

Clinical Categorization of Under Five Wheezers

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Abstract

Introduction: The incidence of wheeze is very high in children, approximately 25–30% of infants will have had at least one wheezing, by 3 years of age, an episode of wheeze will have occurred in 40% of children and 50% will have at least one episode of wheezing by 6 years.

Aim of the Study: The aim of the study was to categorize different types of wheeze among children aged 6 months–5 years based on history, clinical profile, etiology, and risk factors.

Materials and Methods: All children aged 6 months–5 years admitted in department with definite history of wheezing and respiratory distress with typical clinical features.

Observations and Results: One hundred five children with recurrent wheeze were studied in the age group of 6 months–5 years.

Discussion: There are many children getting admitted with recurrent wheezing in <5 years age group. This study could help in identifying the etiology, categorization of wheezers, and risk factors predisposing these children to wheeze compared to other children.

Conclusion: In our study, various categories for recurrent wheezing based on clinical phenotypes are: Episodic wheeze 40%, multitrigger wheeze 42.8%, asthma 12.3%, and gastroesophageal reflux disease 4.7%.

Key words: Asthma, Child, Wheeze

INTRODUCTION

The incidence of wheeze is very high in children, approximately 25–30% of infants will have had at least one wheezing, by 3 years of age, an episode of wheeze will have occurred in 40% of children, and 50% will have at least one episode of wheezing by 6 years.^[1]

In India, the incidence of wheeze is high in children. It has been found that one in three children has their first episode of wheeze in infancy, and the prevalence of wheeze is nearly 50% by 6 years of age. About 25% of children who develop persistent asthma started to wheeze by age of 6 months and 75% by 3 years of age.^[2]

A recurrent wheeze is estimated to occur in one-third of children of preschool age and can cause significant

morbidity, decrease quality of life, and increase the frequency of the use of health care services and economic costs.^[3]

Data have confirmed that wheezing is clinically heterogeneous in early life in terms of its temporal pattern (i.e., age of onset and duration until symptoms disappear) and its risk factors, which include atopy and genetic or environmental factors, and the outcomes are different for such phenotypes.^[4,5]

Different wheezing phenotypes have been reported in the literature, with the first such report being the Tucson childhood respiratory study of Martinez *et al.*,^[6] in which children were classified into four main subtypes, including never wheezing, early transient wheezing, persistent wheezing, and late-onset wheezing; later reports further categorized patients with persistent wheeze as having nonatopic persistent wheezing or atopic/IgE-associated wheezing.^[7,8]

Regardless of whether five or six different types are included in an assay, it remains difficult to differentiate these phenotypes clinically because the expression of symptoms

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and risk factors can change over time. In addition, different factors, including genetic, environmental, and host factors (and interactions among these factors), can impact a child's condition and contribute to the development of wheezing and the progression of a patient's symptoms.^[9]

Our proposed operational criteria are aimed at simplifying the types of wheezing used to categorize children of preschool age and identifying risk factors for the persistent wheezing subtypes that can impact lung function^[10] or lead to the subsequent development of asthma as these conditions should be treated by appropriate medical interventions.^[11]

Wheeze can be Divided According to its Pattern and Duration

Wheeze subtypes according to pattern (symptomatic classification)

- a. Episodic wheeze: Wheezing within a discrete period that is often associated with clinical evidence of a viral cold. There is no wheezing between episodes^[12]
- b. Multitrigger wheeze: Wheezing presenting with and apart from an acute viral episode.^[12,13]

Wheeze according to duration

- a. Transient early wheeze: This is a type of wheeze that starts early in the 1st year of life and then continues through the 2nd year before beginning to subside after the 3rd year. Most of these patients are not atopic and exhibit no evidence of eosinophilia or other markers of inflammation, which are observed in approximately 16% of affected patients.^[14] The main risk factors in this group are maternal exposure to smoke, prematurity, low maternal age, low socioeconomic status, low birth weight, attending day-care center at an early age, and more than two siblings at home. In addition, in these patients, pulmonary function test scores are low even before the onset of the wheeze, suggesting that affected individuals may have had smaller airways than were observed in the control group and remain slightly lower than those reported in their peers in adolescence^[6]
- b. Late-onset wheeze: This presents as infrequent wheezing from 6 to 42 months old age that becomes more frequent at 42 months of age and then persists to an age of 6 years (approximately 1.7e6%).^[14,15] A skin allergy test usually produces strong results in this group, and this is known to be a major prognostic factor. Allergies in the nose are also commonly associated with late-onset wheezing, similar to smoke exposure, is known to be a risk factor in males^[6,14]
- c. Persistent wheeze: This is wheeze with onset at 6 months of age or later that occurred in approximately 3.1% of patients in the PIAMA study, 4.1% of patients in SIDRIA, and 8.9% of patients in the ALSPAC study.

