Environmental Research 158 (2017) 798–805

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Prenatal particulate air pollution exposure and body composition in urban preschool children: Examining sensitive windows and sex-specific associations

Yueh-Hsiu Mathilda Chiu[a,b], Hsiao-Hsien Leon Hsu[a], Ander Wilson[c], Brent A. Coull[d,e], Mathew P. Pendo[f], Andrea Baccarelli[g], Itai Kloog[h], Joel Schwartz[e], Robert O. Wright[a,i], Elsie M. Taveras[j,k,1], Rosalind J. Wright[a,b,i,*,1]

[a] Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[b] Kravis Children's Hospital, Department of Pediatrics, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[c] Department of Statistics, Colorado State University, Fort Collins, CO, USA
[d] Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[e] Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[f] Center for Medicine, Health and Society, Vanderbilt University College of Arts and Science, Nashville, TN, USA
[g] Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, NY, USA
[h] Department of Geography and Environmental Development, Ben-Gurion University of the Negev, Israel
[i] Institute for Exposomic Research, Icahn School of Medicine at Mount Sinai, New York, NY, USA
[j] Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA
[k] Department of Pediatrics, Massachusetts General Hospital for Children, Boston, MA, USA

ARTICLE INFO

Keywords:
Prenatal exposure
Particulate matter
Child obesity
Anthropometry
Sensitive windows
Sex difference

ABSTRACT

Background: Evolving animal studies and limited epidemiological data show that prenatal air pollution exposure is associated with childhood obesity. Timing of exposure and child sex may play an important role in these associations. We applied an innovative method to examine sex-specific sensitive prenatal windows of exposure to $PM_{2.5}$ on anthropometric measures in preschool-aged children.

Methods: Analyses included 239 children born ≥ 37 weeks gestation in an ethnically-mixed lower-income urban birth cohort. Prenatal daily $PM_{2.5}$ exposure was estimated using a validated satellite-based spatio-temporal model. Body mass index z-score (BMI-z), fat mass, % body fat, subscapular and triceps skinfold thickness, waist and hip circumferences and waist-to-hip ratio (WHR) were assessed at age 4.0 ± 0.7 years. Using Bayesian distributed lag interaction models (BDLIMs), we examined sex differences in sensitive windows of weekly averaged $PM_{2.5}$ levels on these measures, adjusting for child age, maternal age, education, race/ethnicity, and pre-pregnancy BMI.

Results: Mothers were primarily Hispanic (55%) or Black (26%), had ≤ 12 years of education (66%) and never smoked (80%). Increased $PM_{2.5}$ exposure 8–17 and 15–22 weeks gestation was significantly associated with increased BMI z-scores and fat mass in boys, but not in girls. Higher $PM_{2.5}$ exposure 10–29 weeks gestation was significantly associated with increased WHR in girls, but not in boys. Prenatal $PM_{2.5}$ was not significantly associated with other measures of body composition. Estimated cumulative effects across pregnancy, accounting for sensitive windows and within-window effects, were 0.21 (95%CI = 0.01–0.37) for BMI-z and 0.36 (95%CI = 0.12–0.68) for fat mass (kg) in boys, and 0.02 (95%CI = 0.01–0.03) for WHR in girls, all per $\mu g/m^3$ increase in $PM_{2.5}$.

Conclusions: Increased prenatal $PM_{2.5}$ exposure was more strongly associated with indices of increased whole body size in boys and with an indicator of body shape in girls. Methods to better characterize vulnerable windows may provide insight into underlying mechanisms contributing to sex-specific associations.

