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Factors Associated with Severe Disease in a Population of Asthmatic Children of Bogota, Colombia

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Background. There is evidence that prevalence and severity of asthma in children has risen. Risk factors for severe asthma have been studied extensively in children living in developed countries, but little is known about factors determining the severity of asthma in Latin American countries. The aim of this study was to investigate the role of suspected, potential risk factors for asthma severity in a population of children living in urban Bogota. Methods. We studied 175 children, 2 to 16 years old, with asthma attending an asthma clinic. Severe cases and nonsevere asthmatic subjects were compared regarding suspected, potential pre-, peri-, and postnatal risk factors. Results. After controlling for asthma duration, we found that children never breast fed (OR, 11.53; 95% CI, 2.35–56.50; p = 0.003), mothers 30 years or younger at the child’s birth (OR, 3.44; 95% CI, 1.23–9.63; p = 0.019), usual use of acetaminophen for fever in the child in the 12 months previous to the survey application (OR, 3.13; 95% CI, 1.14–8.56; p = 0.026), older siblings at birth (OR, 3.81; 95% CI, 1.28–11.32; p = 0.016), and primary or secondary school as the highest level of education attained by mother (OR, 3.20; 95% CI, 1.01–10.07; p = 0.046) were all independent predictors of severe asthma. Conclusion. No breastfeeding, maternal age at child’s birth of less than 30 years, routine use of acetaminophen for fever in the child in the 12 months previous to the survey application, older siblings at birth, and primary or secondary school as the highest level of education attained by mother were independent predictors of severe asthma. Some of these risk factors are clearly modifiable. Further prospective, population-based studies with a bigger sample size and a more representative sample of the general population residing in the city are needed to retest and clarify these associations.

Keywords risk factors, asthma, asthma severity, childhood asthma, developing countries, Colombia

INTRODUCTION

Childhood asthma is a major public health problem in the United States as well as in many other countries, as Colombia (1, 2) Although only a small minority of asthmatic patients have severe disease, it has a profound impact on health status, and accounts for more than 50% of direct and indirect cost of the disease (3). What determines severity of illness is not very clear. It has been suggested that development of asthma and its severity are determined by genetic predisposition and environmental factors (4, 5). A number of epidemiologic studies have identified potential risk factors for severe asthma, including previous hospitalizations due to asthma, frequent respiratory infections, male gender, family history of asthma, passive smoke exposure, presence of household pets (6), onset of illness before 48 months of age (5), positive skin tests, airways responsiveness to exercise (7), sensitization to house-dust mite, pets, and cockroaches (8), aspirin intolerance, asthma duration exceeding 10 years (9), current keeping of either pets or rugs/carpet, current high-risk occupations (10), counts of peripheral eosinophils (11), African-American ethnicity, and decreased forced expiratory volume in one-second/forced vital capacity (FEV1/FVC) (12).

While the causes of the worldwide increases in asthma and allergic diseases in childhood are not known with certainty, some evidence supports a connection with factors related to modernization and prosperity (13). One potential avenue of research is to study such risk factors for asthma in countries in the midst of the process of modernization. Colombia is representative of such countries; its economy has been on a recovery trend during the last few years despite a serious armed conflict (gross domestic product, real growth rate: 3.6%; 2004 estimate) (14). The economy continues to improve in all sectors, with the volatility of the coffee market determining the relative strength of each. Today Bogota is one of the fastest growing metropolitan areas, not only in Colombia, but also in South America. Further, although childhood asthma is a major public health problem in many South American countries, little is known about the factors that may influence the severity of asthma in these countries, including Colombia. Risk factors in Colombia may teach us something about asthma pathogenesis and may provide data to support regional interventions to improve asthma control for Colombia and other South American nations.

The aim of this study was to investigate the role of suspected, potential risk factors for asthma severity in a population of children living in urban Bogota.

