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Maternal Exposure to Ambient $PM_{2.5}$ During Pregnancy and the Risk for High Blood Pressure in Childhood

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Abstract

Exposure to ambient air pollution has been associated with greater risk of elevated blood pressure (BP) in adults and children. Recent evidence suggests that air pollution exposure in pregnancy may also portend increased risk for the next generation; however, few studies have examined this relationship. We conducted a prospective study of 1,293 mothers in the Boston Birth Cohort (enrolled 1998–2012) and their children who had follow up visits between 3–9 years of age and complete exposure and outcome data. Our primary exposure, ambient particulate matter ≤2.5 microns ($PM_{2.5}$) concentration during pregnancy, was estimated by matching mother's residential address to the U.S. Environmental Protection Agency's air quality monitors. We defined our primary outcome child systolic BP (SBP) percentile according to U.S. reference (Fourth Report) and classified elevated BP as SBP ≥ 90^{th} percentile. Our multivariable-adjusted cubic spline showed a sharp increase in offspring SBP percentile and risk for elevated BP when third-trimester

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CONFLICT(S) OF INTEREST/DISCLOSURE(S)

None.

$PM_{2.5}$ concentration was ≥13 μg/m^3. The highest vs. lowest tertile of third-trimester $PM_{2.5}$ exposure was associated with a 4.85 (95% CI: 1.38–8.37) percentile increase in child SBP or a 1.61 (95% CI: 1.13–2.30) times higher risk of child elevated BP. A 5 μg/m^3 increase in $PM_{2.5}$ during the third trimester was associated with a 3.49 (95% CI: 0.71–6.26) percentile increase in child SBP or a 1.47 (95% CI:1.17–1.85) times higher risk of elevated BP. Our findings suggest that exposure to ambient $PM_{2.5}$ during the third trimester of pregnancy is associated with elevated BP in children, ages 3–9 years.

Keywords

Air Pollution; Particulate Matter; Blood Pressure; Hypertension; Pregnancy; Maternal Exposure; Child Health

INTRODUCTION

High blood pressure (BP) is a major risk factor for cardiovascular disease and the leading modifiable cause of mortality, contributing to an estimated death of 7.5 million worldwide.[1,2] Although great strides have been made to control BP, the global prevalence of elevated BP after age-standardization remains high at 20% to 25% and has recently increased among children and adolescents.[3–5] High BP tracks from childhood to adulthood, and thus it is crucial to start prevention as early as possible.[6]

Air pollution, a significant contributor to morbidity and mortality worldwide,[7] has been associated with elevated BP in both children and adults.[8,9] Air pollution may also have transgenerational effects. Murine models have found that exposure to particulate matter ≤2.5 microns ($PM_{2.5}$) *in utero* affects the development of offspring's cardiovascular system, increasing the risk for elevated BP and other cardiovascular disease events.[10–12] In humans, our team was the first to report the link between maternal exposure to air pollution with offspring low birthweight and shorter gestational age.[13,14] More recently, we reported an association between $PM_{2.5}$ and intrauterine inflammation,[15] as well as a combined effect of maternal exposure to $PM_{2.5}$ and pre-pregnancy obesity on childhood overweight or obesity.[16] However, data on the transgenerational effects of air pollution on BP are sparse. Van Rossem et al. found $PM_{2.5}$ exposure in the third trimester related with elevated BP among newborns.[17] Breton and colleagues, on the other hand, did not find such association among 11-year-old teenagers using retrospectively collected pollutant data.[18]

In light of this literature gap, we sought to test the hypothesis that exposure to $PM_{2.5}$ during pregnancy is associated with higher offspring systolic BP (SBP) in childhood, using longitudinal data from the Boston Birth Cohort, a large, predominantly urban, low income minority population.

METHODS

Our manuscript adheres to the American Heart Association Journals' implementation of the Transparency and Openness Promotion (TOP) Guidelines. Dr. Xiaobin Wang, the Principal Investigator of the Boston Birth Cohort, has full access to all of the data in the study and

takes responsibility for the integrity of the data and the accuracy of the data analysis. The data, analytic methods, and study materials that support the findings of this study will be available from Dr. Xiaobin Wang (xwang82@jhu.edu) upon request, after the request is submitted and formally reviewed and approved by the institutional review board of the Boston University Medical Center and Johns Hopkins Bloomberg School of Public Health.

STUDY PARTICIPANTS

Participants for our study are from the Boston Birth Cohort, an ongoing prospective birth cohort that began recruiting mother-child pairs in Boston University Medical Center starting from 1998 on a rolling basis. The cohort consists of a predominantly urban low-income minority population rich in preterm birth and low birth weight infants.