Abbreviations: AOD, aerosol optical depth; BDLIM, Bayesian distributed lag interaction model; BMI-z, body mass index z-score; CDC, Centers for Disease Control; DLM, distributed lag model; LUR, land-use regression; OS, oxidative stress; PAHs, polyaromatic hydrocarbons; ROS, reactive oxygen species; SES, socioeconomic status; SS, subscapular skinfold; TS, triceps skinfold; WHR, waist-to-hip ratio

* Corresponding author at: Department of Environmental Medicine and Public Health, Icahn School of Medicine at Mount Sinai, New York, NY, USA.
[1] Co-senior authors.

http://dx.doi.org/10.1016/j.envres.2017.07.026
Received 18 March 2017; Received in revised form 14 June 2017; Accepted 11 July 2017

1. Introduction

Nearly one third of children in the United States (U.S.) are overweight or obese, a proportion that has more than doubled since 1980 (Ogden et al., 2016). While some data suggest that U.S. obesity rates are stabilizing, rates remain high in preschoolers (CDC, 2013) and continue to show disparities for lower-socioeconomic status (SES) groups (Yanovski and Yanovski, 2011). Moreover, correlated phenotypes in infants and toddlers, such as faster weight gain and higher body fat, predict later life obesity-related trajectories (Barker, 2012; Taveras et al., 2009). For example, children who are obese are five times as likely as those who are not to be obese adults (CDC, 2013). Moreover, obesity increases the risk of a number of physical and mental health disorders over the life course (Bogers et al., 2007; CDC, 2013; Strazzullo et al., 2010). Such trends result in U.S. spending approaching nearly $190 billion annually on obesity related healthcare expenses (Cawley and Meyerhoefer, 2012). Identifying potentially modifiable risk factors is a research priority.

While current standards mandate prevention to start soon after birth (Task Force on Childhood Obesity, 2010), research increasingly shows that programming of obesity begins prenatally (Sutton et al., 2016). Moreover, while attempts to curb childhood obesity have largely focused on physical activity and diet, childhood obesity is likely influenced by a range of environmental factors beyond nutrition and exercise (Birch et al., 2011). Recent evidence points to a role for chemical environmental exposures in programming obesity (Vrijheid et al., 2016).

Emerging evidence specifically supports a role for particulate air pollution, a pro-oxidant environmental exposure, in obesity programming. Particulate air pollution has been increasingly linked to obesity and related phenotypes in animal models (Bolton et al., 2014). Oxidative stress (OS) plays a role in the generation and maintenance of an obesity phenotype in both isolated adipocytes and animals (Aroor and DeMarco, 2014; De Marchi et al., 2013; Imhoff and Hansen, 2010; Ye et al., 2015). Notably, obesity involves excess accumulation of adipose tissue, as well as dysregulation of glucose and lipid metabolism. Reactive oxygen species (ROS) promote adipogenic signaling pathways and disrupted adipogenesis (Atashi et al., 2015; Iyer et al., 2010). Moreover, recent prospective epidemiological data link early postnatal ambient pollution to child obesity (McConnell et al., 2015), and also link ambient pollution exposure, even below air quality guidelines, to glucose tolerance during pregnancy and food reward hormone dysregulation (Calderon-Garciduenas et al., 2015; Fleisch et al., 2014), both of which are identified intermediate pathways to offspring/child obesity (Hillier et al., 2007; Jastreboff et al., 2014; Kubo et al., 2014; Poston, 2010).

Ambient air pollution effects likely begin *in utero*. In pregnant women, inhaled particles translocate from the lungs via the blood to other organs including the placenta (MohanKumar et al., 2008). Particulate matter can also invoke a chronic inflammatory process in the mother's lung resulting in systemic inflammation and consequent placental OS (Liu et al., 2016). Our group and others have linked *in utero* air pollution exposure with low birth weight, a potential predecessor of overweight/obesity in later life (Bell et al., 2007; Kloog et al., 2012; Lakshmanan et al., 2015; Padula et al., 2012).

