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Migrant population is more vulnerable to the effect of air pollution on preterm birth: Results from a birth cohort study in seven Chinese cities

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ABSTRACT

Background: Studies have reported that exposure to air pollution during pregnancy was associated with preterm birth (PTB). However, it remains unknown whether this association differs between local residents and migrants.
Objective: This study aimed to differentiate the associations between maternal air pollution exposure and PTB between local residents and migrants.
Methods: We established a retrospective birth cohort in seven Chinese cities in Pearl River Delta (PRD) region during 2015–2017. The mothers were included in the cohort at their first time of hospital visit for pregnancy, and the endpoint events were identified using the birth registry. The air pollution exposure was estimated based on the daily air pollution concentrations in the nearby air monitoring stations during different pregnancy periods. Cox proportional hazards models were utilized to estimate the associations between each air pollutant and PTB for different pregnancy periods.
Results: Our cohort included a total of 628,439 mother-and-live-birth pairs. Among them, 308,201 women were local residents, and 320,238 were migrants. We observed stronger effects of air pollutants among the migrants than the local residents. For the exposure during the entire pregnancy, the hazard ratio (HR) among the migrants and local residents were 1.56 (95% CI: 1.50, 1.63) and 0.98 (95% CI: 0.93, 1.02) for each 10 μg/m^3 increase in $PM_{2.5}$, 1.32 (95% CI: 1.27, 1.39) and 1.18 (95% CI: 1.12, 1.23) for each 10 ppb increase in O_3, and 1.48 (95% CI: 1.40, 1.57) and 0.99 (95% CI: 0.93, 1.05) for each 10 μg/m^3 increase in SO_2, respectively. Similarly higher effects were observed among the migrants for the exposures in different trimesters of pregnancy. However, the effects of NO_2 were comparable between the two groups.
Conclusion: Our study suggests that maternal $PM_{2.5}$, O_3 and SO_2 exposures might be important risk factors of preterm birth, particularly among the migrants. More specific protective and education measures should be considered for the migrant pregnant women.

1. Introduction

Widespread evidence shows that the atmospheric pollution could affect human health (Chung et al., 2017; Qiu et al., 2018; Xue et al., 2018). Most of the previous studies have focused on the association of air pollution on cardiovascular and respiratory mortality and morbidity (Ai et al., 2018; Lin et al., 2017b; Zhang et al., 2018). However, some populations might be more vulnerable to the effect of air pollution than others, for example, a potential link between air pollution and adverse pregnancy outcomes has become an important issue in recent years (Guo et al., 2018; Quinn et al., 2016; Wang et al., 2018a). In particular, low birth weight and preterm birth have been of great concern as

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important adverse birth endpoints (Liang et al., 2014; Liu et al., 2017).

Preterm birth (PTB, < 37 weeks of gestation) is one of many important neonatal health problems, accounting for about 11.1% of all newborns worldwide during 2010 (Blencowe et al., 2012; Li et al., 2018). It has been widely documented that preterm birth is strongly related to infant mortality (Liu et al., 2012; Ryan and Dogbey, 2015) and has long-term effects in childhood development (Arhan et al., 2017; Boptom et al., 2017). The impacts of air pollution on PTB have been explored in a few previous studies (Huang et al., 2018; Johnson et al., 2016; Malley et al., 2017). However, they were mainly conducted in developed countries. The studies in Asian countries have been lacking, though higher levels of air pollution usually exist (Li et al., 2017; Yang and Zhang, 2018).

Furthermore, the health effects of environmental exposures among the migrant population have been largely neglected. Studies have suggested that the migrants are the vulnerable subpopulation to be affected by a variety of environmental factors, mainly due to their poor living conditions (Liming et al., 2014), limited health knowledge (Shi et al., 2012), as well as lacking of social support and social integration (Li, 2013). More efforts should be put on this vulnerable population (Zeng et al., 2015). The Pearl River Delta (PRD) region is a major industrial and developed region, and one of the most important destinations for internal labor migrants in China (Guo and Shen, 2014). This region provided an opportunity for us to study the effects of maternal air pollution exposures on PTB among the migrants. However, no such study has been conducted yet.

