Indoor Exposure to Particulate Matter and Age at First Acute Lower Respiratory Infection in a Low-Income Urban Community in Bangladesh


* Correspondence to Dr. Emily S. Gurley, Centre for Communicable Diseases, International Centre for Diarrhoeal Disease Research, Bangladesh, 68 Shaheed Tajuddin Ahmed Sarani, Mohakhali, Dhaka-1212, Bangladesh (e-mail: egurley@icddrb.org).

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The timing of a child’s first acute lower respiratory infection (ALRI) is important, because the younger a child is when he or she experiences ALRI, the greater the risk of death. Indoor exposure to particulate matter less than or equal to 2.5 µm in diameter (PM2.5) has been associated with increased frequency of ALRI, but little is known about how it may affect the timing of a child’s first ALRI. In this study, we aimed to estimate the association between a child’s age at first ALRI and indoor exposure to PM2.5 in a low-income community in Dhaka, Bangladesh. We followed 257 children from birth through age 2 years to record their age at first ALRI. Between May 2009 and April 2010, we also measured indoor concentrations of PM2.5 in children’s homes. We used generalized gamma distribution models to estimate the relative age at first ALRI associated with the mean number of hours in which PM2.5 concentrations exceeded 100 µg/m3. Each hour in which PM2.5 levels exceeded 100 µg/m3 was independently associated with a 12% decrease (95% confidence interval: 2%, 21%; P = 0.021) in age at first ALRI. Interventions to reduce indoor exposure to PM2.5 could increase the ages at which children experience their first ALRI in this urban community.

Acute lower respiratory infection; Bangladesh; child health; particulate matter; survival analysis

Abbreviations: ALRI, acute lower respiratory infection; CI, confidence interval; ICDDR,B, International Centre for Diarrhoeal Disease Research, Bangladesh; PM2.5, particulate matter less than or equal to 2.5 µm in diameter.
younger age at first ALRI could lead to interventions to reduce severity of and risk of death from ALRI.

Children in both urban and rural Bangladeshi households are exposed to concentrations of particulate matter inside their homes many times higher than the World Health Organization recommended guideline of <25 μg/m³ (9–12). Indoor exposure to particulate matter has been consistently associated with increased risk of lower respiratory infection in children (13–17). One study from urban Bangladesh showed that infants, in particular, were at increased risk of ALRI from indoor exposure to particulate matter less than or equal to 2.5 μm in diameter (PM$_{2.5}$) (14), but there are no data available on how exposure to PM$_{2.5}$ may affect the timing of a child’s first ALRI. Our objective in this analysis was to estimate the association between indoor PM$_{2.5}$ concentration and age at first ALRI among children under 2 years of age in a low-income, urban cohort in Dhaka, Bangladesh.

METHODS

Enrollment in the birth cohort

Between January 2008 and March 2009, investigators at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) enrolled a cohort of newborns in Mirpur, a densely populated, low-income community in Dhaka (18), to study the etiology of childhood infections and cognitive development (19). The study area comprised approximately 3 km$^2$ with a population of approximately 19,000 persons. All pregnant women in the study area were identified through house-to-house visits, and all women who were planning to reside there for the next 2 years were invited to participate in the study. In exchange for participation, mothers were offered free primary medical care for their children from the study clinic. Mothers of all children enrolled in this birth cohort who were still participating in the study during April 2009 were invited to participate in our study examining the relationship between indoor air pollution and acute respiratory infection (10, 14).

Child follow-up and surveillance for ALRI

A detailed description of the methods used for children’s enrollment and follow-up has been published elsewhere (14). Trained research assistants used standard protocols to measure children’s weight and length within 72 hours of birth and at approximately 3 and 6 months of age. All enrolled children were visited every 3–4 days by trained community health workers for the duration of the study to identify signs and symptoms of illness. Children were referred to the study clinic if they experienced 1 major sign of illness (subjective fever; rapid, labored, or noisy breathing; inability to eat or drink; convulsion; cyanosis) or 2 minor signs (cough; rhinorrhea; sore throat; muscle or joint pain; chills; headache; irritability; repeated vomiting) on the day of the visit (2). Study children lived within approximately 2 km of the study clinic. Pediatricians at the study clinic recorded the symptoms reported by the mother or caretaker and physically examined the children.

