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An exploratory analysis of the relationship between ambient ozone and particulate matter concentrations during early pregnancy and selected birth defects in Texas

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ABSTRACT

We performed an exploratory analysis of ozone (O_3) and fine particulate matter ($PM_{2.5}$) concentrations during early pregnancy and multiple types of birth defects. Data on births were obtained from the Texas Birth Defects Registry (TBDR) and the National Birth Defects Prevention Study (NBDPS) in Texas. Air pollution concentrations were previously determined by combining modeled air pollution concentrations with air monitoring data. The analysis generated hypotheses for future, confirmatory studies; although many of the observed associations were null. The hypotheses are provided by an observed association between O_3 and craniosynostosis and inverse associations between $PM_{2.5}$ and septal and obstructive heart defects in the TBDR. Associations with $PM_{2.5}$ for septal heart defects and ventricular outflow tract obstructions were null using the NBDPS. Both the TBDR and the NBPDS had inverse associations between O_3 and septal heart defects. Further research to confirm the observed associations is warranted.

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1. Introduction

Ozone (O_3) and particulate matter (PM), two of the criteria air pollutants regulated by the Clean Air Act, have been investigated for increasing the risk of several birth outcomes, including preterm birth, low birthweight, and birth defects (US EPA, 2009, 2013). Some of those previous studies have investigated associations between birth defects and air quality in Texas. One study reported an association between increased PM_{10} concentrations and higher odds of certain cardiovascular defects (Gilboa et al., 2005). Living in census tracts with higher levels of modeled environmental exposure to benzene, estimated using the EPA Assessment System for Population Exposure Nationwide (ASPEN), was associated with greater risk of having offspring with spina bifida (Lupo et al., 2011) but not oral clefts (Ramakrishnan et al., 2013). Close residence near Toxic Release Inventory sites was associated with increased odds of oral clefts, neural tube defects, and chromosomal abnormalities (Brender et al., 2006, 2008; Suarez et al., 2007), particularly in infants of older women. There was no association with conotruncal heart defects (Langlois et al., 2009).

The goal of the current study was to perform an exploratory analysis examining broad groups of birth defects to assess the potential for associations with O_3 and fine particulate matter ($PM_{2.5}$) concentrations. Most studies of this nature utilize data from air monitors, limiting the women included in the studies to those living near monitors, which are mostly urban areas (Gilboa et al., 2005). However, in the current study, all participants residing in the study area were included; a Bayesian hierarchical model that combined modeled air pollution concentrations with air monitoring data to create bias-corrected concentrations across Texas provides information on concentrations of $PM_{2.5}$ and O_3 regardless of proximity to an air monitor. Evaluation for possible associations with birth defects was performed utilizing two study populations,

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the Texas Birth Defects Registry (TBDR) and Texas data from the National Birth Defects Prevention Study (NBDPS). Utilizing two study populations allowed us to compare results and look for similar patterns across the studies. The TBDR covers the entire state resulting in a wide variety of exposure and a large sample size, which afforded the opportunity to investigate multiple defects. Although the NBDPS is smaller in size, limiting the number of defects able to analyzed compared to the TBDR, there is more information on maternal covariates that may add insight into whether the TBDR is biased by not including these covariates.

2. Materials and methods

2.1. Data from the Texas Birth Defects Registry

The TBDR is a population-based active surveillance system that includes the entire state of Texas (Miller, 2006). Staff visit hospitals, birthing centers, and midwives throughout Texas and identify children or pregnancies with birth defects diagnosed prenatally or up to one year after delivery. Mothers must be a resident in Texas at the time of delivery. The data from medical charts are abstracted and entered into a web-based system where they undergo extensive quality control. These data are then linked to vital records (birth, fetal death, and death certificate data).

For the current study, cases with one or more of a range of defects were obtained from this registry for singleton live births with a delivery date between 2002 and 2006. Individuals with more than one birth defect were included in all the appropriate birth defect groupings. Live-born controls from the same time period were obtained from Texas birth certificate data, and any children with birth defects were excluded.

