CI 1.08 to 1.38) or SO_2 (OR 1.26, 95% CI 1.07 to 1.47). $PM_{2.5}$, NO_2 and SO_2 were also positively related to CHDs (ORs=1.36–1.84). Elevated hazard of orofacial clefts was observed among women who conceived in the cold season exposed to heavy NO_2 concentrations (OR 1.85, 95% CI 1.16 to 2.93). However, in the warm season, the odd of total birth defects was elevated among women exposed to PM_{10} (OR 1.12, 95% CI 1.00 to 1.24).

DISCUSSION

In the current study, the prevalence of birth defects was close to what was reported in Hunan Province (19.18‰) and higher than that of Jiangsu Province (7.15‰).[20 21] Moreover, this study examined the associations between birth defects and air pollutants exposure in the first trimester, and we further explored the relationships stratified by fetal sex and season of conception.

This study showed that maternal exposure to ambient air pollutants including PM_{10}, $PM_{2.5}$, NO_2 and SO_2 during the first trimester could have higher odds of birth defects, which has been well documented previously. Moreover, we have adopted peak exposure on the thresholds at the 95th percentile to derive the accumulated days of high dose exposure, which further confirmed the positive association between high dose of NO_2 exposure during the

Table 2 Quartile concentrations (μg/m^3) of exposure for ambient air pollutants among birth defects groups in first trimester of pregnancy in Wuhan, China

Air pollutants	Non-defects N=69 502	Birth defects N=1352	CHDs N=265	Limb defects N=210	Orofacial clefts N=119
PM_{10}					
Min	36.86	39.08	49.82	40.76	48.85
25th	80.84	84.05	84.05	85.86	83.98
Median	102.42	101.78	99.46	105.80	96.77
75th	123.86	124.39	120.48	127.34	116.36
Max	231.49	225.91	225.91	220.82	191.37
$PM_{2.5}$					
Min	21.27	21.27	22.77	22.16	22.98
25th	39.37	45.02	44.88	42.63	41.26
Median	59.21	61.98	61.33	63.00	60.98
75th	80.20	80.73	78.81	84.66	77.38
Max	178.20	165.92	154.42	154.79	155.35
NO_2					
Min	9.71	15.22	29.03	25.78	16.89
25th	43.40	45.70	45.49	44.31	44.09
Median	51.49	53.64	53.69	53.43	53.84
75th	59.08	59.98	59.46	62.84	59.99
Max	93.60	93.37	92.93	93.37	87.58
SO_2					
Min	2.93	3.02	3.93	3.77	3.99
25th	9.07	9.36	9.43	10.55	9.46
Median	14.47	13.97	13.77	16.09	12.55
75th	23.54	23.87	23.36	25.23	21.28
Max	71.74	63.36	63.36	62.99	53.75

CHDs, congenital heart defects; NO_2, nitrogen dioxide; PM_{10}, particulate matter ≤10 μm diameter; SO_2, sulfur dioxide.

first trimester and birth defects (online supplemental table 5). A case–control study conducted by Al Noaimi *et al* showed a positive association between $PM_{2.5}$ exposure in the first trimester of pregnancy and birth defects (OR=1.05).[22] Wang *et al* applied Poisson generalised additive models on the time-series data adjusted for temperature, relative humidity, season and time trend, which showed that maternal exposure to PM_{10} and NO_2 in early pregnancy significantly increased the risk of birth defects by 10.3% per 10 μg/m^3 and 3.4% per 10 μg/m^3, respectively.[23]

As was observed among the total participants, the risk of birth defects among both male fetuses and female fetuses was significantly related to PM_{10}, $PM_{2.5}$, NO_2 and SO_2. The underlying mechanisms between air pollutants exposure and the development of birth defects are still unclear. Maternal air pollutants exposures might cause changes in epigenetic signatures and permanent modifications in gene expression.[24] Animal studies showed that maternal exposure to $PM_{2.5}$ during pregnancy leads to spatial memory dysfunction, neurodevelopmental impairment and disturbed cerebral cortex development of mice offspring.[25 26] Another study showed that maternal exposure to a high concentrate of $PM_{2.5}$ during the first trimester of pregnancy could result in the decreased placental expression of *BDNF* and *SYN1*, which may undermine fetal neurodevelopment.[27] Moreover, SO_2 is a systemic toxic agent which can induce chromosomal aberrations, sister chromatid exchanges and micronuclei in mammalian cells.[28]

