

Original research article

Prospective Observational Study of Wheezing Disorder in Children Below 5 Years of Age.

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Abstract

Background: Wheezing in early life is a common disorder, with approximately 50% of children having an episode of wheezing in the first year of life. 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. In young children, wheezing, either transient or persistent, can be severe and cause a poor quality of life with frequent use of health care system and economic costs.

Aims and Objectives: To study the demographic and clinical profile of children presenting with wheeze, monitor their clinical course and relation to environmental factors if any.

Material and Methods: Prospective observational clinical study was done which included children from 6 months to 5 years of age presented with wheeze and admitted in pediatric ward November 2018 to April 2019. Every patient was managed according to GINA guidelines and followed up for 1 year since their admission.

Results: Wheeze accounted for 34% of total paediatric admissions in ward with male-female ratio 2:1. 82% were episodic wheezers, of which 52.2% were first time wheezers. All risk factors studied, co-related with most previous studies. No significant correlation was found between wheezers and monthly AQI during study. Over 1 year, 64.8% patients could be followed up as per protocol, 52.8% of followed up patients, had at least one episode of wheeze. Low birth weight, 1st episode of wheeze in infancy and episodic wheeze were found to be significant risk factors for repeat episode of wheeze.

Conclusion: A complex relationship exists between various factors which may be responsible for the recurrence of wheeze. Proportion of morbidity caused by wheeze is quite high in

comparison to other respiratory diseases. It poses a great challenge for a clinician not only to diagnose and effectively treat the child but also identify risk factors so that steps may be taken to eliminate them if possible.

Keywords: AQI, Asthma, Children, Wheezing

Introduction

Wheezing in early life is a common disorder, with approximately 50% of children having an episode of wheezing in the first year of life. 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.^[1] In young children, wheezing, either transient or persistent, can be severe and cause a poor quality of life with frequent use of health care system and economic costs.^[2] Parents of infants with recurrent wheezing often ask the pediatrician: “Will my children develop asthma?” This is a crucial question that involved also clinician in the diagnostic and therapeutic attempts. Proper identification of children at risk of developing asthma at school age may predict long-term outcomes and improve treatment and preventive approach, but the possibility to identify these children at preschool age remains limited. Wheezing is a multi-factorial symptom, usually related to bronchiolitis or asthma, but other less common conditions may be considered in case of atypical presentation.^[2] To better define the patients with wheezing, attempts of classification, identification of asthma risk factors, genetic and environmental factors has been proposed to improve the characterization of children with recurrent wheezing. Over last few years, the presentations of respiratory diseases in young children are changing.^[3] Many young infants present with wheeze at a very early age. Environmental factors like temperature, humidity, air pollution, living conditions, and other host factors also seem to be responsible for increased incidence of wheezing. Whether the environmental factors affect the host immune system or increase the occurrence of viral infection is still a subject of detailed study.^[3]

Material and Methods:

Prospective observational clinical study was done which included children from 6 months to 5 years of age presented with wheeze and admitted in pediatric ward November 2018 to April 2019. Every patient was managed according to GINA guidelines and followed up for 1 year since their admission. Patients of Vomiting associated with respiratory symptoms (GERD), Tuberculosis, Broncho-pulmonary dysplasia, Airway malacia., Cerebral palsy or muscle dystrophy, Structural or focal lung disease, Congenital heart disease, Severe acute malnutrition were excluded from the study.

The patient were classified in groups based on symptom pattern at the time of admission.

A. 1st episode of symptoms(wheeze, cough, heavy breathing.)

2nd episode onwards:

B. Symptoms for <10 days with/without upper respiratory tract infection (URTI) (2-3 episodes / year),no symptoms between episodes.

C. Symptoms for >10 days with or without URTI. (>3 episodes/ year or severe episodes and/or night worsening) child may have occasional symptoms.

D. CAT-C + child has symptoms regularly between episodes during play or when laughing.

All patients were managed as per 2018 GINA guidelines:

A. symptomatic treatment

B. reliever bronchodilator as and when required

- C. low dose inhaled corticosteroid.
D. double low dose ICS or low dose ICS+ LTRA.

All patients were monitored and called to designated asthma OPD at least once a month by telephonic call. On follow up they were monitored as per GINA protocols. Air quality index (AQI) was documented daily. At the end of the study period, the patients were reclassified according to their wheezing episodes over the period of 1 year. The patients who had no episode of wheeze were continued to be referred as category A and others were categorized to B, C and D according to the symptom control. The patients who could not be contacted or were not followed up according to the set protocol were documented as LOST to follow-up.

