Prevalence and risk factors for wheezing in Salvador, Brazil: a population-based study

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Summary

Background: Wheezing is one of the most frequent causes of visit to emergency rooms among children. However, data on wheezing burden are mostly provided at healthcare setting, and particularly only for infants.

Aims: We sought to estimate the prevalence of wheezing in children under 4 years and to assess potential risk factors in the community.

Design: This was a cross-sectional analysis of a population-based cohort study.

Methods: The sample comprised children aged <4 years living in Salvador, Brazil. Data were collected via home visits when the parents/guardians were interviewed. Data were recorded on standardized forms.

Results: Of 1534 children, mean age was 21 ± 14 months (minimum 3 days; maximum 47 months; 6% <2 months); 780 (51%) were males and 501 [33%; 95% confidence interval (95% CI): 30–35%]

reported wheezing in the last 12 months. Among wheezers, 321 (64%) had occasional wheezing. Overall, 180 (12%; 95% CI: 10-14%) had recurrent wheezing and 157 (10%; 95% CI: 9-12%) had asthma. For children in the first, second, third and fourth year of life wheezing was reported in 23, 41, 34 and 37%, respectively. Mother atopic-related disease was independently associated with recurrent wheezing (Adj PR[95% CI]: 1.54 [1.12-2.11]) and asthma (AdiPR[95% CI]: 1.54 [1.10-2.16]). Smoker at home (AdjPR[95% CI]: 1.34 [1.07-1.67]) and low birth weight (AdiPR[95%CI]: 1.38 [1.05-1.81]) were independently associated with occasional wheezing. Conclusions: One-third of under 4 years reported wheezing; history of mother's atopic-related disease was an independent risk factor for recurrent wheezing and asthma; smoker at home and low birth weight were independent risk factors for occasional wheezing.

Introduction

Wheezing is one of the most frequent causes of visit to emergency rooms or primary healthcare settings among children in different continents.¹ It is also a

common cause of hospital admission, particularly during the first year of life.² Recurrent wheezing imposes a high economical cost to the healthcare system³ and negatively impacts upon the quality of

life of patients and their families. Wheezing early in life has been found to predispose to asthma in adolescence and adulthood, being asthma a leading chronic illness with severe consequences for the whole life.

The prevalence of childhood wheezing and associated risk factors has been investigated in several countries. Nonetheless, parents/guardians were mostly interviewed during visits to primary healthcare units or well baby clinics, especially for scheduled immunization or during vaccine campaigns. Therefore, those data somehow depend on the family's behaviour in seeking healthcare assistance: if the family does not go to the healthcare unit or does not take the child to receive vaccine, this child will not be found to be included in the study. Herein, we aimed to estimate the prevalence of wheezing in children aged <4 years in the community and to assess potential risk factors in the city of Salvador, Northeast Brazil.

Methods

This was a cross-sectional analysis of a population-based cohort study. The sample comprised children younger than 4 years living in four neighbourhoods in the city of Salvador, Northeast Brazil, a tropical region. Those neighbourhoods are around the Federal University of Bahia campus, and residents are representative of the rest of the population living in the city of Salvador. The climate in this city is tropical rainforest with no discernible dry season. The temperatures are relatively constant throughout the course of the year, featuring warm and humid conditions.⁸

According to the Local Council's Department of Health in Salvador, there were 2156 children in this age group living in the study area. Sample size calculation considered an estimated prevalence of 20% of one potential risk factor, with an expected difference of this prevalence between the affected and unaffected children equal to 5%, at power = 90% and a 5% two-tailed test. Then, the estimated sample size was 1462 children. Data collection was performed via home visits when the parents/ guardians gave written informed consent and were interviewed by trained medical/pharmacy students in the year 2006. The visited homes were identified in the street map of the four neighbourhoods and were consecutively visited until the sample size was completed. Data were recorded on standardized forms containing identification, socio-demographic and epidemiological information which were entered into EPI INFO and analysed using STATA version 11.0.

Prevalence and the respective 95% confidence interval (95% CI) were estimated. The guestions "Has your child had wheezing or whistling in the chest in the last 12 months?" and "Has your child ever been diagnosed with asthma by a doctor?" were employed. Definitions used were as follows: occasional wheezing (≤2 episodes per year), recurrent wheezing (≥3 episodes per year) and severe recurrent wheezing (>6 episodes per year). Potential risk factors were investigated, and the frequency was calculated. Low birth weight was considered <2500 g. Number of people in the child's bedroom was dichotomized as ≤ 3 or >4. Bivariate and multivariate analyses, using Poisson regression models, with robust variance, were performed to identify possible associations between wheezing and report of asthma diagnosed by physician with 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. The study was approved by the Ethics Committee at the Federal University of Bahia.

