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Exposure to ambient air pollution during trimesters of pregnancy and childhood allergic diseases in Wuhan, China

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ABSTRACT

The study explored the associations between maternal exposure to air pollution during different trimesters and allergic diseases including asthma, allergic rhinitis, allergic conjunctivitis or/and eczema. Individual exposure to air pollutants was assessed by an inverse distance weighted (IDW) method using daily concentrations of SO₂, NO₂, PM₁₀, and PM_{2.5} from air quality monitoring stations. Multiple logistic regression model was performed to estimate the associations between air pollution during each trimester of pregnancy and childhood allergic diseases. A total of 332 children (51.3%) were reported by their parents having been diagnosed with allergic diseases. After adjusting for covariates, allergic diseases were significantly associated with per interquartile range (IQR) increase in NO₂, PM₁₀, PM_{2.5} during the second trimester with odds ratios (ORs) and 95% confidence intervals (95%CI) being 1.292 (1.005,1.662), 1.210 (1.042,1.405) and 1.270 (1.004,1.606), respectively. These findings suggest that maternal exposure to certain air pollutants during pregnancy, especially in the second trimester, is associated with childhood allergic diseases.

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Air pollution; Maternal exposure; Pregnancy; Trimester

Introduction

Allergic diseases mainly refer to allergic reactions caused by exposure to various allergic substances, including asthma, allergic rhinitis, allergic conjunctivitis, and eczema, and so on (Yu et al. 2019). The World Allergy Organization (WAO) reported that about 30% to 40% of the global population suffer from more than one allergic disease. Asthma is one of the common allergic diseases, which contributed 417,918 deaths and 24.8 million disability-adjusted life years (DALYs) globally in 2016 (WHO 2020), and whose prevalence is still increasing worldwide, especially in childhood (Weinberg 2011; Boehmer et al. 2018; Chen 2018; Hu et al. 2020). Epidemiological studies have demonstrated that allergic diseases may affect children's physical and mental health, even their adulthood life (Sears et al. 2003; Chen et al. 2013; Ramirez et al. 2019).

It has been reported that different types of allergic diseases often occur concomitantly (Okayama et al. 2020). A meta-analysis showed that comorbidity of allergic rhinitis with asthma in Chinese children was as high as 54.93% (Kou et al. 2018). Meanwhile, a growing body of studies have found that allergic diseases share common risk factors, including stress during pregnancy, high birth weight

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(Yu et al. 2019), cesarean section (Kim et al. 2019), secondhand smoke, and air pollutants (Burbank et al. 2017). And an increasing number of epidemiological evidence revealed that early-life exposure increased the risk of childhood allergic diseases (Deng et al. 2015a, 2015b; Suk et al. 2016).

The hypotheses of the fetal origins of disease reveal that adverse exposure during pregnancy can cause consequent susceptibility to certain chronic diseases, especially allergic diseases (Gluckman et al. 2008; Eriksson 2016; Carpinello et al. 2018). Because the development of human immune and respiratory systems starts from the early embryonic stage to the early postnatal period, adverse exposure in early life could increase the risk of immune and respiratory systems diseases (Cao et al. 2016). At present, the majority of studies on exposure in early life focused on maternal diet, nutrition, stress during pregnancy (Garcia-Larsen et al. 2018), cesarean section, exposure to environmental toxicants and air pollutants (Thacher et al. 2016; Zou et al. 2018). Due to different properties of pollutants and characteristics of pollution and environment, existing studies show inconsistent results (Gehring et al. 2010; Sugiyama et al. 2019).

For example, a research found that NO₂ during the entire pregnancy may increase the risk of allergic rhinitis (Deng et al. 2016b). However, no such association was found in another study (Huang et al. 2019). Other studies have also found that the associations of allergic diseases with different air pollutant within the same exposure window and with the same air pollutant during different exposure windows were inconsistent (Lu et al. 2017, 2020; Deng et al. 2019; Huang et al. 2019). Moreover, the majority of studies focusing on allergic diseases and early life exposure to air pollution usually divided the exposure window into the entire pregnancy and the early postnatal period (Gluckman et al. 2008; Hsu et al. 2015; Deng et al. 2015b, 2019; Kravitz-Wirtz et al. 2018; Huang et al. 2019; Lu et al. 2020), while only several studies focused on the three trimesters of pregnancy (Aguilera et al. 2013; Deng et al. 2016b; Lu et al. 2017). Therefore, it can increase new evidence to investigate the impact of exposure to air pollution in different trimesters on the risk of childhood allergic diseases.

In this study, we aimed to evaluate the associations between maternal exposure to air pollution during three critical trimesters of pregnancy and childhood allergic diseases among preschool children in Wuhan, and to identify the sensitive air pollutants and sensitive trimesters for providing epidemiological evidence for further study and intervention.

Methods

Participants and procedure

From November to December 2017, a survey on childhood allergic diseases was conducted in three kindergartens in Wuchang and Qingshan districts of Wuhan, the capital city of Hubei Province. Wuhan (29°58'~31°22'N and 113°41'~115°05'E), is one of the megacities in central China, which is the hub of transportation and the major link of west and east China. Vehicle exhaust, industrial emission, and construction dust are the main sources of air pollution in Wuhan, and the concentration of PM_{2.5} in Wuhan far exceeds that of other provincial central China (Mbululo et al. 2019). The Medical Ethics Committee of Wuhan University approved this research. The informed consents were received from the parents of recruited preschool children before the survey.

A total of 882 preschool children in three kindergartens were recruited. Teachers asked the children to take questionnaires to their parents or other guardians to fill them out and return them within one week. A total of 784 (88.9%) questionnaires were returned and 121 questionnaires were excluded due to missing data of allergic diseases. Moreover, the study limited that the maternal exposure windows were between 2013 and 2014; thus, 16 children were excluded and 647 were included in the final analysis.

Exposure assessment

In this study, the entire pregnancy was divided into three different trimesters, namely, the first, second, and third trimesters of pregnancy that are from the 1st week to the 13th week, from the 14th week to the 27th week, and from the 28th week to delivery, respectively (Becerra et al. 2013; Ren et al. 2019).