We therefore performed this study in seven major cities of the Pearl River Delta region in Southern China. The aims of this study included: 1) to quantify the association between maternal air pollution exposures and preterm birth in migrants and local residents during different periods of pregnancy; 2) to investigate whether migrant status could modify the association between maternal air pollution exposures and preterm birth.

2. Material and methods

2.1. Study settings

The PRD region had about 26.8 million migrant population at the end of 2017. We selected seven cities in the PRD region for this study. They were Guangzhou, Shenzhen, Zhuhai, Dongguan, Foshan, Jiangmen, and Zhongshan (Fig. 1). These cities are the major cities in the PRD region with similar geographical, climate, and cultural conditions. They had a typical subtropical climate with dry, cool to mild winters and wet, hot summers.

Approval to conduct this study was obtained from the institutional ethical committee board of Guangdong Women and Children Hospital.

We collected the data of all singleton births between January 1, 2015 and December 31, 2017 from the birth registry database. According to the regulations of Guangdong Province, the birth information should be reported to the system by all midwifery clinics and hospitals in this province. Birth certificate is one of the components of the system (He et al., 2016; Liang et al., 2019). In accordance with previous studies (He et al., 2016; Wang et al., 2018a), all singleton vaginal live births with available maternal Hukou information at 20–44 weeks of gestation were included in the present study. The information included maternal age, date of birth, delivery mode, infant sex, gestational age at birth, birth weight, parity and registered residence. Registered residence represents the permanent residence in the system of household registration (the Hukou system) in China.

The conception date was estimated according to the ultrasound examination and the mother's last menstrual period, and then the pregnancy periods of the first, second and third trimesters were estimated (He et al., 2016). Any birth with < 37 weeks of gestational age was defined as PTB (Blencowe et al., 2012; Liang et al., 2018). In order to examine the effects of air pollutants on the timing for natural labor, we excluded cesarean section deliveries as their delivery date was more likely to be affected by other factors, especially the preference of the parents (Vicedo-Cabrera et al., 2014).

2.2. Definition of migration

In accordance with previous studies and the resident registration system in China (Mou et al., 2015), we defined a “migrant” as a person who has settled permanently or temporarily in the seven cities of present study other than his/her own Hukou (household registration) place in China.

2.3. Exposure assessment

Air pollution concentration data were measured at the air monitoring stations for the period from January 1, 2014 to December 31, 2017. The number of air monitoring stations differed in the seven cities: 10 in Guangzhou, 11 in Shenzhen, 4 in Zhuhai, 5 in Dongguan, 8 in Foshan, 4 in Jiangmen, and 4 in Zhongshan (Fig. 1). The details about the air monitoring system have been introduced previously (Lin et al., 2017c). In brief, the monitored air pollutants included $PM_{2.5}$, nitrogen dioxide (NO_2), sulfur dioxide (SO_2) and ozone (O_3). The daily concentrations were measured following strict, standard quality assurance and quality control procedures in accordance with the National Environmental Protection Administration of China. There were few observation days with missing data (fewer than 5% for all the air pollutants across the seven cities). We imputed the missing values using linear interpolation based on the na.approx function in the R package.

To examine the effects of air pollution on the risk of PTB at different pregnancy periods, the daily mean concentrations of each air pollutant were computed for each pregnancy stage: 0–12 weeks as the first trimester, 13–28 weeks as the second trimester, and after 28 weeks as the third trimester, as well as the entire pregnancy (Chen et al., 2018). In order to capture the acute effect, we also assessed exposures during the 2 weeks prior to delivery.

We estimated the air pollution exposures according to the combination of air monitoring information in a nearby monitoring station during the pregnancy period of the mothers. Specifically, the exposures were estimated based on the mother's residential districts at birth, and the districts without an air monitoring station were excluded from the analysis. Finally, a total of 30 districts were included in the study and the average radius of the districts was about 10 km.

Daily meteorological data were collected for the same time period from the National Weather Data Sharing System, including daily average temperature (°C) and relative humidity (%). They were matched to the different pregnancy periods using the same approach as that of air pollution.

We considered a few covariates in this study, including continuous variables [such as the age of the mother at delivery, birth weight (grams), and gestational age (in weeks)], and categorical variables [including the sexes of the newborns (male or female), previous pregnancy (yes or no), and previous delivery (yes or no)].

