Maternal Exposure to Particulate Matter during Pregnancy and Adverse Birth Outcomes in the Republic of Korea

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Abstract: Air pollution has become a global concern due to its association with numerous health effects. We aimed to assess associations between birth outcomes in Korea, such as preterm births and birth weight in term infants, and particulate matter < 10 µm (PM10). Records from 1,742,183 single births in 2010–2013 were evaluated. Mean PM10 concentrations during pregnancy were calculated and matched to birth data by registered regions. We analyzed the frequency of birth outcomes between groups using WHO criteria for PM10 concentrations with effect sizes estimated using multivariate logistic regression. Women exposed to PM10 > 70 µg/m³ during pregnancy had a higher rate of preterm births than women exposed to PM10 ≤ 70 µg/m³ (7.4% vs. 4.7%, P < 0.001; adjusted odds ratio (aOR) 1.570; 95% confidence interval (CI): 1.487–1.656). The rate of low birth weight in term infants increased when women were exposed to PM10 > 70 µg/m³ (1.9% vs. 1.7%, P = 0.278), but this difference was not statistically significant (aOR 1.060, 95% CI: 0.953–1.178). In conclusion, PM10 exposure > 70 µg/m³ was associated with preterm births. Further studies are needed to explore the pathophysiologic mechanisms and guide policy development to prevent future adverse effects on birth outcomes.

Keywords: maternal exposure; particulate matter; preterm birth

1. Introduction

Air pollution in the Republic of Korea (Korea) has been an issue for many years. In particular, the particulate matter (PM) component of air pollution is becoming increasingly important due to several factors, including geographical characteristics, the chemical evolution in Seoul, and overcrowding in urban areas. In 2016, the United States National Aeronautics and Space Administration, the Ministry of Environment in Korea, and the National Institute of Environmental Research studied PM in Korea and released the Korea–United States Air Quality Study, reporting that the PM emitted domestically may exceed the recommendations outlined in the World Health Organization (WHO) air quality guidelines [1]. In previous studies, PM such as PM2.5 (fine inhalable particles with diameters that are generally smaller than 2.5 µm) and PM10 (inhalable particles with
diameters that are generally smaller than 10 µm) have been associated with increased mortality and morbidity from multiple health conditions, including cardiovascular disease, lung cancer, acute respiratory infections, asthma, and diabetes [2–9]. Moreover, other studies have reported that maternal exposure to PM during pregnancy may increase the risk of preterm birth (gestational age < 37 weeks) [10–12], low birth weight (birth weight < 2500 g) in term infants [13–15], and congenital malformation [16] through processes related to inflammation, oxidative stress, endocrine disruption, and impaired oxygen transport across the placenta [17]. In addition, there have been several studies reporting on the long-term effects of prenatal air pollution exposure on neurodevelopment and respiratory outcomes [18,19].

Preterm birth has short-term effects on respiratory, central nervous system, and cardiovascular functions in the form of patent ductus arteriosus, respiratory distress syndrome, and intravascular hemorrhage [20]. There are also, long-term consequences for physical health, neurodevelopment, pulmonary function, and adult health (cerebral palsy, asthma, growth impairment, and hypertension) [21]. Preterm birth is the second-most common cause of mortality in children under five years of age, and low-birth weight infants (LBWIs) have a 20-fold higher mortality rate than infants with a birth weight > 2500 g [22,23].

Given the increasing attention on the relationship between exposure to PM and adverse birth outcomes, this study aimed to assess the association of birth outcomes, such as preterm births and low birth weight in term infants, with PM in ambient air pollutants in Korea. We used a cutoff value for PM concentration of 70 µg/m³ to indicate high levels of exposure. This reference value of 70 µg/m³ was based on the interim target-1 in the WHO air quality guidelines [1] and is associated with a 15% higher long-term mortality risk relative to the guideline level of 20 µg/m³. We hypothesized that air pollution would be negatively associated with birth outcomes, particularly preterm births and low birth weight.