Detailed methods of recruitment and data collection have been described previously.[19] The enrollment period for the current analytic data set was from 1998 to 2012. Recruitment was conducted 24–72 hours after the child were born with written consent from all mothers. A standardized questionnaire interview of mothers was used to collect information on socio-economic status, lifestyle and environmental factors. Multiple-gestation pregnancies and newborns with major birth defects were excluded from the study. Postnatal follow-up was limited to children who were enrolled in the study and received primary care at the Boston University Medical Center between January 2001 to December 2014.

Figure S1 (please see http://hyper.ahajournals.org) illustrates how participants were selected for our analysis. Of the 2,890 mothers under postnatal follow-up, 1,877 had their child's BP measured on at least one well-child visit from 3 to 9 years old. We excluded 6 pairs who did not complete maternal questionnaire and 578 pairs who had missing data for $PM_{2.5}$ exposure during preconception or any trimester during pregnancy, which reduced our sample size to 1,293 mother-child pairs.

The study was approved by the institutional review board of Boston University Medical Center and Johns Hopkins Bloomberg School of Public Health.

EXPOSURES

The primary exposure for this study was mothers' exposure to ambient $PM_{2.5}$ during pregnancy. Pregnancy exposure periods were divided into the first trimester (days 1–90 of pregnancy), the second trimester (days 91–180), third trimester (days 181-birth). We created a combined exposure from the first to third trimester as a proxy of exposure during entire pregnancy. We also examined the preconception (90 days before pregnancy) and postnatal (first two years of life) $PM_{2.5}$ exposure.

To determine ambient $PM_{2.5}$ concentration, we matched each mother's residential address by street level to the nearest U.S. Environmental Protection Agency's (EPA) air quality monitor using Euclidean minimum distance and recorded daily $PM_{2.5}$ concentration from this monitor.[16] A map showing the locations of participants relative to the monitors can be found in our previous paper.[15] If the participant moved away from the previous address during pregnancy, $PM_{2.5}$ concentration was recorded from the nearest monitor matched to

the new address since the date she moved. Individual exposure to $PM_{2.5}$ during each period was calculated as the geometric mean of the daily concentration during this time. We treated $PM_{2.5}$ concentration both as a continuous variable (scaled to 5μg/m^3 increase) and as a categorical variable (deriving tertiles of exposure separately for each period).

OUTCOME

The primary outcome was child SBP at the last recorded well-child visit at the Boston University Medical Center, which fell between 3 and 9 years of age. Child BP was measured at the right brachial artery by the clinical staff using the validated automatic sphygmomanometer Masimo Set (2003–2008: the Welch Allyn 420 Spot Vital Signs monitor; 2008–2014, the Welch Allyn 45MT0 Spot Vital Signs LXi monitor). We transformed SBP for each child into percentile based on the U.S reference (The Fourth Report).[20] We chose to use SBP in lieu of diastolic BP (DBP) because it is a better predictor of adult hypertension and adverse cardiovascular outcomes.[21,22]

We modeled SBP as a continuous variable and as a binary variable (having elevated BP or not). We defined elevated BP as SBP percentile ≥90 in accordance to the Fourth Report which is the reference standard for child hypertension diagnosis.[20]

COVARIATES

We extracted information on mother's pre-pregnancy weight, height, race, education, smoking status and alcohol consumption from the standardized questionnaire. Maternal pre-pregnancy body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. We further categorized it as underweight (BMI < 18.5 kg/m^2), normal weight (18.5 kg/m^2 ≤ BMI < 25 kg/m^2), overweight (25 kg/m^2 ≤ BMI < 30 kg/m^2) and obesity (BMI ≥ 30 kg/m^2). Maternal race was categorized as Black, Hispanic and Other (including White, Asian, any other self-reported race or mixed race).

Covariates included maternal age at delivery, maternal hypertensive disorders, birth weight, gestational age, child sex and delivery type, all of which were extracted from electrical medical records. Maternal hypertensive disorder was defined by having chronic hypertension or one of the pregnancy-induced symptoms including gestational hypertension, eclampsia, pre-eclampsia or hemolysis, elevated liver enzymes, and low platelet count (HELLP syndrome).[23] Gestational age was modelled both continuously and categorized as preterm birth (<37 weeks) or not (≥37 weeks).

