A quantile regression approach to examine fine particles, term low birth weight, and racial/ethnic disparities

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Background: Exposure to fine particulate matter (PM_{2.5}) during pregnancy has been shown to be associated with reduced birth weight and racial/ethnic minorities have been found to be more vulnerable. Previous studies have focused on the mean value of birth weight associated with PM_{2.5}, which may mask meaningful differences. We applied a quantile regression approach to investigate the variation by percentile of birth weight and compared non-Hispanic (NH) Black, NH White, and Hispanic mothers.

Methods: Data for singleton births in California from October 24, 2005 to February 27, 2010 were collected from the birth records accessed from the California Department of Public Health. Air pollution monitoring data collected by the California Air Resources Board and interpolated for each zip code using an inverse-distance weighting approach, and linked to maternal zip code of residence reported on the birth certificate. Multilevel linear regression models were conducted with mother’s residential zip code tabulation area as a random effect. Multilevel quantile regression models were used to analyze the association at different percentiles of birth weight (5th, 10th, 25th, 50th, 75th, 90th, 95th), as well as examine the heterogeneity in this association between racial/ethnic groups.

Results: Linear regression revealed that a 10 μg/m³ increase in PM_{2.5} exposure during pregnancy is associated with a mean birth weight decrease of 7.31 g [95% confidence interval (CI): 8.10, 6.51] and NH Black mothers are the most vulnerable. Results of the quantile regression are not constant across quantiles. For NH Black mothers whose infants had the lowest birthweight of less than 2573 g (5th percentile), a 10 μg/m³ increase in PM_{2.5} exposure is associated with a decrease of 18.57 g [95% CI: 22.23, 14.91], while it is associated with a decrease of 7.77 g [95% CI: 8.73, 6.79] for NH White mothers and 7.76 [8.52, 7.00] decrease for Hispanic mothers at the same quantile.

Conclusion: Results of the quantile regression revealed greater disparities, particularly for infants with the lowest birth weight. By identifying vulnerable populations, we can promote and implement policies to confront these health disparities.

Keywords: Quantile regression; Air pollution; Low birth weight; Health disparities

Introduction

Air pollution exposure during pregnancy has been shown to be associated with adverse birth risks such as intrauterine growth restriction, which can result in infants born with a low birth weight (LBW).1–4 LBW infants have higher morbidity and mortality compared to normal weight infants.5,6 Mothers’ high exposure to fine ambient particles under 2.5 μm (PM_{2.5}) during pregnancy may precede these adverse birth weight outcomes. Several studies investigating the relation between PM_{2.5} and birth weight at term report an inverse association.8–13 However, a couple of other studies detected no such association.14,15 Maternal socioeconomic status has been shown to modify the association between air pollution and birth outcomes.6,15 A recent review on LBW published in 2017 found that women with low socioeconomic status were generally more vulnerable to LBW from air pollution,16 possibly from lower maternal immune defense and sensitivity to oxidative stress and inflammation, which increases vulnerability of the mothers’ air pollution exposures, and consequently the developing infant in utero.14 In the United States, racial and ethnic (R/E) disparities in birth outcomes have also been documented; for example, non-Hispanic (NH) Black mothers appear more vulnerable to PM_{2.5} exposure than NH White mothers.8,17–19

What this study adds

Health disparities in the association between air pollution and birth outcomes have also been documented; for example, non-Hispanic (NH) Black mothers appear more vulnerable to PM_{2.5} exposure than NH White mothers.8,17–19

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Although the association between air pollution during pregnancy and birth weight among term infants has been well studied, the majority of this work has employed regression methods, like Ordinary Least Square models, which typically reported the change in the mean value of the birth weight distribution associated with a given change in exposure (e.g., gestational exposure to air pollution). Other studies focused on binary birth outcomes such as term LBW (defined as <2,500 g) or small for gestational age (commonly defined as birth weight below the 10th percentile for gestational age). However, focusing on changes in birth weight mean or dichotomization of the outcome may not capture the heterogeneity in the influence of air pollution exposure during pregnancy on birth weight. Higher variance can have a greater potential to promote interventions that improve the health of disadvantaged populations.

