

FACTORS IMPEDING A SATISFACTORY CLINICAL RESPONSE IN CHILDREN UNDER THE AGE OF FIVE WITH WHEEZING

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Abstract

Background: Paediatric wheezing poses a significant health burden and requires comprehensive investigation into associated factors resulting in hospital visit. This cross-sectional study, conducted at a tertiary care centre and in a Paediatric outpatient clinic in Chennai aimed to explore the demographic, clinical, and environmental determinants which contributed to wheezing in under five children and also severity of the episodes requiring hospital stay and healthcare utilisation among these children.

Methods: Data was collected using questionnaires, clinical histories, and physical examinations. Healthcare utilisation metrics included Emergency Room (ER) visits, hospitalisations, and Intensive Care Unit (ICU) admissions. Statistical analyses were performed using chi-square tests and Mann-Whitney U tests, and a p-value <0.05 was considered significant. **Results:** A total of 75 children were included in this study, of whom 40 were male (53.3%). Among the socioeconomic groups, no significant association was found between wheezing severity and hospitalisation needs. Irregular use of metered-dose inhalers (MDIs) was associated with mild wheezing episodes ($p = 0.003$) and lower hospitalisation rates ($p = 0.001$). Additionally, there were no significant differences in wheezing severity across different age groups ($p = 0.341$). However, significant differences were observed in the mean number of exacerbations per week ($p = 0.001$) and year ($p = 0.001$) based on wheezing severity. Children with severe wheezing experienced exacerbations more frequently than those with mild or moderate wheezing. **Conclusion:** Regular MDI use emerged as a crucial factor in mitigating wheezing severity and reducing hospitalisation rates among children. This highlights the importance of adherence to prescribed inhaler regimens and following the proper technique of drug administration for the management of paediatric wheezing.

Keywords: Wheezing, Paediatric Population, Paediatric Health, Pulmonary Tests, Metered-Dose Inhalers.

INTRODUCTION

Wheezing during early childhood is prevalent and affects approximately 50% of infants within their first year of life.¹ Recurrent wheezing is estimated to affect one-third of preschool-aged children, leading to notable morbidity, reduced quality of life, heightened healthcare utilisation, and an increased economic burden.² Research has established the clinical diversity of wheezing in early childhood, including variations in age of onset, duration of symptoms, and associated risk factors such as atopy, genetic predisposition, and environmental influences, each contributing to distinct outcomes.^{3,4} The characterisation of different wheezing phenotypes dates back to seminal studies such as the Tucson Childhood Respiratory Study by Martinez et al., which classified children into four primary subtypes: never wheezing, early transient wheezing, persistent wheezing, and late-onset wheezing.⁵ Subsequent investigations further refined these classifications, delineating nonatopic persistent wheezing,

atopic/IgE-associated wheezing, and additional subtypes through longitudinal analyses.⁶⁻¹³

Despite these advancements, the clinical differentiation of these phenotypes remains challenging because of the dynamic nature of symptom expression and evolving risk factors. Various factors, including genetic variations, environmental exposures, host-related elements, and their intricate interplay, contribute to the development and progression of wheezing in affected individuals.¹³ Wheezing is a complex symptom that typically correlates with bronchiolitis or asthma, although less common conditions should be considered for atypical presentations.¹ While approximately 60% of

patients are anticipated to recover and become symptom-free by age 6 years, the majority continue to remain asymptomatic at ages 11 and 16 years.^{14,15}

Overall, this study aimed to provide a comprehensive understanding of the demographic, clinical, and environmental factors resulting in poor clinical response in children under 5 years of age with wheezing, with the ultimate goal of improving the diagnosis, management, and parental education resulting in improving the outcome of paediatric patients with these conditions.

MATERIALS AND METHODS

This cross-sectional study was conducted in 75 patients at a tertiary care centre and an Outpatient clinic in Chennai in collaboration with paediatric and pulmonary departments of Saveetha medical college. Before initiating the study, approval was obtained from the ethics committee and informed consent. Upon recruitment, accompanying parents or guardians completed questionnaires assessing demographic and environmental risk factors, under the guidance of trained physicians. Additionally, a detailed clinical history was obtained and a physical examination was conducted for each participant.

Following their initial ER visit or hospitalisation, all children were invited to return for a follow-up appointment two weeks later. During this follow-up, blood samples were collected for further analysis, and skin prick testing (SPT) was performed to evaluate allergic sensitisation and potential triggers of wheezing in these children.