DATA ANALYSIS

We first estimated the effect of $PM_{2.5}$ exposure on SBP percentile using multivariable generalized linear regression model (GLM). Poisson regression with robust variance was used to examine the relative risk of elevated BP in relation to $PM_{2.5}$ exposure.[24] In all the models, $PM_{2.5}$ exposure was treated as both a continuous variable scaled to 5μg/m^3 increases and a categorical variable by tertile. We also examined the possible non-linear relationship using the restricted cubic spline regression model.[25]

To address confounding, we identified covariates related to both the $PM_{2.5}$ exposure and the outcome of BP and which were not in the causal pathway between the exposure and the outcome. We began with the crude model, and then added confounders into the regression model, including maternal age at delivery (continuous), maternal self-reported race (Black/African American; Hispanic; other), maternal marital status (married; other), maternal education (middle school or below; high school; college or above), maternal smoking history (never smoking; quit smoking; continued smoking during pregnancy) and maternal alcohol intake (yes; no). All missing values for categorical variables were coded as a separate category. There were no missing values for the continuous variable maternal age at delivery.

Potential effect measure modifiers (EMM) considered included: maternal hypertensive disorders (yes; no), maternal pre-pregnancy BMI (normal weight; overweight; obesity), child sex (male; female), preterm birth (yes; no), birth weight for gestational age (small for gestational age; appropriate for gestational age; large for gestational age). We conducted subgroup analysis stratified by each potential EMM. Likelihood ratio test was conducted to compare two models with and without the interaction term (the product of the potential EMM and the continuous $PM_{2.5}$ concentration scaled to $5\mu g/m^3$). All missing values for potential EMM were excluded from the analysis when conducting the stratified analysis and in the likelihood ratio test.

We then considered birthweight (continuous), gestational age (continuous) and child BMI-z score (continuous) as potential mediators since they may be in the causal pathway between prenatal $PM_{2.5}$ exposure and child BP. We conducted mediation analysis by adding each mediator into the confounder model and estimated the degree of mediation individually and jointly.

To assess potential selection bias due to the missingness of the BP data, we conducted sensitivity analyses using the stabilized inverse probability weighting method by calculating the chance of having missing BP based on a set of baseline covariates and applying them to the regression model.[26] In estimating the probability, we included all the potential confounders identified above and also maternal hypertensive disorders, maternal BMI, child sex, parity, low birth weight, preterm birth and delivery type. We used multiple imputation by chained equation method in the prediction model to deal with the missing values.[27]

All tests were based on a two-sided $p<0.05$ defined as statistically significant. Data management and analysis were conducted using Stata 14.2 (Stata Corp, College Station, TX) and SAS 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

Table 1 provides characteristics of mother-child pairs according to $PM_{2.5}$ levels in the third trimester (characteristics by $PM_{2.5}$ levels during whole pregnancy is provided in Table S1 on http://hyper.ahajournals.org). Compared to mothers exposed to the lowest tertile of $PM_{2.5}$ during the third trimester, those exposed to the highest tertile were more likely to be unmarried, have lower educational achievement, have maternal hypertensive disorders and have higher pre-pregnancy BMI. Children whose mothers were exposed to the highest $PM_{2.5}$

level were more likely to have been born preterm, low birth weight, and tended to have higher BMI z-scores in childhood.

In Table 2, we show the results for the associations of maternal exposure to ambient $PM_{2.5}$ concentrations in each period with childhood SBP percentile. Associations were significant for $PM_{2.5}$ exposure in the third trimester. Compared to those in the lowest third trimester $PM_{2.5}$ tertile, those in the highest tertile had a 4.62 (95% CI: 1.12, 8.12) percentile higher SBP after adjusting for confounders. This estimate increased to 4.79 (95% CI: 0.21, 9.37) after controlling postnatal $PM_{2.5}$ concentration. Modelled as a continuous exposure, a 5 $\mu g/m^3$ increase in $PM_{2.5}$ concentration exposure in the third trimester was associated with a 3.39 (95% CI: 0.63, 6.15) percentile increase in child SBP. Based on multivariable cubic spline model (Figure 1), the SBP percentile increased monotonically and sharply after a threshold of 13 $\mu g/m^3$ $PM_{2.5}$ exposure in the third trimester. Childhood SBP percentile was not associated with exposure to ambient $PM_{2.5}$ in the preconception period (adjusted β=1.05, 95% CI: −1.59, 3.68), first trimester (adjusted β =1.16, 95% CI: −1.63, 3.95) or second trimester (adjusted β =1.18, 95% CI: −1.75, 4.11).