Aims and Objectives

Aim of the study

The aim of the study was to categorize different types of wheeze among children aged 6 months–5 years based on history, clinical profile, etiology, and risk factors.

Objectives of the Study

The objectives of the study were as follows:

1. To assess case burden of wheeze presenting with recurrent wheezing in children from age group of 6 months–5 years
2. Evaluate various etiologies and prognosis.

MATERIALS AND METHODS

Type of Study

Descriptive study

Period of study: December 2018 to November 2020

Inclusion Criteria

All the patients between 6 months and 5 years of age who presented with wheeze (recurrent wheeze or persistent wheeze) were included in the study.

Exclusion Criteria

The following criteria were excluded from the study:

- Children above 5 years of age group and <6 months
- Known or suspected immunodeficiency
- Other chronic diseases (TB, bronchiectasis, cystic fibrosis, and CHD).
- Foreign body aspiration.

Sample Size

All children aged 6 months–5 years admitted in department with definite history of wheezing and respiratory distress with typical clinical features.

MATERIALS AND METHODS

- All children aged 6 months–5 years admitted in the department with a definite history of wheezing and respiratory distress with typical clinical features
- Routine and specific diagnostic tests.
- Detailed history, clinical examinations, and required baseline investigations such as hemogram, total leukocyte count, and absolute eosinophil count, chest radiography, Mantoux test would be done.

Source of Data

Cases were admitted in Mahatma Gandhi Memorial Hospital, Warangal, during the study period.

Statistical Data Analysis and Interpretation

Data were entered into Microsoft Excel (Windows 10; Version 2019) and analyses were done using the Statistical Package for the Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation for continuous variables, frequencies, and percentages were calculated for categorical Variables were determined. Bar charts and pie charts were used for visual representation of the analyzed data.

OBSERVATIONS AND RESULTS

One hundred five children with recurrent wheeze were studied in the age group of 6 months–5 years.

Demographic Characteristics

Total no. of males = 55 (52.38%).

Total no. of females = 50 (47.61%).

No predilection to sex was observed.

The study population comprises 55% male and 50% female, there is no significant difference ($P = 0.6255$) in male-female distribution when we consider the study population in total [Table 1]. Of these in infancy, there is male predominance, 7 out of 11 were male, constituting 63.6% of the total population in infancy.

Out of 105 children, 11 (10.4%) were <1 year of age; 18 (17.1%) belonged to the age group 1–2 years; 23 (21.9%) to the age group 2–3 years; 27 (25.7%) to the age group 3–4 years; and 26 (24.7%) children to the age group 4–5 years.

In the study population, 41 (39.04 %) had onset of symptoms <1 year of age and 64 (60.95 %) had symptoms onset after 1 year of age [Table 2].

Table 3 shows that 10 (9.5%) of the study population had eczema, 18 (17.1%) had rhinitis, and 43 (40.9%) had a family history of atopy.

One hundred (95.2%) children with recurrent wheeze had a good response to short-acting beta analog (SABA) and 5 (4.7%) had poor response to SABA [Table 4].

Episodic wheezers had 100% association with viral-induced wheeze and fever, multitrigger wheezers have 100% association with other triggers such as exposure to cold, sweet, chocolate, and cool drinks, asthma group has in addition to triggers personal atopy in the form of eczema 8 (61.5%), rhinitis 11 (84.6%), and family history of atopy 100%.

Clinical features in various etiology of recurrent wheeze.

Table 1: Age and sex distribution in the study population

Age (years)	Male n (%)	Female n (%)	Total n (%)
6 months–1 year	7 (63.6)	4 (36.3)	11 (10.4)
1–2 years	8 (44.4)	10 (55.5)	18 (17.1)
2–3 years	13 (56.5)	10 (43.4)	23 (21.9)
3–4 years	14 (51.8)	13 (48.1)	27 (25.7)
4–5 years	13 (50)	13 (50)	26 (24.7)
Total	55 (52.3)	50 (47.6)	105 (100)

Table 2: Age of onset of symptoms in the study population

Age of onset	Cases (n=105)	Percentage
<1 year	41	39.04
>1 year	64	60.95

Out of the 42 children with episodic wheeze, 23 (54.7%) were male and 19 (45.2%) were female, showing no sex predilection. Seventeen (40.4%) had onset before 1 year and 25 (59.5%) had onset after 1 year. All 42 children had fever, cough, 10 (23.8%) had noisy breathing, none had personal atopy, and 8 (19.04%) had family H/O atopy. All of them had wheeze in response to viral infection and all of them responded well to SABA.