2. Materials and Methods

2.1. Study Design and Participants

This nationwide registry-based study analyzed data from 1,862,441 live births in 2010–2013 registered in the Korean national birth registry. The birth weight of term infants and the proportions of preterm births and low birth weight were analyzed according to the concentration of PM_{10} during pregnancy. In Korea, all parents must report their child’s birth within 1 month and include the following information: month and date of birth; maternal residential address at the time of birth; place of birth (hospital or elsewhere); parental ages; gestational age (weeks and days); sex; birth weight; birth order; total number of births; and parental education, occupation, and nationality. All data were acquired from Statistics Korea [24], which offers data (except for date of birth and days of gestational age, which are withheld for reasons of privacy protection) to all researchers who submit the objective of a study to their website. Because the individual identifier number was removed from the individual record to protect the privacy of the individuals, each birth record was treated as a separate family member, even though a couple may have had more than one child during the study period. Since multiple births are a major factor associated with preterm birth and low birth weight, 59,516 records (3.2%) involving multiple births were excluded. In addition, we excluded 1299 records with a gestational age < 23 weeks or a birth weight of <400 g according to the guideline for withholding of neonatal resuscitation [25]. Moreover, to compare premature births with normal births, we excluded 59,443 observations with a gestational age of ≥42 weeks or a birth weight > 4000 g (Figure 1). Thus, this study evaluated data from 1,742,183 records.

2.2. Air Monitoring Data

To assess PM_{10} exposure, we obtained daily mean levels from the National Health Insurance Service (NHIS), which makes air pollution data available through its data sharing website [26]. The level of PM_{10} was measured using the β-ray absorption method at 266 monitoring stations.
scattered throughout Korea during 2009–2013 [27]. Residential addresses (city, county, district; or si, gun, gu in Korean) at birth were utilized for spatial exposure assessment and assignment of PM$_{10}$ concentrations during pregnancy were assigned according to the address; the study population was postulated to be stable (did not change) over the exposure time period. We calculated monthly averages of PM$_{10}$ concentrations for each address and matched them to individuals based on their gestational age.

![Flow diagram of the study population](image)

**Figure 1.** Flow diagram of the study population.

2.3. **Statistical Analysis**

Using ArcGIS Maps for Office (ESRI Inc., Redlands, CA, USA), we visualized PM$_{10}$ concentrations and the proportion of preterm births in Korea according to addresses (city, county, district; or si, gun, gu) of monitoring stations and residences. We performed multiple linear regression analysis to assess correlations between mean PM$_{10}$ level and birth weight in term infants. Multivariable logistic regression was used to assess the effect of PM$_{10}$ in each residential region on birth weight in term infants and preterm births. The mean PM$_{10}$ concentrations were categorized in two ways. First, we compared birth outcomes of subjects in the lower first to third quartiles with the subjects in the fourth quartile. As the 75th percentile of the concentration was 54.5325 μg/m$^3$, we calculated odds ratios (ORs) using ≤54.5325 μg/m$^3$ as the reference category. Second, proportions and ORs were analyzed based on ≤70 μg/m$^3$, which is the interim target-1 of the WHO [1]. To evaluate the difference between metropolitan areas (Seoul, Busan, Daegu, Incheon, Gwangju, Daejeon, and Ulsan) and nonmetropolitan regions, we performed sensitivity analyses and assessed differences in ORs among both regional groups. We estimated adjusted ORs (aORs) after controlling for variables known to affect birth outcomes [28–30], including season at birth, parity, and parental job, education level, age, nationality, and residential region (capital region or not).

2.4. **Ethics Statement**

This study was granted ethical exemption by the institutional review board at Kyung Hee University Hospital (Seoul, Korea), since this was a secondary analysis of de-identified data (IRB No. 2018-01-091). The study was conducted in accordance with the Declaration of Helsinki.

3. **Results**

3.1. **Demographic and Birth-Related Characteristics**

Table 1 presents the baseline characteristics of the analyzed birth records. Overall, the mean ± standard deviation of gestational age and birth weight were 38.7 ± 1.5 weeks and 3200 ± 400 g, respectively. Preterm infants accounted for 4.7% of neonates and LBWIs accounted for 3.8%. Rates of preterm births and low birth weight increased over the observation period. Preterm births accounted for 4.6% of births in 2010 and increased to 4.9% in 2013. Proportions of low birth weight among term infants (28,728/1,659,659 × 100) were constant at 1.7% over the observation period.
Table 1. Background characteristics of births between 2010 and 2013 in Korea.

