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Seasonal analyses of the association between prenatal ambient air pollution exposure and birth weight for gestational age in Guangzhou, China

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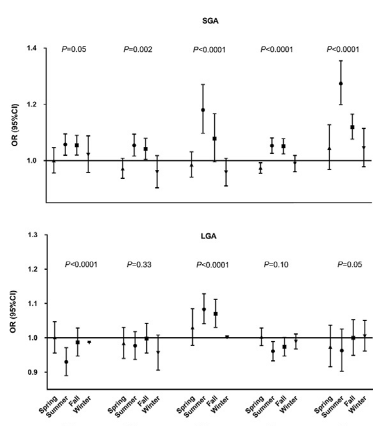
HIGHLIGHTS

- Prenatal $PM_{2.5}$, NO_2, SO_2, and O_3 exposures increased the risk of SGA.
- Prenatal exposure to $PM_{2.5}$, PM_{10}, SO_2, and O_3 decreased the risk of LGA.
- Effects of prenatal air pollution exposure on SGA may be modified by season.
- Effects of air pollution on SGA were observed for pregnancies conceived in summer or fall.

GRAPHICAL ABSTRACT



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ABSTRACT

Ambient air pollution has been linked to small for gestational age (SGA); however, the relationship with large for gestational age (LGA) is unclear and very few studies have investigated seasonal effects on the association between air pollution and SGA or LGA. Using birth registry data of 506,000 singleton live births from 11 districts in Guangzhou, China between January 2015 and July 2017, we examined associations between ambient air pollutants ($PM_{2.5}$, PM_{10}, NO_2, SO_2, and O_3) and SGA/LGA, and further assessed the modification effect of season. Daily concentrations of air pollutants from 11 monitoring stations were used to estimate district-specific exposures for each participant based on their district of residence during pregnancy. Two-level binary logistic regression models were used to evaluate associations between air pollution and SGA/LGA. Stratified analyses by season and a Cochran Q test were performed to assess the modification of season. Exposure to $PM_{2.5}$, NO_2, SO_2, and O_3 was significantly associated with increased risk of SGA, especially for exposure during the second and third

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Large for gestational age
Season
Effect modification

trimester. For an interquartile range (IQR) increase in $PM_{2.5}$ (6.5 μg/m^3), NO_2 (12.7 μg/m^3), SO_2 (2.8 μg/m^3) and O_3 (20.8 μg/m^3) during the entire pregnancy, SGA risk increased by 2% (OR = 1.02, 95% CI: 1.00–1.04), 8% (OR = 1.08, 95% CI: 1.04–1.12), 2% (OR = 1.02, 95% CI: 1.01–1.03), and 14% (1.14, 1.11–1.17), respectively. A decreased risk of LGA was found for $PM_{2.5}$, PM_{10}, SO_2, and O_3 during the first trimester or entire pregnancy. When examined by season, significant associations between air pollutants and SGA were observed for women who conceived during summer or fall, and the patterns were consistent for all pollutants. Our study suggests that conception during different seasons might modify the association between ambient air pollution and SGA.

1. Introduction

Small for gestational age (SGA) and large for gestational age (LGA) are defined as birth weight less than the 10th percentile or more than the 90th percentile, respectively, of a population-based birth weight reference at a given gestational age, while an appropriate size for gestational age (AGA) is defined as birth weight within the 10th to 90th percentile of the reference value (Khambalia et al., 2017; Mikolajczyk et al., 2011). SGA has been associated with children's morbidity and mortality (Moraitis et al., 2014) and complications later in life, including cardiovascular disease and diabetes (Baker et al., 2008; Risnes et al., 2011). High birth weight or being LGA increases the mother's risk for genital tract injury, postpartum bleeding (Surkan et al., 2004), while longer term it increases the risk of metabolic disorders for infants in later life (Boney et al., 2005).