Air pollutants including sulfur oxide (SO₂), nitrogen dioxide (NO₂), particulate matter with an aerodynamic diameter <10 µm (PM₁₀), and particulate matter with an aerodynamic diameter <2.5 µm (PM_{2.5}) were selected as representative of outdoor air pollution (Norback et al. 2019; Yang 2019). The average daily concentrations of SO₂, NO₂, PM₁₀, and PM_{2.5} were obtained from five municipal air pollution monitoring stations during 2013–2014. Daily mean concentrations of pollutants were interpolated to each kindergarten, using the inverse distance weighting (IDW) method (Rivera-Gonzalez et al. 2015; Deng et al. 2015a; Kravitz-Wirtz et al. 2018). We used the air pollutants exposure in the kindergartens to replace maternal exposure during three trimesters of pregnancy, because the children generally went to the kindergarten closest to where they lived or where their parents worked (Deng et al. 2015a).

Health outcome

The outcome variable was the physician-diagnosed allergic diseases, which was estimated by the questions: “Has your child ever been diagnosed with asthma/allergic rhinitis/allergic conjunctivitis/eczema by a doctor (Yes/No)?”

Covariates

Based on the prior investigations (Deng et al. 2016b, 2019), the covariates were divided into three categories: the personal factors mainly including gender (male or female), age (3 or 4 years old), delivery (early-term, full-term or later term), cesarean section (yes/no), birth weight (≥2500 g or <2500 g), only child (yes/no), milk powder feeding (born or a few months after born) and birth season (spring, summer, autumn or winter); the parental factors mainly including maternal productive age (≤30 or >30 years old), weight gaining during pregnancy (≤10 kg, 10 ~ 20 kg or >20 kg), maternal education (junior college or below, undergraduate college or above), maternal occupation (technical/clerical/management or business/service/production, etc.), paternal occupation (technical/clerical/management or business/service/production, etc.), and gestational diabetes (yes, no or unknown); the residential factors mainly including environmental tobacco smoke (ETS) (yes/no), house size (≥100 m² or <100 m²) and the distance to the main road (≤100 m, 100 ~ 300 m or >300 m). About occupation, technical/clerical/management included professional and technical personnel, clerical, administrative and management personnel; business/service/production, etc., included business, service, production, transportation and material moving workers, etc.

Statistical analysis

The chi-square test was used to analyze differences in various covariates among preschool children with and without allergic diseases. Multiple logistic regression models were used examined the association of maternal exposures to air pollutants with allergic diseases. Three models (Model a, Model b and Model c) were developed, with Model a including different air pollutant and personal factors, Model b considering parental factors besides the factors entering Model a and Model c including all covariates. Odds ratios (ORs) and 95% confidence intervals (95% CIs) associated with per interquartile range (IQR) increase in each pollutant were presented. $P < 0.05$ was considered statistically significant. SPSS 22.0 was performed to conduct all analysis.

Results

Table 1 shows the characteristics among 647 preschool children stratified by covariates. Of 647 children, 332 (51.3%) had a history of physician-diagnosed allergic diseases. The prevalence was higher in preschool children who were only child and whose maternal education was undergraduate college or above ($p < 0.05$). Compared with those children whose paternal occupational was business/service/production, the prevalence was higher in the children whose fathers engaged in technical/clerical/management work.

Table 2 shows the status of air pollutants in different exposure windows. The average concentrations of SO_2 , NO_2 , PM_{10} , and $\text{PM}_{2.5}$ (Mean $\pm$ SD) in the second trimester were $40.0 \pm 12.1 \mu\text{g}/\text{m}^3$, $47.9 \pm 15.8 \mu\text{g}/\text{m}^3$, $122.5 \pm 41.1 \mu\text{g}/\text{m}^3$, and $92.9 \pm 43.0 \mu\text{g}/\text{m}^3$, respectively. The average exposure levels of individuals in the three trimesters were not significantly different, but the four pollutants showed a decreasing trend from the first trimester to the third trimester. The interquartile range of (IQR) of PM_{10} at different periods was higher than other air pollutants.

Table 3 describes the correlations of four air pollutants in each trimester and the association of air pollutants between different exposure period. Correlations between different pollutants in each exposure window were moderate or strong (from 0.617 to 0.974). Correlations in each air pollutant between different exposure period were weak or strong (from -0.019 to -0.922).

Table 4 summarizes associations of maternal exposure to air pollutants during each trimester of pregnancy with allergic diseases among preschool children. In the model a, the ORs (95%CI) of childhood allergic diseases with per IQR increase in SO_2 , NO_2 , PM_{10} , and $\text{PM}_{2.5}$ in the second trimester were 1.149 (1.003,1.317), 1.349 (1.049,1.735), 1.257 (1.083,1.460) and 1.270 (1.005,1.606), respectively. After adjusting all covariates, the ORs (95%CI) were 1.292 (1.005,1.662) for NO_2 , 1.210 (1.042,1.405) for PM_{10} , and 1.270 (1.004,1.606) for $\text{PM}_{2.5}$.

The association between exposure to air pollutants during trimesters of pregnancy and allergic diseases was further assessed by sensitivity analysis for sex and all significant covariates, including only child, maternal educational level, and paternal occupation. **Figure 1** shows the associations between exposure to air pollutants during trimesters of pregnancy and allergic diseases stratified by sex. After adjusting for all covariates, the OR (95%CI) was 1.501(1.030, 2.190) for NO_2 in the male population during the second trimester. **Figure 2** shows the OR (95%CI) was 1.257 (1.005, 1.573) for PM_{10} in preschool children who were only child during the second trimester. The associations between air pollutants exposure during trimesters of pregnancy and allergic diseases stratified by maternal educational level or paternal occupation were also assessed by sensitivity analysis (see supplementary materials).

Discussion

In this research, the prevalence of allergic diseases in preschool children was 51.3%, which was slightly higher than in infants under 2 years old in China (49.9%) reported in 2015 (Brozek et al. 2016) and 49.07% in preschool children in Yangzhou reported in 2019 (Zhang and Zhang 2019), and it was similar to the results of the China, Children, Homes, Health (CCHH) study, which reported that the prevalence of one manifestation of wheeze, rhinitis or eczema in children aged 3–6 years was higher than 50% (Zhang 2013). Differences in the prevalence of childhood allergic diseases may be associated with different exposure factors due to regional differences, as well as different judgment criteria for allergic diseases and the age of the subjects (Deng et al. 2016a).