Out of 45 children with multi-trigger wheeze, 23 (51.1%) were male, 22 (48.8%) were female, showing no sex difference. Fourteen (31.1%) had onset of symptoms before 1 year of age and 31 (68.8%) had onset of symptoms after 1 year of age. Forty-two (93.3%) had cough, 10 (22.2%) had fever, 5 (11.1%) had noisy breathing, 2 (4.4%) had eczema, 7 (15.5%) had rhinitis, 22 (48.8%) had family H/O atopy, 7 (15.5%) had wheeze associated with a viral infection, all of them had triggers other than viral infection, and all of them responded well to SABA.

Out of 13 children with asthma, 7 (53.8%) were male, 6 (46.1%) were female showing no sex difference. Six (46.2%) had onset of symptoms before 1 year of age and 7 (53.8%) had onset of symptoms after 1 year of age. All of them had cough, none had fever noisy breathing, 8 (61.5%) had eczema, 11 (84.6%) had rhinitis, all had family H/O atopy, all of them had triggers other than viral infection, and all of them responded well to SABA.

Out of 5 children with gastroesophageal reflux disease (GERD), 2 (40%) were male and 3 (60%) were female. Four (80%) had onset of symptoms before 1 year of age, 1 (20%) had onset of symptoms after 1 year of age, 4 (80%) had cough, none had fever, 1 (20%) had noisy breathing, and 5 (100%) had either poor or partial response to SABA.

Of the 105 cases under our study, 59 (56.1%) were of rural location and 46 (43.8%) were of urban location.

Table 3: Personal and family H/O atopy in the study population

H/O	6 months– 1 year n=11 (%)	1–2 years n=18 (%)	2–3 years n=23 (%)	3–4 years n=27 (%)	4–5 years n=26 (%)	Total n=105(%)
Eczema	0	0	4 (17.3)	5 (18.5)	1 (3.8)	10 (9.5)
Rhinitis	0	1 (5.5)	6 (26.0)	7 (25.9)	4 (15.3)	18 (17.1)
Family H/O atopy	2 (18.1)	6 (33.3)	11 (47.8)	14 (51.8)	10 (38.4)	43 (40.9)

Table 4: Response to short-acting beta analog in the study population

Response to short acting beta analogue	6 months to 1 year n=11 (%)	1–2 years n=18 (%)	2–3 years n=23 (%)	3–4 years n=27 (%)	4–5 years n=26 (%)	Total n=105(%)
Good	8 (72.7)	16 (88.8)	23 (100)	27 (100)	26 (100)	100 (95.2)
Poor	3 (27.2)	2 (11.1)	0	0	0	5 (4.7)

In our study, 90 (85.7%) were born at term, while 15 (14.2%) were born preterm.

In our study, the majority were of normal weight at birth while 18 (17.1%) were low birth weight.

In our study, 47 (44.7%) were exclusively breastfed, 17 (16.1%) were partially (mixed) breastfed, and 41 (39.0%) were formula-fed children.

Of the 105 cases of our study population, 89 (84.7%) were nutritionally healthy, while 16 (15.2%) were underweight [Tables 5-9].

DISCUSSION

There are many children getting admitted with recurrent wheezing in <5 years age group. This study could help in identifying the etiology, categorization of wheezers, and risk factors predisposing these children to wheeze compared to other children.

The exact proportion of various causes of wheeze is not yet published in the Indian population. Causes of recurrent wheeze in infants, toddlers, and preschool children may vary that need to be emphasized.

A descriptive study was conducted at MGM Hospital, Warangal, to find out the demographic characteristics, clinical profile, etiology, and risk factors of recurrent wheeze based on which categorization is done in children <5 years of age.

One hundred five children of age group between 6 months and 5 years admitted at our institution who met the inclusion and exclusion criteria were recruited. We had 42 (40%) episodic wheezers, 45 (42.8%) multitrigger wheezers, 13 (12.3%) asthma, and 5 (4.7%) GERD.

In our study, 55 were male and 50 were female, showing no difference sex-wise, but in age <1 year, there was male predominance. Out of 105 children, 11 (10.4%) were <1 year of age; 18 (17.1%) belonged to the age group 1–2 years; 23 (21.9%) to the age group 2–3 years; 27 (25.7%) to the age group 3 to 4 years; and 26 (24.7%) children to the age group 4 to 5 years.

LY *et al.* found no significant difference in gender in early-onset wheeze (<3 years) which is consistent with our study. Patra *et al.* report in children <2 years, there was male predominance.

In the study population, 41 (39.04%) had onset of symptoms <1 year of age and 64 (60.95%) had symptoms onset after 1 year of age.