Results

Of 1549 evaluated children, 15 (1%) were excluded (1 reported neurological illness, 2 refused to give informed consent, 12 did not inform about wheezing). Therefore, the study group comprised 1534 children who lived in the following neighbourhoods: Alto das Pombas (n = 521; 34%), Nordeste de Amaralina (n=390; 25%), Federação (n=380; 25%) and Garcia (n = 243; 16%). Informant was the mother (77%), grandmother (9%), father (7%) or other family member (7%). There were 780 (51%) males, the mean age was 21 ± 14 months, median age was 20 months, minimum 3 days and maximum 47 months and 6% were younger than 2 months. Running water supply (100%), sewers supply (99%), electricity supply (100%) and regular trash collection (95%) were registered. There was no change in the environment, like the establishment of a smoke-producing factory, during the period considered in the study (12 months before and during recruitment).

Wheezing in the last 12 months was reported for 501 (33%; 95% CI: 30–35%) children, mean number of episodes 3 ± 3 (median 2, variation 1–24). Among wheezers, 321 (64%) had occasional wheezing, 126 (25%) had recurrent wheezing and 54 (11%) had severe recurrent wheezing. Overall, 180 (12%; 95% CI: 10–14%) reported recurrent

Table 1 Prevalence and number of episodes of wheezing by age strata

| Year of life | N | Wheezing in the | Number of episodes | | Wheezing | | |
|--------------|-----------|-----------------|--------------------|--------------------------------|------------|-----------|------------------|
| on interview | | last 12 months | $Mean \pm SD$ | Median $(p^{25th} - p^{75th})$ | Occasional | Recurrent | Severe recurrent |
| First | 513 (34%) | 119 (23%) | 2 ± 3 | 1 (1 – 2) | 94 (18%) | 17 (3%) | 8 (2%) |
| Second | 386 (25%) | 159 (41%) | 3 ± 3 | 2(1-3) | 101 (26%) | 42 (11%) | 16 (4%) |
| Third | 340 (22%) | 115 (34%) | 4 ± 4 | 2(1-4) | 64 (19%) | 35 (10%) | 16 (5%) |
| Fourth | 295 (19%) | 108 (37%) | 3 ± 3 | 2 (1 – 1) | 62 (21%) | 32 (11%) | 14 (5%) |

Total number of children: 1534.

wheezing. Table 1 shows the prevalence of wheezing by age strata. Overall, for children in the first, second, third and fourth year of life wheezing was reported in 23, 41, 34 and 37%, respectively. Children with report of wheezing in the last 12 months were older on recruitment than those without it $(23.5 \pm 13.1 \text{ months vs. } 20.2 \pm 14.6 \text{ months};$ P < 0.001). Report of asthma diagnosed by physician was informed for 157 (10%; 95% CI: 9-12%) children, who were older than non-asthmatic individuals $(26 \pm 13 \text{ months vs. } 21 \pm 14 \text{ months};$ P < 0.001). Table 2 depicts the overall frequency of potential risk factors. Altogether, rhinitis or asthma or bronchitis or eczema was reported for mothers (18%), fathers (13%) and other siblings (14%). Smoker at home, irrespective of who smoked, was reported for 22% (331/1515) households. The comparison of potential risk factors is presented in Table 3. Mother atopic-related disease was independently associated with recurrent wheezing (AdiPR[95% CI]: 1.54 [1.12-2.11]) and asthma (AdiPR[95% CI]: 1.54 [1.10-2.16]). Smoker at home (AdiPR[95% CI]: 1.34 [1.07-1.67]) and low birth weight (AdiPR[95%CI]: 1.38 [1.05-1.81]) were independently associated with occasional wheezing.

Discussion

This study, undertaken in a tropical region of South America, shows that one-third of children under 4 years among those living in an urban area have wheezed at least once in the last 12 months. Overall, approximately one-tenth reported recurrent wheezing or asthma. Report of mother's atopic-related disease was an independent risk factor for recurrent wheezing and asthma, whereas presence of a smoker at home and low birth weight were independent risk factors for occasional wheezing.