Data collection

Patient data, including demographic details, economic status of parents, history of wheezing, incidence of allergic rhinitis (AR), severity of wheezing, exposure of what allergen resulted in exacerbation and MDI use with the treatment provided, were obtained and included in an Excel sheet.

Three metrics were used to assess healthcare utilisation during wheezing episodes in this study: the number of Emergency Room (ER) visits within the preceding year due to wheezing, a history of hospitalisations due to wheezing within the previous year, and any admissions to an Intensive Care Unit (ICU) attributed to wheezing. To accommodate for the sample size, the frequency of ER visits was categorised into two groups: <5 and ≥5 episodes. The groups "frequent episodes" and "persistent wheezers" were defined by GEMA¹⁵. These metrics were provided by parents through questionnaires administered during their children's ER visits.

Statistical analysis

Group proportions were assessed using either the chi-squared test or Fisher's exact test, depending on the number of observations in each group. As IgE levels were not normally distributed, comparisons involving continuous variables were conducted using the Mann-Whitney U test or Kruskal-Wallis test as applicable. Correlations were determined using the Spearman's test. Statistical significance was set at $p < 0.05$. The analysis was performed using the IBM SPSS statistics 20.0.

RESULTS

This study included 40 male (53.3%) and 35 female (46.7%) children. Among the participants, 23 (30.7%) were from lower-income families, 31 (41.3%) were from middle-income families, and 21 (28%) were from upper-income families. Regarding preschool attendance, 36 children (48%) did not attend preschool, 21 (28%) attended Balwadi, and 18 (24%) attended preschool. Additionally, 48 children (64%) had no family history of wheezing, while 27 (36%) had a positive family history of wheezing.

Table 1: Demographic characteristics of patients

		Number of cases	Percentage
Gender	Male	40	53.3
	Female	35	46.7
Socioeconomic status	Lower	23	30.7
	Middle	31	41.3
	Upper	21	28
Attending preschool	Nil	36	48
	Balwadi	21	28
	Pre School	18	24
Family history	No	48	64
	Yes	27	36

Among the participants, 68% had no history of allergic rhinitis, whereas 32% reported a history of allergic rhinitis. Additionally, 62.7% of children were found to use Metered Dose Inhalers (MDIs) regularly, while 37.3% did not use MDIs regularly. Most participants knew about the technique of MDI administration (65.3%) and (34.6%) were not aware of the technique of drug administration using the MDI. Regarding the severity of wheezing, 50.6% of cases were classified as mild and 28% were classified as moderate and 21.3% were classified as severe. Exacerbations occurred following various exposures, with 40% attributed to infections, 16% to animal dander, 14.7% to smoke, 10.7% to pollen, 8% to cold air, 5.3% to stress, and 5.3% to poor MDI compliance. Furthermore, 60% of the patients did not require hospitalisation during wheezing episodes, while 40% required hospitalisation. In terms of treatment, 56% received nebulization with bronchodilators, 21.3% received a combination of steroids and nebulization with bronchodilators, and 22.7% received a combination of steroids, nebulization, and magnesium sulfate (MgSO₄) therapy.

Table 2: Patient history and severity of wheezing

		Number of cases	Percentage
History of Allergic rhinitis	No	51	68
	Yes	24	32
Using MDI Regularly	No	28	37.3
	Yes	47	62.7
Technique known	Yes	49	65.3
Severity	No	26	34.6
	Mild	38	50.6
	Moderate	21	28
Exacerbation following what exposure	Severe	16	21.3
	Smoke	11	14.7
	Infection	30	40
	Pollen	8	10.7
	Cold air	6	8
	Stress	4	5.3
	Poor MDI compliance	4	5.3
Required hospitalisation	Animal dander	12	16
	No	45	60
Treatment given	Yes	30	40
	Nebulization	42	56
	Steroid + Nebulization	16	21.3
	Steroid + Nebulization + MgSo4	17	22.7

The mean age for mild, moderate, and severe wheezing groups was 1.85 years (standard deviation [SD] = 1.50), 1.69 years (SD = 1.40), and 2.40 years (SD = 1.62), respectively, with no significant difference found ($p = 0.341$). Children were diagnosed as wheezers at an average age of 1.16 years (SD = 0.99) for mild wheezing, 1.10 years (SD = 1.01) for moderate wheezing, and 1.36 years (SD = 1.11) for severe wheezing, with no notable distinction observed ($p = 0.72$).

