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Particulate air pollution, fetal growth and gestational length: the influence of residential mobility in pregnancy

Gavin Pereira^{*,1}, Michael Bracken², and Michelle L. Bell³

¹School of Public Health, Curtin University, Perth, WA 6845, Australia

²Center for Perinatal Pediatric and Environmental Epidemiology, School of Medicine, Yale University, New Haven, CT 06511, USA

³School of Forestry and Environmental Studies, Yale University, New Haven, CT 06511, USA

Abstract

Background—It remains unclear as to whether neglecting residential mobility during pregnancy introduces bias in studies investigating air pollution and adverse perinatal outcomes, as most studies assess exposure based on residence at birth. The aim of this study was to ascertain whether such bias can be observed in a study on the effects of PM₁₀ on risk of preterm birth and fetal growth restriction.

Methods—This was a retrospective study using four pregnancy cohorts of women recruited in Connecticut, USA (N=10,025). We ascertained associations with PM₁₀ exposure calculated using first recorded maternal address, last recorded address, and full address histories. We used a discrete time-to-event model for preterm birth, and logistic regression to investigate associations with small for gestational age (SGA) and term low birth weight (LBW).

Results—Pregnant women tended to move to areas with lower levels of PM₁₀. For all outcomes, there was negligible difference between effect sizes corresponding to exposures calculated with first, last and full address histories. For LBW, associations were observed for exposure in second trimester (OR 1.09; 95% CI: 1.04 – 1.14 per 1µg/m³ PM₁₀) and whole pregnancy (OR 1.08; 95% CI: 1.02 – 1.14). For SGA, associations were observed for elevated exposure in second trimester (OR 1.02; 95% CI: 1.00 – 1.04) and whole pregnancy (OR 1.03; 95% CI: 1.01 – 1.05). There was insufficient evidence for association with preterm birth.

Conclusion—PM₁₀ was associated with both SGA and term LBW. However, there was negligible benefit in accounting for residential mobility in pregnancy in this study.

Corresponding author: School of Public Health, Curtin University, PO Box U1987, Perth, WA 6845, Australia. gavin.f.pereira@curtin.edu.au, Phone: +61 (08) 9266 3940.

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Ethical approval for this study was obtained from the Yale Human Investigation Committee.

Keywords

residential mobility; pregnancy; preterm birth; fetal growth; exposure misclassification

Background

Epidemiological studies indicate that exposures to particulate matter air pollution may have adverse effects on pregnancy outcomes^{1, 2}, with fetal growth and gestational length among the outcomes commonly investigated. Most often, ground-level measurements from a government monitoring network are used to derive exposure at a single residential address, usually recorded at delivery. However, as approximately 9% – 32% of women move during pregnancy there is potential for a high degree of exposure misclassification³. Patterns of residential mobility among pregnant women are largely unknown but studies indicate that moving is more likely among mothers who are younger^{4–6}, have lower parity^{4, 5, 7}, and have lower socioeconomic status^{4, 5}, all of whom have greater risk of delivering smaller babies and delivering preterm. Exposure misclassification might be minimal if women tend to move short distances (median, <10km)^{5, 8, 9}. In a New York cohort, whole pregnancy exposure to particulate matter with aerodynamic diameter $\leq 10 \mu\text{m}$ (PM_{10}) was essentially unchanged when based on residence recorded by maternal interviews ($20.11 \mu\text{g.m}^{-3}$) compared to that based on the residential location recorded at delivery ($20.09 \mu\text{g.m}^{-3}$)⁵. In a UK cohort, annual PM_{10} derived using the residential location at delivery was highly correlated with that derived using residential locations throughout pregnancy (Pearson $r=0.88$)¹⁰. In contrast, in another study, estimated PM_{10} exposure based on address at delivery compared to complete residential history differed by more than one standard deviation in 16% of pregnancies¹⁰. Consequently, it remains unclear as to whether final effect estimates on preterm birth and fetal growth restriction are biased by ignoring residential mobility in the derivation of PM_{10} exposure^{5, 11–15}.

The aim of this study was to compare effect estimates of particulate matter (PM_{10}) exposure on fetal growth and gestational length, with and without accounting for residential mobility using four large pregnancy cohorts in Connecticut, between 1988 and 2008.