METHODS

Study Site

Bogota, the capital city of Colombia, is located at an elevation of about 2650 m. (8660 ft.) on a mountain-rimmed plateau high in the Cordillera Oriental of the Andes Mountains and lies only 4°36’ north of the equator. Its average...
annual temperature is 14.8°C, with daily variations that range between 1 and 26°C. The average annual precipitation in the city is about 672 mm and average annual wind speed is 1.5 m/s. Two main seasons are recognized in the city: the dry season, running from December to March and from June to August; and the rainy season, running from March to May and from September to November approximately. Yearly emissions by fixed sources of air pollution in Bogota amount to about 2.198 tons of dust, 6.503 tons of SO2, and 1.687 tons of NO2. Industrial kilns and furnaces represent 75% of fixed sources of air pollution. The technological deficiencies of small and medium industrial enterprises have been associated with high levels of industrial pollution in the city (15).

**Study Population and Procedures**

The study examined a consecutive sample of pediatric patients between 2 and 16 years of age with asthma attending an asthma clinic and education program in Bogota, Colombia, over a six-month period between May and November 2005. Children less than four years of age were eligible if they met the stringent definition of asthma from the Asthma Predictive Index (16). This stringent definition of asthma yielded a sensitivity from 14.8% to 27.5%, and a specificity from 96.1% to 97% for the prediction of active asthma at different school ages (16). Older children and adolescents were eligible if they had typical symptoms of asthma, including cough, wheezing, chest tightness, and shortness of breath, and evidence of an increase of 12% or more in forced expiratory volume in one second (FEV1) after bronchodilator medication. All patients were diagnosed as having asthma by a pediatric pulmonologist, based on the above-mentioned criteria. All parents or guardians provided informed consent prior to enrollment in the study. The study was approved by the local ethics board.

The parents or guardians of participating children completed a questionnaire regarding demographics, current child’s asthma medication use, medication compliance, and potential risk factors for severe asthma. To collect current child’s asthma medication use as accurately and consistently as possible, parents were asked to bring the medications to their study visit. Parent-reported medication doses, frequency, and routes of administration were summarized as appropriate maintenance treatment for each level of asthma severity (i.e., mild intermittent, mild persistent, moderate persistent, and severe persistent asthma).

In order to determine the symptom components of the Global Initiative for Asthma (GINA) severity scale, parents ranked responses to questions such as: “In the past 6 months, how often, on average, has your child had a dry cough, wheezing or whistling in the chest at night, apart from a cough associated with a cold or chest infection?” on a 4-point ordinal scale, with 1 corresponding to “not more than twice a month,” 2 corresponding to “more than twice a month, but less than once a week,” 3 corresponding to “more than once a week,” and 4 corresponding to “frequently.”

The combination of the subjective report of current daytime and nighttime symptoms and the current maintenance treatment step were used to establish the patient’s asthma severity (17). So, a patient with ongoing symptoms of mild persistent asthma present before treatment was begun was regarded as having mild persistent asthma, but the same patient being on the appropriate maintenance treatment for this step was regarded as having moderate persistent asthma. Similarly, a patient with ongoing symptoms of moderate persistent asthma present before treatment was begun was regarded as having moderate persistent asthma, but the same patient being on the appropriate maintenance treatment for this step was regarded as having severe persistent asthma. While spirometric measures can also be used to assign severity level, they were not included in our assessment of asthma severity because not all small children can easily perform spirometry. Before analysis, the responses were assigned to 1 of 4 asthma severity categories (mild intermittent, mild persistent, moderate persistent, and severe persistent asthma).

Potential risk factors for severe asthma were chosen a priori, and many of them were evaluated in the same standardized way as they are evaluated in the International Study of Asthma and Allergies in Childhood (ISAAC) (1). Questions regarding pre- and perinatal exposures included maternal smoking during pregnancy (yes or no), birth weight (<2500 vs. >2500 g), child ever breastfed (yes or no), family history of asthma and allergies, and maternal age at the child’s birth (30 years of age or younger vs. 31 years of age or older).