Studies have applied quantile regression to investigate the effect of air pollution exposure on birth weight. Recently, Fong et al. revealed a negative relationship between PM2.5 and LBW, particularly at lower quantiles, while Stickland et al. found contrary results with greater reductions in birth weight for higher weight babies. Additionally, Smith et al. used quantile functions to study ozone exposure and birth weight and found that ozone is negatively associated with lower quantiles of gestational age. Infants at both tails (i.e., low weight and macrosomic infants) require much more clinical attention and induce greater risk of morbidity than the majority of births delivered within one standard deviation of the mean birth weight. The key benefit of quantile regression (vs. traditional Ordinary Least Square) involves the ability to identify potential heterogeneity in population responses to exposure across the range of a continuous health outcome. In the same vein, although effect modification of R/E has been investigated extensively, few studies have examined these disparities beyond the birth weight mean.

California has a large, diverse population and there is variation in particulate matter exposure by region; therefore, it is an interesting location to study the effects of air pollution on birth outcomes across R/E groups. A study conducted in 2005 investigated the relationship between air pollution and birth weight infants born at term in California in 2000 and found a higher odds of being born small for gestational age and a slight decrease in birth weight with higher PM1.0 exposure. In 2013, a study used linear and logistic regression models to show that PM1.0 and several of its constituents were associated with increased risk of LBW at term.

In this study, we investigated how the effect of mother's exposure to PM1.0 on birth weight for at term singleton births in California varied by birth weight quantile. We also examined whether NH Black, NH White, or Hispanic mothers were more vulnerable to these effects, and if these changes occurred primarily in the higher or lower ends of the birth weight distribution. As LBW infants have been shown to be particularly vulnerable, we hypothesized that adverse effects of PM1.0 are greater at lower birth weight quantiles. We also hypothesized that small infants born to NH Black mothers may be even more affected due to increased vulnerability from underlying social and structural factors that have been shown to affect perinatal outcomes. By understanding which mothers were more susceptible to gestational exposure to air pollution at each birth weight quantile, attention can be given to reduce exposure and concurrently decrease health inequities.

Methods

Study population and outcome definition

Data for singleton births in California from October 24, 2005 to February 27, 2010 were collected from the birth records accessed from the California Department of Public Health. The study population included all singleton live births in California that had data available from birth certificates for birth date, birth weight (in grams), gestational age (in weeks), and maternal residential zip code tabulation area (ZCTA). Gestational age was determined from birth certificates by clinical estimates, involving a combination of ultrasound and gestational age assessment at birth. Researchers have examined variation in birth weight in full-term infants or birth weight adjusted for gestational age to separate fetal growth from length of gestation. We restricted our population to term singleton births (>37 weeks of gestation) to focus on fetal growth. We created a cohort defined by the date of conception including births conceived between January 1, 2005 and February 20, 2010 to allow births of all gestational lengths to be included in the study. The State of California and the University of California, Irvine, approved the study (IRB protocol approval#13-06-1251 and 2013–9716).

Exposure measurements

Air pollution measures on PM2.5 concentrations were collected by the California Air Resources Board from monitors in California. PM2.5 estimates for each ZCTA were interpolated with an inverse-distance weighting approach using measurements from the three nearest fixed-site monitoring stations within 20 km of the zip code centroid. Maternal ZCTA of residence reported on the birth certificate was linked to air pollution monitoring data to determine PM2.5 (μg/m3) exposure during pregnancy. For each birth included in the study, mean PM2.5 was calculated from daily estimates for the full gestational period. ZCTAs without at least three monitors within 20 km were excluded from analysis.

Covariates

We considered the following covariates collected from the birth certificates as potential confounders for all models: maternal age (18–25, 26–34, and 35+ years), insurance status (Medicaid or not), maternal education (less than high school, high school/ equivalent, any college, and beyond), parity (first birth or previous births), and an indicator for year of birth and season of birth (fall, summer, spring, and winter). For heterogeneity analyses, we focused on NH White, NH Black, and Hispanic (Mexican/Mexican American/Chicano, Puerto Rican, Cuban, Central/Southern American, and other Spanish/Hispanic) mothers.