The study found that the prevalence of allergic diseases was higher among preschool children with higher maternal educational level (undergraduate college or above), which was consistent with previous studies (Shaw et al. 2011). We also observed the prevalence was higher among children who were only children or whose paternal occupation was technical/clerical/management personnel, which was also consistent with previous study (Deng et al. 2019). The association of socio-economic status of the family with allergic diseases in the offspring has been well known (Gluckman

Table 1. Characteristics and prevalence of allergic diseases in children stratified by covariates.

Characteristic	Total population	Allergic diseases n(%)		p-value
		Yes	No	
N	647 (100.0)	332 (51.3)	315(48.7)	
Personal				
Gender				0.175
Male	334 (51.6)	180 (53.9)	154 (46.1)	
Female	313 (48.4)	152 (48.6)	161 (51.4)	
Age(year)				0.460
3	356 (55.0)	178 (50.0)	178 (50.0)	
4	291 (45.0)	137 (47.1)	154 (52.9)	
Low birth weight				0.981
≥2500 g	614 (94.9)	315 (51.3)	299 (48.7)	
<2500 g	33 (5.1)	17 (51.5)	16 (48.5)	
Delivery categories				0.665
Early term	309 (47.8)	163 (52.8)	146 (47.2)	
Full term	221 (34.2)	108 (48.9)	113 (51.1)	
Later term	117 (18.1)	61 (52.1)	56 (47.9)	
Cesarean section				0.792
No	237 (36.6)	120 (50.6)	117 (49.4)	
Yes	410 (63.4)	212 (51.7)	198 (48.3)	
Milk powder feeding				0.625
Born	78 (12.1)	38(48.7)	40 (51.3)	
A few months after born	569 (87.9)	294 (51.7)	275 (48.3)	
Only child				0.021
Yes	488 (75.4)	263 (53.9)	225 (46.1)	
No	159 (24.6)	69 (43.4)	90 (56.6)	
Birth season				0.466
Spring	172 (26.6)	75 (43.6)	97 (56.4)	
Summer	219 (33.8)	112 (51.1)	107 (48.9)	
Autumn	168 (26.0)	85 (50.6)	83 (49.4)	
Winter	88 (13.6)	43 (48.9)	45 (51.1)	
Parental				
Maternal productive age(years) ^a				0.530
≤30	412(65.3)	214(51.9)	198(48.1)	
>30	219(34.7)	108(49.3)	111(50.7)	
Weight gaining during pregnancy				0.338
≤10 kg	170 (26.3)	79 (46.5)	91 (53.5)	
10 ~ 20 kg	339 (52.4)	180 (53.1)	159 (46.9)	
>20 kg	138 (21.3)	73 (52.9)	65 (47.1)	
Gestational diabetes				0.189
No	590 (91.2)	299 (50.7)	291 (49.3)	
Unknow	3 (0.5)	3 (100.0)	0 (0)	
Yes	54 (8.3)	30 (55.6)	24 (44.4)	
Maternal educational level				0.005
Junior college or below	198 (30.6)	85 (42.9)	113 (57.1)	
Undergraduate college or above	449 (69.4)	247 (55.0)	202 (45.0)	
Maternal occupation				0.634
Technical/clerical/management	429 (66.3)	223 (52.0)	206 (48.0)	
Business/service/production etc.	218 (33.7)	109 (50.0)	109 (50.0)	
Paternal occupation				0.021
Technical/clerical/management	433 (66.9)	236 (54.5)	197 (45.5)	
Business/service/production etc.	214 (33.1)	96 (44.9)	118 (55.1)	
Residential				
Environmental tobacco smoke (ETS)				0.203
No	564 (87.2)	284(50.4)	280(49.6)	
Yes	83 (12.8)	48 (57.8)	35 (42.2)	
House size (m ²) ^a				0.801
≥100	405 (66.3)	206 (50.9)	199 (49.1)	
<100	206 (33.7)	107 (51.9)	99 (48.1)	
The distance to the main road(m) ^a				0.567
≤100	307(48.7)	153(49.8)	154(50.2)	
100 ~ 300	209(33.1)	108(51.7)	101(48.3)	
>300	115(18.2)	64(55.7)	51(44.3)	

^aSum of the number is not 647 due to missing data. The values p < 0.05 were in bold.

Spring: March–May, Summer: June–August, Autumn: September–November, Winter: December–February

Technical/clerical/management: professional and technical personnel; clerical; administrative and management personnel

Business/service/production etc.: business; service; production: installation, maintenance, and repair; production; and transportation and material moving workers etc.

Table 2. Statistics of the children’s exposure to air pollutants (n = 647).

Variables	Mean	SD	Min	P25	P50	P75	Max	IQR
1st trimester								
SO ₂ (μg/m ³)	44.1	10.3	26.8	36.3	40.3	49.7	64.8	13.3
NO ₂ (μg/m ³)	50.0	17.1	24.3	35.9	47.3	63.8	80.8	27.9
PM ₁₀ (μg/m ³)	125.7	45.7	64.3	86.8	118.1	157.1	213.3	70.3
PM _{2.5} (μg/m ³)	97.8	51.0	32.7	53.2	86.2	139.1	197.8	85.9
2nd trimester								
SO ₂ (μg/m ³)	40.0	12.1	15.0	34.3	37.9	44.2	64.8	9.9
NO ₂ (μg/m ³)	47.9	15.8	24.3	35.1	46.5	56.5	80.7	21.4
PM ₁₀ (μg/m ³)	122.5	41.1	65.2	99.6	113.0	137.7	213.3	38.1
PM _{2.5} (μg/m ³)	92.9	43.0	32.5	65.4	80.9	125.2	197.6	59.9
3rd trimester								
SO ₂ (μg/m ³)	36.1	13.9	12.7	27.7	37.1	42.1	64.3	14.4
NO ₂ (μg/m ³)	43.2	17.3	7.1	28.5	43.1	50.7	80.3	22.2
PM ₁₀ (μg/m ³)	114.4	39.9	63.4	82.9	107.6	127.9	212.2	45.0
PM _{2.5} (μg/m ³)	87.4	43.2	33.5	54.6	77.4	108.5	192.7	53.9

SO₂: sulfur dioxide; NO₂: nitrogen dioxide; PM₁₀: particulate matter≤10 μm in aerodynamic diameter; PM_{2.5}: particulate matter≤2.5 μm in aerodynamic diameter; SD: standard deviation; P25: 25th percentile; P50: 50th percentile; P75: 75th percentile; IQR: interquartile range.

