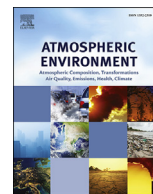




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Association between exposure to ambient air pollution before conception date and likelihood of giving birth to girls in Guangzhou, China



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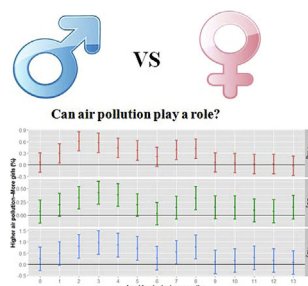
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HIGHLIGHTS

- We compared air pollution exposures of parents of boys and girls in Guangzhou.
- Air pollution exposure was associated with higher chance of giving birth to girls.
- Exposure of about one week before conception date was effective for this effect.

GRAPHICAL ABSTRACT



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ABSTRACT

A few studies have linked ambient air pollution with sex ratio at birth. Most of these studies examined the long-term effects using spatial or temporal comparison approaches. This study aimed to investigate whether parental exposure to air pollution before conception date could affect the likelihood of the offspring being male or female. We used the information collected in a major maternal hospital in Guangzhou, China. The parental exposure to air pollution was assessed using the air pollution concentration before the conception date. Logistic regression models were used to assess the association between air pollution exposure and birth sex with adjustment for potential confounding factors, such as maternal age, parental education levels, long-term trend, season, and weather condition (mean temperature and relative humidity). The analysis revealed that higher air pollution was associated with higher probability of female newborns, with the effective exposure around one week prior to conception date. In the one-pollutant models, PM₁₀, SO₂ and NO₂ had significant effects. For example, the excess risk was 0.61% (95% confidence interval (95% CI): 0.36%, 0.86%) for a 10 µg/m³ increase in lag 2 day's PM₁₀.

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0.42% (95% CI: 0.21%, 0.64%) for lag 3 day's SO₂ and 0.97% (95% CI: 0.44%, 1.50%) for lag 3 day's NO₂; and in two-pollutant models, PM₁₀ remained statistically significant. These results suggest that parental exposure to ambient air pollution a few days prior to conception might be a contributing factor to higher probability of giving birth to female offspring in Guangzhou.

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1. Introduction

Previous studies have linked air pollutants to various health outcomes (Peters et al., 2000; Brook et al., 2004). Their effects on perinatal outcomes have recently drawn more attention, particularly low birth weight and preterm birth (Legro et al., 2010; Miraglia et al., 2013; Fleischer et al., 2014; Zhao et al., 2015). And a few epidemiological studies have reported that exposure to higher ambient air pollution might lead to more female babies, and thus impact the sex ratio at birth (Lloyd et al., 1985; Mackenzie et al., 2005).

The sex ratio at birth, also called secondary sex ratio, has been suggested as a sentinel indicator of the reproductive health of a population (Davis et al., 1998). Worldwide, the human live birth sex ratio is remarkably constant. However, a declining trend in male-to-female sex ratio has been observed in a number of countries during the past decades, which has been partly ascribed to a number of environmental and occupational factors (Allan et al., 1997; Fukuda et al., 2002; Mackenzie et al., 2005). Though the sex of the human embryo is mainly genetically controlled and determined at the time of conception, there is evidence that the sex ratio can be partially influenced by both endogenous and exogenous factors (Terrell et al., 2011). Parental endogenous hormone concentration of gonadotropins and/or testosterone at the time of conception are suspected to play an important role in determining the sex of the newborns (James, 2004).

Exogenous factors such as stress, parental diseases, and exposure to air pollution appear to have some influence on sex ratio of the newborns (James, 2004). The association between air pollution and birth sex ratio was supported by a few studies, including one experimental study (Lichtenfels et al., 2007). The mechanism of how these factors could affect the sex ratio of births remained largely unclear, it has been hypothesized that some of these environmental factors may act as endocrine disrupting compounds, influencing the sex ratio by changing the hormonal milieu of the parents (James, 1996), or by inducing sex-specific mortality in utero (Sakamoto et al., 2001).

Most previous studies reported the long-term association between air pollution and sex ratio at birth using either spatial analysis, which compared the sex ratio between locations with different levels of ambient air pollution (Williams et al., 1992; Williams et al., 1995; Yang et al., 2000a), or time-series studies that related temporal changes in birth sex to fluctuations in air pollution (Zhang et al., 1995; Allan et al., 1997; Astolfi and Zonta, 1999; Tragaki and Lasaridi, 2009; Miraglia et al., 2013). Most of the spatial comparison and temporal studies were subject to potential confounding bias because they did not consider some covariates at the individual level, such as maternal age, education level, etc. As an effective exposure window has not been assessed, it is unclear that how long of parental exposure to air pollution prior to the pregnancy was effective.

Air pollution has been a major environmental concern in Guangzhou, China alongside its rapid economic growth in recent decades (Jahn et al., 2011). However, there have been limited efforts to examine the reproductive health effects of ambient air pollution

in Guangzhou (Zhao et al., 2011).

The current study, therefore, was designed to explore the hypothesis that the sex ratio of births would be altered, to either high or low, by exposure to higher level of air pollution before/around the conception date. We used a logistic regression model with adjustment for some potential confounding factors at the individual level to assess the impact of parental exposures to ambient particulate matter of median aerometric diameter less than 10 microns (PM₁₀), sulfur dioxide (SO₂), and nitrogen dioxide (NO₂) on birth sex.

2. Data collection and methods

2.1. Data collection

This study was conducted among women who delivered first singleton live infants without malformations at a major maternal hospital in Guangzhou, China between January 2006 and November 2011. The hospital covers about 10% of newborns in Guangzhou City, and there was comparable distribution of gestational age (272.6 days VS 272.3 days), maternal age (28.1 yrs VS 27.5 yrs), birth weight (3148 g VS 3173 g) and male-to-female sex ratio of newborns (1.08 VS 1.15) with the whole city (Guo et al., 2014; He et al., 2014), suggesting a relatively good representativeness of this hospital. To minimize the impact of sex-selective abortion, we restricted the subjects to the singleton term, first pregnancy and first birth live newborns for the analysis.

In China, every birth is required to be registered by the law. It is the responsibility of the parents or the family concerned to register all births within 15 days after the birth of a new baby. A birth certificate must be submitted to the household registration office (no matter whether the infant is a male or a female), even if stillbirths or malformations occurred, they were included in the system (Li et al., 2010). In recent years, most deliveries in Guangzhou take place in a hospital or clinic.

The research protocol was reviewed and approved by medical ethical committee of Guangdong Provincial Center for Disease Control and Prevention.

2.2. Exposure assessment

Daily (24-hr) averaged concentrations of ambient PM₁₀, NO₂ and SO₂ were collected from 9 air monitoring stations located in Guangzhou for the period from 1 January 2006 through 31 December 2011. There were no changes in the placement of the stations or the monitoring instruments during the study period. Details on the monitoring stations have been described elsewhere (Yu et al., 2012; Lin et al., 2014). The daily concentration of the 9 stations was averaged to obtain the daily concentration for the whole city.

We estimated the effect of air pollution on birth sex according to different lag structures, including current day (lag0) up to 13 days before (lag13). Exposure to air pollution for each subject was estimated as the air pollution level at and prior to the conception date. Dates of the air pollution records were matched temporally to

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