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First Trimester Exposure to Ambient Air Pollution, Pregnancy Complications and Adverse Birth Outcomes in Allegheny County, PA

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Abstract

Despite numerous studies of air pollution and adverse birth outcomes, few studies have investigated preeclampsia and gestational hypertension, two pregnancy disorders with serious consequences for both mother and infant. Relying on hospital birth records, we conducted a cohort study identifying 34,705 singleton births delivered at Magee-Women's Hospital in Pittsburgh, PA between 1997 and 2002. Particle (<10 μm-PM_{10}; <2.5 μm-$PM_{2.5}$) and ozone (O_3) exposure concentrations in the first trimester of pregnancy were estimated using the space–time ordinary Kriging interpolation method. We employed multiple logistic regression estimate associations between first trimester exposures and preeclampsia, gestational hypertension, preterm delivery, and small for gestational age (SGA) infants. $PM_{2.5}$ and O_3 exposures were associated with preeclampsia (adjusted OR = 1.15, 95 % CI = 0.96–1.39 per 4.0 μg/m^3 increase in $PM_{2.5}$; adjusted OR = 1.12, 95 % CI = 0.89–1.42 per 16.8 ppb increase in O_3), gestational hypertension (for $PM_{2.5}$ OR = 1.11, 95 % CI = 1.00–1.23; for O_3 OR = 1.12, 95 % CI = 0.97–1.29), and preterm delivery (for $PM_{2.5}$ ORs = 1.10, 95 % CI = 1.01–1.20; for O_3 ORs = 1.23, 95 % CI = 1.01–1.50). Smaller 5–8 % increases in risk were also observed for PM_{10} with gestational hypertension and SGA, but not preeclampsia. Our data suggest that first trimester exposure to particles, mostly $PM_{2.5}$, and

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ozone, may increase the risk of developing preeclampsia and gestational hypertension, as well as preterm delivery and SGA.

Keywords

Air pollution; Particulate; Preeclampsia; Gestational hypertension; Preterm; Small for gestational; age (SGA)

Introduction

Preeclampsia is a pregnancy disorder characterized by hypertension and proteinuria. It develops in the course of pregnancy after mid-gestation and is a major cause of maternal and neonatal mortality and morbidity [1]. For pregnant women diagnosed with preeclampsia, delivery is the only cure. Thus, preeclampsia causes 15 % of all preterm births (defined as delivery at less than 37 weeks of gestation) that are induced to prevent progression of preeclampsia [2]. While it has been postulated that reduced perfusion of the placenta contributes to preeclampsia, this alone is not sufficient to cause this syndrome, which must be complemented by other genetic, behavioral, and/or environmental factors [3]. Without signs of preeclampsia, failure of vascular remodeling that reduces blood supply to the placenta also contributes to both intrauterine growth restriction (IUGR) and to an estimated 30 % of spontaneous preterm births [4, 5].

Previously, both ambient and traffic-related air pollution have been linked to adverse birth outcomes such as low birth weight, preterm birth, and small for gestational age infants (SGA) [6-9]. Thus far, few studies have investigated preeclampsia and gestational hypertension [10-13]. A California birth cohort study of air pollution investigated preeclampsia based on birth certificates and reported positive associations with higher carbon monoxide (CO) and sulfur dioxide (SO_2) exposures during pregnancy [11]. Recently, a smaller cohort study conducted in western Washington state identified 117 preeclamptic womenandreported increasedrisks withambient CO and $PM_{2.5}$ exposures [10]. Furthermore, we previously observed adverse effects of traffic-related nitrogen oxides (NO_x) and $PM_{2.5}$ exposures on preeclampsia in Southern California [12]. A Dutch study did not find associations for residential proximity to traffic with preeclampsia or gestational hypertension [13], but an excess in risk emerged for whole pregnancy PM_{10} and nitrogen dioxide (NO_2) exposures when improved exposure modeling methods were employed [14].

We re-examined the relatively new hypothesis that air pollution influences the occurrence of preeclampsia and gestational hypertension, and also report on the more commonly examined adverse birth outcomes such as preterm delivery and SGA. We assessed air pollution in early pregnancy (i.e., first trimester) because this is the period when we would expect this exposure to interfere with maternal vascular remodeling processes. Most previous air pollution and adverse birth outcome studies have also examined the influence of air pollution in this period. It is thought that a root cause of preeclampsia is a failed remodeling of the maternal spiral arteries supplying the placenta. This results in reduced placental perfusion and oxidative stress, and occurs between 9 and 18 weeks of gestation [3]. Employing data from a major hospital in Pittsburgh Allegheny County collected from 1997 to 2002, we had access to information on maternal smoking, which previously often could not be taken into account. This cohort included a higher proportion of African-American women living in a historically industrial region that continues to rank low with respect to air quality. Thus, these data provide us with the unique opportunity to study the influence of air pollution on less studied pregnancy complications, while taking into account maternal smoking.

Methods

Study Population and Design

For this hospital-based cohort study, we obtained data from the Magee Obstetric Medical and Infant (MOMI) database, established in 1995, which routinely collects detailed information on maternal, fetal, and neonatal outcomes from electronic and medical records for all women delivering at Magee-Women's Hospital in Pittsburgh, PA. Approximately 60 % of all women in Allegheny County deliver at this hospital.

The information in the MOMI database includes maternal age, race/ethnicity, education level, mother's marital status, year and date of birth, infant gender, gestational age at delivery, cigarette smoking during pregnancy, parity, insurance type, preeclampsia, gestational hypertension, SGA (defined as birth weight below 10th percentile for gestational age according to growth curves based on California normograms [15]), and maternal residential zip code at delivery. Gestational hypertension was defined as systolic blood pressure (SBP) ≥140 mmHg or diastolic blood pressure (DBP) ≥90 mmHg during the second half of pregnancy, whereas preeclampsia was defined as gestational hypertension accompanied by proteinuria after 20 weeks of gestation. Gestational age at delivery was estimated based on the last menstrual period (LMP) and certain other measurements, including uterine size, detection of fetal heartbeat, and first or second trimester ultrasonography if available. This study was approved by the Institutional Review Board at the University of Pittsburgh.

