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Frequency of Gastroesophageal Reflux Disease in Children with Persistent Cough and Wheezing

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ABSTRACT

Objective: To determine the frequency of gastroesophageal reflux disease (GERD) in children with persistent cough and wheezing. **Study Design:** Cross-sectional study. **Settings:** Department of Pediatric Medicine, Children's Hospital & The Institute of Child Health, Multan Pakistan. **Duration:** Six-months from 1st December 2023 to 31st May 2024. **Methods:** A total of 113 children aged 6 months to 12 years of either gender presenting with persistent cough and/or wheeze were consecutively enrolled. Children with developmental delay, congenital heart disease, or other congenital malformations were excluded. GERD was diagnosed on barium swallow study if any one or more of the following findings were present: reflux of gastric contents into the lower esophagus, hiatal hernia, signs of reflux esophagitis, or impaired gastric motility. Descriptive statistics in the form of mean ± SD for numerical and frequency and percentages were calculated for qualitative data. Confounding was assessed through stratification using a chi-square test at a 5% significance level. **Results:** The study enrolled children with a mean age of 3.9±1.8 years, 69% male, a mean BMI of 17.1±0.7 kg/m², and a mean illness duration of 3.3±0.6 weeks. GERD was diagnosed in 45.1% of cases, with significantly higher prevalence among premature children (82.5% vs. 24.7%, p <0.001) and those with positive family history of atopy (71.4% vs. 29.6%, p < 0.001). **Conclusion:** GERD is a common finding in children presenting with persistent cough and wheeze. The condition is notably more prevalent in children born prematurely and with a family history of atopy.

Keywords: *Gastroesophageal reflux, Chronic cough, Wheezing, Prematurity.*

INTRODUCTION

A common physiological occurrence that occurs frequently throughout a 24-hour duration in healthy infants, children, and even adults is gastroesophageal reflux (GER).[1] GER is frequently characterized by sporadic relaxation of the lower esophageal sphincter (LES), regardless of eating, allowing stomach contents to pass into the oesophagus.[2] It is linked to several difficulties. Numerous respiratory symptoms have been documented to coexist with gastroesophageal reflux.[3] There is little information available on the frequency and natural history of GER in children. The majority of infants with reflux get well by the time they are one year old, but very few continue to develop gastroesophageal reflux disease later in life.[4]

Chronic symptoms related to the lungs, such as a persistent cough, frequent wheezing, and respiratory distress, can be a sign of gastroesophageal reflux.[5] One of the issues that causes children to see pediatricians frequently is a persistent cough, and one of the most common causes of this condition is gastroesophageal reflux disease.[6] Asthma symptoms can occasionally be alleviated by intensive anti-reflux medication, and GER is a known possible asthma trigger.[7]

Praveen PN *et al* enrolled a total of 30 children (1-12 years of age) who presented with persistent cough and wheezing of duration above 3 months. They found a 63.3% frequency of GER in their study.[8] Aslam M *et al* included a total of 75 patients (between 2 months to 2 years of age) with chronic cough. Out of the total cases, GERD was observed in 39% of patients confirmed on barium study.[9]

There is not much literature on the relationship between GER and lung conditions among pediatric patients

previously published from our country. With this background, we wanted to document the magnitude of GER in children having persistent cough so that we may identify treatable etiology of chronic respiratory symptoms. If timely managed, many long-term complications of GER, e.g., feeding difficulties, failure to thrive, esophageal narrowing, and damage to the tissue in the esophagus (called Barrett's syndrome), can be prevented. If GERD is diagnosed correctly, unnecessary use of bronchodilators, corticosteroids, and antibiotics can be avoided.

METHODS

This hospital-based cross-sectional study was conducted at the Department of Pediatric Medicine, Children's Hospital & the Institute of Child Health Multan after approval from the institutional ethics review committee (No: 2148/CH&ICH Multan, dated: 29-11-2023) throughout 6 months from 1st December 2023 to 31st May 2024. Children 6 months to 12 years, either male or female gender and presenting with persistent cough and/or wheeze were consecutively recruited in the study after obtaining informed consent from the parents. Children with developmental delay, with congenital heart disease, or other congenital malformation were excluded from the study.