Table 3. Spearman correlation between exposures to air pollutants and between trimesters.

Air pollutants	Between air pollutants				
	SO ₂	NO ₂	PM ₁₀	PM _{2.5}	Between trimesters
1st trimester					2nd trimester
SO ₂	1	0.897**	0.909**	0.823**	−0.384**
NO ₂		1	0.974**	0.936**	−0.103*
PM ₁₀			1	0.880**	−0.050
PM _{2.5}				1	0.048
2nd trimester					3rd trimester
SO ₂	1	0.792**	0.705**	0.625**	0.252**
NO ₂		1	0.916**	0.916**	0.108*
PM ₁₀			1	0.855**	−0.019
PM _{2.5}				1	0.111*
3rd trimester					1st trimester
SO ₂	1	0.846**	0.714**	0.617**	−0.753**
NO ₂		1	0.914**	0.882**	−0.819**
PM ₁₀			1	0.908**	−0.724**
PM _{2.5}				1	−0.922**

*Correlation was significant at the 0.05 level (2-tailed); **Correlation was significant at the 0.01 level(2-tailed)

Table 4. Associations between exposure to outdoor air pollutants during pregnancy and childhood allergic diseases.

	Allergic diseases		
	Adjusted ^a	Adjusted ^b	Adjusted ^c
1st trimester			
SO ₂	0.887(0.683,1.152)	0.875(0.656,1.167)	0.911(0.683,1.214)
NO ₂	0.846(0.609,1.174)	0.846(0.609,1.174)	0.894(0.610,1.311)
PM ₁₀	0.932(0.708,1.228)	0.869(0.660,1.144)	0.932(0.707,1.227)
PM _{2.5}	0.842(0.602,1.179)	0.842(0.602,1.179)	0.842(0.601,1.179)
2nd trimester			
SO ₂	1.149(1.003,1.317) *	1.138(0.974,1.330)	1.137(0.973,1.329)
NO ₂	1.349(1.049,1.735) *	1.321(1.027,1.698) *	1.292(1.005,1.662) *
PM ₁₀	1.257(1.083,1.460) *	1.210(1.042,1.405) *	1.210(1.042,1.405) *
PM _{2.5}	1.270(1.005,1.606) *	1.270(1.005,1.606) *	1.270(1.004,1.606) *
3rd trimester			
SO ₂	1.029(0.869,1.218)	1.044(0.882,1.236)	1.014(0.856,1.201)
NO ₂	0.978(0.787,1.215)	1.000(0.805,1.242)	0.978(0.787,1.215)
PM ₁₀	0.956(0.801,1.140)	0.956(0.801,1.140)	0.956(0.801,1.140)
PM _{2.5}	1.114(0.902,1.375)	1.114(0.902,1.375)	1.114(0.901,1.375)

^aAdjusted personal factors, ^b adjusted personal factors and parental factors, ^c adjusted personal factors, parental factors, and residential factors.

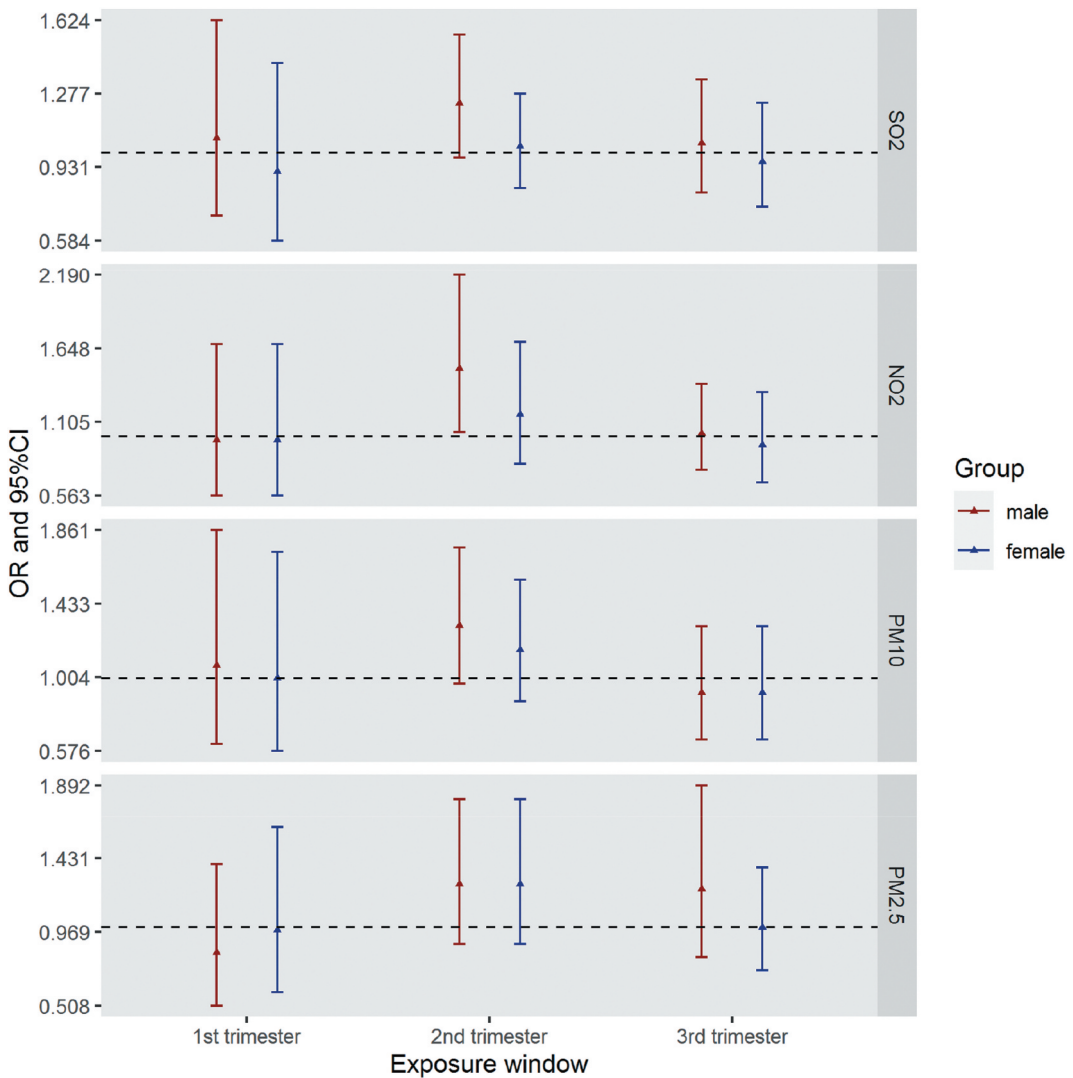


Figure 1. Estimated odds ratios (ORs) and 95% confidence intervals (95% CIs) of allergic diseases per interquartile range (IQR) increase of air pollution among male and female.