An incident of ALRI was defined as an acute respiratory illness observed by the study physician that included either cough or difficult breathing and either age-specific tachypnea or physician-observed chest in-drawing, per criteria proposed by the World Health Organization (20). Tachypnea was defined as a measurement of ≥60 breaths/minute for children aged <2 months, ≥50 breaths/minute for children aged 2–11 months, and ≥40 breaths/minute for children aged 12–23 months (21).

Measurement of household risk factors and indoor particulate matter levels

All children still participating in the birth cohort during April 2009 were eligible to participate in our study of particulate matter exposure and incidence of ALRI. One child was enrolled per household. Every child was visited during May 2009, and characteristics of the household were recorded on a structured questionnaire, as previously described (14). We recorded the type of stove and fuel used in the home, indoor cigarette smoking, the number of people residing in the house, and measures of education and household wealth.

The yearly average concentrations of fine particulate matter in the child’s sleeping space were measured. Typically, the place where the child slept and spent the vast majority of his or her time was also the primary living space for the family. Details on the methods used for measurement of indoor particulate matter concentrations in these households have been published elsewhere (10, 14). In brief, once per month from May 2009 through April 2010, a particulate matter air monitor manufactured by the Berkeley Air Monitoring Group (University of California, Berkeley, California) (10, 22, 23) was placed on the wall approximately 2 feet (0.6 m) above the child’s sleeping space. The monitor logged the average PM$_{2.5}$ concentration in the preceding 60 seconds once per minute for a 24-hour period, following the manufacturer’s instructions. Children who had at least 11 monthly measurements, with at least 1,300 minute readings each, were included in the analysis.

Statistical analyses

We used descriptive statistics to characterize study children and their households. The particulate matter monitors we used had a minimum limit of detection of 50 μg/m³ (24). Therefore, we used threshold metrics to summarize PM$_{2.5}$ concentration measurements from each child’s sleeping space. Specifically, we calculated the mean number of hours for which the PM$_{2.5}$ concentration exceeded 100 μg/m³ (daily hours >100 μg/m³) over the year in which PM$_{2.5}$ concentrations were measured. Although daily hours of a PM$_{2.5}$ level greater than 100 μg/m³ is not a threshold known to be associated with illness, we chose this threshold because it represented twice the limit of detection of the monitors and 4 times the World Health Organization guidelines for mean daily indoor-air particulate matter concentrations (25 μg/m³) (9). We also calculated the mean number of hours in which PM$_{2.5}$ exceeded thresholds of 50 μg/m³ and 250 μg/m³ (5 times the limit of detection) and the time-weighted mean of PM$_{2.5}$ for sensitivity analyses.

The time origin for the survival analysis was birth, the time axis was the age (in months) of the child, and events were defined as the first ALRI. Children were censored from the analysis after their first ALRI or when they reached their second birthday. First, we fitted Kaplan-Meier curves (25) to graph the proportion of children who had not yet experienced their first ALRI over time. To explore whether children’s ages at first development of ALRI differed by particulate matter exposure, we classified children as being exposed either above the median PM$_{2.5}$ concentration (>100 µg/m$^3$ for ≥5.3 hours/day) or below the median PM$_{2.5}$ concentration (>100 µg/m$^3$ for <5.3 hours/day) and fitted Kaplan-Meier curves (25) for each group. We recorded the signs and symptoms children experienced during their first ALRI.

Our primary interest was to quantify the relative time to first ALRI associated with PM$_{2.5}$ exposure rather than the relative hazard. We therefore used the generalized gamma distribution, which is a parametric approach that yields relative times as the measure of association (26). The time axis represented the age of the child, so the relative time measure of association in this model was equivalent to the relative age of children at the first ALRI. An added benefit of using the generalized gamma distribution is that the method does not assume that the ratio of hazards remains constant over time (26). This model was implemented using the streg command in Stata 10 (StataCorp LP, College Station, Texas) (26).