Table 2 Overall frequency of potential risk factor for wheezing

| Potential risk factors | Freq | uency |
|--|------|---------|
| Mother's disease (n=1506) | | |
| Rhinitis | 159 | (10.6%) |
| Asthma | 77 | (5.1%) |
| Bronchitis | 21 | (1.4%) |
| Eczema | 6 | (0.4%) |
| Father's disease $(n=1421)$ | | |
| Rhinitis | 109 | (7.7%) |
| Asthma | 55 | (3.9%) |
| Bronchitis | 20 | (1.4%) |
| Eczema | 2 | (0.1%) |
| Siblings' disease $(n = 1224)$ | | |
| Rhinitis | 70 | (5.7%) |
| Asthma | 67 | (5.5%) |
| Bronchitis | 30 | (2.5%) |
| Eczema | 2 | (0.2%) |
| Low birth weight ^a $(n=1468)$ | 161 | (11%) |
| Day care centre attendance | 283 | (18.4%) |
| Other child <5 years old at home | 474 | (30.9%) |
| Number of people in the | 360 | (23.5%) |
| child's bedroom ≥4 | | |
| Mould at home $(n=1531)$ | 628 | (41%) |
| Smoking | | |
| Mother $(n = 1525)$ | 121 | (7.9%) |
| Other person at home $(n=1518)$ | 272 | (17.9%) |
| Mother during pregnancy $(n=1524)$ | 103 | (6.8%) |

^aLow birth weight <2500 g.

The prevalence of wheezing ever was quite similar to the results reported in Tucson (USA) for those aged under 3 years (34%)¹¹ as well as to the results reported from the cities of Zwolle, in The Netherlands (29.5%)¹² and Salamanca in Spain (32.3%),¹³ both estimated among infants during the first year of life. On the contrary, such prevalence was lower than those reported in other studies from other Brazilian cities and from Havana in

Table 3 Comparison of potential risk factors for wheezing, occasional wheezing, recurrent wheezing and asthma

| Characteristics ^a | Wheezing in the last 12 months | last 12 months | Analysis | Asthma | | Analysis |
|---|--|-----------------|----------------------------|--|---------------|----------------------------|
| | Yes $(n = 501)$ | No $(n = 1033)$ | _{Adj} PR (95% CI) | Yes $(n=157)$ | No $(n=1377)$ | _{Adj} PR (95% CI) |
| Age on interview | | | | | | |
| First year of life | 119 (24) | 394 (38) | _ | 29 (19) | 484 (35) | |
| Second year of life | 159 (32) | 227 (22) | 1.94 (1.58–2.37) | 43 (27) | 343 (25) | 2.05 (1.30–3.24) |
| Third year of life | 115 (23) | 225 (22) | 1.50 (1.20–1.89) | 43 (27) | 297 (22) | 2.24 (1.42–3.54) |
| Fourth year of life | 108 (21) | 187 (18) | 1.58 (1.26–1.99) | 42 (27) | 253 (18) | 2.40 (1.51–3.82) |
| Mother's atopic-related disease ^{a,b} | 95/487 (20) | 168/1019 (17) | 1.18 (0.98–1.41) | 38/156 (24) | 225/1350 (17) | 1.54 (1.10–2.16) |
| Smoker at home ^a | 135/492 (27) | 196/1023 (19) | 1.29 (1.10–1.52) | 46/157 (29) | 285/1358 (21) | 1.31 (0.93–1.84) |
| Low birth weight ^a | 63/479 (13) | 98/989 (10) | 1.26 (1.02–1.56) | 21/151 (14) | 140/1317 (11) | 1.31 (0.86–2.02) |
| ≥4 people in the child's bedroom ^a | 137/499 (27) | 223/1033 (22) | 1.17 (0.99–1.38) | 51/157 (32) | 309/1375 (22) | 1.53 (1.10–2.11) |
| Characteristics ^a | Occasional wheezing in the last 12 months | szing in | Analysis | Recurrent wheezing in the last 12 months | ng in S | Analysis |
| | Yes $(n=321)$ | No $(n=1033)$ | _{Adj} PR (95% CI) | Yes $(n=180)$ | No $(n=1033)$ | _{Adj} PR (95% CI) |
| Age on interview | | | | | | |
| First year of life | 94 (29) | 394 (38) | | 25 (14) | 394 (38) | _ |
| Second year of life | 101 (32) | 227 (22) | 1.73 (1.35–2.23) | 58 (32) | 227 (22) | 3.89 (2.44–6.20) |
| Third year of life | 64 (20) | 225 (22) | 1.21 (0.90–1.63) | 51 (28) | 225 (22) | 3.17 (1.95–5.13) |
| Fourth year of life | 62 (19) | 187 (18) | 1.34 (1.00–1.79) | 46 (26) | 187 (18) | 3.14 (1.91–5.15) |
| Mother's atopic disease ^{a,b} | 51/313 (16) | 168/1019 (16) | 1.05 (0.81–1.36) | 44/174 (25) | 168/1019 (17) | 1.54 (1.12–2.11) |
| Smoker at home ^a | 85/314 (27) | 196/1023 (19) | 1.34 (1.07–1.67) | 50/178 (28) | 196/1023 (19) | 1.35 (0.98–1.85) |
| Low birth weight ^a | 44/310 (14) | 98/989 (10) | 1.38 (1.05–1.81) | 19/169 (11) | 98/989 (10) | 1.13 (0.73–1.74) |
| ≥ 4 people in the child's bedroom ^a | 83/319 (26) | 223/1033 (22) | 1.15 (0.92–1.44) | 54/180 (30) | 223/1033 (22) | 1.29 (0.95–1.75) |
| | | | | | | |