Children with cough and wheeze (on clinical assessment) lasting for more than two weeks were labelled as having persistent cough and wheeze. Age, gender, duration of illness (weeks), prematurity, family history of atopy, and body mass index (BMI) were recorded. BMI was measured by the formula –weight in kg/height in meters^2. Weight was measured on a weighing scale and height on a stadiometer. All children underwent a barium swallow study from the radiology department. Gastroesophageal reflux disease (GERD) was labelled if any one or more findings of (i) reflux of gastric contents into the lower esophagus, (ii) hiatal hernia, (iii) signs of reflux esophagitis, (iv) impaired gastric motility were present. Patients positive for GERD were treated in consultation with a pediatric gastroenterologist.

A minimum sample size of 113 children was calculated through the WHO sample size calculator using a one-proportion formula, taking a 39% prevalence of GERD in children with persistent cough and wheeze,[9] 95% confidence level, and 9% precision. Data was analyzed through SPSS version 23. Normality of numerical data was assessed through the Shapiro-Wilk test. Age, duration of illness, and BMI are presented as mean ± SD. Gender, prematurity, family history of atopy, and GERD are presented as frequencies and percentages. Confounding was assessed through stratification on demographic variables using a chi-square test at a 5% significance level.

RESULTS

The mean age of the participants was 3.9 ± 1.8 years and included 69% (n=78) males. The mean body mass index was 17.1 ± 0.7 kg/m^2, and the mean duration of illness was 3.3 ± 0.6 weeks. In 35.4% (n=40) cases, children were born premature, and 37.2% (n=42) had a family history of atopy. Gastroesophageal reflux disease (GERD) was diagnosed in 45.1% (n=51). Table 1

Table 1: Characteristics of children presenting with persistent cough and wheezing (N=113)

Age (years)	3.9 ± 1.8
Gender	
Male	78 (69)
Female	35 (31)
Body Mass Index (kg/m^2)	17.1 ± 0.7
Duration of Illness (weeks)	3.3 ± 0.6
Prematurity (Yes)	40 (35.4)
Family History of Atopy (yes)	42 (37.2)
Gastroesophageal Reflux Disease (yes)	51 (45.1)

The prevalence of GERD was remarkably high in children born prematurely compared to full-term born (82.5% vs. 24.7%, p-value < 0.001). Similarly, the prevalence of GERD was substantially higher in children with a family history of atopy compared to no family history (71.4% vs. 29.6%, p-value < 0.001). Table 2

Table 2: Relationship between demographic characteristics and gastroesophageal reflux disease in children presenting with persistent cough and wheezing (N=113)

Demographic Characteristics		Gastroesophageal Reflux Disease		p-value*
		Yes	No	
Age	< 5-years	37 (46.8)	42 (53.2)	0.579
	≥ 5-years	14 (41.2)	20 (58.8)	
Gender	Male	33 (42.3)	45 (57.7)	0.368
	Female	18 (51.4)	17 (48.6)	
Duration of Illness	≤ 3-weeks	29 (40.3)	43 (59.7)	0.169
	> 3-weeks	22 (53.7)	19 (46.3)	
Body Mass Index (kg/m^2)	15.4 – 17.0	29 (46.0)	34 (54.0)	0.829
	17.1 – 18.5	22 (44.0)	28 (56.0)	
Prematurity	Yes	33 (82.5)	7 (17.5)	< 0.001
	No	18 (24.7)	55 (75.3)	
Family History of Atopy	Yes	30 (71.4)	12 (28.6)	< 0.001
	No	21 (29.6)	50 (70.4)	

**chi-square test*

DISCUSSION

The movement of stomach contents into the esophagus is known as gastroesophageal reflux disease (GERD), which

involves problematic symptoms or complications related to GER.[10] GERD is different from GER. Esophageal and extra-esophageal symptoms are common in children with gastroesophageal reflux. The two most prevalent extra-esophageal respiratory symptoms of GER are persistent coughing and frequent wheezing.[11] The condition of gastroesophageal reflux has a broad spectrum in children, ranging from a physiological process in infants to pathological repercussions in children and teenagers, which is known as gastroesophageal reflux disease.[12]

In our study, the mean age of the patients was 3.9±1.8 years, and included 69% males. While in children positive with GER, there was no prominent difference between age groups of <5 and ≥5 years, as well as between male and female genders. According to Praveen PN *et al*, GER was more common in males (63.1%) and more common in children under the age of five (40%) than in children above the age of five (25.5%).[8] According to a study by Aslam *et al*, the prevalence was highest at ages under a year, with 20 (27%) of the 29 patients being between the ages of 2 and 9 months and 9 (12%) being between the ages of 10 and 17 months. The prevalence of GER was higher in males (24%) than in females (15%).[9]

