Short-term Associations of Air Pollution with Postneonatal Infant Death in Seoul, Korea, 1999-2003

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ABSTRACT

Objective to assess whether exposure to air pollutants is associated with postneonatal infant death, using a time-series methodology, between 1999 and 2003 in Seoul, Korea. Methods We investigated the short-term effects of air pollution for 548,725 live births during the study period. The daily count of postneonatal infant deaths from all causes and from SIDS (sudden infant death syndrome) by birth order was analyzed by a Generalized Additive Poisson model, with controlling for the effects of seasonal trends, air temperature, relative humidity, barometric pressure, and day of the week as covariates. Results During the study period, we observed 699 deaths from all causes and 47 deaths from SIDS. We did not find any significant associations between daily mortality and ambient levels of air pollutants except for CO and NO2. The estimated relative risk of postneonatal infant death from all causes was 1.17 (95% CI=1.04-1.32) and 1.16 (95% CI=1.03-1.29) by IQR (interquartile range) for CO and NO2 respectively. Also, we observed no clear trend of the mortality effects of air pollution by birth orders. Conclusion In conclusion, our findings suggest that air pollution, in general, influenced adversely postneonatal infant death from all-cause and SIDS although it was not statistically significant. This study may support that the rationale

Keywords: Air pollution, Postneonatal infant death, Birth order

I. Introduction

Over the past decade, many epidemiologic studies have examined the associations of short-term exposure to ambient air pollution with all-cause, respiratory and cardiovascular mortality in various countries or cities. However, most of these previous studies focused on adult and elderly populations. Very few studies have focused on mortality in infants in relation to outdoor air pollution with a time-series approach.

Infants may be a susceptible population who could be vulnerable to the effects of air pollutants. In a study in the United States, PM2.5 (particulate matter less than or equal to 2.5 μm in aerodynamic diameter) was found to be associated with postneonatal infant mortality from respiratory causes. Kaiser and his colleague reported that the estimated proportion of all-cause mortality, SIDS (sudden infant death syndrome), and respiratory disease mortality attributable to PM10 (particulate matter less than or equal to 10 μm in aerodynamic diameter) above the national standard was associated with postneonatal infant mortality in 23 U.S. metropolitan areas.

Especially, the previous time-series studies relating infant death have not been determined personal information because it could not include information about birth order or biologically abnormal babies such as low birth weight and premature infant. It also was not easy to evaluate the relationship between air pollution and infant deaths relating birth order in time-series study.

Among the birth order, first-born babies have consistently been shown to be at a higher than average risk of infant death. Most recently, Mathews and MacDorman (2006) reported infant mortality rates were generally higher for first
births than for second births, and then rates generally increased as birth order increased.\textsuperscript{11} Therefore, the purpose of this study is to assess the influence of air pollution according to birth order in postneonatal infant death, using a time-series methodology, between 1999 and 2003 in Seoul, South Korea.

II. Methods

Death related birth certificate records were obtained from the Korea National Statistical Office for births occurring between 1999 and 2003. A total of 548,725 births and 1,164 infant deaths (83 SIDS) were recorded. Deaths due to accidents and deaths occurring outside of the city were excluded from this analysis. The death data also were restricted to daily counts of postneonatal deaths, defined here as the death of an infant over 27 days old and less than 1 yr of age at the time of death. We also excluded neonates less than 27 days of age from this analysis because neonates are influenced easily by perinatal conditions.\textsuperscript{12-13}

Ambient air data were provided by the Ministry of Environment of the Republic of Korea. Exposure measurements from air pollution data for particulate matter less than or equal to 10 μm in aerodynamic diameter (PM\textsubscript{10}), carbon monoxide (CO), sulfur dioxide (SO\textsubscript{2}), nitrogen dioxide (NO\textsubscript{2}), and ozone (O\textsubscript{3}) during the study period were obtained from ambient monitoring stations located in each of 27 administrative districts in Seoul, South Korea. We calculated the daily maximum of the 8-hour moving average for CO and O\textsubscript{3} and daily means for the other pollutants. Information on the 24-hour average temperature (°C), relative humidity (%), and barometric pressure (hPa) from the same calendar year was available from the Korea Meteorological Administration. Figure 1 shows the 27 administrative districts in Seoul, South Korea. The total population size of this city during the study period was about 10 million, and the major air pollution source was automobile exhaust emissions and domestic heating.