et al. 2008; Andrusaityte et al. 2017; Ofenloch et al. 2019). In this study, the information of childhood allergic diseases was collected by their parents' self-report, and those mothers with higher levels of education and fathers engaging in technical/clerical/management work might know better about allergic diseases or pay more attention to the diseases (Ofenloch et al. 2019).

The study found that NO₂, PM₁₀ and PM_{2.5} exposures were all significantly associated with childhood allergic diseases, which concurred with most previous studies (Kim et al. 2013; Bowatte et al. 2015; Hsu et al. 2015). For example, one longitudinal retrospective study conducted between 1997 and 2006 showed a decrease in PM and carbon with a decrease in the yearly prevalence of allergic rhinitis (Bhattacharyya 2009). Similar results were observed in a cross-sectional study in Changsha demonstrating maternal exposure to air pollution during pregnancy could increase the risk of childhood asthma. Specifically, exposure to NO₂ significantly increased childhood asthma with odds ratio = 1.21 (95% CI: 1.02–1.45) (Deng et al. 2015b). Allergic diseases belong to inflammatory

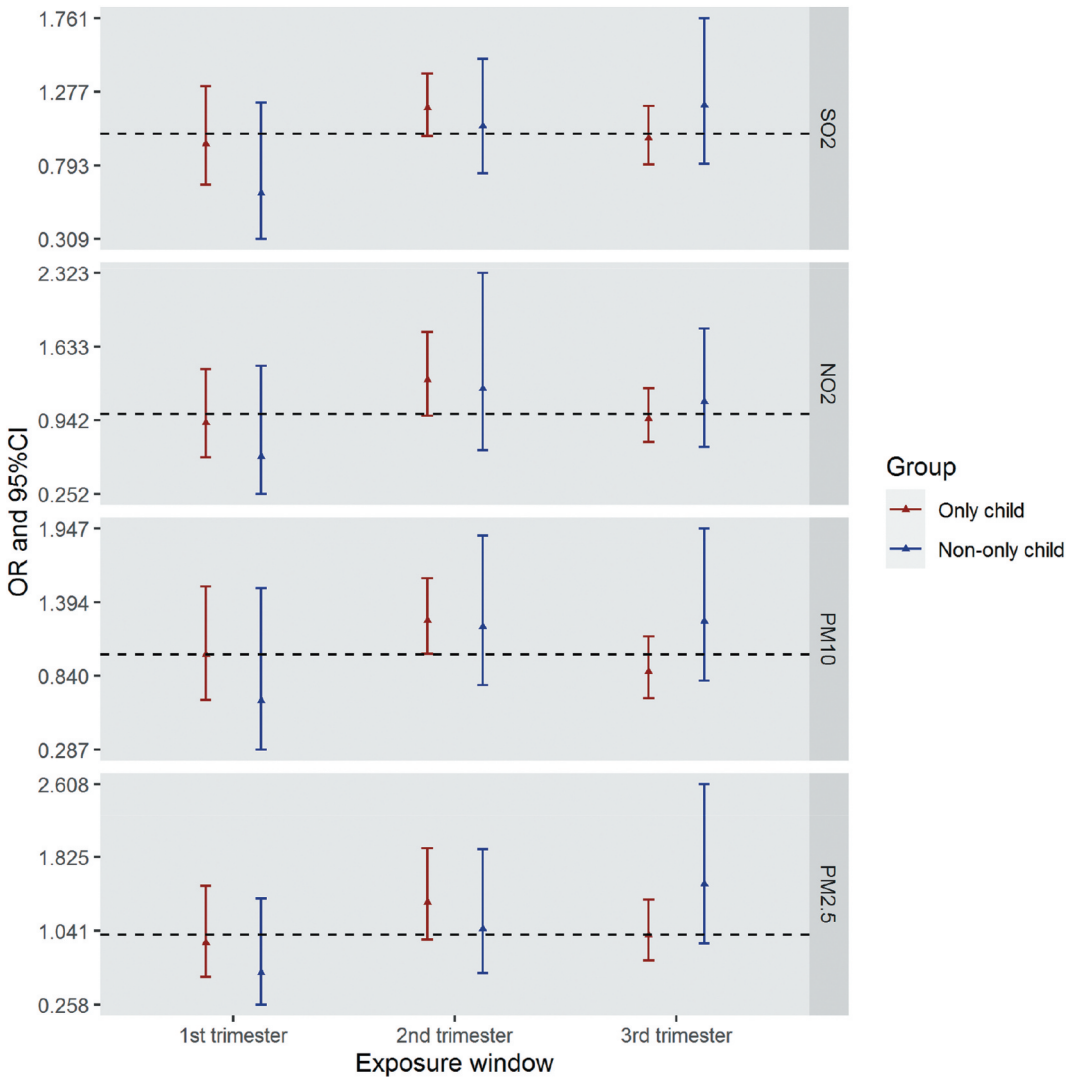


Figure 2. Estimated odds ratios (ORs) and 95% confidence intervals (95% CIs) of allergic diseases per interquartile range (IQR) increase of air pollution among only-child and no-only child.

diseases, and air pollutants might enhance children's sensitivity to allergens, inflammatory pathways, immune responses, and epigenetics by involving with oxidative stress and damage (Yang 2019).