3. Statistical analysis

We performed a Cox proportional hazards model to examine the effects of air pollution exposures on preterm birth at different periods of pregnancy for local residents and migrants, respectively. In the model, the preterm birth was used as the outcome variable, and the gestational age was used as the time axis (Xiao et al., 2018).

The births were considered as censored data at the end of the 36th week of gestation. To account for the non-linear effects of the meteorological factors, the ambient temperature and relative humidity were adjusted using natural cubic splines with degrees of freedom of 6 and 3, respectively (Liang et al., 2016). We also controlled for other covariates in the model, such as maternal age, baby's gender, previous pregnancy,

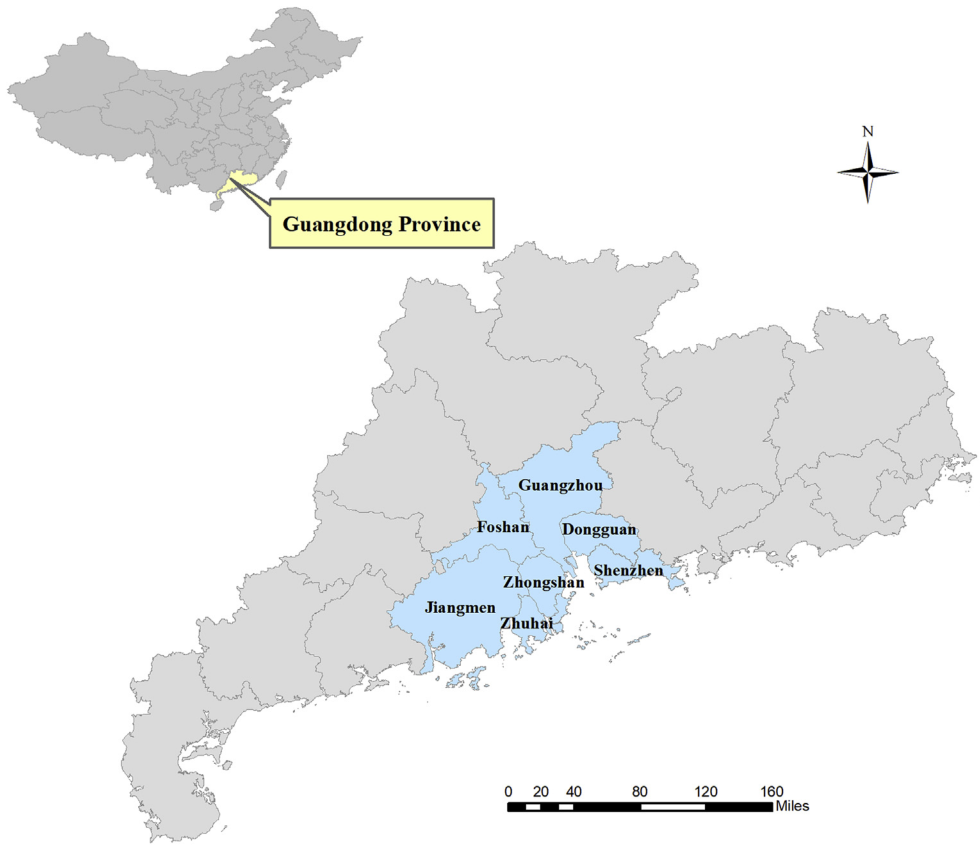

Fig. 1. The geographical distribution of the seven study cities in China.

and previous delivery. Individual model was constructed for PTB and each stage of pregnancy.

The effects were examined by both single-pollutant and two-pollutant models. The linearity of the concentration–response associations between pollutant exposures and PTB was also evaluated using a natural spline smoothing function (Lin et al., 2017a). A number of sensitivity analyses were performed by changing the degrees of freedom for mean temperature (5–7 degrees of freedom), and relative humidity (2–4 degrees of freedom). To avoid the potential impact of the cesarean deliveries on the estimates, we also performed one additional analysis by further incorporating the cesarean deliveries into the analysis. We further conducted one additional analysis by controlling for conception season to check the robustness of our findings.

The associations were illustrated as hazard ratios (HRs) and the 95% confidence intervals (95% CIs) for each 10 $\mu g/m^3$ increase in the concentrations of $PM_{2.5}$, NO_2, and SO_2, and each 10 parts per billion (ppb) increase in the concentration of O_3. We performed all statistical analyses using R software (version 3.4.4). The “survival” and “smoothHR” packages were used to fit Cox proportional hazards regression models.