Postnatal variables included the presence of allergic rhinitis (yes or no), usual use of acetaminophen in the first 12 months of the child’s life for fever (yes or no), usual use of acetaminophen for fever in the child in the 12 months previous to the survey application (yes or no), use of any antibiotics in the first 12 months of the child’s life (yes or no), dog or cat ownership during the first year of the child’s life (yes or no), dog or cat ownership in the 12 months previous to the survey application (yes or no), number of older siblings at birth (0 vs. 1 or more older siblings), highest level of education attained by mother (primary or secondary school vs. college, university, or other form of tertiary education), exposure to maternal smoking during the child’s first year of life (yes or no), exposure to maternal or female guardian smoking (yes or no), exposure to paternal or male guardian smoking (yes or no), traffic density on street of residence (trucks pass through the street where the child lives on weekdays never or seldom vs. frequently through the day or almost the whole day), age of illness onset (before 48 months or after 48 months of age), and asthma duration (less than two years vs. more than two years). Values for maternal age at the child’s birth, age of illness onset, and asthma duration were dichotomized according to the median values. Severe cases and nonsevere asthmatic subjects were compared regarding all these potential risk factors.

**Statistical Methods**

The analytic strategy involved several steps. First, a bivariate analysis was conducted to assess the association between severe asthma with predictor variables using contingency tables and the chi-square test or Fisher’s exact test, depending on sample size. Variables showing strong associations in the bivariate analysis (defined by a p-value < 0.20) were selected to be included in a multivariate analysis logistic regression model. The alpha level of 0.20 was chosen to reduce the likelihood of missing important predictors whose bivariate relationship with the outcome is confounded.
FACTORS ASSOCIATED WITH SEVERE ASTHMA

by other variables (18). From prior research, we know that the relation between breastfeeding and childhood asthma may be altered by the presence of maternal asthma (19). Therefore, to determine whether the presence of maternal asthma modified the association between breastfeeding and asthma severity, we compared logistic regression models with and without an interaction term between maternal asthma and breastfeeding, using likelihood ratio tests. The goodness of fit of the logistic regression models was assessed by using the Hosmer-Lemeshow statistic (20). All statistical tests were two-tailed, and the significance level used was 0.05. The data were analyzed with the Statistical Package Stata 8.0 (Stata Corporation, College Station, Texas, USA).

RESULTS

Of the total number of children ever coming to the asthma clinic (n = 1832), a total of 414 subjects were screened in the clinic during the study period; of these subjects, only 178 (43%) met our eligibility criteria, and 175 (98.3%) were enrolled in the study (Figure 1). Of the remaining 236 patients, the majority were excluded because they didn’t meet the stringent definition of asthma from the Asthma Predictive Index, or because they didn’t have evidence of an increase of 12% or more in FEV1 after bronchodilator medication. A total of three patients were not enrolled because they declined to complete the questionnaires. Of the study participants, 104 (59.4%) were male and 71 (40.6%) were females. The mean age ± standard deviation (SD) of the study subjects was 5.2 ± 3.4 years, and it was not significantly different in patients with severe asthma compared with patients with nonsevere asthma (5.8 ± 3.6 vs. 5.1 ± 3.3 years; p = 0.42). The study participants had a history of asthma symptoms for an average of 42 months (range, 2–178). Sixteen percent (n = 28) of the subjects had severe persistent asthma.

Detailed frequencies of exposures in both severe and non-severe asthmatic children according to pre-, peri-, and post-natal variables are shown in Tables 1 and 2. The majority of these associations are self-explanatory. However, some deserve special attention. Children never breastfed, mothers 30 years or younger at the child’s birth, routine use of acetaminophen for fever in the child in the 12 months previous to the survey application, older siblings at birth, primary or secondary school as the highest level of education attained by mother, and asthma duration of less than two years were all significantly associated with severe asthma. No statistically significant differences in paternal or maternal history of asthma and allergies, exposure to maternal or paternal smoking, and age of illness onset were found between subjects with and without severe asthma (Tables 1 and 2).