A total of 45,228 live infants were delivered at Magee-Womens Hospital between 1997 and 2002. We excluded multiple births (n = 1,806), women with chronic hypertension (n = 615), chronic diabetes (n = 291), gestational weeks at delivery recorded as less than 15 or greater than 45 weeks (n = 40), and a residential zip code outside of Allegheny County, PA (n = 7,771). This rendered a total of 34,705. The women we excluded were similar in age to those included but were more often of Caucasian race and reported to have been smokers during pregnancy.

For quality control, entries in the MOMI database are periodically compared to randomly sampled patient charts. In addition, outliers are identified and discrepancies between the database and medical charts are verified and corrected [16].

Exposure Assessment

Maternal exposure to ambient air pollution during pregnancy was estimated based on air monitoring data collected by the Allegheny County Health Department (ACHD) and the US Environmental Protection Agency (EPA) between 1996 and 2002. We examined ambient air pollutant concentrations for PM_{10}, $PM_{2.5}$ and O_3. These are so-called "criteria pollutants" measured routinely at government monitoring stations. The major sources of particle pollutants include coke and coal-fired power plants, road dust, and motor vehicles. Ozone is a photochemical pollutant formed by the chemical reaction of nitrogen oxides and volatile organic compounds in the presence of sunlight.

To optimize spatial variability information for each pollutant, we also incorporated air monitoring data for each pollutant collected in the neighboring counties within 50 km of the Allegheny County (AC) boundary. During the study period, 40 stations (including 18 monitoring stations in AC) collected PM_{10} daily or every 3rd or 6th day. $PM_{2.5}$ data were not available before 1999, and 23 monitoring stations (including 13 monitoring stations in AC) collected daily or every 3rd or 6th day data from 1999 to 2001. For O_3, hourly measurements were available at 15 stations in AC and its neighboring counties during the study period (Fig. 1).

The exposure assessment has been described in more detail elsewhere [17]. Briefly, we performed the space–time ordinary kriging (STOK) interpolation to estimate daily air pollution concentrations at each centroid of a grid (0.46 $mile^2$) in AC, using daily average concentrations calculated (for O_3) or collected (for PM_{10} and $PM_{2.5}$) from air monitoring data. We fitted the spatial and temporal variograms separately, using a spherical semivariogram model, and also combined the individual variograms into one space–time variogram by fitting a general product-sum model [18] (model parameter estimates are presented in Table 5 in "Appendix").

To obtain zip code-level pollutant concentrations, we averaged daily concentrations for each pollutant estimated for each grid centroid within each zip code. For example, to calculate the daily zip code-level concentrations for a pollutant, we would average 10 estimated daily concentrations at the centroid of 10 grids contained in the zip code. There are 109 zip codes in AC, with a mean area of 16.8 km^2 and an average of 10 grids in each zip code (range 1–84 grids).

Since we were interested in early pregnancy exposure, we then calculated the zip code-level first trimester air pollution concentrations for each woman. We averaged daily concentrations for each zip code over the first trimester (defined as the first 12 weeks of gestation) according to estimated gestational age.

Statistical Analysis

We performed multiple logistic regression to evaluate associations between first trimester air pollutant exposures and preeclampsia, gestational hypertension only, preterm delivery, and SGA, with robust variance estimators to account for non-independence, since many women lived within the same zip code. The coefficient estimates are the same as those based on the standard maximum-likelihood variance estimator in logistic regression, but they have slightly different standard errors, since the robust variance estimators take the non-independence of maternal residences within zip codes into account. We treated pollutant concentrations as continuous variables and reported the associations as per interquartile range (IQR) and per-unit increases. We calculated IQR for each pollutant based on first trimester average exposure concentrations of each pollutant, and only evaluated single-pollutant models, due to high colinearity between pollutants.

Based on previously published literature [7, 14, 19] and visualization, using causal diagram methods, as well as change in estimate criteria [20], we selected maternal age (years), race/ethnicity (Caucasian, African-American, other races), parity (nulliparous, parous), number of cigarettes smoked during pregnancy, season of birth, and year of conception as potential confounders for inclusion in adjusted models. We also examined other potential confounders, including maternal education level, mother's marital status, insurance type, and route of delivery, but since they did not change the estimates for pollutants by more than 10 %, these variables were not included in final models. Furthermore, we conducted several sensitivity analyses stratifying by maternal race/ethnicity (Caucasian, African-American) and smoking status (yes/no) during pregnancy.

Women diagnosed with preeclampsia who deliver a preterm infant (before 37 weeks of gestation) are generally more severely affected than those who deliver at term (after 37 gestational weeks), and have a greater risk of later life cardiovascular disease [21, 22]. Therefore, we also conducted stratified analyses for preeclampsia by preterm delivery (yes/no). For preterm deliveries, we furthermore investigated labor type (spontaneous/indicated). We used STATA (version 8.0; STATA Corporation, College Station, TX) to perform all statistical analyses.

Results

The mean maternal age at delivery was 29 years (SD = 6.1), and women reported an average of 14 (SD = 2.3) years of education. Most of the cohort members were Caucasian (77 %), married (64 %), reported no smoking during pregnancy (84 %), and were covered by health insurance during pregnancy (73 %) (Table 1). The incidence of preterm delivery and SGA during the study period was 9.0 and 8.5 %, respectively, and 6.0 % of the pregnant women were diagnosed with gestational hypertension and 3.3 % developed preeclampsia. Mean pollutant concentrations and correlations for the first trimester of pregnancy are shown in Table 2. PM_{10} was highly correlated with $PM_{2.5}$ and O_3 (r = 0.9 and 0.7, respectively), and $PM_{2.5}$ was moderately correlated with O_3 (r = 0.5).