Ethical aspects: Written informed consent of the patients was taken and confidentiality of the data maintained.

Results:

Wheeze accounted for 34% of total paediatric admissions in ward. Out of 111 patients enrolled 74(66.6%) were males and 37(33.3%) were females, which is statistically significant at confidence level of 95%.

Table 1: Age wise Distribution

	A (N=58)		B (N=40)		C (N=13)		TOTAL
	< 2 yrs	> 2 yrs	< 2 yrs	>2 yrs	< 2 yrs	>2 yrs	
BRONCH-IOLITIS	18	0	11	0	0	0	29 (26.1%)
WALRI	28	11	15	8	0	0	62 (55.8%)
MULTI-TRIGGER WHEEZER	0	0	4	1	5	7	17 (15.3%)
ASTHMA	0	1	0	1	0	1	3 (2.8%)
TOTAL	46 (79.3%)	12 (20.7%)	30 (75%)	10 (25%)	5 (38.5%)	8 (61.5%)	111

The patients were classified among 4 primary clinical conditions: Bronchiolitis, Wheeze Associated Lower Respiratory Infection (WALRI), multi-trigger wheezer and Asthma. The number of first-time wheezers enrolled during the study was 58, 46(79.3%) of them were below 2 years age.

The total number of episodic wheezers was found to be 91 (82%). 72 (79.1%) of the episodic wheezers were of 2 years of age or younger when they presented.

Table 2 : AGE AT 1ST EPISODE OF WHEEZE:

DIAGNOSIS	AGE AT 1ST EPISODE	
	< 1 YR (N=81)	>1 YR (N=30)
BRONCHIOLOITIS	28 (34.6%)	1 (3.3%)
WALRI	36(44.4%)	26 (86.7%)
MULTI-TRIGGER WHEEZERS	15(18.5%)	2 (6.7%)
ASTHMA	2 (2.5%)	1 (3.3%)
TOTAL	81 (72.9%) (N=111)	30 (27.1%) (N=111)

Of 111 patients in the study, 81 (72.9%) had their first episode of wheeze at an age below 1 year.

Table 3 : RELATION WITH LOW BIRTH WEIGHT (LESS THAN 2.5 KG)

DIAGNOSIS	LOW BIRTH WEIGHT (N=111)	
	YES	NO
BRONCHIOLITIS	11 (9.9%)	18(16.2%)
WALRI	16 (14.4%)	46 (41.5%)
MULTI-TRIGGER WHEEZERS	9 (8.1%)	8 (7.2%)
ASTHMA	1 (0.9%)	2 (1.8%)
TOTAL	37(33.3%)	74 (66.7%)

Birth weight of all the patients was recorded, we found that 37 (33.3%) of the 111 study patients had LBW (<2.5kg).

Table 4 : RELATION WITH NICU ADMISSION:

DIAGNOSIS	NICU ADMISSION (N=111)	
	YES	NO
BRONCHIOLITIS	8 (7.2%)	21 (18.9%)
WALRI	6 (5.4%)	56 (50.5%)
MULTI-TRIGGER WHEEZERS	5 (4.5%)	12 (10.8%)
ASTHMA	0	3 (2.7%)
TOTAL	19(17.7%)	92(82.3%)

On eliciting detailed history 19(17.17%) of the study patients had history of NICU admission.

Table 5 : RELATION WITH PASSIVE SMOKING:

DIAGNOSIS	PASSIVE SMOKING (N=111)	
	YES	NO
BRONCHIOLITIS	16 (14.4%)	13 (11.7%)
WALRI	18 (16.2%)	44 (39.7%)
MULTI-TRIGGERWHEEZERS	9 (8.1%)	8 (7.2%)
ASTHMA	1 (0.9%)	2 (1.8%)
TOTAL	44(39.6%)	67(60.4%)

39.6% of the patients were exposed to tobacco smoke due to use by family members.

RELATION TO AQI:

According a previous study done by our institute, we found a strong co relation between seasonal variation in AQI with number of respiratory admissions.