The mean number was 1.00 for mild wheezing, 1.19 for moderate wheezing, and 2.31 for severe wheezing showed a significant difference among the groups ($p = 0.001$). Similarly, the mean number of exacerbations per week was 1.08 for mild wheezing, 2.76 for moderate wheezing, and 4.81 for severe wheezing was significantly different ($p = 0.001$). Furthermore, the mean number of exacerbations per year was 2.66 for mild wheezing, 5.95 for moderate wheezing, and 9.00 for severe wheezing demonstrated a significant difference among the groups ($p = 0.001$).

Table 3: Association of wheezing and clinical characteristics

	Mild	Moderate	Severe	P value
Age	1.85 ± 1.5	1.69 ± 1.4	2.4 ± 1.62	0.341
Diagnosed as a wheezer when	1.16 ± 0.99	1.1 ± 1.01	1.36 ± 1.11	0.72
Number of exacerbations	1 ± 0	1.19 ± 0.51	2.31 ± 0.79	0.001
Exacerbations in a week	1.08 ± 0.36	2.76 ± 1.41	4.81 ± 1.52	0.001
Exacerbations in a year	2.66 ± 1.36	5.95 ± 2.22	9 ± 2.13	0.001

In this study, the distribution of wheezing severity among different demographic and clinical factors was analysed. Among the males, 23 (60.5%) had mild wheezing, eight (38.1%) had moderate wheezing, and nine (56.3%) had severe wheezing. For females, 15 (39.5%) had mild wheezing, 13 (61.9%) had moderate wheezing, and 7 (43.8%) had severe wheezing. These differences in wheezing severity between sexes

were not statistically significant ($p = 0.246$). Regarding socioeconomic status, lower-income children showed mild wheezing in 11 cases (28.9%), moderate wheezing in six cases (28.6%), and severe wheezing in six cases (37.5%). Middle-income children had mild wheezing in 15 (39.5%), moderate wheezing in eight (38.1%), and severe wheezing in eight (50%). Upper-income children exhibited mild wheezing in 12 cases (31.6%), moderate wheezing in 7 cases (33.3%), and severe wheezing in 2 cases (12.5%). The differences in wheezing severity across socioeconomic statuses were not statistically significant ($p = 0.654$). In terms of preschool attendance, those not attending (Nil) had mild wheezing 17 patients (44.7%) had mild wheezing, 14 (66.7%) had moderate wheezing, and five (31.3%) had severe wheezing. Among the Balwadi attendees, 12 (31.6%) had mild wheezing, 4 (19%) had moderate wheezing, and 5 (31.3%) had severe wheezing. Preschool attendees showed mild wheezing in nine cases (23.7%), moderate wheezing in three cases (14.3%), and severe wheezing in six cases (37.5%). The differences in wheezing severity based on preschool attendance were not significant ($p = 0.247$). When considering family history, those without a family history of wheezing had mild wheezing in 24 cases (63.2%), moderate wheezing in 17 cases (81%), and severe wheezing in seven cases (43.8%). Participants with a family history had mild wheezing in 14 cases (36.8%), moderate wheezing in 4 cases (19%), and severe wheezing in 9 cases (56.3%). The differences in wheezing severity based on family history were not statistically significant ($p = 0.065$).

Regarding the history of allergic rhinitis, 26 patients (68.4%) had mild wheezing, 16 (76.2%) had moderate wheezing, and 9 (56.3%) had severe wheezing. Participants with a history of allergic rhinitis had mild wheezing in 12 cases (31.6%), moderate wheezing in 5 cases (23.8%), and severe wheezing in 7 cases (43.8%). The differences in wheezing severity based on allergic rhinitis history were not statistically significant ($p = 0.435$). Finally, in terms of regular use of Metered Dose Inhalers (MDIs), those not using MDIs regularly had mild wheezing in 8 cases (21.1%), moderate wheezing in 9 cases (42.9%), and severe wheezing in 11 cases (68.8%). Participants using MDIs regularly had mild wheezing in 30 cases (78.9%), moderate wheezing in 12 cases (57.1%), and severe wheezing in five cases (31.3%). Differences in wheezing severity based on regularity of MDI use were statistically significant ($p = 0.003$).