Predictor variables that were associated with severe asthma in the bivariate analysis at a p-value of less than 0.2 were examined in multivariate analysis. After controlling for asthma duration, we found that children never breastfed, mothers 30 years or younger at the child’s birth, usual use of acetaminophen for fever in the child in the 12 months previous to the survey application, older siblings at birth, and primary or secondary school as the highest level of education attained by mother were independent predictors of severe asthma in our sample of patients (Table 3). Children never breastfed (odds ratio [OR], 11.53; 95% confidence interval [CI], 2.35–56.50; p = 0.003) and those with older siblings at birth (OR, 3.81; 95% CI, 1.28–11.32; p = 0.016) remained the strongest predictors associated with severe asthma (Table 3). The other significant associations were mothers 30 years or younger at the child’s birth (OR, 3.44; 95% CI, 1.23–9.63; p = 0.019), usual use of acetaminophen for fever in the child in the 12 months previous to the survey application (OR, 3.13; 95% CI, 1.14–8.56; p = 0.026), and primary or secondary school as the highest level of education attained by mother (OR, 3.20; 95% CI, 1.01–10.07; p = 0.046) (Table 3). After including the interaction term between maternal asthma and breastfeeding, using a log likelihood ratio test (data not shown), it was found that there was no interaction present regarding asthma severity between infant feeding history and presence of maternal asthma (p = 0.46). The Hosmer and Lemeshow goodness-of-fit test showed a significance of 0.15, indicating a good fit of the model.

![Figure 1. Study population.](image-url)
of asthma (26,27) or an increased risk for asthma in atopic
other allergic disease among children (23–25), others have
shown that breastfeeding decreases the risk of asthma and
factors (22).

Patterns associated with different pathogenesis and risk
in childhood is a heterogeneous condition with several dis-

This study is the first to investigate the risk factors as-
sociated with severe asthma in children in Colombia. After
controlling for asthma duration, we found that children never
breasted, mothers 30 years or younger at the child’s birth,
usual use of acetaminophen for fever in the child in the 12
months previous to the survey application, one or more older
siblings, and primary or secondary school as the highest level
of education attained by the mother, were independent predic-
tors of severe asthma in our sample of patients. Although the
observed associations differ from those obtained in previous
studies, our findings strengthen the hypothesis that wheezing
in childhood is a heterogeneous condition with several dis-

tinct patterns associated with different pathogenesis and risk
factors (22).

The relationship between infant feeding practices and
childhood asthma is conflicting. While some studies have
shown that breastfeeding decreases the risk of asthma and
other allergic disease among children (23–25), others have
found no significant relation between infant feeding and risk
of asthma (26,27) or an increased risk for asthma in atopic
children with asthmatic mothers (19). Probably, these con-
flicting findings are due, in part, to differences in study de-
signs, analytical methods, study populations, and possible
biases between studies. For example, Wright and colleagues
found that while in the first years of life, longer exclusive
breastfeeding was associated with lower rates of recurrent
wheeze, regardless of both maternal asthma status and atopy
in the child. It was associated with an increased risk of both
asthma and recurrent wheeze at 6–13 years of age but only in
atopic children of asthmatic mothers (19). Further, they didn’t
find a relation between asthma and infant feeding in children
with nonasthmatic mothers or in those who were themselves
nonatopic (19). Although we assessed a different main out-
come, and a broad range of ages, our findings agree with
that of others that suggest that breastfeeding has a protective
effect against asthma. It is reasonable to speculate that hu-
man milk may confer a protective effect on the development
of severe asthma. This protective effect may be mediated by
several mechanisms, including: the effect of human breast
milk in reducing both exposure and intestinal absorption of
antigenic substances (due to the immunological components
of human breast milk, such as secretory IgA (28), and by
exclusion, of ingestion of milk other than breast milk and its
potentially allergenic components from the infant’s diet [25]);
the promotion of maturation of infant immune competence
due to its specific immunomodulatory, immunoregulatory,
anti-inflammatory, and nutritional factors (29); and its pro-
tective effect against the occurrence of many illnesses in infancy.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Severe asthma (n = 28)</th>
<th>Nonsevere asthma (n = 147)</th>
<th>OR (95% CI)</th>
<th>Significance (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal smoking</td>
<td>0 (0%)</td>
<td>2 (1.4%)</td>
<td>—</td>
<td>1.00</td>
</tr>
<tr>
<td>Birth weight &lt;2500 g</td>
<td>1 (3.6%)</td>
<td>14 (9.5%)</td>
<td>0.32 (0.04–2.55)</td>
<td>0.467</td>
</tr>
<tr>
<td>Maternal history of asthma/allergies</td>
<td>6 (21.4%)</td>
<td>28 (19.0%)</td>
<td>1.13 (0.42–3.05)</td>
<td>0.309</td>
</tr>
<tr>
<td>Paternal history of asthma/allergies</td>
<td>5 (17.9%)</td>
<td>21 (14.3%)</td>
<td>1.27 (0.43–3.72)</td>
<td>0.773</td>
</tr>
<tr>
<td>Maternal age at child’s birth &lt;30 years</td>
<td>19 (67.9%)</td>
<td>70 (47.6%)</td>
<td>2.23 (0.94–5.62)</td>
<td>0.062</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.