We first estimated the association between exposures and children’s ages at first ALRI in bivariate analyses. We primarily investigated the relationship between the number of hours in which PM$_{2.5}$ levels exceeded 100 µg/m$^3$ and first ALRI. Then, we constructed a multivariate model using hours of PM$_{2.5}$ >100 µg/m$^3$ as the exposure variable and adjusted for potential confounders between the risk of ALRI and particulate matter exposure as described in the meta-analysis by Dherani et al. (27). The potential confounders we considered included socioeconomic status, mother’s education, household crowding, malnutrition, and duration of breastfeeding. Ownership of both a television and a cell phone was used as an indicator of household wealth. We created a dichotomous variable for mother’s education to indicate whether or not the mother had more than an elementary school education. We used the indicator of household wealth and mother’s education as proxies for socioeconomic status. Crowding was represented in the model by the number of persons per square meter of household floor space. Children’s mean weight-for-age $z$ scores observed at birth, 3 months of age, and 6 months of age and the duration of breastfeeding (in months) were included in the model as linear variables. Children who weighed less than 2,500 g when they were enrolled in the study within 72 hours of birth were classified as being low birth weight (28).

Exposure to indoor tobacco smoke and vaccination status were also proposed as possible confounders of the relationship between indoor particulate matter exposure and ALRI (27). Exposure to indoor cigarette smoking was not included in our multivariate model because we considered indoor tobacco smoke to be a contributor to our measurement of PM$_{2.5}$, not a confounder. We did not include vaccination status in the model because coverage for measles, diphtheria, and pertussis vaccines was greater than or equal to 95% among cohort children (Rashidul Haque, ICDDR,B, personal communication, 2011). At the time this study was conducted, neither influenza virus nor pneumococcal vaccine was included in the immunization schedule or available commercially in the local market. Haemophilus influenzae type b vaccines were not included in the immunization schedule but were commercially available in the study community for approximately US$7 per dose (Nadira Sultana Kakoly, ICDDR,B, personal communication, 2011). However, we did not collect information about H. influenzae type b vaccination status from study children.

Sensitivity analyses

To explore the sensitivity of our results to the threshold used in the analysis (mean hours of PM$_{2.5}$ levels >100 µg/m$^3$), we conducted the same multivariate analyses using alternative thresholds (50 µg/m$^3$ and 250 µg/m$^3$). In addition, the same analysis was performed using the time-weighted average of PM$_{2.5}$ concentrations.

Human subject considerations

Prior to enrollment and data collection, mothers provided separate informed consent for their children’s participation in the birth cohort and in the substudy on indoor exposure to particulate matter. The study protocol was reviewed and approved by institutional review boards at the ICDDR,B (Dhaka, Bangladesh); the University of Virginia (Charlottesville, Virginia); Johns Hopkins University (Baltimore, Maryland); and the US Centers for Disease Control and Prevention (Atlanta, Georgia).

RESULTS

A total of 265 children were enrolled in the birth cohort through April 2009. Three children had left the study by April, so 262 children were eligible for the air-quality monitoring study and were enrolled. Complete baseline information and PM$_{2.5}$ measurements were available for 257 (98%) of the 262 children enrolled in the air monitoring study, and these children were included in the analysis (Table 1). Cohort children were between the ages of 1 week and 16 months (median, 9 months) when the air-quality monitoring began. Children were breastfed for a median of 30 months, and 36% had low birth weight (i.e., <2,500 g). The study children lived in crowded conditions, with a median of 1.8 m$^2$ of floor space per person. Six percent of the children’s families burned only biomass (including wood, bamboo, and paper) for cooking, but 52% occasionally burned biomass when their natural gas or electricity supply was interrupted. The median time-weighted average PM$_{2.5}$ concentration in the children’s sleeping spaces was 127 µg/m$^3$ (interquartile range, 88–194). PM$_{2.5}$ concentrations were over 100 µg/m$^3$ for a median of 5.3 hours per day (interquartile range, 4.0–6.9) (Table 1). Results of additional analyses showing the seasonal distribution and primary determinants of PM$_{2.5}$ concentrations in these children’s homes are reported elsewhere (10).