Statistical analysis

Linear regression

Multilevel linear regressions were conducted to assess the association between mean PM2.5 exposure during the gestational period at maternal residential ZCTA at the time of birth and their infant’s birth weight in California, adjusted for maternal age, insurance status, parity, year of birth, and season of birth. We included a random effect for the intercept at the maternal ZCTA level (to account for potential clustering and time-fixed spatial patterns). The intraclass correlation coefficient from the univariate model was less than 1% (0.8%). We estimated 95% confidence intervals (CIs) by bootstrapping (500 samples). Results were presented as the change in birth weight mean associated with a 10 μg/m3 increase in PM2.5 exposure.

We estimated stratified models for each R/E group and Cochran Q tests were used to assess the heterogeneity in the association between the R/E groups (see details in supplemental material; http://links.lww.com/EE/A51).

Quantile regression

Multilevel quantile regression was used to analyze the association between PM2.5 during pregnancy (full gestational exposure) on birth weight at different percentiles of the birth weight distribution, including maternal ZCTA as a random effect. Quantile
regression is a statistical technique used to model changes in quantities (i.e., percentiles) within a regression framework. Median regression is a special case of the quantile regression that was used in this study. A detailed description of quantile regression appears elsewhere. To capture a representative range of the birth weight distribution, we considered the following percentiles: 0.05, 0.10, 0.25, 0.50, 0.75, 0.90, 0.95 using a simultaneous quantile regression approach. The same potential confounders were adjusted (with quantile-specific adjustments) for and we estimated 95% CIs by bootstrapping (500 samples). This analysis was conducted for the entire population and stratified by R/E. Results were also presented as the change in birth weight associated with a 10 µg/m³ increase in PM₂.⁵ exposure for each percentile. Cochran Q tests were run to examine heterogeneity in the effect of PM₂.⁵ on birth weight between NH Black and NH White as well heterogeneity between Hispanic and NH White for each quantile. All the analyses were conducted using Stata SE 15 (StataCorp, CollegeStation, TX).

Results

Descriptive statistics

Births with missing maternal residential ZCTA (n = 13,733), birth weight (n = 259), or gestational age (n = 45,691) were excluded from the analysis. After exclusions, 2,768,898 full-term births, nested in 1589 ZCTAs in California between 2005 and 2010 were eligible for analysis. Table 1 presents maternal and infant characteristics as well as descriptive statistics of exposure to PM₂.⁵. The majority (61.5%) of mothers were Hispanic while 32.2% were NH White and 6.3% were NH Black. On average, maternal age at birth was 28 years (SD 6.4); 48.1% of NH Black mothers were under 25 years old, 45.9% of Hispanic mothers, while 26% of NH White mothers were in this age category. About 53% of the mothers attended at least some college and half of the infants born were male. For NH Black mothers, 53% were insured by Medicaid, while only 34.1% of Hispanic mothers and 21.9% of NH White mothers were insured by Medicaid. The mean birth weight among full-term infants was 3324 g (SD: ±586 g), which was slightly higher for NH Black (3361 g (SD: ±592 g) and Hispanic mothers (3304 g (SD: ±582 g)) compared to NH White mothers (3111 g (SD: ±672 g)). The average gestational exposure to PM₂.⁵ was 10.32 µg/m³, with higher exposure for NH Black and Hispanic mothers (10.58 and 10.72 µg/m³, respectively) compared to NH White mothers (9.52 µg/m³).

Linear regression results

Results of the linear regression revealed that per 10 µg/m³ increase in PM₂.⁵ exposure during pregnancy, mean birth weight decreased by 7.31 (8.10, 6.51) g in the total study population. For NH White mothers, an increase in PM₂.⁵ exposure was associated with a decrease in mean birth weight of 6.26 (7.32, 5.21) g. For NH Black mothers, a 10.33 (11.67, 8.98) g decrease in birth weight was observed. For Hispanic mothers, a 6.31 (5.42, 7.20) g decrease in birth weight was observed. The Cochran Q test revealed that the effect between NH Black and NH White was not heterogenous (see supplemental table). Infants in the lowest quantile (5th percentile) revealed a slightly larger association as well as greater R/E disparities, particularly for NH Black mothers. This decrease of 7.99 (8.56, 7.42) g, 6.60 (6.91, 6.30) g, and 7.60 (8.20, 7.01) g, respectively, for every 10 µg/m³ increase in PM₂.⁵ gestational exposure for the entire population.

