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Ambient air pollution and adverse birth outcomes: Differences by maternal comorbidities

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ABSTRACT

Background: Prenatal exposure to ambient air pollution has been associated with adverse birth outcomes, but the potential modifying effect of maternal comorbidities remains understudied. Our objective was to investigate whether associations between prenatal air pollution exposures and birth outcomes differ by maternal comorbidities.

Methods: A total of 818,400 singleton live births were identified in the province of Ontario, Canada from 2005 to 2012. We assigned exposures to fine particulate matter ($PM_{2.5}$), nitrogen dioxide (NO_2) and ozone (O_3) to maternal residences during pregnancy. We evaluated potential effect modification by maternal comorbidities (i.e. asthma, hypertension, pre-existing diabetes mellitus, heart disease, gestational diabetes and preeclampsia) on the associations between prenatal air pollution and preterm birth, term low birth weight and small for gestational age.

Results: Interquartile range (IQR) increases in $PM_{2.5}$ (2 μg/m^3), NO_2 (9 ppb) and O_3 (5 ppb) over the entire pregnancy were associated with a 4% (95% CI: 2.4–5.6%), 8.4% (95% CI: 5.5–10.3%) and 2% (95% CI: 0.5–4.1%) increase in the odds of preterm birth, respectively. Increases of 10.6% (95% CI: 0.2–2.1%) and 23.8% (95% CI: 5.5–44.8%) in the odds of preterm birth were observed among women with pre-existing diabetes while the increases were of 3.8% (95% CI: 2.2–5.4%) and 6.5% (95% CI: 3.7–8.4%) among women without this condition for pregnancy exposure to $PM_{2.5}$ and NO_2, respectively ($P_{int} < 0.01$). The increase in the odds of preterm birth for exposure to $PM_{2.5}$ during pregnancy was higher among women with pre-eclampsia (8.3%, 95% CI: 0.8–16.4%) than among women without (3.6%, 95% CI: 1.8–5.3%) ($P_{int} = 0.04$). A stronger increase in the odds of preterm birth was found for exposure to O_3 during pregnancy among asthmatic women (12.0%, 95% CI: 3.5–21.1%) compared to non-asthmatic women (2.0%, 95% CI: 0.1–3.5%) ($P_{int} < 0.01$). We did not find statistically significant effect modification for the other outcomes investigated.

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Conclusions: Findings of this study suggest that associations of ambient air pollution with preterm birth are stronger among women with pre-existing diabetes, asthma, and preeclampsia.

1. Introduction

Ambient air pollution has been associated with several adverse birth outcomes such as preterm delivery, low birth weight and small for gestational age (Dadvand et al., 2013; Shah et al., 2011; Stieb et al., 2012). The underlying mechanism(s) explaining the impact of maternal air pollution exposures on adverse birth outcomes are not well understood, but it appears that impaired oxygen and nutrient transport to the foetus due to oxidative stress, inflammation and hemodynamic changes may be implicated (Kannan et al., 2006; Schlesinger et al., 2006). For example, some evidence suggests that exposure to particulate air pollution during pregnancy can lead to acute inflammation in the lungs and other organs, including the placenta, thereby increasing the likelihood of preterm labour (Liu et al., 2003). In addition, increased systemic inflammation may also contribute to intrauterine growth restriction due to interference with nutrient transport to the foetus and reduced oxygenation of maternal blood (Kannan et al., 2006).

In general, presence of inflammation is also a common characteristic of individuals with medical conditions such as diabetes and chronic hypertension (Rodriguez-Hernandez et al., 2013) and previous studies have shown that women with pre-existing health problems such as these were at increased risk of adverse birth outcomes (Ankumah et al., 2014; Gilbert et al., 2007; Negrato et al., 2012). In that regard, two recent studies have investigated whether specific maternal health problems and pregnancy complications could modify the impact of air pollution on adverse birth outcomes (Laurent et al., 2014; Lin et al., 2015). These investigations have shown stronger associations between air pollution and low birth weight among infants of mothers with chronic hypertension and diabetes mellitus (Laurent et al., 2014) and preterm birth among infants of mothers with gestational diabetes mellitus (Lin et al., 2015). However, these studies lacked data on smoking during pregnancy and relied on data from ambient air pollution monitoring stations. In addition, other diseases associated with systemic inflammation such as chronic asthma, heart disease and preeclampsia that have not been previously investigated and could also modify the relationship between air pollution and adverse birth outcomes.