Methods

Study design and setting

This was a retrospective study using four pregnancy cohorts of women recruited in Connecticut, USA (N=10,025). Women were interviewed 2–4 times in pregnancy. Women were recruited at <25 weeks gestation for the Asthma in Pregnancy study¹⁶ (AIP; 1996–2000; N=2,255) and the Pink and Blue study¹⁷ (PAB; 2005–2008; N=2,645) of depression in pregnancy. Women were recruited at <16 weeks gestation for the Nutrition in Pregnancy study¹⁸ (NIP; 1996–1999; N=2,344) and Environmental Tobacco Smoke study¹⁹ (ETS; 1988–1991; N=2,781). Further details of the cohorts have been published previously^{16–19}.

Participants

We excluded women with at least one address that could not be geocoded (N=182). We sequentially excluded records with multiple gestations (N=165), missing sex (N=55), and records with missing gestational age (N=1) or gestational age > 42 weeks (N=35), which resulted in a study population of 9,587 singleton pregnancies. Women were not explicitly asked for their residential histories. Day of residential move was ascertained in the course of cohort follow-up from the point of contact at recruitment to the post-partum interview.

Outcome variables

Preterm birth (PTB) was defined as birth before 37 completed weeks of gestation. Period of gestation was obtained from the birth certificate record. This was the clinical best estimate of gestational age, based on ultrasound or last menstrual period if ultrasound was not available. Births were classified as small for gestational age (SGA) if birth weight was <10th centile for gestational age and sex²⁰. Term low birth weight (LBW) was defined as a birth with at least 37 weeks of completed gestation attaining a birth weight <2,500g.

Exposure variables

Daily PM₁₀ measurements from the US Environmental Protection Agency (EPA) monitoring network were obtained for all monitors within 100km of participants' residential addresses. We calculated exposure using measurements from monitors within circular "buffer" radii of 20km, 40km, and 100km from the residential address. At each residential location and gestational week of pregnancy we calculated the 7-day average PM₁₀ concentration using (i) measurements from the closest monitor to the residential location within the buffer distance, and (ii) the inverse distance weighted (IDW) average of measurements from all monitors within the buffer distance. These weekly means were then used to compute average PM₁₀ concentrations for each trimester (< week 14, weeks 15–26, > week 26) and for the whole pregnancy. By definition, pregnancies are not at risk of preterm birth after gestational week 36. For this reason, only measurements prior to either birth or gestational week 36 (whichever was earlier) were included in the calculation of third-trimester and whole-pregnancy exposures for the preterm birth analyses. To ascertain the effects of acute exposure on the risk of preterm birth, we calculated mean PM₁₀ exposure for the week of delivery and the 6-week period prior to delivery. We calculated exposures using (i) the address at recruitment (first address), (ii) the address at delivery (last address), and (iii) all addresses updated throughout pregnancy (updated addresses).

Final study population

The full study population of 9,587 singleton pregnancies was used to investigate SGA. Preterm birth was investigated separately with (i) the full study population (N=9,587), and (ii) further restriction to vaginal deliveries (N=7,334 remaining). By definition, assessment of risk of term LBW required restriction to term births (N=8,997 remaining). Characteristics of the study population are shown in Table 1.

Statistical methods

For all models, adjustment was made for the following variables ascertained at study entry: maternal age (<20, 20–24, 25–29, 30–34, 35–39, 40+ years), race/ethnicity (White, African American, Hispanic, Asian, other), marital status (married, single, divorced/separated), highest level of educational attainment (did not complete high school, high school, post-secondary, graduate and above), parity (0, 1, 2, >=3), pre-pregnancy weight (kg), an indicator for smoking (tobacco), and an indicator for alcohol consumption (beer, wine, liquor). To adjust for temporal confounding by unmeasured factors such as long-term trends and seasonal factors we included an adjustment term for year and season of conception. For Term LBW, we also adjusted for final gestational age (weeks) due to accumulating evidence that perinatal outcomes continue to vary along the gestational age continuum from 37 weeks²¹. Logistic regression was used to calculate odds ratios (OR) for associations between PM₁₀ exposure and term LBW and SGA. For PTB, a discrete time-to-event model²² was used to calculate hazard odds ratios (HOR). This model allowed calculation of prospective risk estimates that ensured comparisons were restricted to only pregnancies at risk at each week of gestation. Pregnancies entered the risk set at gestational week 20, were followed until the earlier of birth or gestational week 36 inclusive, and were censored thereafter. More specifically, we modelled $H_i(t)$, the hazard of preterm birth for pregnancy i at week t , as:

$$\text{logit}(H_i(t)) = \text{logit}(P(Y_i(t)=1|Y_i(t-1)=0)) = h(t) + \gamma Z_i + \beta X_i(t) + \varepsilon_{it}$$

where $Y(t)$ is an indicator for birth at time t , $h(t)$ are the week-specific intercepts, Z is the matrix of adjustment variables with corresponding parameter estimate vector γ , $X(t)$ is the time-varying PM₁₀ exposure with parameter estimate β , and ε denotes the residuals.

