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Epidemiology of wheeze among preschool children: a population-based cross-sectional study from rural Sri Lanka

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ABSTRACT

Objectives To assess the prevalence of wheeze and factors associated with its severity among 3–6 years old children.

Methodology

Design A population-based, cross-sectional study using the WHO 30 cluster methodology with probability proportionate to size sampling.

Setting 36 preschools registered at the divisional secretariat offices of Anuradhapura district, Sri Lanka.

Participants We recruited 1060 preschool children from 36 preschools aged 3–6 years.

Main outcome measurements We used the International Study of Asthma and Allergy in Childhood questionnaire to assess the prevalence, symptomatology and associated factors of wheeze.

Results The study sample consisted of 548 (51.70%) male and 512 (48.30%) female children with a mean age of 4.41 (±0.66) years. At least one wheezing episode ever was reported in 323 (30.47%; 95% CI 27.71% to 33.34%) children and 247 (23.30%; 95% CI 20.79% to 25.97%) children had a wheezing attack in the preceding year. Severe episodes of wheezing were reported in 76 (7.17%; 95% CI 5.69% to 8.89%) participants. However, only 27 (35.53%; 95% CI 24.88% to 47.34%) children with severe wheezing had been diagnosed as asthmatics by a clinician. The identified independent risk factors for severe wheeze were allergic rhinitis (OR 6.90; 95% CI 3.84 to 12.40), domestic dog(s) (OR 2.34; 95% CI 1.01 to 5.40), frequent consumption of skipjack tuna (OR 1.94; 95% CI 1.11 to 3.39) and passive smoking (OR 1.70; 95% CI 0.93 to 3.11) while living in a house with a cement floor is a protective factor (OR 0.41; 95% CI 0.21 to 0.80).

Conclusion Wheezing commonly affects one-fourth of preschool children in rural Sri Lanka. Severe wheezing is often not diagnosed as asthma despite frequent symptoms, probably due to hesitancy in labelling preschool children as asthmatics. Allergic rhinitis, domestic dogs, frequent consumption of Skipjack tuna fish and exposure to passive smoking were independent risk factors for severe wheeze.

Strengths and limitations of this study

- This is the first reported study on the prevalence and factors of wheeze in preschool children from rural Sri Lanka.
- We used a representative sample of 1060 preschool children from 36 preschools in the largest district of Sri Lanka with generalisable results.
- This cross-sectional study reports the prevalence of wheeze in a hitherto underinvestigated age group.
- Factors associated with wheeze are presented but not their causal relationship.
- Only the association of the presence of domestic animals was assessed in this study. The timing of exposure and the level of exposure were not assessed in the current study.

INTRODUCTION

Globally, an estimated 300 million people live with asthma and the prevalence of asthma has a wide geographical distribution with a higher prevalence detected in developed countries.[1] However, the highest incidence of severe asthma is seen in lower-income countries.[2] The WHO states that asthma is the most common chronic disease among children worldwide and the highest incidence of asthma is in children aged 0–9 years.[3] Up to 80% of children with persistent asthma present before 6 years of age.[4] Although self-reported wheezing is a common symptom of asthma, asthma maybe diagnosed in children who never had wheeze and around half of the wheezers may not develop asthma.[5 6] Still wheezing is one of the most common paediatric symptoms with a global prevalence of 11.6% and it is associated significant healthcare cost, morbidity and parental stress.[5 7] A multicentre European cohort study reported the prevalence of 4-year-old children who had at least one wheezing episode during their lifetime ranging from 9.82% in Greece to 55.37% in Spain.[8] A study conducted in Korean preschool children reported a wheeze ever prevalence of 22.4% and current wheeze prevalence of 13.8%.[9]