Investigating the differences in the association between PM₂.⁵ exposure and birth weight for NH White, NH Black, and Hispanic mothers separately using this analysis revealed further disparities (see Figure 1). The largest difference in this association by R/E occurred for infants in 5th percentile. While the impact of PM₂.⁵ on birth weight did not differ greatly between NH White and Hispanic mothers, the difference between NH Black and NH White women was around 11 g for infants at or below the 5th percentile (see Table 2). For NH White mothers, infants weighed 2746 g in the 5th percentile, and a 10 µg/m³ increase in PM₂.⁵ exposure was associated with a birth weight decrease of 7.77 (8.73, 6.79) g. In comparison, NH Black mothers’ infants weighed 2673 g in the 5th percentile, and had a 18.57 (22.23, 14.91) g decrease in birth weight.

Discussion

Summary of the findings

Our results showed that California mothers who lived in areas with higher PM₂.⁵ exposure during pregnancy delivered lower weight infants at term. This finding was consistent with prior literature and robust to both approaches used: the linear regression and quantile regression analyses. While the linear regression showed a 7.31 (8.10, 6.51) g decrease in birth weight associated with a 10 µg/m³ increase in PM₂.⁵ exposure, the decrease in birth weight ranged from 5.77 (6.24, 5.30) to 6.07 (6.40, 5.74) g in the quantile regression approach. Infants in the lowest quantile (5th percentile) revealed a slightly larger association as well as greater R/E disparities, particularly for NH Black mothers. This
demonstrates that the linear regression analysis which examined a change in mean birth weight may have produced a more conservative result by failing to capture the lower end of the distribution of birth weight for which the association is greatest. We found birth weight among NH Black mothers to be consistently more affected by PM$_{2.5}$ exposure than birth weight among NH White and Hispanic mothers. The linear regression analysis revealed an additional $4.33$ g decrease in PM$_{2.5}$ on birth weight for NH Black mothers when compared with NH White mothers. However, results of the quantile analysis revealed further health disparities, particularly for infants in the lowest birth weight quantile ($10.81$ ($13.1, 8.48$) g decrease for NH Black mothers compared with NH White mothers). However, infants in the higher birth weight quantiles were not found to have a higher birth weight due to PM$_{2.5}$ exposure. By understanding the distribution of this association at different levels of air pollution on birth weight, we were able to reveal considerably more R/E inequalities in air pollution effects. This analysis allows a more comprehensive grasp of the magnitude of these disparities, especially for vulnerable infants with the lowest birth weights.

**Comparison with existing research**

Past studies that used linear regression approaches have shown varied results. While some demonstrated an association between PM$_{2.5}$ and LBW,$^{3,19}$ others showed imprecise estimates or no association.$^{13,32,42,43}$ The association revealed in different studies varied greatly, but our results using linear regression were consistent with previous literature published using California data. A study conducted in 2004 revealed a $-29.3$ g ($-42.2, -16.3$) change for each 10 $\mu$g/m$^3$ increase in PM$_{2.5}$. Meanwhile, Basu et al.$^{25}$ used an interquartile range in their analysis and revealed a $-7$ ($-9, -4$) gram change per 7.56 $\mu$g/m$^3$ interquartile range increase. As our study highlights, it is important to consider the associations at different percentiles of the birth weight distribution, and may partially explain the variability in results between previous studies investigating this relationship.