In addition to wheeze and breathlessness, 101 (96.1%) presented with cough, 52 (49.5%) had associated fever, 16 (15.2%) had noisy breathing, 58 (55.2%) had triggers in the form of exposure to cold, consumption of ice cream, cool drinks, chocolate, etc. Forty-nine (46.6%) of the children wheeze during viral illness.

Saglani *et al.* in his study on recurrent wheeze in children between 3 months and 5 years.

The previous study is based on investigations which may not be possible in a resource-poor setting like ours whereas our study is mainly based on clinical features. Viral-associated wheeze is less than in our study. This could be explained by the fact that the previous study was conducted at London, where infection rate is less than our population. Incidence of asthma is very high in the previous study, but they have not attempted to separate multitrigger wheezers.

Mathieu *et al.* found a high prevalence of atopy in children with recurrent wheeze who are at risk of developing asthma. Our study also shows a high association between atopy and wheeze, 19.04% of episodic wheezers had a

Table 5: Location-wise distribution of cases

Location	Case	Percentage
Rural	59	56.1
Urban	46	43.8
Total	105	100

Table 6: Gestation age-wise distribution

Gestational age	Case	Percentage
Term	90	85.7
Preterm	15	14.2
Total	105	100

Table 7: Distribution with relation to birth weight

Birth weight	Case	Percentage
<2500 g	18	17.1
>2500 g	87	82.8
Total	105	100

Table 8: Distribution with relation to different feeding practice

Feeding practice	Case	Percentage
Exclusive breastfeeding	47	44.7
Partially breastfed	17	16.1
Artificial feeding	41	39.0
Total	105	100

Table 9: Distribution with relation to nutritional status

Nutritional status	Case	Percentage
Healthy	89	84.7
Underweight	16	15.2
Total	105	100

family history of atopy, 48.8% of multitrigger wheezers had family H/O atopy, 100% of asthmatics had family H/O atopy, of which 61.5% had personal H/O eczema, and 84.6% had H/O allergic rhinitis.

Litonjua *et al.* showed that odds of having a child with asthma are high with parental history of asthma. This is consistent with our study which shows 100% association of family H/O atopy in asthmatics.

Patra *et al.* found that GER is an important cause for recurrent wheezing among children <2 years of age. This is consistent with our study.

Breastfeeding

It is shown that the duration of breastfeeding should be at least 6 months to be protective against respiratory tract

infections. Recurrent episodes of wheezing decreases were with increasing duration of breastfeeding which is consistent with our study. In our study, children who were partially breastfed (16.1%) and formula-fed (39.0%) for 1st 6 months were found to be recurrent wheezers.

Maternal Smoking in Pregnancy

Maternal smoking in pregnancy is a risk factor for all types of wheezing but not for asthma itself. It increases the risk of transient early wheezing and impaired lung function in infancy but not in later childhood. It appears to affect lung development, resulting in reduced lung capacity and smaller airways, as well as prematurity and low birth weight. In a study by Dezateux *et al.* in 101 infants, the odds of wheezing were significantly increased in those with a family history of asthma and those exposed to maternal smoking during pregnancy. However, in our study, we found maternal smoking is not a risk factor for recurrent wheezing.

Low maternal age: Rusconi, Galassi, Corbo, *et al.* showed that young motherhood (<20 years) has not been found to be a risk factor for wheezing respiratory illness in the 1st years of life because of the low number of mothers younger than 20 years (2.1%). However, in our study, young motherhood found to be a risk factor for recurrent wheezing.

Birth History

In a study done by Sherriffa *et al.*, prematurity was a significant risk factor recurrent wheezing, while our study showed that children who presented with recurrent wheeze predominantly were term according to their gestational age (85.7%).

CONCLUSION AND SUMMARY

There are a very few Indian studies on the study of wheezing <5 years and their follow-up.

1. In our study, various categories for recurrent wheezing based on clinical phenotypes are: Episodic wheeze 40%, multitrigger wheeze 42.8%, asthma 12.3%, and GERD 4.7%
2. Episodic wheezers were usually associated with wheeze during viral illness (100% viral associated) and they were asymptomatic in between
3. In our study, multitrigger wheezers and asthma have wheeze due to various other triggers and some of them had family history of atopy multitrigger (48.8%) and asthma (100%)
4. In our hospital, it is being observed that an increasing number of children with symptom of wheezing are frequently attended by pediatrics in ED, OPD, and ward, thereby proving an added burden to the younger age group

5. In our study, the risk factors identified for recurrent wheezers are male child in infants (63.6%), passive smoking (58%), rural areas (56.1%), and children who were not exclusively breastfed for 6 months (55.1%). However, we could not find maternal smoking as a risk factor in our study due to the sociocultural lifestyle in the study population.

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