First trimester $PM_{2.5}$ but not PM_{10} exposure was associated with preeclampsia (for $PM_{2.5}$ adjusted odds ratios (aORs) = 1.15, 95 % CI = 0.96–1.39 per 4.0 $\mu g/m^3$ increase) (Table 6 in "Appendix"; Table 3, for effect estimates based on per-unit increases). An effect for O_3 was only suggested when we adjusted for maternal smoking (aORs = 1.12, 95 % CI = 0.89–1.42 per 16.8 ppb increase). For gestational hypertension, an IQR increase in $PM_{2.5}$, PM_{10}, and O_3 during the first trimester increased the adjusted odds ratio by 8–12 %. Similarly, 4–23 % increases in the odds were estimated for PM_{10}, $PM_{2.5}$ and O_3, and preterm delivery in adjusted models. A smaller increase in odds for SGA was observed with first trimester PM_{10} and $PM_{2.5}$ exposure.

Effect estimates for preeclampsia and particulate matter were similar in size in smoking and non-smoking women (for smokers, aORs = 1.13, 95 % CI = 0.85–1.50; for non-smokers, aORs = 1.15, 95 % CI = 0.94–1.41 per 4.0 $\mu g/m^3$ increase in $PM_{2.5}$; Table 7 in "Appendix"; Table 4, for effect estimates based on per-unit increases). We observed a stronger association between O_3 and preeclampsia in smokers (for smokers, aORs = 1.23, 95 % CI = 0.68–2.23; for non-smokers, aORs = 1.10, 95 % CI = 0.86–1.41, per 16.8 ppb increase), but the 95 % CIs of the estimates for smokers and non-smokers largely overlapped. Sensitivity analyses for smokers and non-smokers separately suggested that PM_{10} affects gestational hypertension more strongly in non-smokers, while estimated effects were similar for the outcomes of preterm delivery and SGA. $PM_{2.5}$ affected preterm delivery more strongly in non-smokers, while effect estimates were similar for gestational hypertension and SGA in smoker and non-smokers. Generally, for O_3, the estimates for preterm delivery were greater for smokers, but associations for gestational hypertension and SGA were greater in non-smokers than smokers.

Results stratified by race suggested that $PM_{2.5}$ affected preeclampsia in Caucasian (aOR = 1.21, 95 % CI = 0.99–1.50) but not African-American women (aOR = 0.93, 95 % CI = 0.72–1.20) (Table 8 in "Appendix"). Consistent with $PM_{2.5}$ and preeclampsia results, first trimester $PM_{2.5}$ also affected preterm births only in Caucasians, while effects on gestational hypertension and SGA were greater in African-American women (Table 8 in "Appendix"). Generally, for gestational hypertension and SGA, the effects of O_3 and PM_{10} were also greater in African-American than Caucasian women, but the corresponding 95 % CIs largely overlapped. When stratified by preterm status (yes/no), effect estimates for preeclampsia were greater for both particulate matter and ozone in women who had delivered preterm infants (Table 9 in "Appendix"). Stratifying by labor type revealed that air pollutants influenced indicated/induced births more than spontaneous preterm births.

The results reported above for preeclampsia are from analyses in which the control group included women with gestational hypertension, as well as preterm births and SGA infants. When we conducted analyses that employed a single control group that excluded all of the outcomes of interest in this study, effect estimates were almost identical.

Discussion

Our study is one of the few to date that examined preeclampsia and gestational hypertension in relation to ambient air pollutant exposures. In addition, we were able to assess and control for the influence of smoking during pregnancy. We found that higher first trimester $PM_{2.5}$ and O_3 exposures were consistently associated with preeclampsia, gestational hypertension, and preterm delivery. A slightly increased risk of SGA was also observed for first trimester particulate matter (PM) exposures.

Previously, a Californian study analyzed birth certificate data for 2.3 million singleton live births from 1996 to 2004, and found no consistent associations between ambient $PM_{2.5}$ exposure and preeclampsia [11], possibly due to differences in particle composition across this large state. More recently, Rudra et al. [10] reported positive associations between model-based $PM_{2.5}$ concentrations and preeclampsia in a cohort of 3,509 women in western Washington state, but in this small study, effect estimates had wide confidence intervals (fourth vs. first quartile aOR = 1.41; 95 % CI = 0.63–3.18). Relying on measures of traffic density in a population-based cohort study of 7,339 women, Van den Hooven et al. [13] reported odds ratios of 1.07 (95 % CI = 0.75–1.53) and 1.14 (95 % CI = 0.71–1.82) for gestational hypertension and preeclampsia, respectively, for women who lived close to a major road in Rotterdam, Netherlands. We previously applied a sophisticated exposure model, CALINE4, to estimate traffic-generated NO_x and $PM_{2.5}$ concentrations for a cohort of 81,186 singleton births delivered at four hospitals (1997–2006) in Los Angeles and Orange Counties, California (USA), and reported an odds ratio of 1.10 (95 % CI = 1.06–1.15) for preeclampsia per 1.35 $\mu g/m^3$ increase in $PM_{2.5}$ during the first trimester [12]. The magnitude of this estimate is larger than that obtained in our present study, which examined ambient $PM_{2.5}$ exposures in general rather than traffic-related $PM_{2.5}$ exposures (for the current study, the aOR = 1.05 (95 % CI = 0.99–1.12) per 1.35 $\mu g/m^3$ increase in $PM_{2.5}$).