Associations for elevated childhood BP were similar (Table 3). In the third trimester, the relative risk (RR) of elevated BP was 1.60 (95% CI: 1.12, 2.27) times higher for a child whose mother was exposed to the highest $PM_{2.5}$ tertile compared to the lowest tertile after adjustment. After scaling $PM_{2.5}$ to continuous level, the relative risk is 1.46 (95% CI: 1.17, 1.83) times higher per 5$\mu g/m^3$ increase in ambient $PM_{2.5}$ concentration after adjustment. Our multivariable-adjusted cubic spline model (Please see the Figure S2 on http://hyper.ahajournals.org) showed that the risk for elevated BP significantly increased after exposure to a $PM_{2.5}$ threshold of 13 $\mu g/m^3$ in the third trimester. The adjusted RR of elevated BP comparing who have $PM_{2.5}$ exposure ≥13 $\mu g/m^3$ to those <13 $\mu g/m^3$ during the third trimester was 1.80 (95% CI: 1.33, 2.44). Childhood elevated BP was not associated with 5 $\mu g/m^3$ increase in ambient $PM_{2.5}$ concentration in the preconception period (adjusted RR=0.87, 95% CI: 0.67, 1.13), first trimester (adjusted RR=1.19, 95% CI: 0.91, 1.56) or second trimester (adjusted RR =1.11, 95% CI: 0.85, 1.46).

In the mediation analysis, after separately adding birthweight, gestational age and child BMI-z score into the confounder model, the estimated SBP percentile increase changed from 3.39 (95% CI: 0.63, 6.15) to 3.08 (95% CI: 0.33, 5.82), 3.15 (95% CI: 0.40, 5.90) and 2.75 (95% CI: 0.01, 5.50) per 5 $\mu g/m^3$ higher in ambient $PM_{2.5}$ concentration, respectively. When both birthweight and BMI-z score were added to the model, they mediated 35% of the association, and the p-value for the association of $PM_{2.5}$ and childhood SBP was no longer statistically significant (p=0.112); this finding suggests that the effects of $PM_{2.5}$ on weight at birth and weight during childhood mediate part of the association of $PM_{2.5}$ with childhood SBP.

In the subgroup analysis stratified by potential EMMs, all subgroups show a positive increase of SBP percentile with increasing $PM_{2.5}$ concentration (Figure 2) for the third trimester. The p-values for interaction suggests no EMM.

Table S2 (please see http://hyper.ahajournals.org) shows the comparison of the characteristics between the 1293 pairs included in the analysis versus the 619 excluded from the study due to the missing BP measurement. In our sensitivity analyses, after applying stabilized inverse probability weights in the regression model, the association of $PM_{2.5}$ with child SBP was further enhanced. For the third trimester, we see a 3.79 percentile increase in child SBP per 5 $\mu g/m^3$ increase in $PM_{2.5}$ concentration (95% CI: 0.96–6.62, p=0.009) and a 5.21 percentile increase comparing the highest tertile of $PM_{2.5}$ exposure to the lowest tertile (95% CI: 1.70–8.72, p=0.004) after adjusting for potential confounders.

DISCUSSION

In this study, we found that maternal exposure to ambient $PM_{2.5}$ during the third trimester of pregnancy is associated with elevated child BP at 3 to 9 years old, even after adjustment for potential confounders and controlling for postnatal $PM_{2.5}$ exposure. This association was consistent among children who were born healthy, preterm or with low birth weight. It was also consistent across different races and ethnicities. The association was partly mediated by the effects of $PM_{2.5}$ on fetal growth and weight in childhood. As such, our study provides new insights on the underlying pathways by which prenatal $PM_{2.5}$ exposure affects childhood SBP.

Our findings contribute to a very limited literature base on the transgenerational effects of maternal air pollution exposure on childhood BP. Consistent with our findings, in a cohort study of 1,131 mother-infant pairs, van Rossem et al. found that higher $PM_{2.5}$ exposure in the third trimester, but not in the first or second trimesters, was associated with higher SBP in newborns.[17] However, their outcome measure was neonatal BP which may not be a good approximation for effects on childhood BP. Also, their cohort predominantly contained white (68.7%) newborns, with few preterm births (4.2%) or small for gestational age newborns (mean gestational age: 39.7±1.4 weeks), which limits the generalizability of their conclusion. In another study, Breton et al. did not find any association between exposure to $PM_{2.5}$ in pregnancy and BP in offspring at 11 years of age.[18] However, the trimester-specific $PM_{2.5}$ exposures were assigned retrospectively based on the birth certificate and 12% of the mothers moved during pregnancy, thus bias on exposure ascertainment may exist in this study. To our knowledge, our study is the first to investigate the association between prenatal $PM_{2.5}$ exposure and childhood BP using prospectively collected data.