Bias

Multiple imputation using chained equations with 5 imputations and 5 iterations was used to minimize bias due to non-response from missing adjustment variables. Exposure (PM₁₀) variables and outcome variables (birth weight and gestational length) were not imputed or used in the imputation. Smoking in pregnancy, alcohol consumption in pregnancy, maternal ethnicity, maternal education, marital status, pre-pregnancy weight and maternal age were imputed and used in the imputation to impute other variables. The variable “sex” is used to derive the outcome variable small for gestational age and sex (SGA), and consequently the variable “sex” was used to impute other variables but was not imputed itself. The variable “parity” and “study cohort indicator” are potential proxies for a time varying confounder and consequently were used to impute other variables but were not imputed themselves.

Results

Residential mobility

There were 1,061 (11%) women in the study population that moved during pregnancy. The median distance moved was 5km (IQR: 2km – 13km). Compared to women that did not move, women that moved did not have an elevated risk of delivering preterm (RR 1.03, 95%

CI: 0.80, 1.31) or LBW (RR 0.90, 95% CI: 0.51, 1.48). However, SGA was more likely for women that moved (RR 1.40, 95% CI: 1.18, 1.67).

Exposure

There were 8,323 (87% of sample), 9,502 (99% of sample), and 9,587 (100% of sample) women who lived within 20km, 40km and 100km of a monitor during pregnancy. Overall exposure estimates were not sensitive to choice of buffer distance or exposure method (IDW vs closest monitor) (Tables S1 and S2). The median whole-pregnancy PM_{10} exposure was $22 \mu\text{g.m}^{-3}$ (IQR: $19\text{--}27 \mu\text{g.m}^{-3}$) using updated address histories (IDW, 20km buffer). For movers, the influence on exposure estimates of the decision to use first, last or updated address histories was sensitive to buffer distance and method. That is, we are less likely to observe differences in exposure attributable to using first, last and updated address histories with the IDW method as it uses measurements from multiple monitors which introduces greater variability in estimates. Similarly, although exposure misclassification might be reduced using smaller buffer sizes, there is an associated drop in sample size. Consequently, using the IDW method or small buffer distance (20km), exposure estimates were similar using first, last and updated address histories. However, using the closest monitor method (lower variance) and using larger buffer distances (40 km, greater sample size) we observed a small difference between mean whole pregnancy PM_{10} exposures calculated using the last address (l) and updated address (u) histories ($l - u = -0.20 \mu\text{g.m}^{-3}$; 95% CI $-0.37, -0.03 \mu\text{g.m}^{-3}$). Using a 40km buffer and the closest monitor method, whole pregnancy exposure using the last address was consistently less than that calculated using the first (f) address ($l - f = -0.30 \mu\text{g.m}^{-3}$; 95% CI $-0.59, 0.02 \mu\text{g.m}^{-3}$). That is, the magnitude of the difference was small but the direction of the effect was consistent, indicating women who moved tended to relocate to areas with lower levels of PM_{10} .

Associations with pregnancy outcomes

For all outcomes, there was negligible difference between effect sizes corresponding to exposures calculated with first, last and updated address histories (Figures 1–4). That is, there was near complete overlap in the interval estimates (using first, last and updated address histories) for term LBW (Figure 1), SGA (Figure 2), PTB (Figure 3) and vaginal PTB (Figure 4). There was insufficient evidence that effect sizes differed by buffer distance (20km, 40km, 100km). However, statistically significant associations were observed using the 20km buffer but not the 40km or 100km buffer distances for SGA and term LBW. The IDW method resulted in less precise interval estimates (i.e. wider 95% CIs) than using the closest monitor method, with no observable difference (bias) between the point estimates. Consequently, we describe hereon the adjusted odds ratios and hazard odds ratios for increases ($1 \mu\text{g.m}^{-3}$) in PM_{10} using updated address histories, a 20km buffer and the IDW method. For LBW, statistically significant associations were observed for elevated exposure in second trimester (OR 1.09; 95% CI: 1.04 – 1.14) and whole pregnancy (OR 1.08; 95% CI: 1.02 – 1.14) (Figure 1). Similarly, for SGA, associations were observed for elevated exposure in second trimester (OR 1.02; 95% CI: 1.00 – 1.04) and whole pregnancy (OR 1.03; 95% CI: 1.01 – 1.05) (Figure 2). There was insufficient evidence for an association between PTB and exposure to PM_{10} for cumulative exposure in trimesters, cumulative exposure over the whole of pregnancy, or exposure closer in the week preceding delivery or

