

CORRESPONDENCE

Environmental factors independently associated with the first episode of wheezing among children

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To the Editor,

Acute respiratory infections (ARI), mainly attributable to respiratory viruses, are very common among young children when the frequency increases steeply from 6 months of age onwards (1). Wheezing is one of the findings during ARI episodes among those patients, and viral infections are recognized as the major cause of acute wheezing illnesses in childhood (2).

Several pre-disposing factors for recurrent wheezing such as exposure to tobacco smoke, pre-maturity or other comorbidity conditions had been identified (2). Due to the paucity of data on the first episode of wheezing among young children, particularly in tropical regions, much on the natural history of wheezing remains to be learned, including the age and the associated factors. We aimed to detect associated factors with the first episode of wheezing among children aged 6–23 months with ARI.

This was a prospective cross-sectional investigation carried out from September 2009 to June 2011, at the emergency room of the Federal University of Bahia hospital, in Salvador, Northeast Brazil. Patients are brought to this setting on their own, and not by referral. As the central hypothesis was that environmental factors were associated with the first episode of wheezing, those aged under 6 months were excluded because of lesser frequency of wheezing in this age group and shorter exposure to those factors.

Inclusion criteria comprised fever, sneeze, running nose, nasal blockage, or cough for ≤ 7 days and age between 6 and 23 months. Exclusion criteria were transference from other hospital or report of previous episode of wheezing. Parents/legal guardians signed the written informed consent before enrollment, and the study was approved by the ethics research committee.

For data registration, pre-defined forms were used and data on the current illness, obstetric, neonatal, physiologic, personal, and family morbidities, as well as aspects of the environment where the child lives, were asked to the caregiver. Data on physical examination performed by the pediatrician were collected. Patients were examined just after registration of the complaints during medical consultation. Medical students trained for this purpose, under the supervision of a respiratory physiotherapist filled out the pre-defined forms; the physical examination was performed by a pediatrician on duty, and the respective information registered on each medical chart. Data were collected after patient examination and registered on the pre-defined forms by the same student. Physical examinations are standardized in this setting. Nutritional data were evaluated using the software Anthro, version 3.2.2, and severe malnutrition, malnutrition, overweight, and obesity were defined as z-score for weight-for-height index lower than -3,

lower than -2, higher than 2, higher than 3, respectively, according to the WHO standard. Fever was defined as axillary temperature higher than 37.4°C, and tachypnea as respiratory rate (RR) equal or higher than 50 breaths/minute in children aged 6–11 months and RR equal or higher than 40 breaths/minute in children from 12 months of age onwards. Exposure to animals was defined as at least one animal at home where the child lives.

STATA program (version 11.0; Stata Corp, College Station, TX, USA) was used for analysis. The prevalence of the outcome variable (detected wheezing) was estimated along with the respective 95% confidence intervals (95% CI). The frequency of possible associated factors was also calculated. Bivariate and multivariate analyses, using Poisson regression models, with robust variance, were performed to identify possible associations between detected wheezing and the independent variables. Two criteria were used to select variables for the final model: First, p-value ≤ 0.05 in the bivariate analysis and, second, a clear change (10% or more) in the estimates of the effects of the exposures produced by the other variables not selected in the first step of the analysis.

Overall, 451 children were selected, and 170 (37.7%) were excluded: 164 (36.4%) reported previous episode of wheezing, 6 (1.3%) came from other hospital, and 3 (0.7%) reported both. Therefore, 281 (62.3%) children were selected. The median age was 10 months (mean 11.3 ± 4.4), 189 (67.3%) were younger than 1 yr, 40.6% were aged from 6 to 9 months, 140 (49.8%) were males, and 96.1% were born in Salvador (the capital of the Bahia state). In regard to nutritional status, severe malnutrition (0.4%), malnutrition (1.4%), overweight (7.5%), and obesity (2.1%) were detected. Among the mothers, 55.3% spent some time out of home, working or studying, whereas 44.7% stayed at home full time. Most children (94%) were breastfed, and 44.7% were still being breastfed at the time of recruitment. Exposure to cockroaches (68.0%), other insects (mosquitoes and flies though not tested for) (64.4%), house dust (54.1%), mold (27.8%), rats (23.8%), dogs (21.0%), birds (15.3%), cat (6.4%), and chicken (3.9%) at home was reported by parents. This information was given by the caregiver during the interview based on his perception in regard to the environment where the child lives. The child's house was not inspected to search for those animals. No association was found with occurrence of the first episode of wheezing in the multivariate analysis. The baseline characteristics of the study group are described in Table 1. Rhinitis (54.4%), asthma (29.3%), and skin allergy (18.9%) were reported for the family members of the studied patients, for whom rhinitis (8.0%), gastroesophageal reflux disease (7.5%), heart disease, or neurologic disease (2.1% each), sickle cell disease (1.4%),