Based on the International Study of Asthma and Allergy in Childhood (ISAAC) questionnaire, the prevalence of at least one wheezing episode during their lifetime was 37.3% and the prevalence of at least one wheezing attack in the preceding year was 27.5% among 6–7 years old Sri Lankan children.[10] The third leading cause of hospitalisation in Sri Lanka for the year 2018 was diseases of the respiratory system, and diseases of the respiratory system excluding diseases of the upper respiratory tract, influenza and pneumonia were the fourth leading cause of hospital deaths.[11] The morbidity of asthma was 15 753 male children and 12 066 female children aged 5–16 years (Indoor Morbidity and Mortality Report, 2018). A 10-year population-based retrospective birth cohort study conducted in Canada reported that 87.2% of all children with the diagnosis of asthma at the age of 6 years were diagnosed below 3 years of age.[12] However, in Sri Lanka, studies on the prevalence of asthma and wheeze were mainly conducted in the 5–14 year age group and the studies focused on preschool children (3–5 years old) have mainly focused on wheeze in an urban population.[13]

Prevalence data on severe wheeze and factors affecting severe wheeze among Sri Lankan preschool children are scarce in the medical literature. Therefore, this study was designed to assess the prevalence of wheeze among preschool children of a rural district of Sri Lanka. Furthermore, this study attempted to analyse the effect of demographic and domestic environmental factors on severe wheeze.

METHODOLOGY

We conducted a preschool based, cross-sectional study in Anuradhapura district, geographically the largest district in Sri Lanka, with an area of 7719 km^2 and 977 preschools registered at the 23 Divisional Secretariat Offices of the district catering for more than 9000 children. We selected all registered children aged 3–6 years as our study population.

Each preschool was considered a cluster and the WHO 30 cluster method was followed.[14] Preschools were selected using cluster sampling with the probability proportionate to the size and to obtain the minimum sample size of 951 children, 36 preschools were selected. In the absence of asthma prevalence data for Sri Lankan preschool children, the 10.9% prevalence for 6–7 years old children from the ISAAC study was used.[10] A precision of 2% and a dropout rate of 10% were considered in calculating the minimum sample size.

Participant information sheets and consent forms in native languages were provided to the parent(s) or guardian(s) through the preschool and informed written consent from a parent or guardian was obtained by trained medical undergraduates in the research team. Parent/guardian administered, validated Sinhala and Tamil translations of the ISAAC questionnaire for 6–7 years old children, were used to assess the prevalence of wheeze and the severity of wheezing. The definitions recommended by the ISAAC steering committee were used (table 1).

We collected data on demography and symptomatology including symptoms of severe wheeze, associations including allergic rhinitis and eczema, food and environmental triggers and household risk factors. The household risk factors included the number of family members sharing the child's bedroom; exposure to passive smoke; use of mosquito repellents, incense burners and kerosene lamps at home; source of fuel; materials used for roofing, walls of the house and floor of the child's bedroom; and what child sleeps on (online supplemental file 1). Furthermore, we evaluated the dietary pattern of common food items that are considered in the local context to exacerbate wheeze. The evaluated food items included vegetables such as tomato, ridge gourd and ladies fingers (*Abelmoschus esculentus*); fruit such as pineapple and sour banana; dessert such as curd; milk-powder and Skipjack tuna A frequent consumption of these food items was

Table 1 Standard definitions recommended by ISAAC steering committee

Term	Definition
Wheeze ever	Positive response to the question 'Has your child ever had wheezing or whistling in the chest at any time in the past?'
Current wheeze	Positive response to the question 'Has your child ever had wheezing or whistling in the chest in the past 12 months?'
Recurrent wheeze	Positive response to the question 'Has your child ever had more than three episodes of wheeze in the past year?'
Severe wheezing	Positive response to the question 'Has your child ever had ≥4 wheezing episodes or wheeze affecting speech or ≥1 night per week sleep disturbance?' in current wheezers
Allergic rhinitis	Positive response to the question 'In the past 12 months has your child had a problem with sneezing or runny nose or blocked nose when he/she did not have a cold or the flu?'
Eczema	Positive response to the three questions 'Has your child ever had an itchy rash which was periodical at least for 6 months?', 'Has your child had this itchy rash at any time in the past 12 months?' and 'Has this itchy rash at any time affected any of the following places - the folds of the elbow, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears or eyes?'.

considered as more than twice a week consumption. We used the individual χ^2 test to assess the factors associated with severe wheeze. Those factors with a p value less than 0.25 were included in a multivariable binary logistic regression to identify independent risk factors.