Prospective human studies examining the association between prenatal traffic-related air pollution exposure and childhood obesity remain sparse. Rundle et al. (2012) linked prenatal exposure to polyaromatic hydrocarbons (PAHs) to obesity in children assessed at ages 5 and 7 years. Fleisch et al. (2015) showed that prenatal exposure to fine particulate matter was associated with more rapid postnatal weight gain in 6-month-old infants. This group also demonstrated a link between proximity to major roadways at birth (< 50 m) and fat mass at both early- and mid-childhood (median 3.3 and 7.7 years of age) (Fleisch et al., 2016). Lavigne et al. showed that increased exposure to air pollution during pregnancy was associated with higher levels of umbilical cord blood adinopectin, which regulates glucose and fatty acid breakdown in the developing fetus, and may contribute to obesity in later childhood (Lavigne et al., 2016).

Notably, existing studies of prenatal air pollution effects on childhood obesity have considered subjective assignment of exposure timing, such as air pollution exposure in a certain trimester or averaged over the entire pregnancy or over a certain length of time before pregnancy. This makes it difficult to compare the results across studies as well as to better delineate the critical windows affecting fetal programming. Clinically defined trimesters do not necessarily correspond to relevant vulnerable periods of body growth. Measuring exposure in an arbitrarily defined susceptibility window that does not overlap with periods of physiological vulnerability may lead to underestimated or even missed associations (Wilson et al., 2017a). In addition, animal data demonstrate sex-specific vulnerability to prenatal oxidant injury (Minghetti et al., 2013), which has been linked to both air pollution and infant growth (Sun et al., 2009). Recent analyses from our group combined advanced statistical methods with highly temporally resolved exposure data to more objectively identify susceptibility windows and enhance the power to detect associations and identify vulnerable groups (i.e., effect modification) (Chiu et al., 2016; Hsu et al., 2015). These analyses demonstrated sex-specific and time-varying associations of prenatal air pollution exposure on asthma and neurodevelopmental outcomes in children, but to our knowledge, this has not yet been examined for early childhood growth indicators.

We leveraged data on daily exposure to particulate matter with a diameter ≤ 2.5 μm ($PM_{2.5}$) measured over gestation and applied advanced statistical methods to more precisely identify the sensitive windows of time-varying prenatal $PM_{2.5}$ exposure effects on anthropometric measurements in preschool-aged children from an ethnically mixed lower-SES inner city population. We also examined effect modification by child sex.

2. Materials and methods

Participants were from the Asthma Coalition on Community, Environment and Social Stress (ACCESS) project, a pregnancy cohort originally funded to recruit 500 mother-child pairs to examine independent and interactive effects of early life stress and physical toxins on childhood respiratory health (Wright et al., 2008). Between August 2002 and January 2007, English- or Spanish-speaking pregnant women (≥ 18 years old) receiving care at Brigham & Women's Hospital (BWH), Boston Medical Center (BMC), and affiliated community health centers were enrolled (at 28.4 ± 7.9 weeks gestation). Seventy-eight percent (78%) of women receiving prenatal care, who were approached by research staff on select clinic days, were eligible and agreed to enroll. There were no significant differences on race/ethnicity, education, and income between women enrolled and those who declined. A total of 455 women gave birth to a live born infant and continued follow-up. Supplemental funding was obtained to assess anthropometry in children aged 3–5 years; of n = 358 children age-eligible for this initiative, n = 277 completed anthropometry assessments at age 4.0 ± 0.7 years of age. Among these children, n = 30 were born < 37 weeks, and n = 8 did not have prenatal $PM_{2.5}$ data (i.e., did not have accurate addresses during pregnancy), resulting in n = 239 available for analysis. Those included in analyses did not differ significantly from those not included in analyses based on key covariates including race/ethnicity, maternal age at enrollment, maternal educational status, maternal pre-pregnancy weight, prenatal smoking, child's birth weight or gestational age. Procedures were approved by the human studies committees at BWH and BMC. Mothers provided written consent in their preferred language.

2.1. Prenatal $PM_{2.5}$ exposure

As described previously (Chiu et al., 2016), we used a validated hybrid satellite based spatio-temporal prediction model to estimate