4. Results

A total of 636119 births were initially collected in the seven cities. Among them, 5455 were excluded for non-singleton births, 2074 for non-live births, and 151 due to missing information on maternal age or gestational age, and the remaining 628,439 singleton vaginal live births at the gestational age of 20–44 weeks were included in this study during the study period (Fig. S1). Among them, 308,201 (49.0%) were PRD local registered residents, and 320,238 (51.0%) were migrants (Table 1). There were 29,849 (4.8%) preterm births in this study. Among all the mothers, 10.6% were ≥35 years old, 65.3% had previous pregnancy and 44.6% had previous delivery experience.

The characteristics of the air pollution and meteorological factors during pregnancy are summarized in Table 2. The mean daily concentrations for $PM_{2.5}$, O_3, NO_2, and SO_2 during the whole pregnancy were 36.9 $\mu g/m^3$, 25.2 ppb, 42.8 $\mu g/m^3$, and 13.1 $\mu g/m^3$, respectively.

Table S1 shows the results of the relation between air pollutants and meteorological data. Both pollutants were positively correlated with $PM_{2.5}$ (Spearman's correlation coefficient: r ranged from 0.03 to 0.55), NO_2 and SO_2 were negatively correlated with O_3 ($r = -0.39$ and $r = -0.04$) respectively, and a positive correlation between NO_2 and SO_2 is found ($r = 0.20$). The mean of daily average temperature during the entire pregnancy was 22.7 °C and was negatively correlated with air pollutants except for O_3 ($r = 0.37$). The mean of daily average relative humidity during the entire pregnancy was 78.7% and was negatively correlated with air pollutants except for NO_2 ($r = 0.04$).

Table 3 gives the results from the single-pollutant models at different exposure windows. In migrants, we observed statistically significant positive effects of $PM_{2.5,}$ $SO_{2,}$ and O_3 with PTB during the entire pregnancy, and the corresponding HRs were 1.56 (1.50, 1.63) and 1.48 (1.40, 1.57) for each 10 $\mu g/m^3$ increase in $PM_{2.5}$ and SO_2 concentrations, and 1.32 (1.27, 1.39) for each 10 ppb increase in O_3 concentration, respectively. As for the local residents, we observed statistically significant positive associations of O_3 with PTB during the entire pregnancy, with an HR of 1.18 (1.12, 1.23) for each 10 ppb increase in O_3 concentration. However, we did not find any statistically significant positive effects of other air pollutants for the local residents.

Table 4 displays the effects from the two-pollutant models for comparing with single-pollutant models. The associations estimated from the two-pollutant models were basically consistent with those from the single-pollutant models. Hazard ratio estimates during the entire pregnancy on PTB by the two-pollutant models ranged from 1.48 to 1.62 for $PM_{2.5}$, 1.15 to 1.31 for O_3, 0.91 to 0.98 for NO_2, and 1.23 to 1.47 for SO_2 in migrants, respectively. As for local residents, the changes in estimated effects on PTB by two-pollutant models ranged from 0.96 to 1.03 for $PM_{2.5}$, 1.15 to 1.18 for O_3, 0.95 to 0.97 for NO_2,

Table 1
The descriptive characteristics of all participants during the study period.