Because of insufficient sample size, we are unable to assess interaction and effect measure modification between air pollution exposure and birth outcomes for maternal race/ethnicity and smoking status during pregnancy. Rather, we conducted several sensitivity analyses stratifying by maternal race/ethnicity, smoking status, preterm delivery (for preeclampsia analysis), and labor type (for preterm delivery analysis). Although we observed different effect estimates across all strata, effect estimates had wide 95 % confidence intervals and we lacked precision to draw conclusions concerning interaction.

Several previous studies have reported a link between ambient air pollutant exposures, including particles during different trimesters of pregnancy and risk of preterm birth [23-26]. We confirmed a small increase in risk of preterm delivery for first trimester PM exposures, consistent with our previous report for preterm births in Southern California [12]. For example, for California, we reported an odds ratio of 1.03 (95 % CI = 1.00–1.06) for preterm delivery per 1.35 $\mu g/m^3$ increase in ambient $PM_{2.5}$ during the first trimester.

Using SGA based on the weight distribution of all infants born at a specific gestational age alone to determine growth restriction has several limitations, including (1) only capturing growth restriction for infants but not fetuses; (2) being unable to identify fetuses or infants who have not achieved their genetic growth potential but are not small enough to be SGA; and (3) being unable to distinguish fetuses or infants who have already achieved their genetic growth potential but do not have adequate gestational size/weight based on a standard distribution. Thus, special attention needs to be paid when interpreting the results for SGA. In our study, we found only very small increases in risk of delivering SGA infants in relation to ambient PM exposure during pregnancy, but these results are consistent with previous studies [27-29].

Recently, an International Collaboration on Air Pollution and Pregnancy Outcomes study comprised of 14 research groups and nine countries reported estimated ORs for term low birth weight per 10 $\mu g/m^3$ increase in PM_{10} during the entire pregnancy period, which ranged from 0.81 (95 % CI = 0.24–2.76) for the Netherlands to 1.44 (95 % CI = 0.62–3.36) for Vancouver [30]. Dejmek et al. [27] examined the association between $PM_{2.5}$ and PM_{10} air pollution and IUGR in a polluted region of the Czech Republic, and reported that during the first month of pregnancy exposure to PM_{10} was associated with IUGR (OR = 1.19, 95 % CI = 1.06–1.33, for a 10 $\mu g/m^3$ increase). Hansen et al. [29] reported a small increase in risk for delivering SGA infants exposed to PM_{10} during the first trimester, based on a city-wide average of this pollutant in Brisbane, Australia (per 8.1 $\mu g/m^3$ increase in PM_{10} during the first trimester, ORs = 1.04, 95 % CI = 0.96–1.12) [29].

In addition to hypertension, proteinuria is a cardinal symptom of preeclampsia, and pathological kidney changes are found in preeclampsia but not other forms of gestational hypertension, indicating that this syndrome is more than hypertension being simply revealed by pregnancy [3]. Indeed, not all women diagnosed with gestational hypertension are expected to develop preeclampsia. In our population approximately 45 % of women with gestational hypertension did not develop any accompanying and/or new-onset proteinuria. However, similarities in risk factors (such as obesity, diabetes, older maternal age) for these two disorders suggest overlap between the two conditions [31, 32].

The underlying biological mechanisms by which air pollution might cause adverse birth outcomes or pregnancy complications remain to be determined, but some possibilities include its influence on endothelial function, increase in oxidative stress, induction of inflammatory processes, and increased susceptibility to infections [33,34]. In addition, a growing body of research has linked changes in blood pressure (BP) to ambient air pollution; especially PM, not only for elderly persons with pre-existing cardiac disease, but also for healthy individuals [35-37]. However, we argue that the mechanisms by which air pollution influences BP during pregnancy likely differ, and might be more complex than those acting in non-pregnant populations. For example, in most aging populations, clinical changes in BP are commonly attributed to arterial vascular degeneration; however, in pregnant women, changes in BP result from systemic adaptation necessary to accommodate the presence and needs of the developing fetus. Recently, examining a subset of our study population who participated in a pregnancy cohort study, we reported that women exposed to ambient PM_{10}, $PM_{2.5}$, and O_3 during early pregnancy were more likely to have elevated C-reactive protein concentrations (above 8 $\mu g/ml$), a finding that supports the hypothesis that systemic inflammation induced by air pollutants may be a possible mechanism through which the risk of adverse birth outcomes is increased [17].

One strength of our study is that we relied on hospital-based records, which provide more accurate information than birth certificates concerning gestational weeks at delivery and the diagnoses of preeclampsia and gestational hypertension. Furthermore, information about maternal smoking during pregnancy allowed us to adjust for confounding by smoking, an important risk factor for these adverse birth outcomes.

We were unable to examine the influence of other gaseous air pollutants such as CO, NO_2, and SO_2, due to the scarcity of monitoring stations for these pollutants in the study area. Although our O_3 estimates were based on data collected at only 3 monitoring stations, ozone, a photochemical pollutant formed by the chemical reaction of nitrogen oxides and volatile organic compounds in the presence of sunlight, is spatially more homogenously distributed than other gaseous pollutants. In addition, our spatial interpolation model likely has sufficiently represented ozone exposures.

Like most previous air pollution and adverse birth outcome studies, we did not have maternal mobility information and assumed that women did not move or moved within the same zip code during pregnancy, which may result in misclassification of exposure depending upon the frequency of moving during pregnancy in our population. Furthermore, we ignored indoor sources of pollutants and assumed that the outdoor measures represent the women's exposures during pregnancy, at least in a relative manner. Unfortunately we do not have information for potential important indoor sources of PM or activity patterns for our study population to determine whether our assumptions are correct. However, misclassification of exposure would be non-differential for cases and controls, which most likely results in attenuated effect estimates. In addition, examining the influence of maternal mobility on exposure misclassification in New York State, researchers recently reported that low maternal mobility and moving within the same general area resulted in little change in exposure estimates when using birth addresses versus residential history collected in interviews [38].