Patient and public involvement

The conceptualisation of the research idea was based on the respiratory issues that came across by one of the authors during his clinical practice. Discussions were held with preschool teachers, and parents of preschool children before the implementation to improve the study and also to minimise the discomfort, and burden of questionnaire filling.

RESULTS

The study sample consisted of 548 (51.70%) boys and 512 (48.30%) girls. The mean age in years was 4.41 (±0.66), with 92 (8.80%) children aged 3 years, 448 (42.83%) aged 4 years, 493 (47.13%) aged 5 years and 13 (1.24%) aged 6 years. The majority of study participants (845, 81.72%) were born in the Anuradhapura district.

The prevalence of wheeze-ever was 323 (30.47%; 95% CI 27.71% to 33.34%) and the current wheeze was 247 (23.30%; 95% CI 20.79% to 25.97%). Dry cough at night was reported in 318 (30.00; 95% CI 27.25 to 32.86) and exercise-induced wheeze in 92 (8.68%; 95% CI 7.05% to 10.54%) children. The prevalence of physician-diagnosed asthma was 61 (6.39%; 95% CI 4.92% to 8.13%) in the study sample. Severe wheeze was reported in 76 (7.17%; 95% CI 5.69% to 8.89%), with a majority having recurrent wheezing episodes, followed by disturbances to speech and sleep (table 2). However, despite having frequent symptoms, only 27 (35.53%; 95% CI 24.88% to 47.34%) of children with severe wheezing had an established diagnosis of bronchial asthma by a clinician.

Out of 68 current wheezers with allergic rhinitis, 33 (48.53%) had severe wheeze (OR 3.16; 95% CI 1.66 to 6.03; p=0.001) (table 3). Severe wheeze was also present in 3 out of 6 current wheezers with both eczema and allergic-rhinitis (OR 3.00; 95% CI 0.58 to 15.42; p=0.169). In this study, only 3 out of 35 with eczema had severe wheeze, which was not significant (unadjusted OR 0.75; 95% CI 0.07 to 8.20; p=1.000) and none of the 7 current wheezers with eczema only had severe wheeze (figure 1).

Table 3 Prevalence of allergic rhinitis and eczema among preschool children of different wheezing categories

	Prevalence of allergic rhinitis		Prevalence of eczema	
Wheezing category	**n**	**%**	**n**	**%**
Wheeze ever (n=323)	77	25.41	13	4.20
Current wheeze (n=247)	68	28.57	12	5.08
Severe wheeze (n=76)	33	44.59	4	5.63
Recurrent wheeze (n=56)	25	44.64	4	7.55

The majority of children enjoyed an active lifestyle, where 85.66% (908) engaged in daily playing until sweating. Another 6.42% (68) played 4–6 days per week, 4.91% (52) played 2–3 days per week and 1.32% (14) played once a week or less. There was no association between the presence of severe wheeze and activity levels (unadjusted OR 0.77; 95% CI 0.32 to 1.85; p=0.56).

Roofing was not associated with severe wheeze (p>0.186) and the most common roofing in this population was asbestos sheets (table 4). Firewood is used for cooking in 802 (76.45%; 95% CI 73.77% to 78.99%) houses and using firewood for cooking is not associated with severe wheeze (p>0.555) in this population. The identified independent risk factors for severe wheeze using bivariate analysis were allergic rhinitis (OR 6.90; 95% CI 3.84 to 12.40), domestic dog(s) (OR 2.34; 95% CI 1.01 to 5.40), frequent consumption of skipjack tuna (OR 1.94; 95% CI 1.11 to 3.39) and passive smoking (OR 1.70; 95% CI 0.93

Table 2 Symptomatology of preschool children from Anuradhapura district, Sri Lanka (n=1060)

Symptom/symptom combination	Number	Percentage (%)	95% CI Lower	95% CI Upper
Wheezing category				
Wheeze ever	323	30.47	27.71	33.34
Current wheeze	247	23.30	20.79	25.97
Severe wheeze	76	7.17	5.69	8.89
Symptomatology of severe wheeze				
Recurrent wheeze	56	5.28	4.01	6.81
Speech limited by wheeze in the past 12 months	30	2.83	1.92	4.02
Sleep disturbance from wheeze, ≥1 night a week in the past 12 months	17	1.60	0.94	2.56
Other symptoms				
Dry cough at night	318	30.00	27.25	32.86
Exertional wheeze	92	8.68	7.05	10.54