In this study, we found that the second trimester of pregnancy was a sensitive period, which concurred with some previous studies. For example, a study in Spanish among 2199 infants found the risk of eczema was positively associated with traffic-related pollutant NO₂ exposure during the second and third trimesters (Aguilera et al. 2013). Lu's article demonstrated the association of eczema and exposure to NO₂ in the first two trimesters (Lu et al. 2017). Deng et al. found that exposure to SO₂+ PM₁₀ during the second trimester increased the risk of allergic asthma in children (Deng et al. 2016a). Moreover, the stratified results showed the effects of air pollution on childhood allergic diseases can be observed among boys or only child, which suggested boys and only child need be paid more attention after they are born.

This study provided new evidence for policy-makers and health educators to take measures to prevent childhood allergic diseases. Firstly, pregnant women need reduce the chance of exposure to air pollution during pregnancy, especially the second trimester, by taking protective measures, such as stopping high-exposure occupations or reducing outdoor activities during poor air quality. Secondly, formulating policies to reduce the burning of fossil fuels, strictly controlling the factories emission standards, and adopting traffic control measures have important impact on reducing NO₂ and PM (Liu et al. 2019).

Several limitations exist in the research. First, due to unavailability of information on individual exposure to air pollution of residential area, concentrations of air pollution derived from the environmental monitoring stations nearest kindergartens were used to represent the maternal air pollution exposure during pregnancy, which may underestimate the difference in level of exposure between individuals. Moreover, we did not collect information on moving home or children's migration from one kindergarten to another, which might cause exposure level different from pregnancy period. However, in general, moving home or children's migration in a long distance isn't common, and it has been verified that moving home or children's migration had no significant effect on the results (Deng et al. 2015a). Second, due to the limited sample size, this study used combining allergic diseases as outcome variable, which may cause different results from other studies focusing on a specific type of allergic disease. Third, some potential confounders, such as parental atopy, indoor air pollution, climate factors (air temperature and humidity) and so on, were not included in this study. In future studies, more factors need to be considered.

Conclusion

This study indicated that exposures to NO₂, PM₁₀ and PM_{2.5} during the second trimester of pregnancy were significantly associated with childhood allergic diseases. The findings highlight the significant effect of air pollutants on human health, which provide new evidence for air quality improvement and policy-making. Further prospective research is needed to determine the causal association of exposure to air pollutants in early life with allergic diseases and possible mechanisms.

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Disclosure of potential conflicts of interest

No potential conflict of interest was reported by the author.

Ethical approval

This study was approved by the Medical Ethics Committee of Wuhan University.

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Supplementary materials

Table S1. Associations between air pollutants and allergic diseases stratified by gender

	Male			Female		
	Adjusted ^a	Adjusted ^b	Adjusted ^c	Adjusted ^a	Adjusted ^b	Adjusted ^c
1st trimester						
SO ₂	1.000(0.676,1.480)	1.013(0.667,1.540)	1.069(0.704,1.624)	0.887(0.584,1.348)	0.911(0.584,1.421)	0.911(0.584,1.421)
NO ₂	0.894(0.547,1.463)	0.920(0.562,1.504)	0.972(0.563,1.680)	0.920(0.562,1.504)	0.972(0.563,1.680)	0.972(0.563,1.680)
PM ₁₀	0.932(0.617,1.409)	1.000(0.576,1.735)	1.073(0.618,1.861)	0.932(0.617,1.409)	1.000(0.576,1.735)	1.000(0.576,1.735)
PM _{2.5}	0.842(0.508,1.395)	0.842(0.508,1.395)	0.842(0.508,1.395)	0.918(0.554,1.520)	0.918(0.554,1.520)	0.982(0.593,1.626)
2nd trimester						
SO ₂	1.196(0.965,1.482)	1.208(0.975,1.497)	1.232(0.975,1.557)	1.072(0.882,1.303)	1.061(0.857,1.315)	1.030(0.832,1.277)
NO ₂	1.501(1.030,2.190)*	1.439(0.986,2.098)	1.501(1.030,2.190)*	1.212(0.867,1.695)	1.238(0.849,1.806)	1.162(0.796,1.694)
PM ₁₀	1.306(1.044,1.634)*	1.306(0.968,1.761)	1.306(0.968,1.761)	1.165(0.931,1.458)	1.210(0.967,1.514)	1.165(0.864,1.571)
PM _{2.5}	1.270(0.894,1.806)	1.270(0.894,1.806)	1.270(0.894,1.806)	1.197(0.842,1.701)	1.349(0.949,1.918)	1.270(0.894,1.806)
3rd trimester						
SO ₂	1.059(0.846,1.326)	1.090(0.846,1.404)	1.044(0.811,1.345)	0.986(0.787,1.234)	0.958(0.744,1.234)	0.958(0.744,1.234)
NO ₂	1.000(0.738,1.355)	1.045(0.771,1.417)	1.022(0.754,1.385)	0.957(0.706,1.296)	0.915(0.675,1.240)	0.936(0.661,1.324)
PM ₁₀	0.914(0.701,1.191)	0.956(0.734,1.246)	0.914(0.642,1.301)	0.956(0.734,1.246)	0.914(0.701,1.191)	0.914(0.642,1.301)
PM _{2.5}	1.175(0.856,1.613)	1.240(0.904,1.702)	1.240(0.813,1.892)	1.000(0.729,1.373)	1.000(0.729,1.373)	1.000(0.729,1.373)

^a adjusted personal factors, ^b adjusted personal factors and parental factors, ^c adjusted personal factors, parental factors and residential factors.

Table S2. Associations between air pollutants and allergic diseases stratified by maternal educational level