Table 1 Baseline characteristics of children aged 6–23 months with acute respiratory infection on recruitment

Characteristics	n (%)	Duration (mean $\pm$ SD, min–max)
Current History		
Cough	247 (87.9)	3.7 $\pm$ 1.7, 1–7†
Runny nose	243 (86.5)	3.7 $\pm$ 1.6, 1–7†
Fever	235 (83.9)*	3.1 $\pm$ 1.6, 1–7†
Sneeze	217 (77.2)	3.8 $\pm$ 1.7, 1–7†
Wheezing	124 (44.1)	2.6 $\pm$ 1.7, 1–10†
Hoarseness	77 (27.4)	2.9 $\pm$ 1.7, 1–7†
Dyspnea	68 (24.2)	3.2 $\pm$ 1.8, 1–7†
Vomiting	31 (11.0)	1.9 $\pm$ 1.2, 1–5†
Earache	23 (8.2)*	2 (2, 3), 1–60†‡
Thoracic retraction	19 (6.8)	3.2 $\pm$ 2.1, 1–7†
Diarrhea	8 (2.8)	1.9 $\pm$ 1.2, 1–4†
Eye finding§	7 (2.5)	3.1 $\pm$ 2.5, 1–7†
Ear secretion	7 (2.5)	3.1 $\pm$ 1.5, 2–6†
Cyanosis	3 (1.1)	3 $\pm$ 2, 1–5†
Obstetric History		
Prenatal assistance	271 (96.4)	
C-section	107 (38.1)	
Birth weight $\leq$ 2500 gr	42 (15.3)*	
Disease on birth	56 (19.9)	
Early respiratory distress	24 (8.6)*	
Hospitalization on birth	67 (23.8)	
Pre-maturity	34 (12.1)	
Oxygen use	21 (7.5)*	2.5 (1, 4), 1–60†‡
Cephalic halo	11 (3.9)*	
Mechanical ventilator	9 (3.2)*	
Smoking mother during pregnancy	8 (2.8)	
Smoking mother nowadays	11 (3.9)	
Drug-addicted mother	3 (1.1)	
Flu vaccine during pregnancy	142 (52.4)*	
Physiologic history		
Sitting (month)	259 (92.17)	5.7 $\pm$ 1.2, 3–11¶
Walking (month)	101 (35.94)	10.4 $\pm$ 1.8, 7–16¶
Breastfeeding		
Exclusive	232 (82.9)*	4.8 $\pm$ 2.1, 1–13**
Mixed	161 (57.3)	8.3 $\pm$ 4.2, 5–22**
Child lifestyle		
Shared bed	203 (72.2)	
Someone smokes at home	53 (18.9)	
Absence of ventilation at home	79 (28.1)	

*The denominator was not 281 because data were missing.

†Duration in days.

‡Median (25th percentile, 75th percentile), min–max.

§Eye alteration includes redness, itching, and crying.

¶Age of beginning.

**Duration in months.

bronchopulmonary dysplasia or malformation (0.4% each) were reported.

