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Air pollution exposure during pregnancy and ultrasound and birth measures of fetal growth: A prospective cohort study in Korea

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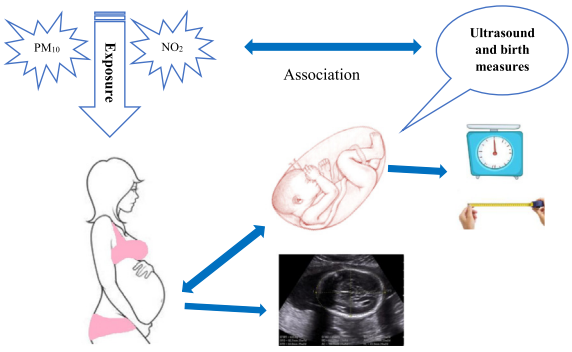
HIGHLIGHTS

- We examined the relationship of maternal air pollution exposure with fetal growth.
- NO_2 was associated with decreased biparietal diameter (BPD) in second trimester.
- PM_{10} was inversely associated with BPD in third trimester.
- Air pollution in third trimester was inversely associated with birth head circumference.

GRAPHICAL ABSTRACT



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ABSTRACT

Few studies have examined the effects of air pollution on fetal growth based on ultrasound measures during pregnancy. More data is needed to evaluate the windows of special vulnerability. Our aim was to investigate the association of ambient air pollution during pregnancy with fetal and neonatal characteristics in a cohort of Korean women. Maternal exposure to particulate matter with an aerodynamic diameter < 10 μm (PM_{10}) and nitrogen dioxide (NO_2) was estimated using land-use regression models based on residential address. The biparietal diameter (BPD), abdominal circumference (AC), femur length (FL), and estimated fetal weight (EFW) were evaluated via ultrasonography, and birth weight (BW), birth length (BL), and head circumference at birth (BHC) were obtained from medical records. The multiple linear regression model was used to adjust for confounders, and the mixed-effect model was used to evaluate longitudinal effect. The negative effects for NO_2 and PM_{10} were estimated; in the adjusted analyses the decreases of BPD were −0.26 mm (95% confidence interval [CI] = −0.41 to −0.11, with a 10 μg/m^3 increase) in the second trimester for NO_2, and −0.30 mm (95%

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CI = −0.59 to −0.03, with a 10 μg/m^3 increase) in the third trimester for PM_{10}. Both NO_2 and PM_{10} levels (10 μg/m^3) during third trimester were inversely associated with BHC, and NO_2 level was inversely associated with BL in all exposure windows. No significant associations for AC, FL, and EFW were observed. The longitudinal analyses showed inverse association of NO_2 exposure with head and length growth ($P < 0.001$). Our findings suggest that ambient air pollution is associated with impaired fetal head size from mid-gestation onwards.

1. Introduction

Numerous epidemiologic studies have demonstrated the association between air pollution and birth outcomes, including low birth weight, small head circumference, and other impaired fetal growth markers (Ballester et al., 2010; Dadvand et al., 2013; Ebisu et al., 2016; Ha et al., 2001; Leem et al., 2006; Pedersen et al., 2013). However, most of these studies assessed fetal parameters at birth and did not provide the evidence of critical windows of exposure at which fetal growth failure begins in utero because air pollution may have transient effect on fetal growth (Slama et al., 2008a).

Previous studies yielded inconclusive results with respect to the trimester which has the greatest association (Lamichhane et al., 2015; Stieb et al., 2012); reported associations are somewhat more consistent for first and third trimester (Woodruff et al., 2009). Air pollution during early pregnancy may have the potential to cause deleterious effects on fetal tissues (Tanner, 1978), which, in turn, lead to growth retardation throughout the gestation (Dejmek et al., 2000). On the other hand, air pollution during late pregnancy may interfere with the period of rapid fetal growth (Kline et al., 1989).