Table 4: Association of patient history with severity of wheezing

		Severity			P value
		Mild	Moderate	Severe	
Gender	Male	23 (60.5%)	8 (38.1%)	9 (56.3%)	0.246
	Female	15 (39.5%)	13 (61.9%)	7 (43.8%)	
Socioeconomic status	Lower	11 (28.9%)	6 (28.6%)	6 (37.5%)	0.654
	Middle	15 (39.5%)	8 (38.1%)	8 (50%)	
	Upper	12 (31.6%)	7 (33.3%)	2 (12.5%)	
Attending preschool	Nil	17 (44.7%)	14 (66.7%)	5 (31.3%)	0.247
	Balwadi	12 (31.6%)	4 (19%)	5 (31.3%)	
	Pre School	9 (23.7%)	3 (14.3%)	6 (37.5%)	
Family history	No	24 (63.2%)	17 (81%)	7 (43.8%)	0.065
	Yes	14 (36.8%)	4 (19%)	9 (56.3%)	
History of Allergic rhinitis	No	26 (68.4%)	16 (76.2%)	9 (56.3%)	0.435
	Yes	12 (31.6%)	5 (23.8%)	7 (43.8%)	
Using MDI Regularly	No	8 (21.1%)	9 (42.9%)	11 (68.8%)	0.003
	Yes	30 (78.9%)	12 (57.1%)	5 (31.3%)	

In terms of hospitalisation requirements, the data showed that among males, 23 (51.1%) did not require hospitalisation, while 17 (56.7%) did. For females, 22 (48.9%) did not require hospitalisation and 13 (43.3%) did. However, these differences in hospitalisation rates between sexes were not statistically significant ($p = 0.637$). Regarding socioeconomic status, 12 patients (26.7%) did not require hospitalisation and 11 (36.7%) required hospitalisation. Middle-income participants had 19 cases (42.2%) that did not require hospitalisation and 12 (40%) that required hospitalisation. Fourteen patients (31.1%) did not require hospitalisation, and seven (23.3%) required hospitalisation. These differences in hospitalisation rates across socioeconomic statuses were also not statistically significant ($p = 0.607$).

When considering preschool attendance, 22 cases (48.9%) of those not attending (Nil) did not require hospitalisation, while 14 cases (46.7%) did require hospitalisation. Among the Balwadi attendees, 14 (31.1%) did not require hospitalisation and 7 (23.3%) did. Nine preschool attendees (20%) did not require hospitalisation and 9 (30%) required hospitalisation. The differences in hospitalisation rates based on preschool attendance were not statistically significant ($p = 0.561$). Regarding family history, 31 patients (68.9%) without a family history of wheezing did not require hospitalisation, and 17 patients (56.7%) did. Fourteen patients (31.1%) did not require hospitalisation and 13 (43.3%) required hospitalisation. However, the differences in hospitalisation rates based on family history were not statistically significant ($p = 0.28$).

Among those with no history of allergic rhinitis, 33 (73.3%) did not require hospitalisation and 18 (60%) did. Twelve patients (26.7%) had a history of allergic rhinitis and 12 (40%) required hospitalisation. These differences in hospitalisation rates based on allergic rhinitis history were not statistically significant ($p = 0.225$). Regarding the regular use of Metered Dose Inhalers (MDIs), 9 cases (20%) of non-regular MDI users did not require hospitalisation, whereas 19 (63.3%) required hospitalisation. Participants using MDIs regularly had 36 cases (80%) that did not require hospitalisation and 11 (36.7%) that required hospitalisation. These differences in hospitalisation rates based on regularity of MDI use were statistically significant ($p = 0.001$).

Table 5: Association of patient characteristics with hospitalisation need

		Required hospitalisation		P value
		No	Yes	
Gender	Male	23 (51.1%)	17 (56.7%)	0.637
	Female	22 (48.9%)	13 (43.3%)	
Socioeconomic status	Lower	12 (26.7%)	11 (36.7%)	0.607
	Middle	19 (42.2%)	12 (40%)	
	Upper	14 (31.1%)	7 (23.3%)	
Attending preschool	Nil	22 (48.9%)	14 (46.7%)	0.561
	Balwadi	14 (31.1%)	7 (23.3%)	
	Pre School	9 (20%)	9 (30%)	
Family history	No	31 (68.9%)	17 (56.7%)	0.28
	Yes	14 (31.1%)	13 (43.3%)	
History of Allergic rhinitis	No	33 (73.3%)	18 (60%)	0.225
	Yes	12 (26.7%)	12 (40%)	
Using MDI Regularly	No	9 (20%)	19 (63.3%)	0.001
	Yes	36 (80%)	11 (36.7%)	

DISCUSSION

The findings of this study shed light on several key aspects of wheezing in children. The demographic distribution indicated a slightly higher prevalence of wheezing in males (53.3%) compared to females (46.7%). The socioeconomic status of the participants varied, with 30.7% from lower-income families, 41.3% from middle-income families, and 28% from upper-income families. Furthermore, 48% did not attend preschool, 28% attended Balwadi, and 24% attended preschool. Moreover, a notable proportion of the children had a family history of wheezing (36%), while 64% did not.