A generalized additive model (GAM) that uses nonparametric smoothing was applied to allow for highly flexible fitting of seasonality and long-term time trends, as well as nonlinear associations with weather variables such as air temperature and relative humidity.\textsuperscript{14} Using the generalized additive model, we controlled for these long-term temporal variations. With this model, we introduced weather variables, such as air temperature, relative humidity, and barometric pressure, to improve the postneonatal infant mortality predictions. Also, daily postneonatal infant mortality figures were fitted to the generalized additive model, which included the locally-weighted running-line smoother (LOESS) function of time, to capture seasonal and long-term trends. The modeling strategy was a systematic approach, building from simpler to more complicated models with an increasing number of covariates. We first incorporated nonlinear time and weather terms into the generalized additive model. After controlling for time and weather, ambient air pollutant concentration was added to the model. Also, the generalized additive model was used with a more stringent convergence criterion than default values of S-plus to avoid biased estimates of regression coefficient and standard error.\textsuperscript{15-16} The model is described by the following equation:

\[
\text{Log}[E(Y)] = \beta_0 + S(X_1) + \beta_1(P_t)
\]

where \(Y\) = daily number of deaths for postneonatal infants by birth order; \(X_1\) = an indicator for day of week; \(X_2\) = air temperature; \(X_3\) = relative humidity;
X₄ = air pressure; Sᵣ = the smoothing function; and
Pᵣ = concentration of air pollutant. The linear
effects of pollution on the log relative risk of death
for postneonatal infants by birth order were
determined and are reported in units of their
interquartile ranges (IQR), of their daily averages
(PM₁₀, SO₂, and NO₂), or of their maximum 8-hour
moving average levels (O₃ and CO). Moreover,
previous studies indicated that an acute effect
could be observed on the same day or within one
to five days of exposure to air pollution. So, we
selected a lag time for each pollutant showing the
highest association with death for first-born post-
neonatal infants. To compare the relative quality
of the postneonatal infant mortality predictions
across these non-nested models, Akaike's Infor-
mation Criterion (AIC) was used as a measure of
how well the model fit the data.¹⁷-¹⁸ Smaller AIC
values indicate the preferred model. All analyses
were carried out using both SAS (SAS Institute,
Cary, NC) and S-plus (Statistical Sciences, Seattle,
WA).

### III. Results

Table 1 describes the number and crude
mortality rate of postneonatal deaths among total
birth cohorts between 1999 and 2003. In the both
of all-cause and SIDS, postneonatal infant
mortality rates were generally higher for first
births than for second births, and then generally
increased as birth order increased. In postneonatal
deaths from all-cause, the crude death rate for first
births (2.35) was 34 percent higher than for
second births (1.75). The rate for third and higher
order births (2.41) was 38 percent higher than the
rate for second births. Those results from SIDS
were similar to the results from all-cause. The
higher parities and therefore the highest order
births are more likely to be associated with older
maternal age, socioeconomic status and so on.