In recent years, studies on the effect of air pollution during pregnancy have focused on the use of ultrasound measures of fetal size in order to explore the period (s) of gestation when the air pollution may be associated with the reduction of fetal size. To date only ten studies, five of them included in a recent review (Smarr et al., 2013), in Europe (Aguilera et al., 2010; Iñiguez et al., 2012, 2016; Malmqvist et al., 2016; Slama et al., 2009; van den Hooven et al., 2012), South and North America (Carvalho et al., 2016; Ritz et al., 2014), Australia (Hansen et al., 2008), and China (Wang et al., 2017) have investigated the impact of prenatal air pollution exposure on fetal growth measured via ultrasounds (Table S1). All these studies with exception of one study (Carvalho et al., 2016) are supportive of an association between ambient air pollution and reduction in biparietal diameter or head circumference. However, the results of these studies were inconsistent with regard to impacts on fetal growth since the studies had assessed different air pollutants, used different study design with different exposure assessment, and varied sample size and adjusted potential confounders. Only one known study has evaluated exposure to air pollution using ultrasounds data in Asia with high ambient air pollution level (Wang et al., 2017); however, in that study, nitrogen dioxide (NO_2) levels were assessed only in 10 monitoring sites to develop the land-use regression (LUR) models.

As with other Asian countries, Korea has experienced rapid economic development, accompanied by increased industrialization and air pollution. Nonetheless, there is considerable heterogeneity in the population, socioeconomics, and pollution characteristics across Asian nations. We report here the Korean results in a prospective birth cohort study, aiming to investigate associations of NO_2 and particulate matter with aerodynamic diameter < 10 μm (PM_{10}) levels during pregnancy with fetal growth characteristics assessed during pregnancy by ultrasonography and at birth.

2. Materials and methods

2.1. Study subjects

This study was embedded in the Mothers and Children's Environmental Health (MOCEH) study, a multicenter prospective birth cohort study in South Korea. The MOCEH study has recruited pregnant women who met the inclusion criteria of being >18 years of age and were before 20 weeks of their pregnancies and were living in the targeted study site (i.e., Seoul, Ulsan, and Cheonan). Among the 1825 pregnant women recruited between 2006 and 2011, exposure levels of PM_{10} and NO_2 were estimated for 1498 mother-child pairs, who provided the required information on residential address and birth date. In this study, we included only non-smoking women with a singleton live birth for whom exposure to PM_{10} and NO_2 were assessed. We excluded mothers reporting chronic disease such as diabetes and hypertension, cases of abortion, and missing covariate information. Supplementary file (Fig. S1) shows the detail of exclusion criteria and final study population. The final study population consisted of 648 pregnant women and their babies for birth weight (BW), 609 for birth length (BL), and 485 for birth head circumference (BHC), and the sample size varied from 289 to 461 for fetal ultrasound measures. The characteristics of excluded participants did not differ from the study population in terms of the recorded characteristics; however, they did differ in the maternal educational level, season of birth, and the location of study (Table S2). Before enrollment, written informed consent was obtained from each eligible woman. Trained interviewers administered a standardized questionnaire to obtain information on sociodemographic characteristics and prior medical history. The study protocol was approved by the ethical committee of Ewha Womans University (approval No. 12-07B-15), Dankook University Hospital (approval No. 2011-09-0340), and Ulsan University Hospital (approval No.06-29).

2.2. Fetal ultrasound measures and birth outcomes

We measured fetal growth in the second and third trimester using gestational age based on ultrasound examination. We had access to the records of ultrasound examinations conducted between 12 and 27 gestational weeks (second-trimester examination) and between 28 and 40 gestational weeks (third-trimester examination). The estimation of gestational age was based on ultrasound examination during first trimester scans (<12 weeks gestation), which were typically made at 9–11 weeks of gestation. The fetal characteristics measured in the second and third trimesters were biparietal diameter (BPD), femur length (FL), abdominal circumference (AC), and estimated fetal weight (EFW) (Hadlock et al., 1985). Birth outcome variables were BW (grams), BL (centimeters), and BHC (centimeters) and were collected from the medical records.

2.3. Exposure assessment

Each participant's exposure to air pollutants was assessed on the basis of the residential address, using geographical information system (GIS) variables, and estimated NO_2 and PM_{10} concentrations from a LUR model, a standardardized method that has been described previously (Lee et al., 2012). We first obtained monthly concentration of PM_{10} and NO_2 measured at all general monitoring stations throughout Korea from 2006 to 2012. The number of national air quality monitoring station in 2006 was 202 and was reached to 246 by 2012. We then calculated the monthly exposure levels at the participants' addresses in the three regions (Seoul, Ulsan and Cheonan), using a modeling method with a GIS (ArcGIS 9.3, Arc Map 9.3; ESRI Inc., Redlands, CA, USA).