Results in n (%). Adj PR, adjusted prevalence ratio. ^aDifferent denominators due to missing data. ^bRhinitis, asthma, bronchitis and eczema.

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Cuba, which ranged from 43 to 45.4% for children attending polyclinics or primary healthcare centres from 12 to 15 months of age. 14-16 Likewise, the reported prevalence of wheezing ever was 45.2% in an international study performed in 17 centres in Latin America and Europe when infants aged 12-15 months had their caregivers interviewed at primary care health clinics. Interestingly, by observing the prevalence of wheezing in the last 12 months stratified by age on interview, we can notice that the prevalence peaked up to 41% for those during the second year of life (Table 1). That is, by employing the question about ever wheezed during the past 12 months for children aged between 12 and 15 months, there is an overestimation for wheezing during the past 12 months.

Overall, 12% had recurrent wheezing in the last 12 months and 10% had asthma diagnosed by a doctor. By stratifying the prevalence of recurrent wheezing by age on interview, it is possible to observe that the prevalence is stable for those over the second, third and fourth year of life (Table 1). This result is also similar to the result found in The Netherlands (14.5%) when parents or caregivers of 13-month-old infants brought their babies for measles-mumps-rubella-vaccine and were interviewed. 12 Again, this finding was much lower (about half) than those reported in other studies when caregivers of children aged between 12 and 15 months were interviewed (range: 20.0-24.8%).^{2,14–16} Therefore, methodological differences may explain those different findings. Conversely, the estimated prevalence of physiciandiagnosed asthma herein was close to data reported from European and Latin American centres (8.5%),² as well as to data from studies in other cities (Curitiba 10.9%¹⁴ and São Paulo 9.1%¹⁷ in Brazil).

Age was different when wheezers were compared with non-wheezers, or when asthmatic children were compared with non-asthmatic ones. In both comparisons, the affected children were older than the non-affected ones. Indeed, the incidence of first wheezing episode declines with age during childhood when a sharp decline from the third year onward was described.⁵ That means, the significant difference in age reported herein looks like paradoxical and limiting age to under 4 years in the inclusion criteria of this investigation may have played a role on this finding. In addition to that, different patterns of wheezing (transient, non-atopic and atopyassociated asthma) can occur early in childhood, 18 which leads to an increasing prevalence of wheezing during early life.

Different independent risk factors were identified for occasional or recurrent wheezing: presence of a smoker at home and low birth weight were risk

factors for occasional wheezing, whereas mother's atopic-related disease was a risk factor for recurrent wheezing (Table 3). Curiously, the risk factor found for recurrent wheezing was the same that was identified for asthma (Table 3). These findings are in agreement with the understanding that wheezing disorders comprise a heterogeneous group of conditions that begin in childhood in most cases.¹⁹ Moreover, asthma has a strong genetic component.¹⁹ History of maternal asthma has been previously identified as an independent predisposing factor towards recurrent wheezing.^{13, 20} Although most asthma starts early in life, no valid test is able to identify asthma in that age period.²¹ Based on the aforementioned findings, it is possible to infer that recurrent wheezing (three or more wheezing episodes) and mother's atopic-related disease may alert to the possibility of asthma among early wheezers.

In conclusion, one-third of under 4 years reported wheezing; history of mother atopic-related disease was an independent risk factor for recurrent wheezing and asthma; presence of smoker at home and low birth weight were independent risk factors for occasional wheezing.