Of the 257 children, 169 (66%) experienced their first ALRI before 2 years of age. Ten percent of the children...
experienced an ALRI by 1.7 months of age, 25% by 3.3 months of age, and 50% by 8.5 months of age (Figure 1). Ninety-three percent (157/169) of the children had physician-observed tachypnea during their first ALRI, and 52% (88/169) had chest in-drawing (Table 2). No hospitalizations or deaths from ALRI were observed among cohort study children.

Children exposed to PM2.5 concentrations above 100 µg/m³ for 5.3 or more hours per day (the median value) experienced their first ALRI at a median of 3.8 months of age. For children exposed to concentrations above 100 µg/m³ for less than 5.3 hours per day, the median age at first ALRI was 8.5 months (Figure 2). In bivariate analyses, each 1-hour increase in the number of hours for which mean PM2.5 concentrations exceeded 100 µg/m³ was associated with a 13% decrease in children’s age at first ALRI (95% confidence interval (95% CI): 4, 21; P = 0.005) (Table 3). Children who lived in households with both a television and a cell phone were 60% older (95% CI: 5, 142; P = 0.028) when they first experienced ALRI than children whose families did not have these assets. In multivariate analysis, each hour that PM2.5 concentrations exceeded 100 µg/m³ was associated with a 12% decrease (95% CI: 2, 21; P = 0.021) in children’s age at first ALRI, after adjustment for potential confounders. Indoor PM2.5 concentration was the only exposure that was independently associated with children’s age at first ALRI (Table 3).

Table 1. Baseline Characteristics of Children Enrolled in the Mirpur Birth Cohort (n = 257) and Their Households, Dhaka, Bangladesh, 2008–2011

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No.</th>
<th>%</th>
<th>Median</th>
<th>Interquartile Rangea</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Child or Mother</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex</td>
<td>137</td>
<td>53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weighed &lt;2,500 g within 72 hours of birth</td>
<td>93</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean weight-for-age z score from birth to age 6 monthsb,c</td>
<td></td>
<td></td>
<td>−1.4</td>
<td>−1.9 to −0.8</td>
</tr>
<tr>
<td>Duration of breastfeeding, months</td>
<td>30</td>
<td>23–35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of exclusive breastfeeding, months</td>
<td>4</td>
<td>2–6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Experienced ALRI during the first 2 years of life</td>
<td>169</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at first ALRI, months</td>
<td>8</td>
<td>3 to &gt;24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highest level of formal education completed by mother</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No formal education</td>
<td>92</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elementary school</td>
<td>92</td>
<td>36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Middle school</td>
<td>69</td>
<td>27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High school</td>
<td>4</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Household</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of household members</td>
<td>5</td>
<td>4–6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Living space floor area, m²</td>
<td>9.6</td>
<td>7.8–11.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of people per m² of floor space</td>
<td>1.8</td>
<td>1.4–2.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of external windows and doors in the home</td>
<td>2</td>
<td>1–3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ownership of a cell phone</td>
<td>173</td>
<td>67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ownership of a television</td>
<td>160</td>
<td>62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cookstove located inside the home</td>
<td>84</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of cooking fuel used in the home</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only clean-burning fuels</td>
<td>107</td>
<td>42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Only biomass fuels</td>
<td>16</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primarily clean fuels but sometimes biomass</td>
<td>134</td>
<td>52</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usually burning kerosene in the home for any purpose</td>
<td>119</td>
<td>46</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tobacco smoking inside the home</td>
<td>72</td>
<td>28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of particulate matter measurements per household</td>
<td>12</td>
<td>11–12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily duration of PM2.5 concentrations &gt;100 µg/m³, hours</td>
<td>5.3</td>
<td>4.0–6.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time-weighted mean PM2.5 concentration, µg/m³b</td>
<td>127</td>
<td>88–194</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ALRI, acute lower respiratory infection; PM2.5, particulate matter less than or equal to 2.5 µm in diameter.

a 25th–75th percentiles.

b The mean value was calculated for each individual; the median value for the entire cohort is presented.

c Normal range for z scores.
Sensitivity analyses showed similar estimates of relative age at first ALRI, regardless of the PM$_{2.5}$ exposure metric used (see Web Tables 1–3, available at http://aje.oxfordjournals.org/).