Variables	Local residents (n = 308,201)	Migrants (n = 320,238)	Preterm live births (n = 29,849)	Term live births (n = 598,590)	Total (n = 628,439)
Preterm birth	15089 (4.9%)	14760 (4.6%)	–	–	29849 (4.8%)
Baby gender					
Male	162497 (52.7%)	169471 (52.9%)	17929 (60.0%)	314039 (52.4%)	331968 (52.8%)
Female	145695 (47.2%)	150758 (47.0%)	11916 (39.9%)	284537 (47.5%)	296453 (47.1%)
Uncertain	9 (0.1%)	9 (0.1%)	4 (0.1%)	14 (0.1%)	18 (0.1%)
Maternal age					
< 35 years	267442 (86.7%)	293899 (91.7%)	25531 (85.5%)	535810 (89.5%)	561341 (89.3%)
≥ 35 years	40720 (13.2%)	26263 (8.2%)	4306 (14.4%)	62677 (10.4%)	66983 (10.6%)
Missing	39 (0.1%)	76 (0.1%)	12 (0.1%)	103 (0.1%)	115 (0.1%)
Previous pregnancy					
Yes	179358 (58.2%)	230966 (72.1%)	18970 (63.5%)	391354 (65.4%)	410324 (65.3%)
No	128355 (41.6%)	88133 (27.5%)	10800 (36.2%)	205688 (34.3%)	216488 (34.4%)
Unrecorded	488 (0.2%)	1139 (0.4%)	79 (0.3%)	1548 (0.3%)	1627 (0.3%)
Previous delivery					
Yes	141490 (45.9%)	138539 (43.3%)	13334 (44.6%)	266695 (44.5%)	280029 (44.6%)
No	166194 (53.9%)	180641 (56.4%)	16438 (55.1%)	330397 (55.2%)	346835 (55.2%)
Unrecorded	517 (0.2%)	1058 (0.3%)	77 (0.3%)	1498 (0.3%)	1575 (0.2%)

Table 2
Summary of air pollution and weather conditions during pregnancy of all participants.

Pollutants	Mean	Min	Max	Percentiles		
				25th	50th	75th
Trimester 1						
$PM_{2.5}$ (μg/m^3)	38.4	11.6	73.2	31.0	37.7	45.2
O_3 (ppb)	25.3	10.0	46.8	20.2	25.3	29.8
NO_2 (μg/m^3)	43.3	9.2	84.0	33.6	42.3	52.4
SO_2 (μg/m^3)	13.6	4.3	42.1	10.3	12.6	15.9
Temperature (°C)	22.3	13.5	29.8	17.6	22.6	27.3
Relative humidity (%)	78.2	62.5	90.0	76.2	78.7	81.3
Trimester 2						
$PM_{2.5}$ (μg/m^3)	36.7	13.3	70.8	28.7	36.1	43.8
O_3 (ppb)	25.0	11.0	48.8	21.0	25.2	28.6
NO_2 (μg/m^3)	42.6	9.7	81.7	33.6	41.5	51.5
SO_2 (μg/m^3)	13.1	4.5	41.1	10.2	12.2	15.1
Temperature (°C)	22.7	13.4	29.6	18.3	23.4	27.3
Relative humidity (%)	78.7	63.5	89.8	76.3	79.1	82.8
Trimester 3						
$PM_{2.5}$ (μg/m^3)	35.7	8.3	81.0	28.1	34.8	41.7
O_3 (ppb)	25.3	3.7	56.7	21.1	25.4	29.2
NO_2 (μg/m^3)	42.6	6.7	108.8	33.6	41.6	50.5
SO_2 (μg/m^3)	12.6	3.8	49.0	10.2	11.9	14.2
Temperature (°C)	23.1	7.2	30.7	18.6	24.6	27.7
Relative humidity (%)	79.0	53.9	94.0	76.6	79.4	82.9
2 weeks prior to delivery						
$PM_{2.5}$ (μg/m^3)	35.7	7.7	105.7	26.8	34.0	42.5
O_3 (ppb)	25.5	3.6	69.7	19.0	24.9	31.2
NO_2 (μg/m^3)	43.0	6.7	119.5	31.5	41.1	52.1
SO_2 (μg/m^3)	12.5	3.1	56.3	9.5	11.7	14.6
Temperature (°C)	23.2	9.0	31.2	18.4	24.7	27.9
Relative humidity (%)	79.0	51.9	96.9	74.7	79.5	84.0
Entire pregnancy						
$PM_{2.5}$ (μg/m^3)	36.9	18.8	60.0	33.4	36.7	40.9
O_3 (ppb)	25.2	12.0	41.3	22.3	25.0	28.0
NO_2 (μg/m^3)	42.8	12.9	75.4	35.8	42.5	50.0
SO_2 (μg/m^3)	13.1	4.8	33.2	10.5	12.3	14.8
Temperature (°C)	22.7	16.2	28.4	21.2	22.6	24.3
Relative humidity (%)	78.7	66.3	86.1	76.5	79.2	81.5

and 0.99 to 1.00 for SO_2, respectively.