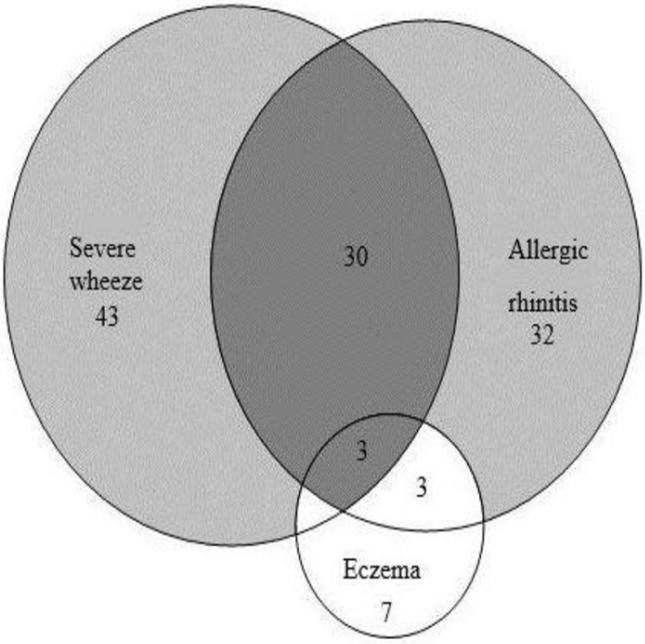

Figure 1 Prevalence of severe asthma, allergic rhinitis and eczema among children with current wheeze (n=247)

to 3.11) while living in a house with a cement floor is a protective factor (OR 0.41; 95% CI 0.21 to 0.80).

DISCUSSION

This study provides the first reported estimates of the prevalence of wheezing and severity of wheeze among preschool children in rural Sri Lanka. We detected that almost one out of four preschool children (23.30%) in this study population had current wheeze, while severe wheeze was present in 7.17%.

The limited data on the prevalence of current wheeze from Sri Lanka shows slightly different estimates for urban settings. In the Colombo municipal council area (urban Sri Lanka) current wheeze, defined as physician-diagnosed wheezing in the past 12 months, was reported as 21.3% (95% CI 17.6% to 25.0%),[13] an estimate closer to the present study finding. However, the said study reports the percentage of children with wheeze-ever, defined as physician-diagnosed wheezing/whistling of the chest in their lifetime, as 38% (95% CI 33.6% to 42.5%), a comparatively higher prevalence. In India, the asthma prevalence among children aged less than 5 years was 13%,[15] which was considerably higher than in our study. However, Kumar *et al* have used two criteria to calculate asthma prevalence: an affirmative answer to the question 'have you been previously diagnosed with asthma' and a history of shortness of breath with cough in the past 30 days, which contributes to the higher prevalence rate, therefore, direct comparison is not possible.

Physician-diagnosed asthma prevalence is reported as 6.7% in a survey conducted in Changsha, China in 2011–2012 and as 2.3% (1.3%–3.9%) in a nationwide cross-sectional survey conducted in Korea from 2008 to 2017.[16 17] However, the number of physician-diagnosed asthma children in our sample is lower compared with the Changsha study. Both studies used affirmative answer to the question have you been previously diagnosed with asthma, to calculate physician-diagnosed asthma similar to ISAAC protocols. However, childhood asthma is diagnosed in only about 30% of preschool children with wheeze.[18] One main reason for such under-diagnosis is hesitancy in labelling a preschool child as an asthmatic.[19] Furthermore, diagnosis of asthma in preschoolers with recurrent wheeze is complicated by different wheezing phenotypes, different disease progression and the difficulties of performing spirometry.[18 20]