Table 2 shows a statistical summary of daily
counts for postneonatal infant deaths from all
causes and from SIDS by birth orders, as well as
daily concentrations of the five air pollutants and

<table>
<thead>
<tr>
<th>Table 1. Number and crude mortality rate of postneonatal deaths among total birth cohorts between 1999 and 2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth-order from all-cause</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>Total birth count (persons)</td>
</tr>
<tr>
<td>Total death count (persons)</td>
</tr>
<tr>
<td>CDR</td>
</tr>
</tbody>
</table>

Note: Missing value in birth order was excluded in death count (N=234), CDR : Crude death rate (1000 person)

<table>
<thead>
<tr>
<th>Table 2. Summary statistics for daily postneonatal infant deaths, air pollutants and weather in Seoul, Korea, 1999-2003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>All-cause death count</td>
</tr>
<tr>
<td>SIDS death count</td>
</tr>
<tr>
<td>PM₁₀ (µg/m³)</td>
</tr>
<tr>
<td>SO₂ (ppb)</td>
</tr>
<tr>
<td>NO₂ (ppb)</td>
</tr>
<tr>
<td>O₃ (ppb)</td>
</tr>
<tr>
<td>CO (ppm)</td>
</tr>
<tr>
<td>Air temperature (°C)</td>
</tr>
<tr>
<td>Relative humidity (%)</td>
</tr>
<tr>
<td>Air pressure (hPa)</td>
</tr>
</tbody>
</table>

¹N : number of sample size; ¹Min : minimum; ¹Max : maximum; ³SD : standard deviation; ³IQR : interquartile range.
weather variables in Seoul, South Korea, from 1 January 1999 to 31 December 2003. There were 1,164 postneonatal infant deaths from all causes during the study period, an average of 0.64 deaths per day. Daily mean concentrations of the five air pollutants in Seoul were 70.1 μg/m³, 5.6 ppb, 35.6 ppb, 25.6 ppb, and 1.0 ppm for PM₁₀, SO₂, NO₂, O₃, and CO, respectively. Daily concentration levels for the five air pollutants remained below the Korean national ambient air quality standards.

Figure 2 shows that there were clear seasonal patterns in ambient CO, NO₂, SO₂, and O₃. Sulfur dioxide and CO were negatively associated with ozone. It can also be seen in Figure 2 that CO and SO₂ levels decreased over a calendar period. However, NO₂, PM₁₀, and O₃ levels did not show any trend by calendar year. The weather variables such as air temperature, relative humidity, and air pressure also showed clear seasonal patterns (Figure 3).

Table 3 shows that the estimated relative risk and its 95% confidence intervals of postneonatal infant mortality from all causes and from SIDS by birth order associated with interquartile range increases in the daily concentration of five air pollutants after controlling for temporal trends, weather conditions, and days of the week by a single pollutant model in Seoul during the period from 1999 to 2003. The estimated relative risk of postneonatal infant death from SIDS were generally higher for first births than for second births, and then generally increased as birth order increased. However, an inverse relationship was found in the results from all cause. The risks of

![Daily infant death counts & Smoothing Curve](image1)

![Daily Mean CO & Smoothing Curve](image2)

![Daily Mean NO₂ & Smoothing Curve](image3)

![Daily Mean SO₂ & Smoothing Curve](image4)

![Daily Mean PM₁₀ & Smoothing Curve](image5)

![Daily Maximum O₃ & Smoothing Curve](image6)

**Fig. 2.** Time trends of the daily number of total infant death counts and daily average concentrations of CO, O₃, PM₁₀, NO₂ and SO₂ in Seoul, Korea, 1999-2003.
Fig. 3. Time trends of the daily mean temperature, relative humidity, and air pressure in Seoul, Korea, 1999-2003.