Sensitivity analyses by changing the degrees of freedom for the adjustment of temperature and relative humidity did not substantially alter the effect estimates for the associations of pollutants with PTB in this study. For example, the hazard ratios of $PM_{2.5}$ during the entire pregnancy ranged from 1.56 to 1.58 and 1.39 to 1.60 for the migrants, and ranged from 0.96 to 0.99 and 0.98 to 0.99 for the PRD local residents. (See Supplementary Table S2). When including the cesarean deliveries, we observed the consistent effect estimate at any trimester

Table 3
Migrant status-specific HRs (95% CIs) in single-pollutant models at different exposure windows during pregnancy in PRD region.

Trimesters	Local residents	Migrants
Trimester 1		
$PM_{2.5}$	0.93 (0.91, 0.96)	0.94 (0.91, 0.96)
O_3	1.01 (0.97, 1.05)	1.01 (0.98, 1.05)
NO_2	0.97 (0.96, 0.99)	1.01 (0.99, 1.03)
SO_2	0.96 (0.92, 1.00)	0.98 (0.94, 1.02)
Trimester 2		
$PM_{2.5}$	0.97 (0.94, 1.01)	1.04 (1.01, 1.07)
O_3	0.92 (0.89, 0.96)	1.03 (0.99, 1.06)
NO_2	0.98 (0.96, 0.99)	1.01 (0.99, 1.02)
SO_2	1.00 (0.95, 1.05)	1.02 (0.97, 1.07)
Trimester 3		
$PM_{2.5}$	0.98 (0.95, 1.01)	1.14 (1.10, 1.17)
O_3	1.08 (1.04, 1.13)	1.08 (1.04, 1.12)
NO_2	1.01 (0.99, 1.02)	1.05 (1.03, 1.07)
SO_2	0.90 (0.86, 0.95)	1.06 (1.01, 1.11)
2 weeks prior to delivery		
$PM_{2.5}$	1.02 (1.00, 1.04)	1.03 (1.01, 1.05)
O_3	1.01 (0.99, 1.03)	1.00 (0.98, 1.03)
NO_2	0.99 (0.98, 1.00)	1.01 (0.99, 1.02)
SO_2	1.07 (1.03, 1.11)	1.02 (0.99, 1.06)
Entire pregnancy		
$PM_{2.5}$	0.98 (0.93, 1.02)	1.56 (1.50, 1.63)
O_3	1.18 (1.12, 1.23)	1.32 (1.27, 1.39)
NO_2	0.96 (0.94, 0.98)	0.95 (0.94, 0.97)
SO_2	0.99 (0.93, 1.05)	1.48 (1.40, 1.57)

Table 4
Estimated HRs (95% CIs) for PTB associated with maternal exposure to air pollutants during the entire pregnancy in two-pollutant models in PRD region.

Pollutants	Local residents	Migrants
$PM_{2.5}$	0.98 (0.93, 1.02)	1.56 (1.50, 1.63)
$PM_{2.5}$ + O_3	0.96 (0.92, 1.00)	1.49 (1.42, 1.56)
$PM_{2.5}$ + NO_2	1.03 (0.98, 1.08)	1.62 (1.55, 1.70)
$PM_{2.5}$ + SO_2	0.98 (0.93, 1.03)	1.48 (1.42, 1.55)
O_3	1.18 (1.12, 1.23)	1.32 (1.27, 1.39)
O_3 + $PM_{2.5}$	1.18 (1.12, 1.24)	1.15 (1.09, 1.20)
O_3 + NO_2	1.15 (1.09, 1.21)	1.31 (1.25, 1.37)
O_3 + SO_2	1.18 (1.12, 1.23)	1.23 (1.18, 1.29)
NO_2	0.96 (0.94, 0.98)	0.95 (0.94, 0.97)
NO_2 + $PM_{2.5}$	0.95 (0.94, 0.97)	0.91 (0.90, 0.93)
NO_2 + O_3	0.97 (0.96, 0.99)	0.98 (0.96, 1.00)
NO_2 + SO_2	0.96 (0.94, 0.98)	0.96 (0.94, 0.97)
SO_2	0.99 (0.93, 1.05)	1.48 (1.40, 1.57)
SO_2 + $PM_{2.5}$	1.00 (0.94, 1.07)	1.23 (1.15, 1.31)
SO_2 + O_3	0.99 (0.93, 1.05)	1.36 (1.28, 1.44)
SO_2 + NO_2	0.99 (0.94, 1.05)	1.47 (1.39 1.56)