Our estimates of individual exposure to air pollutants were based on interpolation methods that relied on data collected from ambient monitoring stations. We ignored atmospheric influences on the dispersion of pollutants and assumed that air pollution concentrations measured at each monitoring station represent the regional exposure. Although we have examined and controlled for a number of important potential confounders in our analyses, certain other potential confounders such as second-hand smoking, maternal occupational exposures, and stress are not available in our study. However, we previously found that for pollutants that change seasonally and averages for shorter pregnancy periods such as trimesters, factors that do not change seasonally are not strong confounders for birth outcomes [7]. Our first trimester air pollution exposure would thus be less likely to be confounded by these factors. Smoking was self-reported after delivery, and women with pregnancy complications may report smoking differently. However, we believe that any differential reporting of smoking is most likely independent of air pollution concentrations in the first trimester, since women likely did not know the concentration of air pollution around their home, making confounding bias less likely.

Conclusions

Relying on obstetric medical and birth records from a large hospital in Pittsburgh, we found that particulate matter (mainly $PM_{2.5}$) and ozone air pollutant exposures during the first trimester were associated with increased risk of developing preeclampsia, gestational hypertension, and preterm delivery. Particulate exposures also minimally increased the risk for delivering a SGA infant. Our results provide some evidence that ambient particulate matter and ozone exposures during the first trimester of gestation may induce pregnancy complications, specifically, preeclampsia and gestational hypertension, which can lead to preterm births and possibly SGA.

Appendix

See Tables 5, 6, 7, 8, 9.

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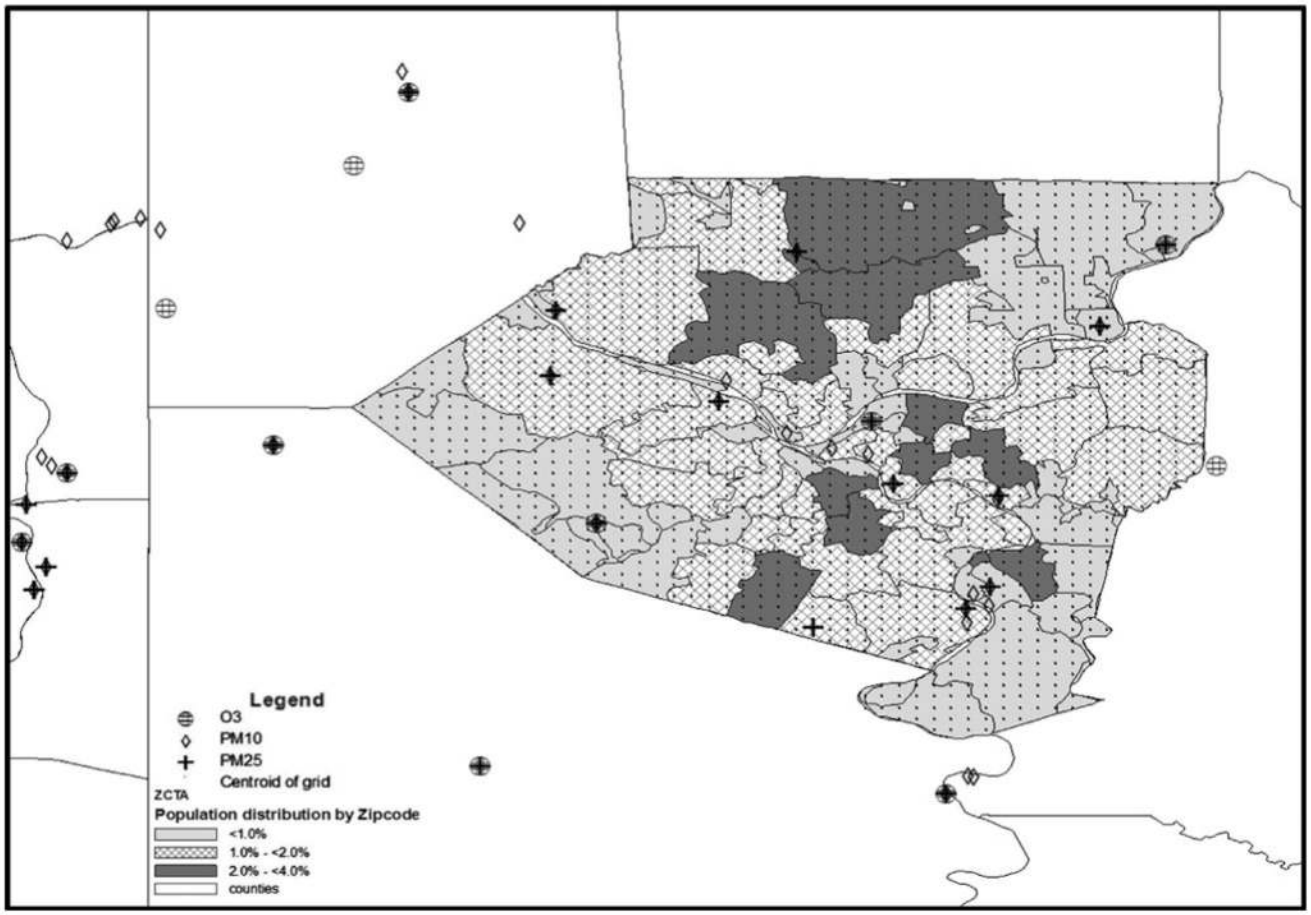

Fig. 1.
The distribution of air monitoring stations in Allegheny County, PA

Table 1

Characteristics of the study population (n = 34,705)