6 weeks preceding delivery (Figure 3, Figure 4). The adjusted HOR of PTB for whole pregnancy exposure was 1.01 (95% CI: 0.98 – 1.04) and 1.00 (95% CI: 0.99 – 1.01) for elevated exposure during the week preceding delivery (Figure 3). The results were similar for PTB after restricting to vaginal deliveries. The adjusted HOR of PTB for whole pregnancy exposure was 1.01 (95% CI: 0.98 – 1.03) and 1.00 (95% CI: 0.99 – 1.01) for elevated exposure during the week preceding delivery (Figure 4).

Discussion

Key results

We compared effect estimates of particulate matter (PM₁₀) exposure on fetal growth and gestational length, with and without accounting for residential mobility using four large pregnancy cohorts in Connecticut and western Massachusetts, between 1988 and 2008. The results indicate that, at the levels of residential mobility observed in this study population (11%), the induced level of exposure misclassification for PM₁₀ had a negligible influence on overall effect estimates. It is plausible that the influence on final effect estimates of moves over short distances is negligible, because residential exposure is intended to be proxy for exposure for time spent in the broader region about the residence. Interestingly, women who moved tended to move to areas of lower PM₁₀ air pollution, characterized in this study by movement away from a city. This observation was not due to decreasing temporal trend because for each address, exposure was calculated for the same period. That is, exposure was calculated using the first address for each exposure period (trimesters and whole pregnancy), then calculated using the last address for each exposure period, and finally calculated using updated address histories for each exposure period. Therefore, we could compare spatial differences in results independently of temporal trend.

Interpretation

Exposure misclassification is induced by residential mobility during pregnancy when the time of ascertainment of the residential location is not temporally well aligned with the exposure period under investigation. We observed that such misclassification had little influence on the observed estimates of the effect of PM₁₀ exposure on restricted fetal growth and gestational length in this study population. This provides greater credibility to past perinatal studies when the particulate matter exposure contrast under investigation is largely due to city-wide spatial comparisons and daily temporal comparisons^{12–15, 23, 24}. For fetal growth endpoints (SGA and term LBW), choice of method of exposure assessment (closest monitor vs IDW) and buffer size had greater influence on effect estimates and their precision than the extent of ascertainment of residential mobility in pregnancy.

Generalisability

A combination of factors contribute to the influence of residential mobility in pregnancy on effect estimates. Exposure misclassification increases with the fraction of women that move during pregnancy (11% in this study). An inherent assumption is that the process that governs residential mobility in pregnancy does not differ by outcome status (e.g. PTB vs term birth). The link between residential mobility and socioeconomic factors alone is sufficient reason to suggest that this assumption is often violated^{3, 25}. However, this

assumption is only important to these epidemiological investigations if exposure misclassification from inaccurate assessment of residential mobility leads to differential exposure misclassification. Although we did not observe differences in effect estimates obtained with and without accounting for residential mobility in this study, this result is not necessarily generalizable to other studies. For our study, a small fraction of women moved (11%), and women moved short distances (median 5km) relative to the spatial scale of exposure assessment (city-wide comparisons). Moreover, the exposure periods of interest for pregnancy outcomes (e.g., trimesters) are often long enough so that the recorded residential address is accurate for at least a portion of that exposure period. Naturally, greater misclassification is expected, for example, when residential address is recorded at delivery but used to calculate exposure near conception. The choice of the outcome itself influences the comparability in levels of residential mobility by outcome status. Inherently, preterm birth provides less opportunity to move than a term pregnancy. Finally, we note that it remains possible that the influence of residential mobility might not be observable overall but might be observable for sub-populations already at elevated risk of restricted fetal growth or gestational length e.g., socioeconomically disadvantaged groups. Assessment of this *a posteriori* hypothesis requires selecting a sample that targets such sub-populations, rather than the population representative samples used in this study.