*During pregnancy.

DISCUSSION

There are very few studies on asthma in Colombia com-
pared with the huge body of information from the developed
countries. The rise in asthma prevalence, morbidity, and mor-
tality over the past three decades has been well documented
(21). Prediction of childhood severe asthma is important and
early prevention strategies should be targeted at those most
at-risk.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Severe asthma (n = 28)</th>
<th>Nonsevere asthma (n = 147)</th>
<th>OR (95% CI)</th>
<th>Significance (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No breastfeeding</td>
<td>4 (14.3%)</td>
<td>7 (4.8%)</td>
<td>3.31 (0.90–12.17)</td>
<td>0.079</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>16 (57.1%)</td>
<td>82 (55.8%)</td>
<td>1.05 (0.47–2.39)</td>
<td>0.894</td>
</tr>
<tr>
<td>Usual paracetamol usea</td>
<td>17 (60.7%)</td>
<td>86 (58.5%)</td>
<td>1.09 (0.48–2.50)</td>
<td>0.828</td>
</tr>
<tr>
<td>Usual paracetamol useb</td>
<td>17 (60.7%)</td>
<td>62 (42.2%)</td>
<td>2.09 (0.91–4.78)</td>
<td>0.076</td>
</tr>
<tr>
<td>Antibiotics usea</td>
<td>14 (50.0%)</td>
<td>72 (49.0%)</td>
<td>1.02 (0.46–2.31)</td>
<td>0.947</td>
</tr>
<tr>
<td>Dog ownershipa</td>
<td>4 (14.3%)</td>
<td>26 (17.5%)</td>
<td>0.76 (0.24–2.38)</td>
<td>0.789</td>
</tr>
<tr>
<td>Cat ownershipa</td>
<td>0 (0%)</td>
<td>5 (3.4%)</td>
<td>—</td>
<td>1.00</td>
</tr>
<tr>
<td>Dog ownershipb</td>
<td>7 (25.0%)</td>
<td>25 (17.0%)</td>
<td>1.62 (0.62–4.23)</td>
<td>0.316</td>
</tr>
<tr>
<td>Cat ownershipb</td>
<td>0 (0%)</td>
<td>3 (2.0%)</td>
<td>—</td>
<td>1.00</td>
</tr>
<tr>
<td>Older siblings at birth</td>
<td>19 (67.9%)</td>
<td>64 (43.5%)</td>
<td>2.73 (1.16–6.45)</td>
<td>0.018</td>
</tr>
<tr>
<td>Primary or secondary schoolc</td>
<td>8 (28.6%)</td>
<td>16 (10.9%)</td>
<td>3.27 (1.24–8.64)</td>
<td>0.013</td>
</tr>
<tr>
<td>Maternal smoking</td>
<td>2 (7.1%)</td>
<td>14 (9.5%)</td>
<td>0.72 (0.15–3.38)</td>
<td>1.00</td>
</tr>
<tr>
<td>Maternal smoking</td>
<td>2 (7.1%)</td>
<td>12 (8.2%)</td>
<td>0.86 (0.18–4.09)</td>
<td>1.00</td>
</tr>
<tr>
<td>Paternal smoking</td>
<td>6 (21.4%)</td>
<td>25 (17.0%)</td>
<td>1.36 (0.49–3.71)</td>
<td>0.547</td>
</tr>
<tr>
<td>Frequently trucks passed</td>
<td>17 (60.7%)</td>
<td>88 (59.9%)</td>
<td>1.03 (0.45–2.36)</td>
<td>0.935</td>
</tr>
<tr>
<td>Asthma onset before 2 years</td>
<td>19 (67.9%)</td>
<td>98 (66.7%)</td>
<td>1.48 (0.56–3.97)</td>
<td>0.427</td>
</tr>
<tr>
<td>Asthma duration less than 2 years</td>
<td>7 (25.0%)</td>
<td>69 (47.0%)</td>
<td>0.42 (0.16–1.07)</td>
<td>0.065</td>
</tr>
</tbody>
</table>