for PTB (Supplementary Table S3). For example, in the migrants, the HR including the cesarean deliveries was 1.50 (95% CI: 1.45, 1.55) for each 10 μg/m^3 increase in $PM_{2.5}$ during the entire pregnancy, which is similar to the HR 1.56 (95% CI: 1.50, 1.63) by excluding the cesarean deliveries. Further, controlling the conception season did not alter the effect estimates (Supplementary Table S4). For example, in the migrants, the HR by controlling the conception season was 1.31 (95% CI: 1.26, 1.37) for each 10 ppb increase in O_3 during the entire pregnancy, which is similar to the HR 1.32 (95% CI: 1.27, 1.39), without controlling the conception season.

5. Discussion

Our study might be the first birth cohort study to examine the association between air pollution and preterm birth among migrant population in China. Using a total of 628,439 singleton vaginally delivered births, this study illustrated that maternal exposures to ambient air pollutants ($PM_{2.5}$, O_3, NO_2, and SO_2) were significantly associated with increased risk of preterm birth, particularly, we observed a stronger association among the migrants than the local residents.

Compared to the local residents, the migrants were found to be more vulnerable to the effects of air pollutants on preterm birth in this study. There are several possible reasons for this phenomenon. First, due to the lower educational attainment level (Zong et al., 2018), most of rural-to-urban migrants have limited knowledge on the reproductive health, and it is relatively more difficult for them to obtain maternal health information (Lu et al., 2012). Second, disparity of health service utilization remained a major public health concern among the migrants due to the relatively lower income and health awareness, lack of time and inconvenience of medical insurance reimbursement (Lu et al., 2014; Zong et al., 2018). In China, public policies have long been based on the household registration (the Hukou) system, and it is relatively more difficult for the migrants to get insurance in the migrant cities. They usually have to get reimbursement in their registered home town. Without a local household registration, the migrants have limited access to the local welfare system (Song et al., 2017). Previous studies have indicated that migrant women's utilization of prenatal care was relatively lower than the local women (Zong et al., 2018). A study in Guangzhou suggested that compared to local residents, migrant women were substantially less likely to have prenatal health examinations (Chen et al., 2004). Finally, the migrants tend to live in places with lower air pollution levels before going to the urban areas, and had fewer opportunities to exposure to high level of air pollution. As a result, they may be less adapted to the high levels air pollution exposure in urban areas.

The observed positive associations between air pollution and preterm birth were generally consistent with previous studies (Arroyo et al., 2016; Laurent et al., 2016). For example, a study of 423,719 singleton births in Florida, USA reported that both O_3 and $PM_{2.5}$ maternal exposures in the entire pregnancy and the three trimesters were significantly positively related to increased risk of PTB (Ha et al., 2014). A prospective birth cohort study of 95,911 infants born between 2011 and 2013 in Wuhan, China also found that there was negligible evidence for NO_2 and SO_2 exposure and increased risk of the premature birth (Qian et al., 2016). On the other hand, inconsistent findings have also been reported in other studies. For example, one Netherlands study including 3,853 singleton births did not find any significant associations of PTB with $PM_{2.5}$ in any pregnancy period (Gehring et al., 2011b). Wang et al. did not find any association between pregnancy SO_2 exposure and the risk of PTB in Guangzhou (Wang et al., 2018b). Compared with these studies, the different study design and sample size may potentially contribute to differential results in our study. First, a large sample size (628,439 newborns) in seven cities of the PRD region was included in our study. Second, we excluded cesarean section deliveries in our study, as the delivery time of section deliveries may be determined by other factors.

Previous studies have reported inconsistent findings in terms of susceptible exposure window, even for the same air pollutants. The third trimester was observed to be the most sensitive exposure window in our study, while some other studies found that the first trimester might be the most sensitive exposure window (Gehring et al., 2011a; Lee et al., 2013). Consistent with ours, De Franco et al. and Hannam et al. found that the third trimester was susceptible exposure window (Defranco et al., 2016; Kimberly et al., 2014). And a meta-analysis also observed a stronger association between $PM_{2.5}$ exposure and preterm birth during the third trimester (Sapkota et al., 2012). However, Pereira et al. and Ritz et al. reported that the first trimester was the more susceptible exposure window for $PM_{2.5}$ and PTB (Gavin et al., 2014; Ritz et al., 2007). Several reasons could explain the inconsistency, including the different sample size, study design, air pollution levels and chemical compositions, and demographic characteristics of the study population.