Exposure to air pollution can induce oxidative stress and can lead to a release of proinflammatory mediators in airway epithelial cells among pregnant women which can trigger preterm delivery (Kannan et al., 2006; Shah et al., 2011; Vadillo-Ortega et al., 2014). Previous studies in non-pregnant adults have suggested that diabetes, heart diseases, asthma and hypertension can modify the effects of outdoor air pollution on adverse health outcomes (Colais et al., 2012; Goldberg et al., 2013; Zanobetti et al., 2000). Oxidative stress and inflammation are hypothesized to be implicated in this enhanced susceptibility to air pollution. For instance, a panel study of elderly persons found that air pollution was associated with systemic inflammation markers (C-reactive protein, interleukin-6, white blood cells), with the largest associations observed amongst persons with diabetes and hypertension (Dubowsky et al., 2006). Given that pregnancy is a state having enhanced susceptibility to oxidative stress and inflammation (Casanueva and Viteri, 2003; Patil et al., 2007) which has implications for fetal growth (Weber et al., 2014), we believe these associations may be enhanced in the presence of maternal health conditions (Laurent et al., 2014). In general, a better understanding of the pathways linking gestational air pollution exposures and adverse birth outcomes is of public health interest given that these conditions can have lifelong consequences (Chernausek, 2012).

This study examined whether selected maternal pre-existing and pregnancy-associated comorbidities modified associations between major ambient air pollutants, namely nitrogen dioxide (NO_2), particulate matter with aerodynamic diameters of ≤ 2.5 μm ($PM_{2.5}$) and ozone (O_3), and adverse birth outcomes.

2. Methods

2.1. Study population

Our study population included a retrospective cohort of pregnant women giving birth in hospitals to live born, non-planned C-sections, singleton infants in Ontario, Canada between January 1st 2005 and March 31st 2012. Birth data were collected from the Better Outcomes Registry & Network (BORN) Ontario, a province wide birth registry that captures maternal health, obstetric, intrapartum, and neonatal information in and around the perinatal period of pregnancy (Dunn et al., 2011). Women were enrolled in the birth registry during the first trimester of pregnancy (6–14 weeks gestation). Birth outcomes examined in this study included preterm birth (gestational age <37 weeks), term low birth weight (LBW, <2500 g) and small for gestational age (SGA, <10th percentile of birth weight for gestational age) (Kramer et al., 2001). Gestational age was determined from the mother's last menstrual period, so there's a potential misclassification of gestational age, but there's no reason to suspect that misclassification differed by air pollution levels. The first trimester of pregnancy was defined as gestational week 1 through week 12, the second trimester as week 13 to week 27 and the third trimester of pregnancy from week 28 to birth. Potential effect modifiers under study included pre-existing maternal comorbidities such as asthma, hypertension, diabetes mellitus (insulin and non-insulin dependent), and heart disease, as well as pregnancy-associated complications such as gestational diabetes and preeclampsia. Information on pre-existing maternal asthma was captured after linking maternal information from the birth registry with the Ontario Asthma Surveillance Information System which is a population-based registry that identifies incident asthma cases using a validated algorithm (Gershon et al., 2009). We obtained information on pre-existing hypertension status among pregnant women by linking maternal information from the birth registry with the Ontario hypertension database, a validated registry of Ontario residents with diagnosed hypertension (Tu et al., 2007). We used the Ontario Diabetes Database, a validated registry of diabetics in Ontario, to identify pregnant women with and without diabetes before their pregnancy (Hux et al., 2002). Heart disease status was captured by linking maternal information with the Discharge Abstract Database, a hospital discharge database that captures all hospital admissions among Ontario residents. Therefore, the linkage of the birth registry with these registries allowed the identification of diagnoses of asthma, hypertension, diabetes and heart disease prior to pregnancy. Gestational diabetes status was assessed between the 24th and 28th week of gestation following the diagnostic criteria of the Canadian Diabetes Association (Canadian Diabetes Association, 2013). The presence of preeclampsia was ascertained through routine measures of blood pressure and proteinuria after 20 weeks of gestation using established diagnostic