On physical examination, cough (75.1%), running nose (70.1%), nasal blockage (65.1%), fever (37.1%), tachypnea (28.7%), and red eyes (24.6%) were registered. Nasal itching

(30.6%), swollen eyes (29.6%), hoarseness (17.4%), and thoracic retraction (4.3%) were also observed. On auscultation, ronchi (37.4%) and crackles (7.8%) were identified in addition to wheezing (16.4%; 95% CI: 12.3%–21.3%). Wheezing was detected in 34 (18.0%; 95% CI: 12.9%–24.4%) children aged under 1 yr and in 12 (13.0%; 95% CI: 7.2%–22.1%) aged 1 yr and above.

Significant differences were found in the multivariate analysis when children with and without wheezing on physical examination were compared (Table 2). All other factors were not associated (data not shown). Moreover, there was a strong indication that age is inversely associated with the detection of wheezing: One month increase in age was associated with 6% decrease in detection of wheezing.

In our study, we identified two environmental factors as independently associated with wheezing detected on physical examination: Day care center attendance and the presence of birds at home (Table 2). Although exposure to birds at home is not a well-known associated factor, the preventive measure in such case is not difficult, that is, to keep the birds somewhere outside home and prevent them to enter home. Day care center attendance has been recognized as an associated factor for ARI in several studies (3). When the child gets over 6 months of age, several factors arise to influence the child's susceptibility to infection, such as clearance of maternal antibodies, ending of breastfeeding, contact with other children more frequently when the adaptive immune system is still immature (1). The inverse association between age and auscultation of wheezing may be due to the airway diameter progression during child's growth: Younger the child, narrower the airway physiologically, that is, easier to present additional narrowing to produce the sound of wheezing. Although smoking is a well-known risk factor for respiratory disease, no association was found herein. The low frequency of smoking during the pregnancy (2.8%) and nowadays (3.9%) may have influenced this result.

Respiratory syncytial virus (RSV) has been largely recognized as a common causative pathogen of ARI in which wheezing is present (4). Recently, evidence has been provided on the infection by RSV in the eyes, and the eye use as a gateway to access the lung (5). Therefore, RSV has been established as an etiologic agent of viral conjunctivitis (6). Here, one can question if the independent association between red eye and wheezing was due to possible infection by RSV. A condition that causes increased airway resistance stimulates a compensatory mechanism: The increase in respiratory rate (7). That is why tachypnea and wheezing were found to be associated.

Methodological flaws must be commented: As an observational study conducted in a pediatric hospital, the results may have been biased by parents' behavior in seeking for health assistance and data on etiology are not available. Herein, children younger than 6 months were not studied. Despite the small number of subjects, others have reported a significant association between upper respiratory tract infections in the first 3 months of life and the first episode of wheezing (8).

In conclusion, environmental factors (day care center attendance and birds at home) were identified as associated factors for detected wheezing in this tropical region and preventive measures may derive from them. Younger the child,

Table 2 Comparison of children with acute respiratory infection with or without wheezing detected on physical examination on admission

Characteristics*	Wheezing		Analysis	
	Yes (n = 46)	No (n = 235)	Unadj PR (95% CI)	Adj PR (95% CI)†
History				
Day care center attendance	8 (17.4)	14 (6.0)	2.48 (1.32–4.64)	2.74 (1.49–5.02)
Birds at home	14 (30.4)	29 (12.3)	2.42 (1.41–4.15)	2.56 (1.56–4.20)
Report of wheezing	30 (65.2)	94 (40.0)	2.37 (1.36–4.16)	2.02 (1.16–3.49)
Physical examination				
Tachypnea	18/44 (40.9)‡	60/228 (26.3)‡	1.72 (1.00–2.96)	1.81 (1.07–3.04)
Red eyes	17 (37.0)	52 (22.1)	1.80 (1.06–3.07)	2.23 (1.37–3.65)

*Results in n (%).

†PR adjusted for the other variables of the table and also for age, as continuous variable (Δ_{adj} PR = 0.94, 95% CI: 0.87–1.02).

‡Different denominator due to missing data.

higher is the chance of wheezing. Presence of red eyes was found to be independently associated with the detection of wheezing on physical examination as it is shown in Table 2.

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Appendix

The Acute Respiratory Infection and Wheezing Study Group Phase I (in alphabetical order)

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