	Junior college or below			Undergraduate college or above		
	Adjusted ^a	Adjusted ^b	Adjusted ^c	Adjusted ^a	Adjusted ^b	Adjusted ^c
1st trimester						
SO ₂	0.887(0.540,1.457)	0.911(0.540,1.537)	0.887(0.499,1.576)	0.830(0.591,1.165)	0.830(0.591,1.165)	0.911(0.632,1.313)
NO ₂	0.920(0.477,1.772)	1.000(0.491,2.035)	1.000(0.491,2.035)	0.778(0.502,1.205)	0.757(0.489,1.172)	0.823(0.531,1.274)
PM ₁₀	0.932(0.537,1.617)	1.000(0.502,1.991)	1.000(0.502,1.991)	0.810(0.536,1.224)	0.810(0.536,1.224)	0.869(0.575,1.313)
PM _{2.5}	0.842(0.430,1.651)	0.918(0.468,1.799)	0.918(0.468,1.799)	0.773(0.467,1.280)	0.709(0.428,1.175)	0.842(0.508,1.395)
2nd trimester						
SO ₂	1.083(0.808,1.450)	1.094(0.801,1.494)	1.138(0.833,1.554)	1.172(0.984,1.397)	1.161(0.974,1.383)	1.138(0.955,1.356)
NO ₂	1.113(0.702,1.765)	1.066(0.645,1.763)	1.162(0.702,1.921)	1.408(1.050,1.888)	1.378(1.028,1.848)	1.349(1.006,1.809)
PM ₁₀	1.121(0.831,1.512)	1.121(0.772,1.629)	1.165(0.802,1.692)	1.306(1.044,1.634)	1.257(1.005,1.573)	1.257(1.005,1.573)
PM _{2.5}	1.127(0.705,1.802)	1.127(0.627,2.026)	1.197(0.666,2.151)	1.270(0.894,1.806)	1.270(0.894,1.806)	1.270(0.894,1.806)
3rd trimester						
SO ₂	0.986(0.723,1.343)	1.014(0.724,1.422)	0.958(0.683,1.342)	1.059(0.870,1.290)	1.074(0.882,1.308)	1.029(0.845,1.253)
NO ₂	0.915(0.619,1.353)	0.936(0.606,1.444)	0.876(0.567,1.352)	1.045(0.806,1.356)	1.045(0.806,1.356)	1.022(0.788,1.327)
PM ₁₀	0.835(0.587,1.189)	0.874(0.562,1.358)	0.798(0.514,1.241)	1.000(0.767,1.303)	1.000(0.767,1.303)	1.000(0.767,1.303)
PM _{2.5}	0.948(0.621,1.445)	0.948(0.621,1.445)	0.898(0.530,1.522)	1.175(0.856,1.613)	1.240(0.904,1.702)	1.175(0.856,1.613)

^a adjusted personal factors, ^b adjusted personal factors and parental factors, ^c adjusted personal factors, parental factors and residential factors.

Table S3. Associations between air pollutants and allergic diseases stratified by only child

	Only child(yes)			Only child(no)		
	Adjusted ^a	Adjusted ^b	Adjusted ^c	Adjusted ^a	Adjusted ^b	Adjusted ^c
1st trimester						
SO ₂	0.887(0.648,1.214)	0.887(0.631,1.246)	0.935(0.666,1.314)	0.776(0.448,1.344)	0.644(0.344,1.206)	0.610(0.309,1.205)
NO ₂	0.846(0.577,1.240)	0.870(0.593,1.275)	0.920(0.594,1.424)	0.778(0.382,1.583)	0.622(0.274,1.413)	0.605(0.252,1.452)
PM ₁₀	0.869(0.575,1.313)	0.932(0.617,1.409)	1.000(0.661,1.512)	0.810(0.407,1.613)	0.656(0.329,1.306)	0.656(0.287,1.499)
PM _{2.5}	0.842(0.602,1.179)	0.842(0.602,1.179)	0.918(0.554,1.520)	0.773(0.333,1.793)	0.651(0.281,1.510)	0.597(0.258,1.386)
2nd trimester						
SO ₂	1.184(0.994,1.411)	1.172(0.984,1.397)	1.172(0.984,1.397)	1.072(0.785,1.464)	1.072(0.770,1.493)	1.051(0.740,1.492)
NO ₂	1.378(1.028,1.848)*	1.349(1.006,1.809)*	1.321(0.985,1.771)	1.378(0.799,2.377)	1.321(0.734,2.375)	1.238(0.660,2.323)
PM ₁₀	1.257(1.005,1.573)*	1.257(1.005,1.573)*	1.257(1.005,1.573)*	1.306(0.899,1.898)	1.257(0.803,1.968)	1.210(0.773,1.895)
PM _{2.5}	1.349(0.949,1.918)	1.270(0.894,1.806)	1.349(0.949,1.918)	1.197(0.666,2.151)	1.197(0.666,2.151)	1.062(0.591,1.909)
3rd trimester						
SO ₂	1.000(0.821,1.218)	1.014(0.833,1.235)	0.972(0.798,1.183)	1.090(0.778,1.527)	1.171(0.812,1.688)	1.188(0.801,1.761)
NO ₂	0.957(0.737,1.241)	0.957(0.737,1.241)	0.957(0.737,1.241)	1.000(0.648,1.544)	1.117(0.693,1.801)	1.117(0.693,1.801)
PM ₁₀	0.874(0.671,1.138)	0.874(0.671,1.138)	0.874(0.671,1.138)	1.094(0.704,1.701)	1.252(0.806,1.947)	1.252(0.806,1.947)
PM _{2.5}	1.055(0.769,1.448)	1.000(0.729,1.373)	1.000(0.729,1.373)	1.458(0.860,2.471)	1.624(0.958,2.752)	1.538(0.908,2.608)

^a adjusted personal factors, ^b adjusted personal factors and parental factors, ^c adjusted personal factors, parental factors and residential factors.

Table S4. Associations between air pollutants and allergic diseases stratified by paternal occupation