Characteristic	Measure
Maternal age (years, mean ± SD)	29.1 ± 6.1
Maternal race/ethnicity (n, %)[a]	
Caucasian	26,356 (76.8)
African-American	6,539 (19.0)
Other[b]	1,435 (4.2)
Maternal education (years, mean ± SD)[a]	14.0 ± 2.3
Parity (n, %)[a]	
Nulliparous	15,239 (44.0)
Parous	19,459 (56.0)
Marital status (n, %)	
Married	22,213 (64.0)
Unmarried	12,492 (36.0)
Gestational age (weeks, mean ± SD)	38.7 ± 2.3
Number of cigarettes smoked per day during pregnancy (n, %)[a]	
0	26,731 (83.5)
1–10	4.54 (12.7)
11–20	1,117 (3.5)
21+	127 (0.3)
Medical insurance type (n, %)	
Private insurance	25,384 (73.1)
Public assistance	9,197 (26.5)
Self-pay	124 (0.4)
Year of conception (n, %)	
1996	4,626 (13.3)
1997	5,415 (15.6)
1998	5,012 (14.4)
1999	5,780 (16.7)
2000	6,256 (18.0)
2001	6,137 (17.7)
2002	1,479 (4.3)
Season of conception (n, %)	
Spring (March–May)	8,327 (24.0)
Summer (June–August)	9,030 (26.0)
Fall (September–November)	8,975 (25.9)
Winter (December–February)	8,373 (24.1)
Route of delivery (n, %)	
Vaginal	28,352 (81.7)
Cesarean	6,353 (18.3)

Characteristic	Measure
Preterm delivery (n, %)	3,109 (9.0)
Preeclampsia (n, %)	1,141 (3.3)
Gestational hypertension (n, %)	2,078 (6.0)
SGA (n, %)[a]	2,958 (8.5)

[a]Missing observations for maternal education (n = 2,192); maternal race (n = 375); parity (n = 7); smoking during pregnancy (n = 2,676); and SGA (missing birth weight, n = 71)

[b]Other races, including Native American, Hispanic, and Asian

Table 2

Descriptive statistics of first trimester air pollution exposures

	Percentile							Pearson correlation		
	IQR	**0th**	**25th**	**50th**	**75th**	**95th**	**100th**	**PM_{10}**	**$PM_{2.5}$**	**O_3**
PM_{10} ($\mu g/m^3$)	7.7	13.9	21.7	24.8	29.4	34.8	42.6	1		
$PM_{2.5}$ ($\mu g/m^3$)[a]	4.0	9.2	13.6	15.6	17.6	21.3	29.0	0.9	1	
O_3 (ppb)	16.8	6.1	13.3	21.7	30.2	36.2	46.8	0.7	0.5	1

[a]For years between 1999 and 2002

Table 3

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per IQR) and preeclampsia, gestational hypertension, preterm delivery, and SGA

Pregnancy condition	Pollutant	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)
Preeclampsia	PM_{10}	1,141	1.03 (0.94–1.14)	1.00 (0.87–1.15)
	$PM_{2.5}$	699	1.15 (1.01–1.30)	1.15 (0.96–1.39)
	O_3	1,141	1.01 (0.91–1.12)	1.12 (0.89–1.42)
Gestational hypertension	PM_{10}	2,078	1.08 (1.02–1.14)	1.08 (0.98–1.20)
	$PM_{2.5}$	1,212	1.10 (1.01–1.19)	1.11 (1.00–1.23)
	O_3	2,078	1.13 (1.05–1.21)	1.12 (0.97–1.29)
Preterm delivery	PM_{10}	3,109	1.02 (0.97–1.07)	1.04 (0.94–1.14)
	$PM_{2.5}$	1,940	1.06 (1.00–1.13)	1.10 (1.01–1.20)
	O_3	3,109	1.01 (0.95–1.08)	1.23 (1.01–1.50)
SGA	PM_{10}	2,958	1.10 (1.04–1.16)	1.05 (0.96–1.15)
	$PM_{2.5}$	1,639	1.05 (0.96–1.14)	1.03 (0.94–1.12)
	O_3	2,958	0.97 (0.90–1.04)	0.98 (0.86–1.11)

[a]Adjusted for maternal age, race, parity, number of cigarettes smoked during pregnancy, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)

Table 4

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per IQR) and preeclampsia, gestational hypertension, preterm delivery, and SGA stratified by maternal smoking during pregnancy

Pregnancy condition	Pollutant	Mother smoked during pregnancy			Mother did not smoke during pregnancy		
		No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)
Preeclampsia	PM_{10}	164	1.04 (0.84–1.27)	1.05 (0.73–1.53)	875	1.02 (0.92–1.12)	1.00 (0.85–1.15)
	$PM_{2.5}$	116	1.08 (0.86–1.36)	1.13 (0.85–1.50)	577	1.17 (1.02–1.34)	1.15 (0.94–1.41)
	O_3	164	1.16 (0.89–1.51)	1.23 (0.68–2.23)	875	1.01 (0.90–1.13)	1.10 (0.86–1.41)
Gestational hypertension	PM_{10}	283	0.97 (0.81–1.18)	0.86 (0.64–1.16)	1,661	1.10 (1.03–1.17)	1.12 (1.01–1.25)
	$PM_{2.5}$	177	1.09 (0.91–1.31)	1.13 (0.88–1.44)	1,027	1.11 (1.02–1.21)	1.11 (0.99–1.24)
	O_3	283	1.05 (0.84–1.30)	0.92 (0.64–1.34)	1,661	1.12 (1.03–1.22)	1.16 (0.98–1.37)
Preterm delivery	PM_{10}	682	0.90 (0.81–1.00)	1.06 (0.85–1.33)	2,117	1.05 (0.99–1.11)	1.02 (0.91–1.15)
	$PM_{2.5}$	465	0.90 (0.78–1.03)	1.04 (0.88–1.24)	1,442	1.09 (1.01–1.16)	1.11 (0.99–1.23)
	O_3	682	0.97 (0.84–1.12)	1.46 (0.99–2.13)	2,117	1.10 (1.01–1.19)	1.15 (0.92–1.45)
SGA	PM_{10}	907	1.06 (0.95–1.18)	1.04 (0.89–1.22)	1,807	1.06 (0.98–1.14)	1.02 (0.90–1.15)
	$PM_{2.5}$	549	0.98 (0.89–1.08)	0.99 (0.88–1.12)	1,073	1.01 (0.91–1.12)	1.01 (0.91–1.12)
	O_3	907	1.06 (0.91–1.23)	0.93 (0.74–1.17)	1,807	0.94 (0.87–1.02)	0.99 (0.84–1.16)