Limitations

As this study was based on pregnancy cohorts, residential mobility prior to recruitment was not ascertainable. Therefore, our results are most relevant for differences in PM₁₀ exposure and associated effects of this exposure after first trimester. This limitation is addressable in future pregnancy cohort studies by retrospective assessment of residential histories at recruitment. In some settings, residential histories can be more objectively ascertained via linkage to national health surveillance systems²⁶. However, these systems tend to record residential location at the time of health service contact, not the time of the move. Diurnal activity patterns may also influence accuracy of exposure classification based on home address in relation to time spent at home. In one study, 3.5 more hours per day were spent at home by pregnant women who did not work, 2.6 more hours were spent at home by those with low income and 1.5 more hours were spent at home by those already at home with children²⁷. It remains uncertain as to whether diurnal activity patterns changed after residential movement and whether this change was associated with both a consistent directional bias in PM_{2.5} exposure and risk of adverse perinatal outcome (SGA, LBW, PTB).

Conclusion

In general, pregnant women tended to move to areas with lower levels of PM₁₀. The influence of residential mobility on effect estimates will be a function of the moving patterns in the population, or subpopulation, and the exposure of interest. In this study, there was negligible benefit in accounting for residential mobility in pregnancy as the observed effects of PM₁₀ exposure on fetal growth and gestational length remained unchanged.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- PM₁₀ exposure was associated with risk of low birth weight and small for gestational age, but not preterm birth.
- We provide empirical evidence that there is negligible difference in effect estimates after accounting for residential mobility in pregnancy, and is generalizable to past studies and other settings for which the spatial variation in assessed exposure was regional (e.g., city-wide) and women tend move short distances.
- Interestingly, women who moved during pregnancy tended to move to areas with lower levels of PM₁₀ air pollution.
- Choice of method of exposure assessment and buffer size had greater influence on effect estimates and their precision than the extent of ascertainment of residential mobility in pregnancy.

Figure 1.

Adjusted log odds ratios for term LBW for a 1 $\mu\text{g.m}^{-3}$ increase in PM_{10} in each trimester (T1, T2, T3) and whole pregnancy (P) ascertained with first address, last address and updated histories. Results presented for each buffer distance (20km, 40km, 100km) and method of exposure assessment (closest monitor, inverse distance weighted).

Figure 2.

Adjusted log odds ratios for SGA for a 1 $\mu\text{g.m}^{-3}$ increase in PM_{10} in each trimester (T1, T2, T3) and whole pregnancy (P) ascertained with first address, last address and updated histories. Results presented for each buffer distance (20km, 40km, 100km) and method of exposure assessment (closest monitor, inverse distance weighted).

Figure 3.

Adjusted log hazard odds ratios for PTB for a $1 \mu\text{g.m}^{-3}$ increase in PM_{10} in each trimester (T1, T2, T3), whole pregnancy (P), week of birth (lag 0) and the 6-week period prior to birth (lag 05). Exposure was ascertained with first address, last address and updated histories. Results presented for each buffer distance (20km, 40km, 100km) and method of exposure assessment (closest monitor, inverse distance weighted).

Figure 4.

Adjusted log hazard odds ratios for PTB for a $1 \mu\text{g.m}^{-3}$ increase in PM_{10} in each trimester (T1, T2, T3), whole pregnancy (P), week of birth (lag 0) and the 6-week period prior to birth (lag 05). Exposure was ascertained with first address, last address and updated histories. Results presented for each buffer distance (20km, 40km, 100km) and method of exposure assessment (closest monitor, inverse distance weighted). Pregnancies were restricted to vaginal births.

Table 1**Maternal Characteristics at Study Entry**

	N women	%
Age		
<20 years	575	6
20–24 years	1,120	12
25–29 years	2,623	27
30–34 years	2,807	29
35–39 years	1,503	16
40+ years	243	3
Missing	812	8
Race/ethnicity		
White	7,337	76
African American	721	7
Hispanic	1,241	13
Asian	183	2
Other	190	2
Missing	11	0
Marital Status		
Married	7,418	77
Single	2,003	21
Divorced/separated	260	3
Missing	2	0
Education (highest level)		
Did not complete High School	819	8
Completed High School	1,601	17
Post-secondary	4,864	50
Graduate and above	2,394	25
Missing	5	0
Parity		
No children	4,251	44
1 child	3,522	36
2 children	1,419	15
3 children	491	5
Pre-pregnancy weight		
<56 kg	2,432	25
56 – 62 kg	2,328	24

	N women	%
63 – 72 kg	2,556	26
73 kg	2,202	23
Missing	165	2
Smoking in pregnancy		
Smoked tobacco	1,657	17
Missing	1,074	11
Alcohol consumption in pregnancy		
Consumed beer, wine or liquor	4,184	43
Missing	4	0
Cohort		
AIP	2,169	22
ETS	2,688	28
NIP	2,213	23
PAB	2,613	27