Except for PM_{10}, this study demonstrated adverse associations of CHDs with $PM_{2.5}$, NO_2 and SO_2 exposure. Previous studies in Taiwan and Northeast England also reported insignificant associations between PM_{10} exposure in the first trimester and CHDs,[29 30] whereas others confirmed the increased risk of CHDs related with PM_{10}.[12 23 31–34] Furthermore, Huang *et al* showed that $PM_{2.5}$ exposure per each interquartile increase during gestational weeks 3–8 was related to an increased risk of CHDs (OR=1.21).[35] Additionally, the positive association between CHDs and maternal exposure to NO_2 and SO_2 was documented by studies conducted by Baldacci

Table 3 Adjusted ORs and 95% CI of ambient air pollutants for each interquartile increase during the first trimester and birth defects in Wuhan, China

	PM_{10}	$PM_{2.5}$	NO_2	SO_2
Birth defects*	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Total				
Birth defects	**1.13** (1.07,1.21)	**1.23** (1.15,1.30)	**1.18** (1.12,1.24)	**1.19** (1.10,1.30)
CHDs	1.08 (0.95,1.24)	**1.21** (1.06,1.38)	**1.13** (1.01,1.27)	**1.24** (1.03,1.48)
Limb defects	1.11 (0.96,1.29)	1.09 (0.93,1.26)	**1.15** (1.01,1.31)	1.16 (0.95,1.43)
Orofacial clefts	0.90 (0.74,1.10)	1.04 (0.85,1.26)	1.10 (0.93,1.31)	0.95 (0.73,1.22)
Male fetus				
Birth defects	**1.13** (1.04,1.22)	**1.23** (1.14,1.34)	**1.18** (1.10,1.26)	**1.19** (1.07,1.33)
CHDs	1.16 (0.96,1.40)	**1.27** (1.06,1.52)	1.11 (0.95,1.30)	1.18 (0.93,1.50)
Limb defects	1.10 (0.91,1.33)	1.08 (0.90,1.30)	1.15 (0.98,1.35)	1.14 (0.89,1.47)
Orofacial clefts	0.86 (0.66,1.12)	1.09 (0.85,1.41)	1.07 (0.86,1.34)	0.99 (0.71,1.37)
Female fetus				
Birth defects	**1.14** (1.04,1.25)	**1.22** (1.12,1.34)	**1.19** (1.10,1.29)	**1.21** (1.07,1.37)
CHDs	0.99 (0.82,1.20)	1.11 (0.91,1.34)	1.14 (0.97,1.34)	1.30 (1.00,1.71)
Limb defects	1.08 (0.84,1.38)	1.15 (0.90,1.47)	1.15 (0.93,1.43)	1.18 (0.84,1.66)
Orofacial clefts	0.98 (0.71,1.34)	0.95 (0.69,1.30)	1.16 (0.88,1.52)	0.88 (0.59,1.30)
Autumn/winter				
Birth defects	1.05 (0.92,1.20)	**1.64** (1.41,1.91)	**1.22** (1.08,1.38)	**1.26** (1.07,1.47)
CHDs	1.05 (0.79,1.39)	**1.84** (1.32,2.57)	**1.36** (1.03,1.80)	**1.43** (1.00,2.03)
Limb defects	1.19 (0.84,1.70)	1.48 (0.99,2.22)	1.35 (0.97,1.87)	1.06 (0.70,1.61)
Orofacial clefts	0.95 (0.61,1.47)	1.63 (0.98,2.70)	**1.85** (1.16,2.93)	1.40 (0.82,2.40)
Summer/spring				
Birth defects	**1.12** (1.00,1.24)	1.06 (0.93,1.21)	1.09 (1.00,1.19)	1.12 (0.98,1.28)
CHDs	0.99 (0.77,1.26)	0.89 (0.65,1.21)	0.88 (0.71,1.08)	1.24 (0.92,1.66)
Limb defects	1.18 (0.92,1.51)	1.21 (0.89,1.63)	1.17 (0.95,1.43)	1.23 (0.89,1.71)
Orofacial clefts	0.72 (0.50,1.03)	0.66 (0.41,1.04)	0.88 (0.65,1.19)	0.72 (0.47,1.10)

Bold values represent statistical significance (two-sided $p<0.05$).
*Adjusted for year of conception, maternal age, gravidity, urban/rural, per capita area of roads, per capita of medication beds, unemployment and per capita of cars.
CHDs, congenital heart defects; NO_2, nitrogen dioxide; PM_{10}, particulate matter ≤10 µm diameter; SO_2, sulfur dioxide.

et al and Vrijheid *et al*.[36 37] Moreover, a case–control study conducted by Jiang *et al* showed that maternal exposure to SO_2 during the first trimester was significantly associated with increased risk of CHD (OR=1.78–2.04), and Hansen *et al* also confirmed that a 0.6 ppb increase in SO_2 was associated with an increased risk of aortic artery and valve defects (OR=10.76).[19 38] The heterogeneity in these studies might be explained by the variation in the population, the gestational periods or the measurement of air pollutants exposure. The physiopathological mechanism of the associations between air pollutants and CHDs was not fully elucidated. It is hypothesised that air pollutants exposure during the first pregnancy might strengthen the genetic and environmental interaction on CHDs.[37] Also, air pollutants might change the molecule of DNA sequence or alter epigenetics related to CHDs.[39]