| Characteristics                  | n (%) or Mean (SD) (n = 1,742,183) |
|----------------------------------|-------------------------------------|
| Infant sex                       |                                     |
| Male                             | 888,711 (51.0)                      |
| Female                           | 853,472 (49.0)                      |
| Marital status                   |                                     |
| Married                          | 1,703,795 (97.9)                    |
| Unmarried                        | 36,857 (2.1)                        |
| Paternal age (years)             |                                     |
| Mean                             | 33.7 (4.6)                          |
| <20                              | 2752 (0.2)                          |
| 20–29                            | 268,567 (15.6)                      |
| 30–39                            | 1,282,258 (74.3)                    |
| ≥40                              | 172,350 (10.0)                      |
| Maternal age (years)             |                                     |
| Mean                             | 31.0 (4.1)                          |
| <20                              | 10,707 (0.6)                        |
| 20–34                            | 1,414,366 (81.2)                    |
| ≥35                              | 316,175 (18.2)                      |
| Area of birth                    |                                     |
| Capital region                   | 885,157 (50.8)                      |
| Others                           | 857,026 (49.2)                      |
| Place of birth                   |                                     |
| Hospital                         | 1,713,436 (98.4)                    |
| Others                           | 27,627 (1.6)                        |
| Paternal education               |                                     |
| University or higher             | 1,227,626 (71.2)                    |
| High school or lower             | 495,918 (28.8)                      |
| Maternal education               |                                     |
| University or higher             | 1,215,714 (70.0)                    |
| High school or lower             | 521,532 (28.0)                      |
| Paternal employment              |                                     |
| Manager or specialist            | 477,105 (27.4)                      |
| Officer                          | 585,437 (33.6)                      |
| Service                          | 296,117 (17.0)                      |
| Blue collar                      | 317,360 (18.2)                      |
| Unemployed a                     | 66,164 (3.8)                        |
| Maternal employment              |                                     |
| Manager or specialist            | 221,519 (12.7)                      |
| Officer                          | 245,619 (14.1)                      |
| Service                          | 78,395 (4.5)                        |
| Blue                             | 34,344 (2.0)                        |
| Unemployed a                     | 1,162,306 (66.7)                    |
| Paternal nationality             |                                     |
| Korean                           | 1,715,981 (99.4)                    |
| Non-Korean                       | 11,048 (0.6)                        |
| Maternal nationality             |                                     |
| Korean                           | 1,679,145 (96.5)                    |
| Non-Korean                       | 60,629 (3.5)                        |
| Parity                           |                                     |
| Primiparous                      | 899,141 (51.7)                      |
| Multiparous                      | 840,365 (48.3)                      |
| Mean gestational age (weeks)     | 38.7 (1.5)                          |
| Preterm infants                  | 82,524 (4.7)                        |
| Mean birthweight (kg)            | 3.2 (0.4)                           |
| Low birthweight in term infants  | 28,728 (1.7 b)                      |

a Unemployed: unemployed, housewife, or student.  
b Proportion of low birthweight in term infants: 28,728/1,659,659 × 100.

3.2. Distribution of PM$_{10}$ and Preterm Births in Korea

Median concentration of PM$_{10}$ over five years decreased from 46 to 43 µg/m$^3$, with the lowest level reported in 2012 (Table 2). Figure 2a illustrates concentrations of PM$_{10}$ in each region divided
into quarters. Concentrations were high in the capital area and metropolitan areas. In the capital area, the quality of air was worse in the west coast areas and rural areas that have factories than it was in Seoul, the capital city. Figure 2b presents proportions of preterm birth by region. Preterm births occurred more frequently in the west coast areas in the capital region and noncapital regions than in Seoul.

**Table 2.** Distribution of particulate matter less than 10 μm (PM$_{10}$) between 2009 and 2013 in Korea.

| PM$_{10}$ (μg/m$^3$) | 2009 | 2010 | 2011 | 2012 | 2013 | Total |
|-----------------------|------|------|------|------|------|-------|
| 1st centile           | 12   | 10   | 9    | 10   | 13   | 11    |
| 25th centile          | 33   | 30   | 30   | 28   | 30   | 30    |
| Median                | 46   | 45   | 44   | 40   | 43   | 44    |
| Mean                  | 53   | 51   | 50   | 45   | 49   | 50    |
| 75th centile          | 65   | 64   | 62   | 56   | 60   | 62    |
| 90th centile          | 91   | 88   | 84   | 76   | 82   | 84    |
| 99th centile          | 167  | 170  | 179  | 118  | 139  | 156   |
| Range                 | 155  | 160  | 170  | 108  | 126  | 145   |