According to the ISAAC study conducted among 6–7 years old children, the global, Indian subcontinent and Sri Lankan prevalence of current wheeze were reported as 11.5%, 6.8%[21] and 27.5%,[10] respectively. In this study, we noted a 23.30% prevalence of current wheeze among preschool children, which is slightly less, but comparable to that of Sri Lankan children aged 6–7 years. Furthermore, self-reported physician-diagnosed asthma has been observed in 364 children out of 3345 (10.9%; 95% CI 9.9% to 12.0%) of 6–7 year aged Sri Lankan children, compared with only 61 of 1060 preschool children (5.75%; 95% CI 4.43% to 7.33%). This lower prevalence in the present study could be partly attributed to the age group difference and also to the low rate of asthma diagnosis in the preschool age. Island-wide regular school medical inspection programmes conducted by the public health sector may also play a role in detecting more respiratory illnesses among school children, compared with preschool children.

In our study sample, the independent risk factors of severe wheeze-related to the domestic environment were exposure to passive smoking, domestic dog(s) and clay floor. The association between passive cigarette smoke exposure and the development of wheeze and asthma is well documented in medical literature.[22] The most common pets in the households of the study sample were dogs followed by cats and birds. In this study, only the presence of domestic animals was assessed. However, the effect of allergens of furry pets is found to be dependent on the age of the child at the time of exposure, where an early-life exposure may play a protective role.[23 24] However, these allergens are capable of exacerbating asthma attacks in sensitised individuals.[25 26] In this study sample, having a clay floor in the house was associated with severe wheeze (p=0.007: unadjusted OR 3.71; 95% CI 1.56 to 8.85) and having a cemented floor was an independent protective factor for the development of severe wheeze (adjusted OR 0.41; 95% CI 0.21 to 0.80). Asbestos exposure is known to increase the risk of respiratory symptoms and asthma in adults; however, the adult subjects have been exposed to asbestos for a prolonged period.[27]

In this study, we considered all the energy sources used for cooking and boiling water not limiting to the major source. Using firewood is not associated with severe wheeze and this observation could be due to several

Table 4 Factors associated with severe wheeze among preschool children of Anuradhapura, Sri Lanka

Risk factor	Children with severe wheezing		Children without severe wheezing		Significance	Unadjusted OR	95% CI	
	N	%	N	%			Lower	Upper
Demographic factors								
Male sex	48	63.16	500	50.81	0.038*	1.659	1.024	2.689
Age 5 or more years	36	47.37	470	48.45	0.855*	0.957	0.600	1.528
Born in Anuradhapura	57	77.03	788	82.08	0.278*	0.732	0.415	1.289
Having elder siblings	37	48.68	548	56.32	0.197*	0.736	0.461	1.174
Having elder brothers	19	25.33	275	28.89	0.512*	0.835	0.487	1.432
Having elder sisters	21	28.00	333	34.98	0.221*	0.723	0.429	1.218
Housing conditions								
Cemented floor	58	76.32	835	85.47	0.032*	0.548	0.314	0.957
Clay floor	7	9.21	26	2.66	0.007†	3.711	1.555	8.854
Tiled floor	9	11.84	85	8.70	0.355*	1.410	0.679	2.927
Concrete floor	‡	2.63	27	2.76	1.000†	0.951	0.222	4.077
Asbestos roof	50	66.67	654	67.35	0.903*	0.969	0.589	1.596
Clay-tile roof	20	26.67	272	28.01	0.802*	0.934	0.550	1.589
Concrete roof	‡	2.67	26	2.68	1.000†	0.996	0.232	4.278
Corrugated metal sheets	3	4.00	18	1.85	0.186†	2.206	0.635	7.665
Plastered walls	59	77.63	804	82.97	0.237*	0.712	0.405	1.253
Behaviour of the child								
Child sleeps on the floor	‡	2.63	17	1.74	0.642†	1.520	0.345	6.704
Child sleeps on a rubber mattress	64	84.21	794	83.14	0.810*	1.081	0.571	2.050
Physically-active child‡	70	92.10	906	93.79	0.472†	0.773	0.322	1.851
Dietary habits								
Frequent consumption of pineapple§	‡	2.70	52	5.52	0.422†	0.475	0.113	1.992
Frequent consumption of Skipjack tuna§	32	44.44	302	32.90	0.046*	1.632	1.005	2.650
Frequent consumption of tomato§	33	44.00	402	43.23	0.896*	1.032	0.642	1.658
Frequent consumption of king coconut§	4	5.48	77	8.54	0.508†	0.621	0.221	1.748
Frequent consumption of sour banana§	11	15.07	281	30.25	0.006*	0.409	0.212	0.789
Frequent consumption of ladies-fingers (*Abelmoschus esculentus*)§	26	34.21	391	41.64	0.205*	0.729	0.446	1.191
Frequent consumption of curd§	9	12.50	137	14.96	0.572*	0.812	0.395	1.672
Frequent consumption of milk powder§	45	59.21	580	63.32	0.476*	0.841	0.522	1.355
Frequent consumption of ridge gourd§	16	21.62	310	33.30	0.039*	0.553	0.313	0.977
Frequent consumption of Centella	32	42.11	470	49.01	0.246*	0.757	0.472	1.214
Domestic animals								
Dogs	66	86.84	730	75.03	0.020*	2.197	1.112	4.340