**DISCUSSION**

Half of all children in this study experienced their first ALRI by 8 months of age, and each hour that PM$_{2.5}$ concentrations exceeded 100 µg/m$^3$ was associated with a 12% decrease in a child’s age at first ALRI. These results suggest that reducing indoor exposure to PM$_{2.5}$ in this low-income urban setting could increase the average age at which children experienced their first ALRI and therefore could decrease the severity of these infections (6–8).

A randomized controlled trial of the introduction of improved cookstoves to reduce indoor exposure to particulate matter in Guatemala found that the intervention was associated with a decrease in the incidence of severe pneumonia episodes but not in the incidence of all pneumonia (29). Our study findings provide one possible explanation for the results of the Guatemala study: The reduction in PM$_{2.5}$ exposure from the intervention may have increased the age at which children first experienced ALRI, reducing the severity but not the incidence of all episodes. Our study findings are limited by our measurements of PM$_{2.5}$ exposure. Children were enrolled as they were born into the community from January 2008 through April 2009, but our measurements of particulate matter did not begin until May 2009. Therefore, our exposure measurements did not temporally overlap with the time at which most children experienced their first ALRI. Rather than a time-varying measure of exposure to PM$_{2.5}$ in the home, our measurements were combined into a crude, yearly average metric of PM$_{2.5}$ concentrations in children’s homes. Nevertheless, we observed a strong association between PM$_{2.5}$ exposure and age at first ALRI, and since we do not suspect that our misclassification of children’s exposure was related to our measurement of age at first ALRI, the magnitude of the true effect may be higher than what we report (30). In addition, the threshold cutoff we used (100 µg/m$^3$) was arbitrary; however, it was preferable to time-weighted average measurements because of the lower limit of detection of our monitors. Despite these limitations in our measurements, they are probably more useful than other proxy measurements of PM$_{2.5}$ exposure in this community, considering that PM$_{2.5}$ concentrations were high in these households, even for homes that used electric...
or natural gas cookstoves. Previous analyses suggested that sources external to the household, such as smoke from neighbors’ homes or ambient pollution (10, 31), could be contributing to exposure in these homes.

We defined ALRI according to criteria suggested by the World Health Organization, based on clinical assessments conducted by study physicians when children appeared at the study clinic for care. This definition is useful because it means that our results are comparable to those of other studies in low-income settings where these clinical criteria are most frequently used. Children in our cohort were visited frequently in their homes to identify the onset of respiratory symptoms and were quickly referred to free, high-quality medical care at the nearby study clinic. This study design is a strength for measuring age at first ALRI because it can be effective in increasing the age at which children experience their first ALRI in this and similar communities. This could, in turn, reduce the severity of first ALRI in the age group most likely to die from these infections (5, 7, 8).

Efforts to reduce reliance on biomass burning may improve indoor air quality in many households, but interventions to reduce particulate matter exposure in households that use cleaner-burning fuels also deserve further investigation.

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Author affiliations: Centre for Communicable Diseases, International Centre for Diarrhoeal Disease Research, Bangladesh, Dhaka, Bangladesh (Emily S. Gurley, Nusrat Homaira, Rashidul Haque, Stephen P. Luby, Eduardo Azziz-Baumgartner); Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Emily S. Gurley, Henrik Salje, William J. Moss); Department of Environmental Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland (Patrick Bryssete); Department of Social and Preventive Medicine, School of Public Health and Health

Proffessions, University at Buffalo, State University of New York, Buffalo, New York (Pavani K. Ram); Departments of Microbiology and Pathology, School of Medicine, University of Virginia, Charlottesville, Virginia (William A. Petri, Jr.); Influenza Division, Centers for Disease Control and Prevention, US Department of Health and Human Services, Atlanta, Georgia (Joseph Bresee, Eduardo Azizz-Baumgartner); and Global Disease Detection Branch, Centers for Disease Control and Prevention, US Department of Health and Human Services, Atlanta, Georgia (Stephen P. Luby).

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Conflict of interest: none declared.

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