	Paternal occupation (technical/ clerical/management)			Paternal occupation (business/service/production)		
	Adjusted ^a	Adjusted ^b	Adjusted ^c	Adjusted ^a	Adjusted ^b	Adjusted ^c
1st trimester						
SO ₂	0.864(0.615,1.213)	0.887(0.631,1.246)	0.974(0.675,1.404)	0.961(0.600,1.538)	0.923(0.562,1.517)	0.847(0.494,1.451)
NO ₂	0.846(0.546,1.310)	0.870(0.562,1.347)	0.970(0.616,1.528)	0.894(0.490,1.632)	0.894(0.490,1.632)	0.845(0.424,1.684)
PM ₁₀	0.869(0.575,1.313)	0.932(0.617,1.409)	1.006(0.655,1.545)	0.932(0.537,1.617)	0.932(0.537,1.617)	0.886(0.463,1.693)
PM _{2.5}	0.842(0.508,1.395)	0.842(0.508,1.395)	0.973(0.606,1.563)	0.842(0.430,1.651)	0.839(0.428,1.643)	0.839(0.428,1.643)
2nd trimester						
SO ₂	1.127(0.945,1.343)	1.116(0.936,1.329)	1.061(0.874,1.290)	1.138(0.883,1.466)	1.138(0.866,1.495)	1.127(0.847,1.500)
NO ₂	1.293(0.964,1.734)	1.265(0.943,1.697)	1.187(0.849,1.659)	1.378(0.906,2.096)	1.321(0.833,2.094)	1.223(0.758,1.972)
PM ₁₀	1.257(1.005,1.573)*	1.210(0.967,1.514)	1.165(0.923,1.470)	1.257(0.932,1.695)	1.210(0.897,1.632)	1.143(0.814,1.606)
PM _{2.5}	1.270(0.894,1.806)	1.171(0.836,1.641)	1.171(0.836,1.641)	1.270(0.795,2.031)	1.171(0.713,1.921)	1.171(0.713,1.921)
3rd trimester						
SO ₂	1.029(0.845,1.253)	1.029(0.845,1.253)	0.981(0.790,1.218)	1.014(0.766,1.344)	1.044(0.766,1.423)	1.044(0.766,1.423)
NO ₂	1.000(0.771,1.298)	0.978(0.754,1.269)	0.936(0.721,1.214)	0.957(0.647,1.414)	1.008(0.675,1.504)	1.008(0.675,1.504)
PM ₁₀	0.956(0.734,1.246)	0.956(0.734,1.246)	0.911(0.697,1.191)	0.956(0.672,1.361)	0.998(0.680,1.466)	0.998(0.680,1.466)
PM _{2.5}	1.114(0.811,1.529)	1.114(0.811,1.529)	1.055(0.769,1.448)	1.055(0.692,1.610)	1.055(0.692,1.610)	1.002(0.637,1.575)

^a adjusted personal factors, ^b adjusted personal factors and parental factors, ^c adjusted personal factors, parental factors and residential factors.

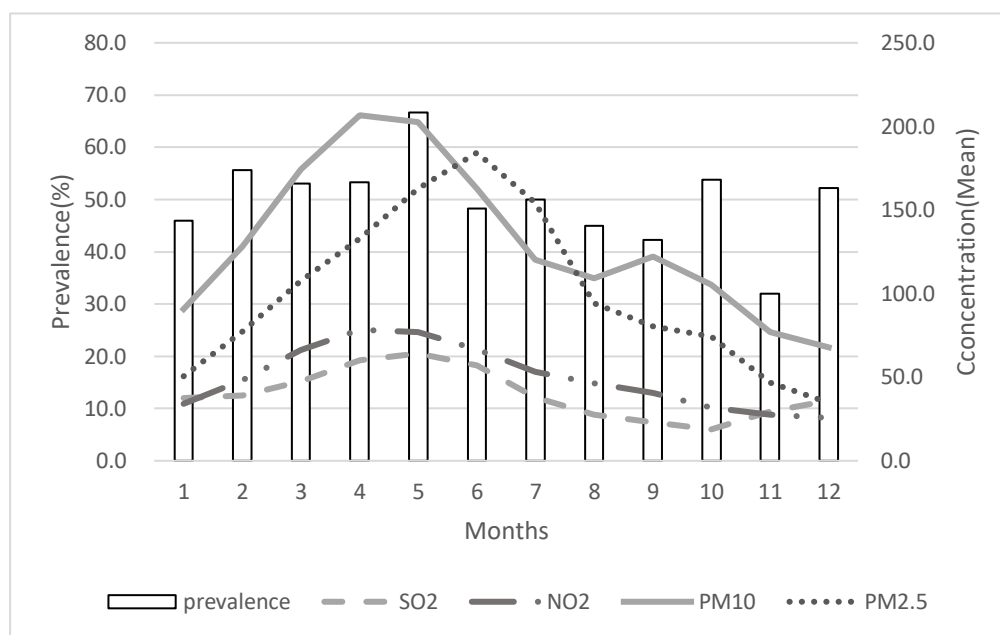


Figure S1. Prevalence of allergic diseases and exposure to air pollutants during the second trimester in 3-year-old children, separated by birth months

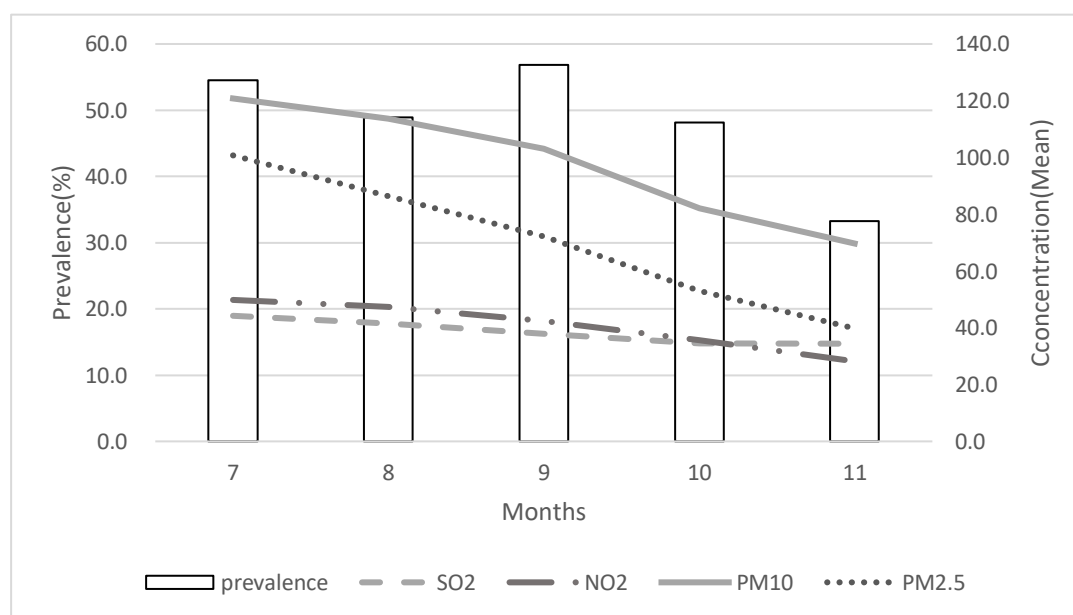


Figure S2. Prevalence of allergic diseases and exposure to air pollutants during the second trimester in 4-year-old children, separated by birth months