Table 3. Relative risks with 95% confidence intervals of postneonatal mortality relating birth-order from all-cause and SIDS* by IQR** increase in daily concentration of five air pollutants using single-pollutant model*** in Seoul, Korea between 1999 and 2003

<table>
<thead>
<tr>
<th></th>
<th>First born</th>
<th>Second born</th>
<th>More than third born</th>
<th>All born</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All-cause</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM_{10} (Lag 0+1)</td>
<td>1.01 (0.95-1.15)</td>
<td>1.04 (0.92-1.18)</td>
<td>1.10 (0.81-1.51)</td>
<td>1.04 (0.97-1.11)</td>
</tr>
<tr>
<td>SO_{2} (Lag 2)</td>
<td>1.09 (0.94-1.26)</td>
<td>0.99 (0.81-1.21)</td>
<td>1.16 (0.68-1.98)</td>
<td>1.03 (0.93-1.16)</td>
</tr>
<tr>
<td>NO_{2} (Lag 0+1)</td>
<td>1.14 (0.98-1.33)</td>
<td>1.22 (1.00-1.49)</td>
<td>1.17 (0.67-2.05)</td>
<td>1.16 (1.03-1.29)</td>
</tr>
<tr>
<td>O_{3} (Lag 0)</td>
<td>0.68 (0.57-0.81)</td>
<td>0.90 (0.72-1.13)</td>
<td>0.91 (0.48-1.73)</td>
<td>0.77 (0.67-0.87)</td>
</tr>
<tr>
<td>CO (Lag 0+1)</td>
<td>1.09 (0.93-1.28)</td>
<td>1.31 (1.06-1.63)</td>
<td>1.59 (0.90-2.81)</td>
<td>1.17 (1.04-1.32)</td>
</tr>
</tbody>
</table>

| **SIDS** |            |             |                      |          |
| PM_{10} (Lag 0) | 1.15 (0.81-1.64) | 0.76 (0.34-1.71) | 1.00 (0.38-2.67) | 1.04 (0.77-1.40) |
| SO_{2} (Lag 0) | 1.36 (0.45-4.13) | 0.61 (0.16-2.36) | 1.52 (0.31-7.37) | 1.17 (0.57-2.39) |
| NO_{2} (Lag 0+1) | 1.63 (0.53-4.97) | 1.37 (0.45-4.16) | 4.83 (0.68-34.48) | 1.76 (0.89-3.46) |
| O_{3} (Lag 1) | 1.22 (0.39-3.82) | 0.71 (0.21-2.45) | 0.60 (0.04-9.98) | 1.09 (0.52-2.27) |
| CO (Lag 0) | 1.03 (0.37-2.87) | 0.70 (0.23-2.19) | 1.83 (0.57-5.80) | 1.33 (0.70-2.53) |

*SIDS: sudden infant death syndrome; **IQR: interquartile range; ***This model adjusted for day of week, and smooth loess functions of date, temperature, relative humidity and barometric pressure as well IQR of PM_{10}, SO_{2}, NO_{2}, O_{3} and CO were 40.8 \mu g/m^{3}, 3.4 ppb, 17.1 ppb, 20.4 ppb and 0.6 ppm, respectively. The Lag n is air pollutant concentration of n days ago.
postneonatal infant death from SIDS among first-born babies were positively associated with all studied air pollutants. However, most of these associations were not statistically significant. The relative risk (RR) of postneonatal infant death from all causes among second-born babies with a 0.6 ppm increment of CO was 1.31 (95% confidence interval, CI = 1.06-1.63) and a 17.1 ppb increment of NO$_2$ was 1.22 (95% confidence interval, CI = 1.00-1.49). In contrast, an increase in the concentration of O$_3$ was negatively associated with postneonatal infant mortality from all causes for all-born babies. This study also evaluated the influence of air pollution and birth order in postneonatal infant death using two-pollutant model. However, all air pollutants effect on mortality was not significant with other pollutants. Therefore, we found that the estimated risk of death by birth order was unaffected by adding the other pollutants to the model.

IV. Discussion

We investigated the influence of ambient air pollutant exposure and birth order in postneonatal infant death from all causes and SIDS using a time-series methodology between 1999 and 2003 in Seoul, Korea.

Our findings showed that the estimated relative risk of postneonatal infant death from SIDS were generally higher for first births than for second births, and then generally increased as birth order increased. This study could confirm that air pollution influenced postneonatal infant death from SIDS by birth order although it was not statistically significant.