Continued

Table 4 Continued

Risk factor	Children with severe wheezing N	%	Children without severe wheezing N	%	Significance	Unadjusted OR	95% CI Lower	Upper
Cats	36	47.37	426	43.74	0.539*	1.158	0.725	1.848
Birds	27	35.53	310	31.83	0.506*	1.180	0.724	1.924
Cows	9	11.84	63	6.47	0.074*	1.942	0.926	4.076
Close contact with animals	23	31.08	216	22.78	0.104*	1.528	0.913	2.558
Inhaled allergens								
Presence of smokers in the house	23	31.08	186	19.79	0.021*	1.828	1.089	3.068
Frequent use of mosquito coils in the house	15	19.74	157	16.14	0.414*	1.278	0.708	2.306
Frequent use of incense burners in the house	55	72.37	709	72.79	0.936*	0.979	0.581	1.650
Using only firewood for fuel	27	35.53	332	34.12	0.804*	1.064	0.653	1.733
Comorbid conditions								
Allergic rhinitis	33	44.59	90	10.01	<0.001*	7.235	4.356	12.018
Eczema	3	75.00	32	80.00	1.000†	0.750	0.069	8.202

*χ^2 test.
†Fisher's exact test.
‡Physically active child is defined as a child playing until sweating for four or more days a week.
§Frequent consumption is defined as consuming twice or more times a week.

factors including the possibility of a limited amount of firewood been used in cooking, firewood cooking in an outdoor environment and the presence of chimneys in houses with indoor firewood cooking.

In Sri Lanka, numerous myths about food and asthma exist. We looked at some of those selected food items popularly believed to be associated with wheeze. Skipjack tuna (*Katsuwonus pelamis*) consumption was an independent risk factor for developing severe wheeze. This could be due to the high histamine content in Skipjack tuna,[28] as histamine plays a pivotal role in asthma.[29] A misconception that banana (Musa spp.) is associated with wheeze and asthma is common in the region, even among healthcare practitioners.[30 31] However, sour banana—locally believed as one of the main allergens for exacerbation of wheeze and asthma—negatively associated with severe wheezing among these children. However, the local practice of avoiding sour banana among children with wheeze and routine consumption of sour banana among non-symptomatic children may have resulted in this observation.

Although male sex showed an association with severe wheeze, in the multivariate analysis it was not an independent risk factor for severe wheezing in this study sample. Current evidence suggests that early-childhood asthma is higher among boys.[32 33] This difference could be due to preadolescent boys having a higher prevalence of atopy and allergen sensitisation with higher serum Ig E levels, eosinophil count compared with girls.[32 34 35]

In conclusion, this study highlights that symptomatic wheezing is common and affects one-fourth of preschool children in rural Sri Lanka. The identified independent risk factors for severe wheezing among preschool children in the study were coexisting allergic rhinitis, presence of domestic dogs, frequent consumption of skipjack tuna and exposure to passive smoking while living in a house with a cement floor was a protective factor. The observed high prevalence of allergic rhinitis among wheezers and its significant association with severe wheeze could be used to define the at-risk population for preventive strategies. Furthermore, early diagnosis of asthma in children with severe wheeze would enable early initiation of long-term control therapy.

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