Previous research by Smith et al.$^{26}$ applied a quantile regression analysis to study ozone exposure on birth weight revealed a negative association, particularly at lower tails of the birth weight distribution. These results are consistent with our findings in this article. Interestingly, two very recent studies conducted a very similar analysis in Massachusetts and Atlanta, Georgia and found contrasting results. While Fong et al.$^{24}$ found that negative association between PM$_{2.5}$ and birthweight was larger in the lowest quantiles, Strickland et al.$^{25}$ found the opposite pattern. Results of our study are more consistent with the findings by Fong et al.,$^{24}$ although they found no evidence of effect modification by individual or community level variables, such as the proportion of Black population in the census tract. However, their study was conducted in Massachusetts and had a predominantly White study population which may explain our differing conclusions.

Quantile regression has also been applied study how various exposures can affect birth outcomes. Abreyava and Dahl$^{44}$ used quantile regression to study maternal smoking and prenatal care and their relationship with birth weight. They found that babies in the median (50th) quantile of birth weight are those most affected by maternal smoking$^{44}$ as compared to other quantiles. Burgette et al.$^{45}$ used the same approach to demonstrate that mothers’ tobacco use on birth weight varied at different percentiles of birth weight and also found the strongest association at the median values. Results of these studies contrasted our results and indicated variation in distributional effects by different exposures.

**Possible mechanisms underlying health disparities**

Air pollution can plausibly affect the course of gestation by accelerating parturition, restricted fetal growth, or both.$^{2,4,46,47}$ Different etiological mechanisms to explain the relationship

| Table 2 | Mean change (with 95% CI) in birth weight (g) for 10 $\mu$g/m$^3$ increase in PM$_{2.5}$ by quantile of birth weight, and R/E differences for each quantile for all California births to NH White mothers, NH Black mothers, and Hispanic mothers from 2005 to 2010. |
|--------|-------------------------------------------------------------------------------------------------|
| Quantile | All population | By R/E | NH White mothers | NH Black mothers | Hispanic mothers |
| 0.05 | $-7.99$ ($-8.56, -7.42$) | $-7.77$ ($-8.34, -7.21$) | $-7.76$ ($-8.52, -7.00$) | $-7.39$ ($-8.56, -7.24$) | $-5.27$ ($-6.05, -4.49$) | $-5.89$ ($-7.19, -4.60$) |
| 0.10 | $-7.16$ ($-7.65, -6.68$) | $-6.07$ ($-6.40, -5.75$) | $-6.59$ ($-6.95, -6.29$) | $-5.99$ ($-6.50, -5.48$) | $-5.84$ ($-6.36, -5.31$) | $-6.69$ ($-7.07, -6.31$) |
| 0.25 | $-5.24$ ($-5.70, -4.79$) | $-4.29$ ($-4.72, -3.86$) | $-5.29$ ($-5.85, -4.73$) | $-4.87$ ($-5.53, -4.21$) | $-5.27$ ($-5.83, -4.72$) | $-6.00$ ($-6.56, -5.44$) |
| 0.50 | $-3.71$ ($-4.21, -3.21$) | $-3.23$ ($-3.64, -2.83$) | $-3.70$ ($-4.24, -3.16$) | $-3.77$ ($-4.32, -3.22$) | $-3.74$ ($-4.29, -3.19$) | $-4.52$ ($-5.08, -3.97$) |
| 0.75 | $-2.67$ ($-3.16, -2.18$) | $-2.10$ ($-2.52, -1.68$) | $-2.64$ ($-3.18, -2.09$) | $-2.57$ ($-3.11, -2.03$) | $-2.54$ ($-3.08, -2.00$) | $-3.27$ ($-3.83, -2.71$) |
| 0.90 | $-1.55$ ($-2.04, -1.06$) | $-1.02$ ($-1.44, -0.60$) | $-1.52$ ($-2.06, -1.00$) | $-1.45$ ($-1.98, -0.92$) | $-1.42$ ($-1.95, -0.89$) | $-2.14$ ($-2.69, -1.59$) |
| 0.95 | $-0.52$ ($-1.04, -0.01$) | $-0.50$ ($-0.94, -0.06$) | $-0.52$ ($-1.04, -0.00$) | $-0.50$ ($-0.94, -0.06$) | $-0.50$ ($-0.94, -0.06$) | $-0.52$ ($-1.04, -0.00$) |
between gestational exposure to air pollution on inhibiting fetal growth have been proposed. These include inflammation, increased blood coagulation and viscosity, or altered vascular function that may affect uteroplacental blood flow and inhibit the placental transfer of oxygen and nutrients from mother to fetus.\textsuperscript{46,48} However, the biological response to health stressors may differ based on vulnerability factors.