**Figure 2.** (a) Distribution of particulate matter less than 10 μm in Korea. (b) Distribution of preterm births in Korea.
3.3. PM10 and Birth Outcomes

A 10 µg/m³ increase in concentration of PM10 during pregnancy was associated with a 1 g decrease in birth weight among term infants \((P = 0.001)\). The proportion of low birth weight in term infants was higher when the exposure to mean PM10 concentration was >70 µg/m³ than it was when exposure was ≤70 µg/m³ \((1.9\% \text{ vs. } 1.7\%)\), although the aOR was not significantly higher than the reference group \((\text{aOR: } 1.060, 95\% \text{ CI: } 0.953–1.178, P = 0.283, \text{ Table 3})\). Women in the highest quartile had higher odds of preterm birth compared with women in the lower three quartiles \((54.5325 \mu g/m^3 \text{ or less})\) of PM10 exposure \((\text{aOR: } 1.044, 95\% \text{ CI: } 1.025–1.062, P < 0.001)\). In particular, women exposed to PM10 >70 µg/m³ during pregnancy had a significantly higher proportion of preterm births \((7.4\% \text{ vs. } 4.7\%)\) than those exposed to ≤70 µg/m³ \((\text{aOR: } 1.570, 95\% \text{ CI: } 1.487–1.656, P < 0.001)\). The aOR for the relationship between exposure to PM10 >70 µg/m³ for very preterm births \((\text{gestational age less than } 32 \text{ weeks})\) was also statistically significant \((\text{aOR: } 1.966, 95\% \text{ CI: } 1.776–2.177, P < 0.001, \text{ Table 3})\).

| Exposure Proportion (%) | P-Value | Adjusted OR (95% CI) |
|-------------------------|---------|---------------------|
| Low birthweights in term infants | 1st–3rd 4th | 1.7 1.8 | 0.495 1.010 (0.981–1.040) |
| ≤70 µg/m³ | >70 µg/m³ | 1.7 1.9 | 0.283 1.060 (0.953–1.177) |
| Preterm infants | 1st–3rd 4th | 1.0 4.7 4.9 | 0.001 1.044 (1.025–1.062) |
| ≤70 µg/m³ | >70 µg/m³ | 4.7 7.4 | <0.001 1.570 (1.487–1.656) |
| Very preterm infants (Gestational age < 32 weeks) | 1st–3rd 4th | 1.0 1.1 | 0.001 1.095 (1.055–1.137) |
| ≤70 µg/m³ | >70 µg/m³ | 1.0 2.0 | <0.001 1.966 (1.776–2.177) |

OR adjusted for parity, parental job, education level, age, nationality, residential regions (capital region or not), and season at birth.

In metropolitan areas, preterm births were more prevalent among those exposed to the highest quartile of PM10 than those exposed to lower PM10 levels \((5.4\% \text{ vs. } 4.6\%)\), and the aOR was statistically significant \((\text{aOR: } 1.156, 95\% \text{ CI: } 1.123–1.190, P < 0.001)\). However, there was no difference between groups in nonmetropolitan regions. aORs for the association between preterm births and mean PM10 exposure > 70 µg/m³, were statistically significant, irrespective of region \((\text{Table 4})\).

| Exposure Proportion (%) | P-Value | Adjusted OR (95% CI) |
|-------------------------|---------|---------------------|
| Metropolitan areas | 1st–3rd 4th | 4.6 5.4 | <0.001 1.156 (1.123–1.190) |
| ≤70 µg/m³ | >70 µg/m³ | 4.7 8.9 | <0.001 1.934 (1.666–2.247) |
| Non-metropolitan regions | 1st–3rd 4th | 4.7 4.7 | 0.127 0.984 (0.963–1.006) |
| ≤70 µg/m³ | >70 µg/m³ | 4.7 7.2 | <0.001 1.521 (1.436–1.611) |

OR adjusted for parity, parental job, education level, age, nationality, and season at birth.
4. Discussion

Using a nationwide registry-based study, we analyzed the associations between preterm births and birth weight of term infants and exposure concentrations of PM$_{10}$ during pregnancy.

