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Maternal exposure to traffic-related air pollution and birth defects in Massachusetts

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ABSTRACT

Exposures to particulate matter with diameter of 2.5 μm or less ($PM_{2.5}$) may influence risk of birth defects. We estimated associations between maternal exposure to prenatal traffic-related air pollution and risk of cardiac, orofacial, and neural tube defects among Massachusetts births conceived 2001 through 2008. Our analyses included 2729 cardiac, 255 neural tube, and 729 orofacial defects. We used satellite remote sensing, meteorological and land use data to assess $PM_{2.5}$ and traffic-related exposures (distance to roads and traffic density) at geocoded birth addresses. We calculated adjusted odds ratios (OR) and confidence intervals (CI) using logistic regression models. Generalized additive models were used to assess spatial patterns of birth defect risk. There were positive but non-significant associations for a 10 $\mu g/m^3$ increase in $PM_{2.5}$ and perimembranous ventricular septal defects (OR=1.34, 95% CI: 0.98, 1.83), patent foramen ovale (OR=1.19, 95% CI: 0.92, 1.54) and patent ductus arteriosus (OR=1.20, 95% CI: 0.95, 1.62). There was a non-significant inverse association between $PM_{2.5}$ and cleft lip with or without palate (OR=0.76, 95% CI: 0.50, 1.10), cleft palate only (OR=0.89, 95% CI: 0.54, 1.46) and neural tube defects (OR=0.77, 95% CI: 0.46, 1.05). Results for traffic related exposure were similar. Only ostium secundum atrial septal defects displayed significant spatial variation after accounting for known risk factors.

1. Introduction

Birth defects are prevalent in 3% of US live births (Parker et al., 2010), with cardiac, orofacial, and neural tube defects among the most common defects observed (Yoon et al., 2001). Exposure to air pollution during pregnancy has been suggested to increase risk of birth defects (Dadvand et al., 2011; Dolk et al., 2010; Gilboa et al., 2005; Padula et al., 2013; Schembari et al., 2014; Vrijheid et al., 2011) in some studies. The time between conception and birth is a sensitive and critical time for fetal development due to rapid cell proliferation and rapid development of various organ systems, thus understanding the influence of ambient exposures on fetal development may elucidate the mechanisms behind abnormal fetal development. Studies of fetal exposure to traffic-related air pollution including particulate matter with a diameter of 2.5 μm or less ($PM_{2.5}$) have shown associations with adverse birth outcomes such as intrauterine growth retardation and preterm births (Brauer et al., 2008; Liu et al., 2007), but investigations of the association of $PM_{2.5}$ on birth defect risk have been inconclusive (Agay-Shay et al., 2013; Hansen et al., 2009; Kim et al., 2007; Stingone et al., 2014; Chen et al., 2014; Marshall et al., 2010; Padula et al., 2013; DJ et al., 2013).

Exposure estimates for earlier studies were constrained to individuals living near air monitoring stations without daily assessments, limiting both spatial and temporal resolution of the exposure assessment resulting in exposure misclassification (Ritz and Wilhelm, 2008; Ghosh et al., 2012). Earlier studies were unable to adjust for important confounders such as individual-level socioeconomic status (SES) and may have been limited by case ascertainment over a short study period (Ritz and Wilhelm, 2008; Ghosh et al., 2012). Only one other study (Padula et al., 2013) to our knowledge has accounted for road density and residential

Abbreviations: AADT, annual average daily traffic; AOD, aerosol optical depth; CI, confidence interval; GAMs, generalized additive models; GOES, Geostationary Operational Environmental Satellite; ICD-9-CM, International Classification of Diseases, Clinical Modification, Ninth Revision; NOS, not otherwise specified; NOAA, National Oceanic and Atmospheric Administration; OR, odds ratio; $PM_{2.5}$, particulate matter with diameter of 2.5 μm or less; SES, socioeconomic status

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distance to roadways, local measures of traffic-related air pollution, in addition to $PM_{2.5}$ estimates when assessing risk of birth defects and exposure to ambient air pollution. Satellite-based $PM_{2.5}$ prediction models can provide additional spatial and temporal information for exposure assessments. Models have evolved from using one single predictor (Wang and Christopher, 2003) to multiple predictors (Liu et al., 2005, 2007, 2009) and from one-stage models (Hu et al., 2013) to multi-stage non-linear models (Hu et al., 2014a, 2014b, 2014c; Kloog et al., 2011).

The objective of this study is to examine the relationship between cardiac, orofacial, and neural tube defects and traffic-related air pollution using satellite-based $PM_{2.5}$ exposure estimates and eight years of birth defects data for Massachusetts. To further assess the influence of $PM_{2.5}$ on birth defect risk, our study includes an analysis of geographic patterns of birth defects across Massachusetts.

2. Methods

2.1. Study population

We obtained all live and still births from the Massachusetts state birth registry with an estimated conception date from January 1, 2001 through December 31, 2008. All births in the Massachusetts Birth Defects Registry having cardiac, orofacial, and neural tube defects (*International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) codes 740.0-743.0, 745.0-748.0 and 749.0-749.3) were identified as cases. The Massachusetts Birth Defects Monitoring Program conducts active surveillance to collect diagnoses made before age one. We randomly selected 1000 infants conceived each year to serve as a common control group among all live births without the defects of interest. We excluded birth addresses that could not be successfully geocoded to *x* and *y* coordinates (2%) and we excluded syndromic births (5%) that were associated with the outcomes of interest (eTable 1) among cases and controls. The Institutional Review Boards of the University of California at Irvine and the Massachusetts Department of Public Health approved this research.