OR, odds ratio; CI, confidence interval.

*During first year of child’s life.

**In 12 months previous to survey application.

*Level of education attained by the mother.

^Through street where child lives.
including lower respiratory tract infections (30). The lack of a significant interaction regarding asthma severity between infant feeding history and presence of maternal asthma in our study is possibly due to the broad range of ages included in our study; while breastfeeding is associated with lower rates of recurrent wheeze in early life, its direct association with later asthma in children of asthmatic mothers has been seen only for allergic asthma (19). Alternative explanations for this lack of significant interaction is that our study employed a different main outcome (i.e., severe asthma) and was underpowered to detect such interaction effect.

Data regarding socioeconomic factors that contribute to asthma morbidity and mortality are conflicting and relatively poorly understood. Socioeconomic status (SES) may be a surrogate measure for the lifestyle characteristics rather than a risk factor. Studies of the relationship between SES and health have shown that SES is multidimensional, incorporating elements of occupational characteristics, education, income, wealth, and residential characteristics (31). There is evidence that improved education levels, increased contraceptive use, and changed family patterns have resulted in more children being born into smaller families or to mothers who typically do not breastfeed (32). The hygiene hypothesis, first articulated in 1976 (33), has, for the last decade, provided a link between epidemiological and immunological observations of atopy, atopic disease, and less consistently asthma. The immunological basis for the hypothesis rests on the concept of immune deviation in early life toward Th1 immune responses encouraged by microbial exposure with Th1 responses, suppressing Th2 responses and IgE production. It has been suggested that infections in early life, associated with larger family size and lower SES, selectively enhances differentiation of T helper cells to the Th1 subtype with resultant suppression of the Th2 subtype, thereby reducing the likelihood of allergy and asthma (34). However, some studies have provided conflicting results on this relationship between early infection and asthma, and not all published data support this hypothesis (35, 36). Explanations for these conflicting results might be the different nature of the infections (37), exposure to other infections, the stage of the immunological development, the timing of the effect of large family size (infant or childhood stage) (36), host characteristics (38), airway size, congenital and acquired dysregulation of airway tone, and altered immune responses to viral infection (39).

In contrast to studies of asthma or wheeze prevalence, studies of severe asthma have consistently shown this presentation of the disease to be more common among low-income or socially deprived groups (40–42). This relationship may be mediated by several mechanisms, including frequent or more severe respiratory infections associated with crowded homes, environmental tobacco smoke, indoor pollution, financial access barriers to good preventive care, under-recognition and consequent undertreatment of asthma (43), and the fact that a young child’s exposure to other children in or out of the home leads to more frequent wheezing during the first years of life (44). Our findings about older siblings at birth and primary or secondary school as the highest level of education attained by the mother as independent predictors of severe asthma agree with these previous studies support the concept that social class, and probably family size, may have a greater effect on severity than on prevalence, as severe asthma is positively associated with lower SES, whereas overall asthma prevalence is greater in higher social classes (40).