The potential mechanisms underlying the observed associations likely include altered fetal and childhood growth, as evidenced by our mediation analyses, along with inflammation, oxidative stress and/or endocrine disruption.[9,28–30] Maternal exposure to $PM_{2.5}$ in pregnancy has been shown to lead to altered trophoblast formation and abnormal vascularization of the placenta and cause defected *in utero* cardiovascular growth.[31] Numerous epidemiology studies including our own have shown that *in utero* $PM_{2.5}$ exposure is related to lower birth weight and preterm birth.[32,33] Animal studies have further demonstrated that *in utero* exposure to $PM_{2.5}$ may increase the risk for altered BP, heart failure and other cardiovascular events in offspring.[10–12] More recent studies also suggest that mothers exposed to high-level $PM_{2.5}$ may give birth to children with shorter telomere length,[34] leading to higher cardiovascular risks.[35]

Our finding that maternal exposure to $PM_{2.5}$ in the third trimester, but not the first or second trimester, was associated with elevated offspring BP is consistent with the findings by Rossem et al.,[17] suggesting that this may be the most etiologically relevant time window for $PM_{2.5}$ exposure. The third trimester is the time when a fetus gains most weight. According to the ultrasound estimation by World Health Organization (WHO), the median fetal weight is 1,039 grams at the end of the second trimester (27 weeks) and 3,617 grams at the end of the third trimester (40 weeks).[36] Thus, one possible explanation is that $PM_{2.5}$ affects child BP by affecting fetal weight gain and development in the third trimester. Again, this is supported by our finding that birthweight and child BMI mediate part of the association between $PM_{2.5}$ and offspring SBP. A possible explanation for why third trimester but not postnatal exposure to $PM_{2.5}$ was associated with offspring BP in our study may be that $PM_{2.5}$ exposure in the third trimester is more critical to development than postnatal exposure. The lack of association for postnatal $PM_{2.5}$ may also be due to the more variable postnatal exposures of a child. After a child is born, he or she might spend time in different locations (for example, in the day-care center) separate from his or her mother, and thus have different $PM_{2.5}$ exposure than his or her mother. Further studies directly assessing $PM_{2.5}$ in infants might help explain this hypothesis.

$PM_{2.5}$ concentration in the third trimester (mean: 10.82 μg/m^3, IQR: 8.86–12.41μg/m^3) in our population was higher than the national average in the U.S. (7.77 μg/m^3 in year 2016).[37] It is estimated that 12.1 million people in the U.S. live in counties where the ambient $PM_{2.5}$ concentrations exceed the EPA's National Ambient Air Quality Standard of an annual mean of 12 μg/m^3.[38,39] Moreover, 92% of the global population live in places where the $PM_{2.5}$ is higher than the WHO's Ambient Air Quality Guidelines of 10 μg/m^3 annual mean worldwide.[40,41] Using these data sources and findings from our study, we estimated that approximately 2.38 million women in the U.S. and 1.51 billion women worldwide at child-bearing age (15–44 years old) are exposed to a $PM_{2.5}$ concentration near or above a threshold that portends higher risk for the development of elevated childhood SBP in offspring.

There are several strengths of our study. First, our study is the first prospective study on this topic, allowing us to determine temporality of the association. Second, in addition to assessing the association of $PM_{2.5}$ during pregnancy, our etiologically relevant time window, we also had data that allowed us to examine the association between preconception $PM_{2.5}$ exposure and offspring SBP. This association, which was null, can be considered as a "negative control" and preconception exposure would not affect the fetus.[42] Third, we had data on postnatal $PM_{2.5}$ exposure, allowing us to determine that the association of third trimester $PM_{2.5}$ was independent of postnatal exposure. Finally, the diversity of our cohort is a strength. Our study population consists more of African American (43.4%), low birth weight (26.5%) and preterm birth (27.3%) children, which improves the external validity of the conclusion.

There are also several limitations of our study. First, as an observational study, residual confounding may be present, although we tried to control for the main confounders. Second, there may be measurement error for child BP, specifically imprecision since it was only measured once at each well-child visit. However, such error would most likely be non-

differential and attenuate findings. Another concern is that the $PM_{2.5}$ data obtained from the EPA air quality monitors may not be precise enough and are likely to cause misclassifications of the $PM_{2.5}$ exposure. However, a recent study by McGuinn et al. found that the monitors are nearly as accurate as any other $PM_{2.5}$ calculating models for showing the long-term association between PM and cardiovascular disease in the urban setting.[43] Moreover, more than 85% of the study participants lived within 10 km of the matched monitors, a distance within which the $PM_{2.5}$ concentrations are spatially homogenous.[15] Finally, although our findings are consistent with prior literature[17], and the p-values for the third trimester are far less than 0.05, we still cannot rule out the possibility of false positive results due to multiple testing.