Our findings suggest that infants born to NH Black women are more vulnerable to air pollution than those born to NH White and Hispanic women, particularly infants born in the lowest percentiles of the birth weight distribution. This health disparity may be explained by societal and economic factors that drive inequalities.\textsuperscript{29} Increased susceptibility to stress due to an increase in allostatic load is an important factor that can increase risk to adverse birth outcomes.\textsuperscript{49} This can be related to economic reasons such as job strain and can also be a consequence of structural and individual racism in society and everyday life.\textsuperscript{49}

While PM\textsubscript{2.5} exposure during pregnancy is higher for NH Black mothers than NH White mothers, it also appears that the effect of PM\textsubscript{2.5} on birth weight is higher among NH Black mothers. In addition, other environmental risks, such as toxins or heat exposure, may contribute to such increased vulnerability of NH Black mothers to air pollution.\textsuperscript{6,18} This double jeopardy is well documented in the environmental justice literature.\textsuperscript{6,17,18} In this article, we additionally show that NH Black mothers, when compared with NH White and Hispanic mothers, are even more vulnerable to the harmful effect of PM\textsubscript{2.5} when focusing on the lowest percentiles of the birth weight distribution. Other unmeasured individual or contextual stressors that are particularly concentrated among NH Black mothers may also have strong impacts on birth weight and then further interact with exposure to PM\textsubscript{2.5} to increase vulnerability of LBW infants. Stress during pregnancy can affect the mother’s body through various physiological pathways such as neuroendocrine pathway, maternal vascular disease pathway, and immune–inflammatory pathway and weaken the pregnant mothers’ ability to cope with other stressors such as air pollution.\textsuperscript{49} In revealing increased R/E disparities in LBW infants, our results indicated the importance of exploring social disadvantage within these particularly vulnerable populations, and targeting interventions to confront these challenges.

Study limitations and recommendations for further research

Noise pollution has also been suggested as a possible confounder, although the evidence to demonstrate the perinatal health outcomes of noise exposure is sparse.\textsuperscript{10} Another limitation of our study is that ambient PM\textsubscript{2.5} was measured from air monitors and estimated at the ZCTA level of the mother’s residence. We alleviated the misclassification of exposure by limiting mothers’ ZCTAs that were located 20 km of a monitor. However, measurement error was possible as we were estimating the mother’s exposure to PM\textsubscript{2.5} by estimating a mean exposure for the gestational period, using the address at the time their child is born, while the mother may have moved or spent part of her pregnancy at a different residence. Yet, a recent study showed such effects remain similar after accounting for residential mobility during pregnancy.\textsuperscript{47,51} Furthermore, data support that mothers’ which change residence during pregnancy usually move short distances (median <10 km) and within the same county or general area.\textsuperscript{52} As the air pollution exposure estimates are calculated at the ZCTA level, it is unlikely that this would results in exposure misclassification. Additionally, certain periods during gestation show more vulnerability to air pollution.\textsuperscript{53} While our study only considers the whole pregnancy period exposure, it would be interesting to use a quantile regression approach to investigate this relationship at different gestational stages in the future.

Last, it has been shown that constituents of PM\textsubscript{2.5} can have a different effect on birth weight.\textsuperscript{20,43,54,55} This separation of constituents was beyond the scope of this paper, but quantile regression analysis could be used to further understand how each PM\textsubscript{2.5} constituent varies by birth weight distribution.

Conclusion

Quantile regression revealed effects that PM\textsubscript{2.5} exposure during pregnancy on birth weight was not completely captured using traditional regression methods, especially when investigating R/E health disparities. This analytical approach has a wide applicability to further study air pollution on birth outcomes as well as on other environmental exposures and associated health disparities.

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