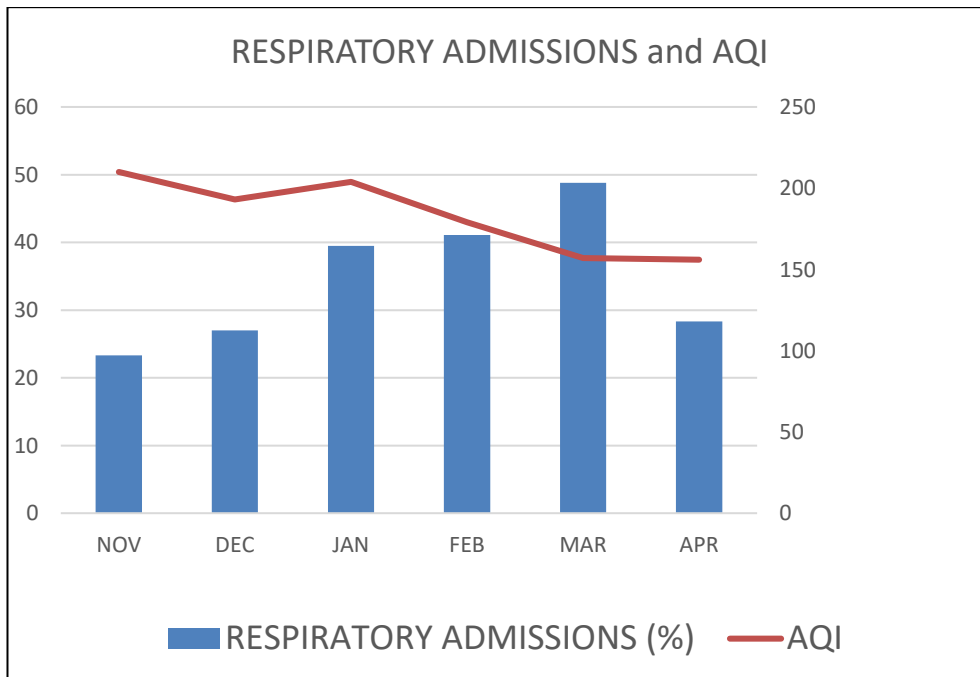


Figure 1: RESPIRATORY ADMISSION AND AQI

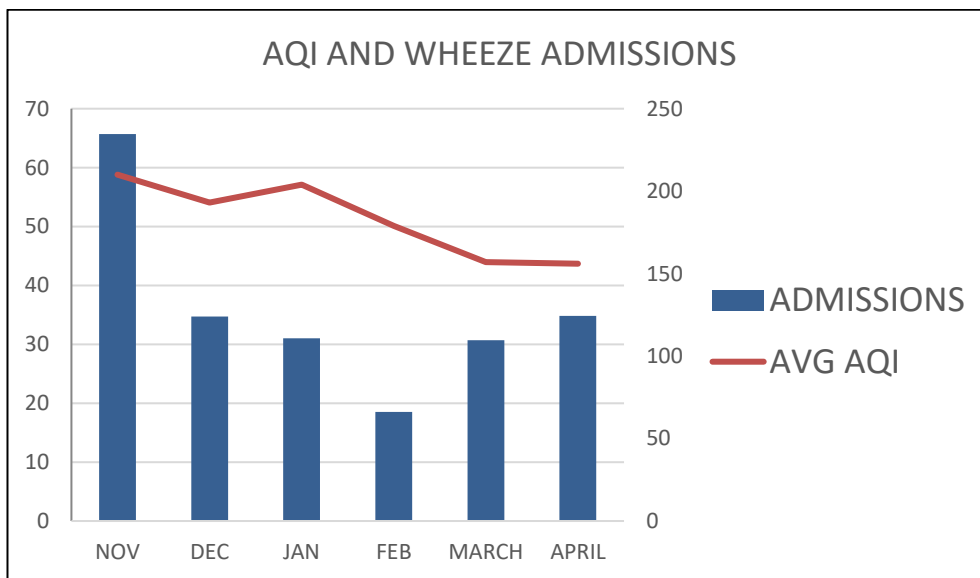


Figure 2: AQI AND WHEEZE ADMISSIONS

It is clear from the above data, that an average 1/3rd of the total admissions of 6 months to five years old children in the studied 6 months are due to respiratory causes and an average of 1/3rd of those respiratory admissions presented with wheeze, after applying the exclusion criteria. March had maximum proportion (48.8%) of respiratory admissions, while November showed maximum proportion (65.7%) of wheeze related admissions. The relationship with AQI is also depicted.

Follow up:

Total 72 (64.8%) of the 111 patients enrolled in the study could be followed up as per set protocol, rest were lost to follow-up due to variety of reasons; chief among them may be migration, social reasons, and lack of priority due to the child being apparently healthy.