PERSPECTIVES

Maternal exposure to ambient $PM_{2.5}$ during the third trimester is associated with elevated BP in children aged 3 to 9 years. The observed association between maternal $PM_{2.5}$ and offspring SBP association appears to be partly mediated by the effects of $PM_{2.5}$ on fetal and childhood weight gain. If further confirmed, our findings provide new insight into early life origins of high blood pressure and opportunities for early screening and primary prevention of hypertension in childhood and beyond.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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NOVELTY AND SIGNIFICANCE

What Is New?

We found that the third trimester during pregnancy may be a critical period during which high maternal exposure to ambient $PM_{2.5}$ ($\geq 13 \mu g/m^3$) portends risk of elevated BP during childhood in offspring.

What Is Relevant?

Our study adds to the literature on the in-utero antecedents of cardiovascular disease, suggesting that reducing maternal exposure to ambient $PM_{2.5}$ may represent an early opportunity for primordial prevention of childhood elevated blood pressure.

Summary

Maternal exposure to ambient PM2.5 during the third trimester of pregnancy is associated with elevated BP in children aged 3 to 9 years.

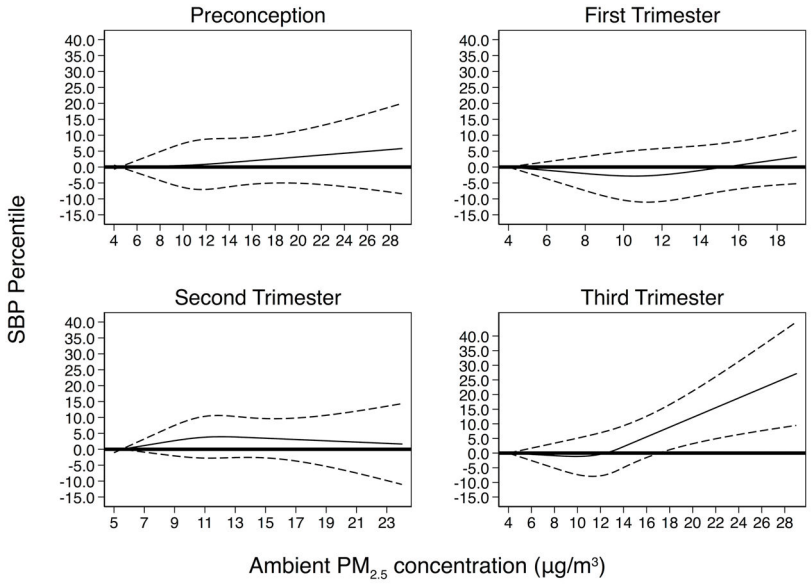

Figure 1.

Relationship between child SBP percentile and maternal ambient $PM_{2.5}$ level in each exposure period estimated by restricted cubic spline regression model

* Model adjusted for maternal age at delivery, self-reported race, marital status, education, smoking history and alcohol intake during pregnancy

† Abbreviations: $PM_{2.5}$ = particulate matter ≤2.5 microns; SBP = systolic blood pressure

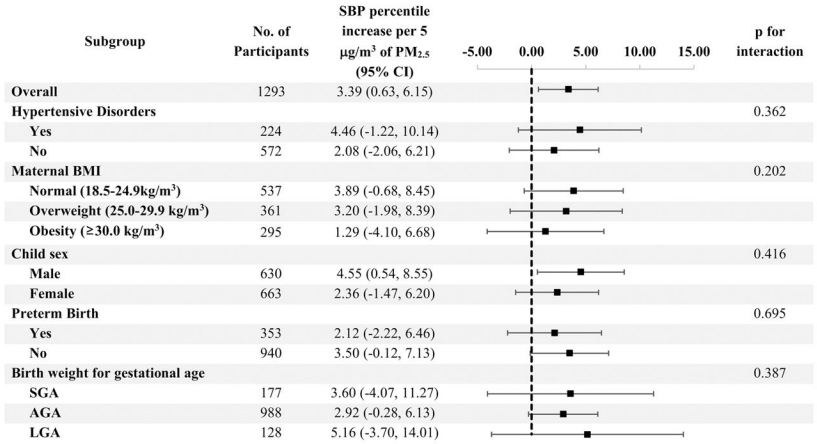

Figure 2.