This study suggested that maternal exposure to air pollution ($PM_{2.5}$, O_3 and SO_2) during the pregnancy may affect the gestation period, especially among the migrants. The biological mechanisms are not yet clear. A few possible biological pathways have been proposed in previous studies. On one hand, the placental DNA adducts produced by air pollution were more common among the mothers exposed to high level of air pollution (Kannan et al., 2006). Higher expression of DNA adducts in a fetus could reduce the DNA repair and detoxification enzymatic capacity (Myllynen et al., 2005). DNA adducts have been associated with decreased length of gestation in previous studies (Liu et al., 2003). On the other hand, the mechanism might be related to hematologic factors. Increased blood viscosity due to the exposure to air pollution and the hematological factors might be related to inadequate placental perfusion and thus lead to PTB (Kannan et al., 2006; Peters et al., 1997). Animal studies also supported the finding that exposure to urban air pollution during pregnancy inhibited fetal growth, which is closely related with the risk of PTB (Veras et al., 2008).

In this study, we did not find a positive association between NO_2 exposure and the risk of PTB among the local residents. Similarly, positive associations between PTB and NO_2 were rarely reported in previous studies. Some previous studies found that PTB was negatively but insignificantly associated with NO_2 (Liu et al., 2003; Qian et al., 2016). The underlying reasons for this observation remained unknown. It was possible that some potential confounding factors were not adjusted in the model, leading to some residual confounding.

One advantage of this study was the large sample size (628,439 newborns) included in the analysis, which covered seven cities in the PRD region. This region had relatively higher air pollution level than that in developed regions where majority of previous studied were conducted. For example, in US, the mean $PM_{2.5}$ concentration during the whole pregnancy ranged between 18.7 μg/m^3 in California and 9.9 μg/m^3 in Florida (Sun et al., 2016). However, the mean $PM_{2.5}$ exposure during the entire pregnancy was 36.91 μg/m^3 in our study. Besides, the PRD region provided an unique opportunity to investigate the effect of maternal air pollution exposure on preterm birth among migrant women. We found that migrant women are more vulnerable to high level air pollution than local residents. And we call for more studies to examine the effects of air pollution on migrant health in future.

There were also some limitations in the present study. First, we did not control for a few important potential confounding factors, such as parental socioeconomic or education status, maternal ethnicity, nutritional status, hypertensive disorders of pregnancy, time of relocation, maternal smoking status and maternal exposure to environmental tobacco smoke, mainly due to the lack of this information in the birth record data. Considering that there was a low smoking rate among the women, especially among the pregnant women, this concern was not likely to bias the results to a great extent (Zhang et al., 2015). Second, the air pollution exposure was assessed based on the measurements from the nearby air monitoring stations, which may not well represent the actual individual exposure. In addition, some women may move during pregnancy. Unfortunately, the information was not available for our analysis. Finally, we can't distinguish spontaneous PTB from medically-indicated PTB, so our study only included the vaginal live births, and preterm birth might be underestimated if air pollution exposure could increase the risk of fetal death. And even few women become pregnant again within 3 years, but due to the lack of individual identifiable information, we did not adjust for within-mother variances in this study.

The findings of this study had some important public health implications. In particular, our study provided further epidemiological evidence on the health effects of air pollution. And regarding the vulnerable subpopulation observed in this study, air pollution protection should be considered for the migrant pregnant women. It is necessary to strengthen the education of reproductive knowledge during the pregnancy for the migrant women. In addition, the government needs to formulate more appropriate policies to provide effective and convenient medical services for the migrant pregnant women.

6. Conclusions

In summary, our study suggests that maternal $PM_{2.5}$, O_3, and SO_2 exposures might be important risk factors of the preterm birth among the migrant women, especially for the women at late stage of pregnancy.

Declaration of interests

The authors declare they have no actual or potential competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijheh.2019.07.004.

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