In line with this study, the epidemiological difference in CHD_S between male and female fetuses has been reported previously.[40 41] This disparity could be explained by the sex chromosome-linked genes expression and their interactions with hormonal effects during early development.[42] Interestingly, only male fetuses showed an elevated risk of CHDs who were exposed to a higher $PM_{2.5}$ concentration. This result indicates that $PM_{2.5}$ might emphasise the disparity in the embryonic origins of sexual dimorphism. Moreover, $PM_{2.5}$ might have a stronger effect on the expression of specific CHDs genes located on the Y chromosome. A study of mice models showed that increased pathological damage in the hearts of offspring mice was observed among maternal mice exposed to $PM_{2.5}$, and these effects in the male group were more obvious than in the female group. $PM_{2.5}$ exposure in utero inhibited the expression of the *GATA4* gene in male mice, which was related to the formation of CHDs.[43]

After stratified by season, maternal exposure of $PM_{2.5}$, NO_2 and SO_2 were positively associated with birth defects in the cold season instead of the warm season. Zhao *et al* reported that the effects of air pollutants on birth defects were more obvious in the warm season in Hohhot.[44] This disparity could be partly explained by the uneven levels of dwellings' air pollutants. Compared with cities with lower GDP, cities with a higher GDP and a large population might have lower concentrations of indoor particulate matter.[45] Moreover, Wuhan is a well-known city with hot summer. Most of the residential buildings are equipped with air conditioners, which could help to improve indoor air quality in hot weather. Thus, the interpretation of results should be cautious that significant associations between air pollutants exposure and birth defects in the warm season in Wuhan.

Strengths

This study first provided evidence on the elevated risk of CHDs among mothers with heavy $PM_{2.5}$ exposure during the first trimester. We also found the increased risks of CHDs and orofacial clefts among women who conceived in the cold season and exposed to high concentrations of air pollutants.

Limitations

This study has several limitations. First, the selected participants are located in a large tertiary maternal care centre in Wuhan and the representative of this study was undermined. Second, the birth defects data of this study are manually collected and checked, but mistakes and omissions are inevitable. Third, maternal air pollutants exposure indoor or in other living residents including work, dining and shopping were not included in this study. Fourth, other risk factors (including ethnicity, smoking, drinking, medications, drug use and family history) were failed to obtain, which might influence the interpretation of the relationship between maternal air pollutants exposure and birth defects. More research is needed to explore the pathogenic mechanism of air pollutants exposure during pregnancy and the associated birth defects.

CONCLUSIONS

Our study confirmed the unfavourable effects of maternal exposure to air pollutants (PM_{10}, $PM_{2.5}$, NO_2 and SO_2) on birth defects during the first trimester of pregnancy. We first provided the evidence on the positive associations between $PM_{2.5}$ exposure and CHDs among male fetuses but not female fetuses. Moreover, stronger effects of $PM_{2.5}$, NO_2 and SO_2 exposure on birth defects were observed in the cold season in Wuhan. As a result, it should be noted for birth defects due to air pollutants, and reducing individual air pollutants exposure during the first trimester might help to birth defect control in the context of the rapid development all over the world. Moreover, the implementation of air quality protection policies on birth defect control should consider seasonal factor, especially for the cold season in Wuhan, China. Future studies of birth defects and air quality data collected by individual air pollutants monitors are promoted.

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Acknowledgements We appreciate all the medical staff of the Maternal and Child Health Hospital ofHubei Province for the data collection used in this manuscript.

Contributors YC and JY contributed equally to this manuscript. YC collected the data, performed data analysis, draft and revised the manuscript. JY collected the data, performed data analysis and edit the manuscript. LY designed the study, collected the data and performed data analysis. MX, XL and WH collected the data, interpreted the data and reviewed the manuscript. GD: collected the data, interpreted the data and revised the manuscript. GS: designed the study, collected the data, and supervised the project. All authors gave final approval of the version to be submitted and agreed to be accountable for all aspects of the work. GD and GS are responsible for the overall content as guarantor.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Ethics Committee of Maternal and Child Health Hospital of Hubei Province (2021IECLW025). This study was based on the retrospective clinical data without any individual patient identifiers.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request. Data for this study are available upon reasonable request from the corresponding author with permission from the Ethics Committee of Maternal and Child Health Hospital of Hubei Province.

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