Similar findings were reported in other studies, where socioeconomic status significantly affected the incidence of wheezing among children. The literature has suggested an association between exacerbation of the disease and poverty, poor hygiene, and recurrent wheezing.¹⁶⁻¹⁹ César et al. reported wheezing in male patients (72%) which was similar to our study findings.¹⁹ The study conducted by Zhu Y et al., reported similar study findings where in 8569 pediatric patients recurrent wheezing was reported among 343 patients. In addition, winter was the most common factor for the onset of wheezing in pediatric patients.²⁰

The analysis of clinical characteristics revealed that 32% of children had a history of allergic rhinitis and 62.7% were regularly using Metered Dose Inhalers (MDIs). All participants (100%) were knowledgeable about MDI usage techniques. The severity of wheezing varied, with 50.7% classified as mild and 49.3% classified as moderate. Exacerbations were triggered by various factors, including infections (40%), animal dander (16%), smoke (14.7%), pollen (10.7%), cold air (8%), stress (5.3%), and poor compliance with MDIs (5.3%).

Additionally, 40% of patients required hospitalisation during wheezing episodes. The severity of wheezing differs from that in our study, in which mild occasional episodic wheezing was reported in 85 patients (66.9%), followed by frequent moderate episodes in 24 patients (18.9%), and severe episodic wheezing in 18 patients (14.2%). The study also reported a significant association between age and incidence of wheezing among children.¹⁹ The multivariate and univariate analysis in pediatric patients reported few independent risk factors that contributed toward wheezing in children including, male gender, history of respiratory or cardiovascular disease, low birth weight, severe pneumonia, and admission to PICU.²⁰

No significant differences were found in wheezing severity based on sex ($p = 0.246$), socioeconomic status ($p = 0.654$), preschool attendance ($p = 0.247$), family history ($p = 0.065$), or allergic rhinitis history ($p = 0.435$). However, a significant association was observed between wheezing severity and regular use of MDIs ($p = 0.003$). The use of MDI, such as montelukast, was proven to be the most protective factor in patients requiring hospitalisation due to wheezing.¹⁹ In addition, few studies have reported that using MDI reduces acute exacerbations that require oral corticosteroids or other treatment methods.²¹

The study conducted by Kim JH et al, reported parallel study results as of our study, where gender and age were the confounding variables for the development of wheezing. In addition, the study also highlighted that parental history of allergic diseases [OR, 20.19, CI: 3.22-126.48], and past history of hospitalization were reported to be independent variables for wheezing.²²

Furthermore, the need for hospitalisation did not significantly differ according to gender ($p = 0.637$), socioeconomic status ($p = 0.607$), preschool attendance ($p = 0.561$), family history ($p = 0.28$), or allergic rhinitis history ($p = 0.225$). However, there was a significant association between hospitalisation needs and regular use of MDIs ($p = 0.001$), indicating that children using MDIs were less likely to require hospitalisation. In a post-interventional study including 140 patients, Basheti et al. reported that the use of MDIs for three months can significantly reduce wheezing and have better outcomes. In addition, the study also reported a mean increase in ACT score of 7.54 (SD 8.18).²²

The study conducted by Costa Bessa OAA et al. among 1209 patients reported a family history of asthma, episodes of cold, and pneumonia as a significant risk factor for the development of recurrent wheezing. However, in our study we did not report similar characteristics as risk factors. In addition, the incidence of nocturnal symptoms and early onset of wheezing were majorly associated with hospitalization. The study also reported that increased incidence of wheezing has been reported as a significant risk factor for hospitalization.²³ Other studies did not report the use of MDI as a significant factor in patients for wheezing.²¹⁻²³ In our study we report that the use of MDI can lower hospitalization rate in children presented with wheezing.

CONCLUSION

In conclusion, our study reports on the intricate web of factors influencing wheezing severity and hospitalisation needs in children under five. While sex, socioeconomic status, preschool attendance, family history of wheezing, and history of allergic rhinitis were not significantly associated with wheezing severity or hospitalisation needs, the lack of regular use of MDIs emerged as a pivotal factor which contributed to wheeze exacerbation in many children ($p = 0.003$).

Children regularly using MDIs exhibited lower wheezing severity and were less likely to require hospitalisation, highlighting the crucial role of proper medication adherence in managing paediatric wheezing. These findings underscore the importance of tailored management strategies, emphasising education and support for families in optimising MDI use to improve outcomes and reduce healthcare utilisation in young wheezers.

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