2.2. Data from the National Birth Defects Prevention Study

A second analysis utilized data from the NBDPS, a population-based case-control study taking place in ten states. Case mothers were selected from active surveillance birth defects registries, and had given birth to a child affected by one or more of 30 birth defects selected for the study. Case records were submitted to in-depth clinical review by clinical geneticists affiliated with the NBDPS. Control mothers had given birth to a child unaffected by birth defects, and were selected from birth certificates or from hospitals in the same area and time period from which cases were drawn. Case and control mothers were invited to participate in a computer-assisted telephone interview which included questions about pregnancy and medical history, diet, lifestyle, occupational exposures, medication use, and where they lived from three months before conception of the index child through the date of delivery. The interview was conducted with women whose infants are between 6 weeks and 2 years of age. More details on the NBDPS can be found elsewhere (Yoon et al., 2001).

For the current study, only women from the Texas enrollment site were included. Because of protocol limitations on participating states, the Texas NBDPS area included only 10–20% of Texas births in any year.

2.3. Exposure data

A hierarchical Bayesian model that combined data from air monitors (provided by the US EPA Air Quality System) with modeled air pollution estimates from the US EPA's Community Multiscale Air Quality (CMAQ) model (which bases its estimates on data from EPA's National Emissions Inventory and meteorological and geographical factors) estimated ambient air concentrations (McMillan et al., 2010). This combination made use of air monitoring data but also provided estimates of air pollutant concentrations for areas where no monitoring data was available. The estimates covered the entire spatial extent of Texas in the form of grid cells (12 km × 12 km) (data available for download here: http://www.epa.gov/esd/land-sci/lcb/lcb_fdaqs_archive.html). For the TBDR, residence at birth was extracted from birth certificates for both cases and controls and geocoded using ARCGIS by the Texas Department of State Health Services. The NBDPS database contained information on all residences during pregnancy, which was geocoded by the Agency for Toxic Substance and Disease Registry at CDC. In the NBDPS data, slightly less than 20% of women moved during the first trimester. To calculate the air pollution concentrations for these women, the air pollution concentrations at each woman's residential address were summed for the time period the woman resided there, and this sum was divided by 90, the number of days in the first trimester.

Each geocoded address was matched to the appropriate CMAQ grid cell. The daily estimates for 24-hour average $PM_{2.5}$ concentrations and 8-hour maximum O_3 concentrations provided by the CMAQ model were then averaged across the first trimester using the grid cell for reported maternal residence to create mean concentration values. A total of 90.2% of the cases and 91.5% of the controls in the TBDR were able to be geocoded and included in the study. Of the addresses provided in the NBDPS, 94.0% were geocoded and assigned a grid cell.

2.4. Statistical analyses

Associations between air pollutant concentrations and birth defects were examined using logistic regression, including both crude and adjusted single-pollutant models. Analysis was limited to birth defects with $N \geq 50$. A Bonferroni multiple comparisons adjustment was performed and reflected in the confidence intervals of the estimates of the TBDR analyses. Due to small numbers for most defects, only a few of the NBDPS birth defects were examined and multiple comparison adjustments were not used. Covariates included in the adjusted analyses were chosen based on those previously reported in the literature and variables thought to be associated with both the exposure and outcome but not on the causal pathway. These included: prenatal care in the first trimester (yes, no), number of previous live births (first birth, second birth, third or greater birth), maternal age (5-year age categories), maternal educational attainment (less than high school degree, high school degree, more than a high school degree), and maternal race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, non-Hispanic other). The TBDR also included a variable for urbanicity (determined using 2003 rural-urban continuum codes (RUCC) assigned based on county; metropolitan urbanized counties [RUCC: 1–3], nonmetropolitan urbanized [RUCC: 4, 5], less urbanized or thinly populated [RUCC: 6–9]) (data available for download here: www.ers.usda.gov/data-products/rural-urban-continuum-codes/.aspx). No covariates were missing more than 5% of their values. Multiple imputation was performed in the TBDR analysis to estimate the values for any missing data on covariates. Information on additional covariates, such as behaviors taking place during the month before pregnancy through the first trimester (i.e., folic acid/multivitamin use, alcohol consumption, and smoking), was available in the NBDPS and used in further adjusted analyses for this study. In addition, co-pollutant analyses that included both the estimated O_3 and $PM_{2.5}$ concentrations, as well as the covariates listed for the adjusted analyses, were performed for both the TBDR and the NBDPS.

This study has been approved by Institutional Review Boards at the Texas Department of State Health Services and the University of North Carolina at Chapel Hill.

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