[a]Adjusted for maternal age, race, parity, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)

Table 5

Estimated spatial and temporal variograms for each pollutant

	Model	Sill	Range[a]	Nugget	Equation[b]
$PM_{2.5}$					
Spatial variogram	Spherical	0.25	31.98	0.02	$\gamma_s(h_s) = \begin{cases} = 0.02 + 0.23\left[(3/2)(h_s/31.98) - (1/2)(h_s/31.98)^3\right], & 0 < h_s \leq 31.98 \\ = 0.25, \quad h_s > 31.98 \end{cases}$
Temporal variogram	Spherical	0.27	3.60	0.08	$\gamma_t(h_t) = \begin{cases} = 0.08 + 0.19\left[(3/2)(h_t/3.60) - (1/2)(h_t/3.60)^3\right], & 0 < h_t \leq 3.60 \\ = 0.27, \quad h_t > 3.60 \end{cases}$
PM_{10}					
Spatial variogram	Spherical	0.25	38.83	0.03	$\gamma_s(h_s) = \begin{cases} = 0.03 + 0.22\left[(3/2)(h_s/38.83) - (1/2)(h_s/38.83)^3\right], & 0 < h_s \leq 38.83 \\ = 0.25, \quad h_s > 38.83 \end{cases}$
Temporal variogram	Spherical	0.27	3.65	0.06	$\gamma_t(h_t) = \begin{cases} = 0.06 + 0.21\left[(3/2)(h_t/3.65) - (1/2)(h_t/3.65)^3\right], & 0 < h_t \leq 3.65 \\ = 0.27, \quad h_t > 3.65 \end{cases}$
O_3					
Spatial variogram	Spherical	0.10	26.09	0.02	$\gamma_s(h_s) = \begin{cases} = 0.02 + 0.08\left[(3/2)(h_s/26.09) - (1/2)(h_s/26.09)^3\right], & 0 < h_s \leq 26.09 \\ = 0.10, \quad h_s > 26.09 \end{cases}$
Temporal variogram	Spherical	0.11	2.15	0.04	$\gamma_t(h_t) = \begin{cases} = 0.04 + 0.07\left[(3/2)(h_t/2.15) - (1/2)(h_t/2.15)^3\right], & 0 < h_t \leq 2.15 \\ = 0.11, \quad h_t > 2.15 \end{cases}$

[a] Unit for spatial variogram is km and for temporal variogram is day

[b] Where γ_s and γ_t are the variogram functions for space and time, respectively; h_s and h_t are the distances in spatial and temporal dimensions, respectively

Table 6

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per unit increase[a]) and preeclampsia, gestational hypertension, preterm delivery, and SGA

Pregnancy condition	Pollutant	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[b] (95 % CI)
Preeclampsia	PM_{10}	1141	1.04 (0.92–1.18)	1.00 (0.84–1.20)
	$PM_{2.5}$	699	1.18 (1.02–1.38)	1.19 (0.95–1.50)
	O_3	1,141	1.01 (0.95–1.07)	1.07 (0.93–1.23)
Gestational hypertension	PM_{10}	2,078	1.10 (1.02–1.19)	1.11 (0.97–1.26)
	$PM_{2.5}$	1,212	1.12 (1.02–1.24)	1.14 (1.01–1.30)
	O_3	2,078	1.07 (1.03–1.12)	1.07 (0.98–1.16)
Preterm delivery	PM_{10}	3,109	1.02 (0.96–1.09)	1.05 (0.92–1.19)
	$PM_{2.5}$	1,940	1.08 (1.00–1.17)	1.13 (1.01–1.26)
	O_3	3,109	1.01 (0.97–1.05)	1.13 (1.00–1.27)
SGA	PM_{10}	2,958	1.13 (1.06–1.21)	1.07 (0.95–1.20)
	$PM_{2.5}$	1,639	1.06 (0.95–1.18)	1.04 (0.93–1.16)
	O_3	2,958	0.98 (0.94–1.03)	0.99 (0.91–1.07)

[a] Per-unit increase for PM_{10} per 10 $\mu g/m^3$; for $PM_{2.5}$ per 5 $\mu g/m^3$; and for ozone per 10 ppb

[b] Adjusted for maternal age, race, parity, number of cigarettes smoked during pregnancy, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)

Table 7

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per unit increase[a]) and preeclampsia, gestational hypertension, preterm delivery, and SGA stratified by maternal smoking during pregnancy