In Mexico City, Loomis et al. (1999) reported a strong association between infant mortality and particulate matter levels. An increase of 10 μg/m$^3$ in PM$_{2.5}$ level over three days was related to an increase of 6.9% in infant mortality with a three-day lag.$^{6}$ Infant mortality was also associated with O$_3$ and NO$_2$ but not as consistently as with particles. More recently, in a study performed in Kaohsiung, Taiwan, using a case-crossover design, air pollutants were found to be associated with mortality from all causes in the postneonatal period.$^{19}$ The authors reported a positive associa-

tion between air pollution and postneonatal infant mortality although, as with our results, it was not statistically significant. Also, a study conducted in California, U.S., showed that PM$_{2.5}$ was associated with postneonatal infant mortality from respiratory causes but not SIDS.$^{8}$ However, we observed a negative association between ambient ozone and daily mortality and it was statistically significant (RR = 0.77, 95% CI = 0.67-0.87). We cannot explain it fully, but it may be affect the threshold for ozone at low levels. Therefore, further study of this finding is needed.

Our findings indicated that the risk of postneonatal infant death from all causes and from SIDS for first-born and second-born babies was positively associated with air pollutants, particularly ambient CO and NO$_2$ from all-cause. The biological mechanism by which exposure to air pollution might influence mortality of postneonatal infants remains to be explained. A number of potential mechanisms for CO have been suggested. Infants may have an increased susceptibility to CO toxicity because of their higher basal metabolic rates and consequent higher tissue oxygen demand. On the other hand, PM$_{10}$ and gaseous pollutants such as SO$_2$ and NO$_2$ lead to pulmonary inflammation with a systemic release of cytokines$^{20}$ and increased blood viscosity.$^{21}$

Previous birth order studies have often been criticized for their lack of consistent findings. In the United States and Norway, an inverse relationship was found, with later-born children more likely to survive in childhood.$^{22,23}$ However, a curvilinear relationship was found, with the middle child most likely to survive childhood in Bangladesh.$^{23}$ Those results are guessed because of the difference of maternal age, nutritional status, level of hygiene, housing status of study population.

There are also biological factors connected to short birth interval and maternal age that speak against the survival of later-born over first-born. Thus, the biological mechanism of the mother has been put forward as an explanation behind the often observed higher mortality of children born towards the end of large sibling.$^{24,25}$

Our study shows considerable strengths. To consider those deaths more plausibly associated
with air pollution, our death data were restricted to daily counts of postneonatal deaths, defined as the deaths of infants of age greater than 27 days and less than 1 year. Neonates younger than 27 days of age are more likely to have less exposure to air pollution because of medical care or conspicuous protection by their parents. Moreover, the other strength of this study relates to use of only first-born babies for the analysis because first-born babies had greater risk of infant death, low birth weight, premature birth and intrauterine growth retardation compared with babies of higher birth order. Most recently, CDC (Centers for Disease Control and Prevention) suggested that first-born babies were generally at higher risk than second-born, and then the risk generally increased as birth order increased. Also, they reported the infant mortality rate for first births was 14 percent higher than for second births, and the rate for fifth and higher order births was 72 percent higher than the rate for second births. In our study, there was a lack of data on maternal status. However, this personal information, socioeconomic status or other demographic features are not a confounder in time-series analysis because those studies are to identify acute effect on the association between ambient air pollution and health effects.

In conclusion, this paper evaluated short-term effects of air pollution on infant mortality from all-cause or SIDS. Although the findings were not statistically significant, we observed the associations were positive which meant air pollution might be a risk factor for early death among infants. We also evaluated the associations separately by birth orders of postneonates. These findings may imply that effective risk management strategies should be applied to minimize the public health impacts for infants.

**Acknowledgements**

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**Abbreviations**

| CI | Confidence interval |

**References**