Subgroup analysis by potential Effect Measure Modifiers

* Model adjusted for maternal age at delivery, self-reported race, marital status, education, smoking history and alcohol intake during pregnancy

† Abbreviations: $PM_{2.5}$ = particulate matter ≤2.5 microns; CI: confidence interval; SBP = systolic blood pressure; BMI = body mass index; SGA = small for gestational age; AGA = average for gestational age; LGA = large for gestational age

Table 1

Characteristics of mother-child pairs in the Boston Birth Cohort by $PM_{2.5}$ level in the third trimester (n=1293)

Variable, Number (%)	$PM_{2.5}$ Level During Third Trimester			p-value
	Tertile 1 (3.79–9.57 μg/m^3)	Tertile 2 (9.57–11.80 μg/m^3)	Tertile 3 (11.80–28.81 μg/m^3)	
Number	431	431	431	
Maternal Characteristics				
Age at delivery, mean (SD)	28.88 (6.76)	28.39 (6.51)	28.32 (6.78)	0.41
African American race	191 (44.3%)	182 (42.2%)	188 (43.6%)	0.82
Married mothers	140 (33.0%)	155 (36.3%)	124 (29.2%)	0.09
Low educational achievement *	122 (28.4%)	126 (29.3%)	137 (32.0%)	0.48
Smoke during pregnancy	43 (10.0%)	44 (10.4%)	47 (11.0%)	0.90
Alcohol intake during pregnancy	35 (8.3%)	31 (7.5%)	27 (6.6%)	0.67
Maternal hypertensive disorder	76 (17.6%)	65 (15.1%)	83 (19.3%)	0.26
Pre-pregnancy BMI (kg/m^2), mean (SD)	26.46 (6.41)	26.37 (5.95)	27.14 (6.43)	0.16
Children Characteristics				
SBP percentile, mean (SD)	56.30 (26.28)	57.35 (25.88)	60.97 (25.78)	0.02
Boys	209 (48.5%)	216 (50.1%)	205 (47.6%)	0.75
Nulliparous	186 (43.3%)	164 (38.1%)	186 (43.2%)	0.21
Preterm birth	122 (28.3%)	98 (22.7%)	133 (30.9%)	0.02
Low birth weight	112 (26.0%)	98 (22.7%)	132 (30.6%)	0.03
Vaginal delivery	279 (64.7%)	270 (62.6%)	280 (65.0%)	0.74
Gestational age in week, mean (SD)	37.66 (3.32)	38.14 (2.83)	37.75 (3.09)	0.06
BMI z-score, mean (SD)	0.62 (1.36)	0.76 (1.24)	0.97 (1.22)	<0.01

*Low educational achievement defined as having the highest education “Middle school or below”

†Abbreviations: $PM_{2.5}$ = particulate matter ≤2.5 microns; SD = standard deviation; BMI = body mass index; SBP = systolic blood pressure; Ref = Reference group

Table 2

Associations of ambient $PM_{2.5}$ level and child SBP percentile in each exposure period (n=1293)

Pregnancy Exposure Periods	$PM_{2.5}$ Levels	Child SBP percentile		
		Crude β (95% CI)	Adjusted β* (95% CI)	p-value
Preconception	Tertile 1 (4.48–9.90 μg/m^3)	Ref.	Ref.	Ref.
	Tertile 2 (9.90–12.08 μg/m^3)	−1.43 (−4.91, 2.05)	−1.37 (−4.88, 2.13)	0.442
	Tertile 3 (12.10–29.00 μg/m^3)	1.85 (−1.63, 5.33)	1.93 (−1.59, 5.46)	0.282
	Per 5μg/m^3 increase	0.94 (−1.64, 3.51)	1.05 (−1.59, 3.68)	0.437
First Trimester	Tertile 1 (4.17–9.72 μg/m^3)	Ref.	Ref.	Ref.
	Tertile 2 (9.72–11.93 μg/m^3)	−1.41 (−4.89, 2.06)	−1.60 (−5.09, 1.90)	0.370
	Tertile 3 (11.93–19.15 μg/m^3)	3.02 (−0.45, 6.49)	2.57 (−0.96, 6.09)	0.153
	Per 5μg/m^3 increase	1.39 (−1.36, 4.15)	1.16 (−1.63, 3.95)	0.415
Second Trimester	Tertile 1 (5.40–9.77 μg/m^3)	Ref.	Ref.	Ref.
	Tertile 2 (9.78–11.91 μg/m^3)	0.30 (−3.18, 3.78)	0.12 (−3.39, 3.64)	0.945
	Tertile 3 (11.91–23.60 μg/m^3)	1.68 (−1.80, 5.17)	1.57 (−1.95, 5.08)	0.382
	Per 5μg/m^3 increase	1.30 (−1.60, 4.20)	1.18 (−1.75, 4.11)	0.429
Third Trimester	Tertile 1 (3.79–9.57 μg/m^3)	Ref.	Ref.	Ref.
	Tertile 2 (9.57–11.80 μg/m^3)	1.05 (−2.42, 4.52)	1.15 (−2.34, 4.64)	0.519
	Tertile 3 (11.80–28.81 μg/m^3)	4.68 (1.21, 8.15)	4.62 (1.12, 8.12)	0.010
	Per 5μg/m^3 increase	3.48 (0.74, 6.23)	3.39 (0.63, 6.15)	0.016
Whole Pregnancy	Tertile 1 (6.15–9.94 μg/m^3)	Ref.	Ref.	Ref.
	Tertile 2 (9.94–11.70 μg/m^3)	1.50 (−1.98, 4.97)	1.13 (−2.37, 4.63)	0.528
	Tertile 3 (11.70–18.43 μg/m^3)	3.56 (0.09, 7.04)	3.34 (−0.19, 6.86)	0.064
	Per 5μg/m^3 increase	3.20 (−0.26, 6.66)	2.99 (−0.51, 6.49)	0.094