Due to differing etiologies, we divided cardiac defects into anatomical groupings based on ICD-9-CM groups. We only included groups with more than 70 cases to ensure sufficient numbers for model convergence. We also assessed the five most common single ICD-9-CM code cardiac defect diagnoses as their own outcome group. In total, there were 17 outcome groups for cardiac anomalies: transposition of great vessels, tetralogy of fallot, ventricular septal defect, ostium secundum atrial septal defect, endocardial cushion defect, pulmonary valve atresia and stenosis, aortic valve stenosis, hypoplastic left heart syndrome, patent ductus arteriosus, coarctation of aorta, pulmonary artery anomalies, insufficiency of the aortic valve, atrial septal defect- not otherwise specified (a subset of ostium secundum atrial septal defect), perimembranious ventricular septal defect (a subset of ventricular septal defect), muscular ventricular septal defect (a subset of ventricular septal defect), single common atrium (a subset of endocardial cushion defects), and patent foramen ovale (a subset of ostium secundum atrial septal defect). Cases of patent ductus arteriosus and patent foramen ovale were excluded if the infant was preterm (<36 weeks, 4% of patent ductus arteriosus and patent foramen ovale cases). Infants with more than one birth defect were categorized into multiple defect groups unless diagnoses were similar (eTable 2). Because the majority of cases had multiple birth defect diagnosis (74%), to assess if there was a difference between infants with multiple defects and isolated defects, these two groups were analyzed separately.

For neural tube defects, spina bifida was the most common defect and was analyzed separately; all other neural tube defects were analyzed together due to small numbers. Anencephaly was excluded (13% of neural tube defects) as those included in the registry may not be representative of all anencephaly cases due to early termination. Orofacial defects were divided into two categories: cleft lip with or without palate and cleft palate only.

2.2. Exposure assessment

Our primary analysis examined the relationship between birth defects and $PM_{2.5}$ exposures modeled using satellite remote sensing, meteorological and land use data. Aerosol optical depth (AOD) is the integral of particle light extinction coefficients from the surface to the top of the atmosphere. It is a measure of the degree to which aerosols prevent light from penetrating the atmosphere and retrieved using wavelengths most sensitive to particles with sizes from 0.1 to 2 μm (Kahn et al., 1998). Thus, AOD is related to the loadings of fine particles in the atmosphere and is a strong predictor of ground-level $PM_{2.5}$ concentrations as most fine particles are emitted and confined in the boundary layer. The number of stationary ambient monitors is limited and the distribution is sparse, while AOD-estimated $PM_{2.5}$ concentrations have the potential to expand the spatiotemporal coverage of ground networks and improve the accuracy of estimates of personal exposure to $PM_{2.5}$ (van Donkelaar et al., 2010). The Geostationary Operational Environmental Satellite (GOES) is the major weather satellite operated by the National Oceanic and Atmospheric Administration (NOAA). GOES provides an aerosol and smoke product (GASP) with AOD retrievals every 30 min from sunrise to sunset at 4 km nominal spatial resolution. We obtained GASP AOD data from the NOAA National Environmental Satellite, Data, and Information Service. In this study, AOD measurements (available from 9 am to 3 pm local time) were averaged to generate daily AOD estimates (Liu et al., 2009).

The 24-hour average $PM_{2.5}$ concentrations from 2001 to 2008 collected from 35U.S. Environmental Protection Agency (EPA) Federal Reference Monitors (FRM) were downloaded from the EPA's Air Quality System Technology Transfer Network (http://www.epa.gov/ttn/airs/airsaqs/). Meteorological fields, including temperature and wind speed, were provided by the North American Land Data Assimilation System (NLDAS) Phase 2 and downloaded from the NLDAS website (http://ldas.gsfc.nasa.gov/nldas/). Elevation data were obtained from the National Elevation Dataset (NED) (http://ned.usgs.gov). Major roads were extracted from ESRI StreetMap USA (Environmental Systems Research Institute, Inc., Redland, CA). Forest cover data were derived from 2001 and 2006 land cover maps downloaded from the National Land Cover Database (NLCD) (http://www.mrlc.gov). Primary $PM_{2.5}$ emissions were obtained from the 2002, 2005, and 2008 EPA National Emission Inventory (NEI) facility emissions reports. We developed a linear mixed effects model with 24-hour average EPA $PM_{2.5}$ measurements from 2001 to 2008 as the dependent variable and AOD, meteorological fields and land use variables as predictors. The model incorporates day-specific random intercepts and slopes for AOD, temperature, and wind speed to account for the temporally varying relationship between $PM_{2.5}$ (based on fixed ground monitors) and AOD. Lee et al., (2011). This model was run annually for a 4 km modeling grid covering the spatial extent of Massachusetts to estimate daily $PM_{2.5}$ concentrations from 2001 to 2008. The model structure can be expressed as

$$\begin{aligned} PM_{2.5,st} = {} & (\beta_0 + \beta_{0,t}) + (\beta_1 + \beta_{1,t})AOD_{st} + (\beta_2 + \beta_{2,t})\text{Temperature}_{st} + (\beta_3 + \beta_{3,t})\text{Wind} \\ & \text{Speed}_{st} + \beta_3\text{Elevation}_s + \beta_4\text{Major Roads}_s + \beta_5\text{Forest Cover}_s \\ & + \beta_6\text{Point Emissions}_s + \varepsilon_{st}(\beta_{0,t}\beta_{1,t}\beta_{2,t}\beta_{3,t}) \sim N[(0, 0, 0, 0), \Psi] \end{aligned}$$