Pregnancy condition	Pollutant	Mother smoked during pregnancy			Mother did not smoke during pregnancy		
		No. of cases	Crude ORs (95 % CI)	Adjusted ORs[b] (95 % CI)	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[b] (95 % CI)
Preeclampsia	PM_{10}	164	1.05 (0.80–1.37)	1.07 (0.66–1.74)	875	1.02 (0.90–1.17)	0.99 (0.81–1.21)
	$PM_{2.5}$	116	1.10 (0.82–1.47)	1.17 (0.82–1.66)	577	1.22 (1.03–1.44)	1.19 (0.93–1.53)
	O_3	164	1.09 (0.93–1.28)	1.13 (0.80–1.61)	875	1.01 (0.94–1.08)	1.06 (0.91–1.23)
Gestational hypertension	PM_{10}	283	0.97 (0.75–1.24)	0.82 (0.56–1.21)	1,661	1.13 (1.04–1.23)	1.16 (1.01–1.34)
	$PM_{2.5}$	177	1.12 (0.89–1.40)	1.16 (0.86–1.58)	1,027	1.14 (1.02–1.27)	1.14 (0.99–1.31)
	O_3	283	1.03 (0.90–1.17)	0.95 (0.77–1.19)	1,661	1.07 (1.02–1.13)	1.09 (0.99–1.20)
Preterm delivery	PM_{10}	682	0.87 (0.76–1.00)	1.08 (0.81–1.44)	2,117	1.07 (0.99–1.15)	1.03 (0.88–1.20)
	$PM_{2.5}$	465	0.88 (0.74–1.04)	1.05 (0.85–1.31)	1,442	1.11 (1.02–1.21)	1.13 (0.99–1.29)
	O_3	682	0.98 (0.90–1.07)	1.25 (1.00–1.57)	2,117	1.06 (1.01–1.11)	1.09 (0.95–1.25)
SGA	PM_{10}	907	1.08 (0.94–1.24)	1.05 (0.85–1.29)	1,807	1.07 (0.98–1.18)	1.02 (0.87–1.19)
	$PM_{2.5}$	549	0.98 (0.86–1.10)	0.99 (0.86–1.15)	1,073	1.01 (0.90–1.15)	1.02 (0.89–1.16)
	O_3	907	1.03 (0.95–1.13)	0.96 (0.84–1.10)	1,807	0.96 (0.92–1.01)	0.99 (0.90–1.09)

[a] Per-unit increase for PM_{10} per 10 $\mu g/m^3$; for $PM_{2.5}$ per 5 $\mu g/m^3$; and for ozone per 10 ppb

[b] Adjusted for maternal age, race, parity, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)

Table 8

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per IQR) and preeclampsia, gestational hypertension, preterm delivery, and SGA stratified by racial group

Pregnancy condition	Pollutant	Caucasian			African-American		
		No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)
Preeclampsia	PM_{10}	789	1.03 (0.92–1.16)	1.00 (0.83–1.20)	301	0.88 (0.74–1.06)	0.94 (0.70–1.26)
	$PM_{2.5}$	467	1.17 (1.02–1.35)	1.21 (0.99–1.50)	200	0.96 (0.79–1.17)	0.93 (0.72–1.20)
	O_3	789	1.06 (0.94–1.19)	1.07 (0.80–1.43)	301	0.88 (0.71–1.09)	1.14 (0.76–1.71)
Gestational hypertension	PM_{10}	1,655	1.07 (1.00–1.14)	1.03 (0.91–1.16)	366	1.12 (0.97–1.30)	1.27 (1.01–1.60)
	$PM_{2.5}$	954	1.10 (1.01–1.19)	1.10 (0.98–1.24)	221	1.08 (0.92–1.26)	1.13 (0.93–1.38)
	O_3	1,655	1.12 (1.03–1.22)	1.12 (0.94–1.33)	366	1.15 (0.94–1.41)	1.15 (0.84–1.57)
Preterm delivery	PM_{10}	2,092	1.00 (0.95–1.05)	1.07 (0.94–1.22)	879	0.96 (0.87–1.07)	1.02 (0.85–1.23)
	$PM_{2.5}$	1,279	1.08 (1.00–1.16)	1.16 (1.04–1.29)	569	0.97 (0.85–1.11)	1.00 (0.83–1.19)
	O_3	2,092	1.06 (0.98–1.15)	1.27 (0.99–1.62)	879	0.97 (0.86–1.11)	1.20 (0.80–1.80)
SGA	PM_{10}	1,801	1.05 (0.98–1.12)	1.03 (0.92–1.16)	986	1.01 (0.91–1.12)	1.11 (0.95–1.29)
	$PM_{2.5}$	943	0.98 (0.88–1.10)	1.00 (0.88–1.13)	598	1.05 (0.95–1.15)	1.09 (0.93–1.28)
	O_3	1,801	1.00 (0.92–1.08)	0.93 (0.79–1.09)	986	0.98 (0.87–1.11)	1.04 (0.81–1.33)

[a]Adjusted for maternal age, parity, number of cigarettes smoked during pregnancy, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)

Table 9

Effect estimates (odds ratio, 95 % CI) for first trimester air pollutant exposures (per IQR) and preeclampsia stratified by preterm status, and preterm delivery stratified by labor type

Pregnancy condition	Pollutant	Normal term			Preterm		
		No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)
Preeclampsia	PM_{10}	739	0.97 (0.87–1.08)	0.91 (0.78–1.05)	402	1.16 (0.99–1.35)	1.27 (1.00–1.61)
	$PM_{2.5}$	445	1.12 (0.98–1.28)	1.11 (0.94–1.30)	254	1.15 (0.95–1.41)	1.24 (0.93–1.66)
	O_3	739	0.99 (0.88–1.11)	1.13 (0.82–1.55)	402	1.04 (0.86–1.24)	1.17 (0.84–1.63)
		Spontaneous			Indicated		
		No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)	No. of cases	Crude ORs (95 % CI)	Adjusted ORs[a] (95 % CI)
Preterm delivery	PM_{10}	1,580	0.98 (0.92–1.05)	0.94 (0.82–1.08)	1,221	1.07 (0.99–1.16)	1.08 (0.90–1.30)
	$PM_{2.5}$	961	1.03 (0.95–1.11)	1.04 (0.91–1.19)	752	1.11 (0.99–1.24)	1.14 (0.98–1.32)
	O_3	1,580	1.04 (0.95–1.13)	1.18 (0.92–1.52)	1,221	1.02 (0.92–1.13)	1.23 (0.92–1.65)

[a]Adjusted for maternal age, race, parity, season of birth, and year of conception (for PM_{10} and O_3: 1996–2002; for $PM_{2.5}$: 1999–2002)