Because the LES is still developing in newborns and young children, the stomach contents frequently reflux into the esophagus. Refluxed material can more easily reach the throat when the esophagus is shorter. The majority of an infant's diet is liquid, which is more prone to reflux than solid meals.[13] GER is a physiological and developmental condition that affects both boys and girls at similar rates in infancy and early childhood, unlike some conditions that are impacted by sex hormones or genetic susceptibility.[14]

In the current study, 45.1% of cases had a diagnosis of gastroesophageal reflux disorder (GERD). In their study, Praveen PN *et al* discovered the prevalence of GER as 63.3%.[8] According to research conducted in Boston by Irwin *et al*, 100% of patients with persistent coughs had gastroesophageal reflux.[15] According to Aslam M *et al*, barium study revealed that 29 (39%) of the 75 subjects with persistent cough had GERD.[9] Twenty-two (46%) of the 48 children with chronic recurrent cough had GER, according to Said M *et al*. It was mild GER in 14 children, moderate in 3, and severe in 5 children.[16]

Fifty-three children with recurrent respiratory tract infections were examined by Lupu VV *et al*, using 24-hour pH-metry to check for gastroesophageal reflux disease. A positive Boix-Ochoa score was reported in 41 (77.3%) of the children. Eight patients still had a positive Boix-Ochoa score two months after starting anti-reflux medication.[17] The variation in prevalence may be owing to the different sample sizes and the cut-off duration of chronic cough used in various studies.

According to a Saudi Arabian study by Saleh Othman *et al*,[18] 43.8% of patients had a chronic cough that was caused by reflux. Like the current study, studies by Khoshoo *et al*[19] and Said M *et al*[16] found no significant correlation between age and GER or between gender and GER. In the present study, frequency of GERD was significantly high in children born premature and those who had positive family history of atopy (p-value < 0.001). Our results contradict those of Gondim MM *et al*. They enrolled 197 infants (less than 24 months), 99 of whom were preterm and 98 of whom were term. Term infants were more likely to regurgitate (35.1% and 15.6%; P < 0.001).[20]

Parents of 582 infants under 6 months old took part in an online survey regarding their child's GER symptoms as part of another cross-sectional study. Compared to infants delivered at later gestational ages, those born at less than 32 weeks showed more GER symptoms. GER symptoms were not linked to the infant's sex or birth mode. GER symptoms were more common in infants with a positive family history of allergies.[21] These findings are relatable to our results. Because of their immature esophageal structure, decreased peristalsis, and slower stomach emptying, preterm infants are more likely to develop GERD.[22]

Thirty-three children with GERD participated in the study, and 67% of them had a positive family history of atopy, compared to just 12% in the control group. This suggests that there is a considerable link between the development of GERD in pediatric patients and familial atopic diseases.[23] This favors our results. When treating GERD in children, more care must be taken. While gastroesophageal reflux's physiological signs are typical in the first few months of life, problematic symptoms can persist and cause issues throughout childhood.

CONCLUSION

Our study concluded that GER prevalence in children with persistent cough and wheezing was 45.1%. Consequently, we suggest GER screening in wheezy children with persistent cough. Children with frequent, chronic symptoms should first undergo lifestyle changes and conservative therapies such as thickened feedings, food restrictions, posture adjustments, and avoiding overfeeding. Most patients can benefit from early diagnosis and timely treatment.

LIMITATIONS

Our study had a limitation that, due to the non-availability of the facility, we could not diagnose GER on esophageal PH monitoring, which is a safe, more sensitive, and specific technique for identifying GERD. The cross-sectional design precludes establishing any causal relationship between GERD and respiratory

symptoms. Additionally, the single-center setting and relatively small sample size (n=113) may limit the generalizability of the findings to broader pediatric populations.

SUGGESTIONS / RECOMMENDATIONS

Future research should consider using a combination of diagnostic tools, including pH monitoring and endoscopy, to more accurately diagnose GERD in children. A multi-center study with a larger and more diverse sample size would enhance the external validity of the findings. Longitudinal studies would be valuable in assessing causal relationships between GERD and persistent respiratory symptoms.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest.

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