Discussion

The number of first-time wheezers enrolled during the study was 58, 46(79.3%) of them were below 2 years of age. The total number of episodic wheezers was found to be 91, which is about 82% of the total enrolled patients. 72 (79.1%) of the episodic wheezers were of 2 years of age or younger when they presented. The mean age of presentation of wheezing in a study of viral etiology of wheeze under 5 years of age was 14.11 ± 12.74 months, and 78 % of children were less than two years old.^[4]

The proportion of wheezing disorders is high in males compared to females which is in accordance with published literature and supported by a Dutch study Visser et al.^[5] which found wheeze to be independently with male infants. This is thought to be due to boys having lower airway function than girls during infancy and childhood. The Prevention and Incidence of Asthma and Mite Allergy (PIAMA) study, have shown this gender disparity in asthma. As children, boys have an increased prevalence of asthma compared to girls with increased atopy, wheeze, serum Ig E levels, and use of asthma medications.

Infants are prone to wheeze because of anatomic factors related to the lung and chest wall in addition to immunologic and molecular influences in comparison to older children. Viral infections lead to immunologic derangements that cause wheezing both in immunocompetent and immunodeficient infants. In Brazil the Estudio Internacional de Sibilancias en Lactantes (EISL), from 3,003 infants in the city of Curitiba, PR; it was observed that, in first 12 months of life, 45.4% had at least one episode and 22.6% had recurrent wheezing episodes, evidencing a high prevalence of wheezing, with early onset and high morbidity.^[6]

Birth weight of all the patients was recorded, we found that 37 (33.3%) of the 111 study patients had LBW (<2.5kg). According to a meta analysis, Low birth weight (<2,500 g) is associated with increased risk of asthma and wheezing both in children and adults and may serve as a mediator between prenatal influences and later disease risk.^[7] A total of 37 studies comprising 1,71,737 participants were included in a meta-analysis which concluded low birth (<2.5 kg) is an independent risk factor for wheezing disorders during childhood and adolescence.^[8]

On eliciting detailed history 19(17.17%) of the study patients had history of NICU admission for one or the other reasons which is in synchrony with a study in Sweden which concluded that treatment with antibiotics in the neonatal period was an independent risk factor for wheezing.^[9] In a study in Japan, the rate of wheezing attack among patients with TTN diagnosis was found to be significantly higher than that in patients who had no TTN diagnosis ($P < 0.01$). TTN was found to be an independent risk factor for wheezing attack (OR, 2.378; 95% CI, 1.20-4.70).^[10]

As 44(39.6%) of the patients were exposed to tobacco smoke due to use by elderly family members. Jing et al.in a study of 378 children with asthma showed that passive smoking induces pediatric asthma by affecting the balance of T-regulatory cells/T-helper type 12 cells ratio. Passive smoking significantly reduced the ratio of T-reg/Th17 cells($p < 0.05$).^[11] In a recent review, exposure to maternal and passive smoking, both pre- and postnatal, was shown to increase the incidence of wheezing and asthma in small children and teenagers up to 18 years of age by at least 20%. Stronger influence of parental smoking is seen on viral associated wheezing particularly maternal smoking for age below 6 years^[12] and weaker relationship with atopic wheezing. The average AQI has a positive correlation with proportion of Wheezers ($r=0.5$) and the strength of correlation (r^2) is 25% but is statistically insignificant at 95% confidence level. The strength of correlation between number of respiratory admissions per month and average AQI is 19% which is also statistically insignificant at 95% confidence level. It is clear that low birth weight, age at 1st episode less than 1 year, and episodic wheeze were

significant risk factors for recurrence of wheeze which may either be episodic or non episodic. Though 86.8% of study subjects lived in overcrowded houses, no significant association was found between overcrowding and propensity to wheeze in the study. Many studies exist which support overcrowding as a risk factor for acute respiratory illnesses but may provide protection against non-episodic wheeze. Contradicting studies also exist, which provides a strong rationale to pursue a robust study on overcrowding and wheeze at a global level.^[13]

Conclusion:

A complex relationship exists between various factors which may be responsible for the recurrence of wheeze. Proportion of morbidity caused by wheeze is quite high in comparison to other respiratory diseases. Although mortality in non-episodic wheeze is low, quality of life is significantly affected in case of improper management leading not only to economical and social losses to the parents but affecting mental, physical growth and development of the child. It poses a great challenge for a clinician not only to diagnose and effectively treat the child but also identify risk factors so that steps may be taken to eliminate them if possible.

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