Ambient air pollution can induce systemic inflammation, oxidative stress, and hemodynamic changes, leading to impaired oxygen and nutrient transport to the fetus, and subsequent abnormal fetal growth (Kannan et al., 2006; Schlesinger et al., 2006). An increasing number of studies have examined the association between prenatal air pollution exposure and SGA (Li et al., 2017; Shah and Balkhair, 2011; Stieb et al., 2012). However, the results from these studies have been inconsistent. A number of prior studies reported increased risk of SGA associated with $PM_{2.5}$ exposure (Hannam et al., 2014; Hyder et al., 2014; Lavigne et al., 2016; Liu et al., 2007; Mannes et al., 2005; Parker et al., 2005; Rich et al., 2009; Stieb et al., 2016) and PM_{10} exposure (Ha et al., 2017; Hansen et al., 2007; Le et al., 2012; Mannes et al., 2005) in various trimesters or the entire pregnancy. However, several studies reported no association (Brauer et al., 2008; Lee et al., 2013; Madsen et al., 2010), and one study reported protective effect (Vinikoor-Imler et al., 2014) of $PM_{2.5}$. Regarding NO_2 and SO_2, previous studies have reported both positive (Brauer et al., 2008; Liu et al., 2003) and no association (Michikawa et al., 2017) with SGA. Most previous studies observed no association between O_3 exposure during pregnancy and SGA (Ha et al., 2017; Hansen et al., 2007; Le et al., 2012; Lee et al., 2013; Liu et al., 2003; Mannes et al., 2005), while fewer studies found positive association (Le et al., 2012; Michikawa et al., 2017; Vinikoor-Imler et al., 2014). Additionally, most of these studies were conducted in areas with relatively low concentrations of air pollution (lower than WHO guidelines (WHO, 2006)), and it is unclear to what extent they are relevant to areas with higher pollutant concentrations, such as China. To our knowledge, no published studies have investigated the association between ambient air pollution and SGA in China.

Recently, an animal study suggested that pregnant mice exposed to air pollution could predispose offspring to weight gain in adulthood (Bolton et al., 2012). One epidemiological study observed positive associations between higher levels of PM_{10} exposure during pregnancy and fetal over-growth (Zhao et al., 2018). Supporting evidence shows that air pollution increases maternal glucose concentration, which could elevate nutrient transfer to the fetus and increase fetal growth (Scholl et al., 2001). Unlike SGA, no study has investigated the association between air pollution and LGA to our knowledge.

Since the chemical composition and concentrations of ambient air pollutants, individual exposures, and biological responses to air pollution may vary with season (Kim et al., 2017), seasonality may affect the association between air pollution and birth outcomes and may contribute to the inconsistency of previous studies, because not all studies adjusted for season of conception/birth in the models (Hyder et al., 2014; Lavigne et al., 2016; Lee et al., 2013; Michikawa et al., 2017; Rich et al., 2009; Vinikoor-Imler et al., 2014). Moreover, season is a temporal factor and changes during the pregnancy, which may lead to complex and unexplained associations between air pollution and birth outcomes; for example, Stieb et al. (Stieb et al., 2016) observed a significant positive association between NO_2 exposure and preterm birth with gestation 20–27 weeks, null association with births in 28–33 weeks, and a negative association with births in 34–36 weeks. It has been shown that associations of prenatal air pollution exposure with preterm birth can be confounded by season (Jalaludin et al., 2007; Olsson et al., 2012; Stieb et al., 2016). However, it is still unclear to what extent season might modify air pollution effects on SGA or LGA.

In this study, we aimed to investigate the effects of prenatal air pollution exposure on both SGA and LGA, and to explore if the season of conception modifies the effects of air pollution on these outcomes.

2. Methods

2.1. Study population

Guangzhou has been one of the cities in China showing high impact of air pollution on total mortality (Shang et al., 2013). Guangzhou also has good birth registry data, which allow us to examine the effects of air pollution on birth outcomes in this city. The study population for this retrospective cohort study was identified from the Birth Registry System in Guangdong province, China, including mothers and their singleton live births in the capital city Guangzhou (population ~ 14.5 million) from January 1, 2015 to July 31, 2017 (n = 506,280). This birth registry commenced and then was refined by adding more quality check steps in 2014 to improve the integrity of collected variables. This system includes all newborns delivered in hospitals, maternity and child care institutions, and at home. Collected variables included the pregnant women's home address during pregnancy at the district level, maternal age, parity, medical conditions during pregnancy (which was an indicator of one or more of several conditions, including placenta abruption, placenta previa, placental accreta, pregnancy-induced hypertension, preeclampsia, eclampsia, oligohydramnios, uterine rupture, and gestational diabetes), delivery mode, gestational age at birth, date of birth, birth weight, and infant sex. The gestational age (week) was determined by combining ultrasound examination and mother-reported last menstrual period to represent the best available clinical estimate for each woman. When available, ultrasound estimates were used; otherwise, the date of the last menstrual period was used. The date of conception was estimated based on the gestational age and the date of birth. We determined the season of conception based on conception date: spring (March–May), summer (June–August), fall (September–November), and winter (December–February).

According to the average age at menarche (12.76 years) (Song et al., 2011) and natural menopausal age (50.76 years) (Shao et al., 2014) in the Chinese population, we excluded 49 pairs with an outlier maternal age (<13 or >50 years).