*Model adjusted for maternal age at delivery, self-reported race, marital status, education, smoking history and alcohol intake during pregnancy

†Abbreviations: $PM_{2.5}$ = particulate matter ≤2.5 microns; CI: confidence interval; SBP = systolic blood pressure; Ref = Reference group

Table 3

Associations of ambient $PM_{2.5}$ level and risk for elevated SBP in each exposure period (n=1293)

Pregnancy Exposure Periods	$PM_{2.5}$ Levels	Child Elevated SBP (defined by ≥90th percentile)			
		Cases (%)	Crude RR (95% CI)	Adjusted* RR (95% CI)	p for adj-RR
Preconception	Tertile 1 (4.48–9.90 μg/m^3)	59 (13.69%)	Ref.	Ref.	Ref.
	Tertile 2 (9.90–12.08 μg/m^3)	58 (13.46%)	0.98 (0.70, 1.38)	0.99 (0.71, 1.39)	0.971
	Tertile 3 (12.10–29.00 μg/m^3)	51 (11.83%)	0.86 (0.61, 1.23)	0.90 (0.63, 1.28)	0.548
	Per 5μg/m^3 increase	N.A.	0.84 (0.65, 1.09)	0.87 (0.67, 1.13)	0.292
First Trimester	Tertile 1 (4.17–9.72 μg/m^3)	52 (12.06%)	Ref.	Ref.	Ref.
	Tertile 2 (9.72–11.93 μg/m^3)	43 (10.00%)	0.83 (0.57, 1.21)	0.83 (0.57, 1.21)	0.336
	Tertile 3 (11.93–19.15 μg/m^3)	73 (16.90%)	1.40 (1.01, 1.95)	1.38 (0.99, 1.92)	0.056
	Per 5μg/m^3 increase	N.A.	1.20 (0.91, 1.56)	1.19 (0.91, 1.56)	0.201
Second Trimester	Tertile 1 (5.40–9.77 μg/m^3)	52 (12.12%)	Ref.	Ref.	Ref.
	Tertile 2 (9.78–11.91 μg/m^3)	54 (12.47%)	1.03 (0.72, 1.47)	1.00 (0.70, 1.44)	0.978
	Tertile 3 (11.91–23.60 μg/m^3)	62 (14.39%)	1.19 (0.84, 1.67)	1.20 (0.85, 1.69)	0.297
	Per 5μg/m^3 increase	N.A.	1.11 (0.85, 1.45)	1.11 (0.85, 1.46)	0.431
Third Trimester	Tertile 1 (3.79–9.57 μg/m^3)	44 (10.21%)	Ref.	Ref.	Ref.
	Tertile 2 (9.57–11.80 μg/m^3)	54 (12.53%)	1.23 (0.84, 1.79)	1.24 (0.85, 1.81)	0.257
	Tertile 3 (11.80–28.81 μg/m^3)	70 (16.24%)	1.59 (1.12, 2.26)	1.60 (1.12, 2.27)	0.009
	Per 5μg/m^3 increase	N.A.	1.47 (1.17, 1.85)	1.46 (1.17, 1.83)	0.001
Whole Pregnancy	Tertile 1 (6.15–9.94 μg/m^3)	51 (11.83%)	Ref.	Ref.	Ref.
	Tertile 2 (9.94–11.70 μg/m^3)	50 (11.60%)	0.98 (0.68, 1.42)	0.95 (0.66, 1.36)	0.767
	Tertile 3 (11.70–18.43 μg/m^3)	67 (15.55%)	1.31 (0.94, 1.84)	1.32 (0.94, 1.85)	0.111
	Per 5μg/m^3 increase	N.A.	1.45 (1.03, 2.04)	1.45 (1.03, 2.05)	0.034

*Model adjusted for maternal age at delivery, self-reported race, marital status, education, smoking history and alcohol intake during pregnancy

†Abbreviations: $PM_{2.5}$ = particulate matter ≤2.5 microns; CI: confidence interval; SBP = systolic blood pressure; RR = relative risk; adj-RR = Relative risk after adjusted; Ref = Reference group