Our results indicate that exposure to PM$_{10} > 70$ µg/m$^3$ during pregnancy may be associated with preterm births. There is an ongoing debate regarding the health effects of exposure to PM$_{10}$ during pregnancy, but our results are consistent with most other studies [11,12]. Our results regarding the association of higher PM$_{10}$ concentrations and increased preterm birthrate closely agree with several previous studies on the effects of PM$_{10}$ exposure on preterm birth in a restricted area in Korea [31,32]. However, unlike previous research, this study analyzed not only the distribution of PM but also the specific standard of 70 µg/m$^3$, which is associated with a higher long-term mortality risk according to the WHO [1]. When the results are visualized geographically, it is clear that preterm births occurred more frequently in west coast areas, and some rural cities in the capital area where there are many more factories than in Seoul. Moreover, exposure to PM$_{10} > 70$ µg/m$^3$ during pregnancy was significantly associated with very preterm births. In addition, mean exposure to PM$_{10} > 70$ µg/m$^3$ resulted in significantly elevated adjusted odds ratios regardless of whether the location was a metropolitan or nonmetropolitan area.

Finally, we found a tendency for increases in PM$_{10}$ to be associated with increased risk of adverse birth outcomes such as low birth weight in term infants. Our data showed a statistically significant ($P = 0.001$) 1 g decrease in birth weight among term infants per 10 µg/m$^3$ increase in PM$_{10}$ exposure during pregnancy. This tendency is consistent with previous research, but the changes in birth weight described previously have been so modest that they may have little clinical importance [33,34]. The proportion of low birth weight in term infants was higher in areas where the mean PM$_{10}$ concentration was $>70$ µg/m$^3$, but the association was not statistically significant, as measured by the aOR.

Although NHIS data showed a decline in PM$_{10}$ concentration over a five-year period, ambient air pollutants—specifically particulate matter—remain a burden on the economy and human society in Korea and worldwide. The Global Burden of Disease, Injuries, and Risk Factors Study of 2016 identified air pollution, especially ambient air pollution, as the sixth leading risk factor for global disease [35]. At the same time, according to 2016 data from the Korean National Statistical Office (KNSO), the frequency of preterm births at a gestational age of <37 weeks increased by 1.5 times from the level seen 10 years previously, to 7.2%. The prevalence of LBWIs (under 2500 g at birth) increased 0.2% from the 2015 level, and steadily increased to about twice the level seen in 1996. Meanwhile, preterm birth is the second-most common cause of mortality in children under 5 years of age, and LBWIs have a 20-fold higher mortality rate than infants of normal birth weight (>2500 g). Therefore, policies are needed to ameliorate modifiable factors for adverse birth outcomes, such as air pollution, to reduce the preterm birthrate and the rate of LBWIs. A campaign is needed to educate the public, especially pregnant women and their families, on methods to reduce or avoid PM.

Our study had several strengths, including adjustment for a number of covariates, including maternal age, parity, infant sex, and parental employment, which have been associated with adverse birth outcomes in previous reports [28–30]. In addition, our analysis was based on the specific criteria of 70 µg/m$^3$ of PM$_{10}$, which is relevant to higher risks. However, it is important to note some limitations. First, when we discuss the association between PM and adverse birth effects, such as preterm birth and low birth weight, we should consider other factors that may affect birth results. These include the family history of preterm births, maternal smoking history, low maternal body mass index, prior preterm birth, medical and pregnancy history, occupational exposure, and other factors. These factors could not be analyzed due to the unavailability of the necessary data. Second, until recently, the concentrations of PM$_{10}$ and PM$_{2.5}$, which is also thought to be related to adverse birth outcomes, had not been measured in Korea [13,14,36,37]. Because there are various types of air pollutants, including SO$_2$, O$_3$, and NO$_2$, comprehensive analyses of the effects of pollutants beyond PM$_{10}$ on birth outcomes are warranted. Lastly, this study did not analyze results by trimester because
detailed data regarding birth history were not available from the KNSO. There was also no data regarding the date of birth or the day of gestational age; therefore, there was no possibility of dividing pregnancies into trimesters.

In April 2017, The Lancet published The Lancet Planetary Health to assess the effects of environment change on human health, but also to investigate other factors such as political, economic, and social systems that govern those effects [38]. This reflects the increasing global emphasis on the importance of the environment on human health.

5. Conclusions

In conclusion, we found that exposure to ambient air pollutants during pregnancy, especially \( \text{PM}_{10} \), was associated with an increased rate of preterm births. Future research priorities should include explorations of the pathophysiological mechanism behind this association. Long-term, multifaceted studies are also needed to guide development of policies to prevent the adverse effects of air pollutants on birth outcomes in the future.

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