Children who usually received acetaminophen for fever in the 12 months previous to the survey application had three times higher odds of having severe asthma than children not using acetaminophen within the 12 months previous to the survey. It has been speculated that frequent use of acetaminophen might influence asthma and rhinitis by depleting levels of reduced glutathione in the nose and airways, thus shifting the oxidant/antioxidant balance in favor of oxidative stress and increasing inflammation (45). It is believed that such a mechanism is plausible for two reasons. First, there are clues that glutathione plays a role in asthma. In adults, airway levels of total and oxidized glutathione are increased in stable asthma (46, 47) and levels of reduced glutathione are decreased in acute asthma (48), indicating a response to oxidative stress. Second, studies in animals and in humans have found that clinically relevant concentrations of acetaminophen deplete glutathione in alveolar macrophages and type 2 pneumocytes in rats and in human pulmonary macrophages (49, 50). These effects in macrophages raise the possibility that acetaminophen might also influence atopic diseases more generally through another mechanism, namely the promotion of atopy, since depletion of glutathione in antigen-presenting cells promotes T helper cell 2-type cytokine responses (51). Our findings with regard to frequent use of acetaminophen and severe asthma may be due to this reduction in the lung of the antioxidant glutathione, increasing inflammation. However, in interpreting this, one important issue to consider is reverse causation; since atopic disorders cause respiratory symptoms, which might be confused with or complicated by infection and fever, established atopic disease could predispose children to treatment with acetaminophen.

A number of studies have shown associations between maternal age and respiratory morbidity in children. Younger mothers are more likely to have children who develop wheezing illnesses in early life, asthma, or other respiratory diseases (52). Both social and biological factors related to maternal age may explain this relationship (52). Maternal age could be a proxy for some unknown social or environmental factors, such as nutrition, poverty, level of education, family support, knowledge about child development and appropriate parenting practices, quality of care for children during early infancy, or quality of the house or health status of the mother, among others (52, 53). Younger mothers may also take less care of themselves during pregnancy and may be more prone to medical complications, including poor maternal weight gain,
anemia, and pregnancy-induced hypertension, increasing the level of stress of the fetus (52, 53). Fetal stress that persists for prolonged periods of time is associated with increased endogenous cortisol secretion (52, 54); antenatal corticoids can arrest alveolarization in animals that initiate alveolarization before birth and has been shown to depress lung growth (55). Martinez and colleagues (56) suggested that smaller airways could predispose to wheezing during respiratory tract infections, as they have shown that infants who subsequently had wheezing lower respiratory tract illness had diminished lung function before any lower respiratory tract illness developed. It is thus possible that factors associated with younger maternal age may affect lung development in the children of younger mothers and predispose them to develop more severe wheezing lower respiratory tract infections during infancy. Our findings about mothers 30 years or younger at the child’s birth as an independent predictor of severe asthma support these hypotheses and agree with previous studies that have shown that children born to younger mothers are at higher risk for wheezing or asthma (52, 57).

The primary limitations of this study are inherent in its design. There is a risk of recall error or bias because of the relatively remote nature of the antecedent events. However, given our current results, only acetaminophen use is likely to be confounded by recall bias. This bias is unlikely to have occurred for the other predictor variables (mother’s age at the child’s birth, presence of older siblings at birth, and the highest level of education attained by the mother). Likewise, there is a risk of reverse causation because established atopic disease could predispose children to treatment with acetaminophen. Again, given our current results, only acetaminophen use is likely to be confounded by reverse causation, and this issue is unlikely to have occurred for the other predictor variables. Moreover, the fact that asthma severity classification was based solely on parental recollection of symptom frequency, and current child’s medication use, not taking into account the contribution of pulmonary function testing, could have underestimated the actual asthma severity of the included patients (58). Another important limitation of the study is the fact that the study population comprised a small sample of pediatric patients attending an asthma clinic, so it may not be representative of the whole population of the city, decreasing the generalizability of the findings. Moreover, as is the case in other observational epidemiologic studies, residual confounding cannot be excluded, so interpretation of our results needs to be cautious.

CONCLUSION

In summary, in Bogota, Colombia, a developing Latin American country, among a population of asthmatic children, children never breastfed, mothers 30 years or younger at the child’s birth, usual use of acetaminophen for fever in the child in the 12 months previous to the survey application, older siblings at birth, and primary or secondary school as the highest level of education attained by the mother were independent predictors of severe asthma. Some of these risk factors are clearly modifiable. Further prospective, population-based studies with a bigger sample size and a more representative sample of the general population residing in the city are needed to retest and clarify these associations.

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