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References

- 1. Bisgaard H, Szefler S. Prevalence of asthma-like symptoms in young children. *Pediatr Pulmonol* 2007; **42**:723–8.
- Mallol J, García-Marcos L, Solé D, Brand P. the EISL Study Group. International prevalence of recurrent wheezing during the first year of life: variability, treatment patterns and use of health resources. *Thorax* 2010; 65:1004–9.

- de Jong BM, van der Ent CK, van Putte Katier N, van der Zalm MM, Verheij TJ, Kimpen JL, et al. Determinants of health care utilization for respiratory symptoms in the first year of life. Med Care 2007; 45:746–52.
- Hafkamp-de Groen E, Mohangoo AD, Landgraf JM, de Jongste JC, Duijts L, Moll HA, et al. The impact of preschool wheezing patterns on health-related quality of life at age 4 years. Eur Respir J 2013; 41:952–9.
- Matricardi PM, Illi S, Grüber C, Keil T, Nickel R, Wahn U, et al. Wheezing in childhood: incidence, longitudinal patterns and factors predicting persistence. Eur Respir J 2008; 32:585–92
- Akinbami LJ, Moorman JE, Bailey C, Zahran HS, King M, Johnson CA, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. NCHS Data Brief 2012; 1–8.
- García-Marcos L, Mallol J, Solé D, Brand PLP. the EISL group. International study of wheezing in infants: risk factors in affluent and non-affluent countries during the first year of life. Pediatr Allergy Immunol 2010; 21:878–88.
- Wikipedia. Salvador, Bahia, Climate. http://www.en.wikipedia.org/wiki/Salvador,_Bahia#Climate (4 August 2014, date last accessed).
- 9. Local Council's Department of Health in Salvador. *Health Information*, 2006. http://www.tabnet.saude.salvador.ba. gov.br/tabcgi.exe?tabpop/populacao.def (9 February 2006, date last accessed).
- Cardoso M-RA, Cousens SN, Siqueira LF, Alves FM, D'Angelo LA. Crowding: risk factor or protective factor for lower respiratory disease in young children? *BMC Public Health* 2004; 4:19.
- 11. Martinez FD. What have we learned from the Tucson Children's Respiratory Study? *Paediatr Respir Rev* 2002; **3**:193–7.

- Visser CA, Garcia-Marcos L, Eggink J, Brand PL. Prevalence and risk factors of wheeze in Dutch infants in their first year of life. *Pediatr Pulmonol* 2010; 45:149–56.
- Pellegrini-Belinchón J, Miguel-Miguel G, De Dios-Martín B, Vicente-Galindo E, Lorente-Toledano F, García-Marcos L. Study of wheezing and its risk factor in the first year of life in the Province of Salamanca, Spain, The EISL Study. *Allergol Immunopathol (Madr)* 2012; 40:164–71.
- Chong Neto HJ, Rosário NA, Solé D, Mallol J. Prevalence of recurrent wheezing in infants. J Pediatr (Rio J) 2007; 83:357–62.
- Medeiros D, Silva AR, Rizzo JÂ, Sarinho E, Mallol J, Solé D. Prevalence of wheezing and associated risk factors among infants in Recife, Pernambuco State, Brazil. Cad Saude Publica 2011; 27:1551–9.
- Venero-Fernández SJ, Suárez-Medina R, Mora-Faife EC, García-García G, Valle-Infante I, Gómez-Marrero L, et al. Risk factors for wheezing in infants born in Cuba. Q J Med 2013; 106:1023–9.
- Sousa CA, César CL, Barros MB, Carandina L, Goldbaum M, Pereira JC. Prevalence of asthma and risk factors associated: population based study in São Paulo, Southeastern Brazil, 2008-2009. Rev Saude Publica 2012; 46:825–33.
- Martinez FD. Development of wheezing disorders and asthma in preschool children. *Pediatrics* 2002; 109(2 Suppl.):362–7.
- 19. Martinez FD, Vercelli D. Asthma. Lancet 2013; 382:1360-72.
- Prietsch SO, Fischer GB, César JA, Cervo PV, Sangaletti LL, Wietzycoski CR, et al. Risk factors for recurrent wheezing in children under 13 years old in the South of Brazil. Rev Panam Salud Pub 2006; 20:331–7.
- 21. Dijk FN, de Jongste JC, Postma DS, Koppelman GH. Genetics of onset of asthma. *Curr Opin Allergy Clin Immunol* 2013; **13**:193–202.