

Prevalence of Gastroesophageal Reflux (GER) in Children with Persistent Cough and Wheezing: A Cross-Sectional Study

Masood Zahir¹, Siddhartha², Ashit Kumar³

¹Senior Resident, Department of Paediatrics, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India

²Senior Resident, Department of Paediatrics, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India

³Associate Professor, Department of Paediatrics, RDJM Medical College and Hospital, Turki, Muzaffarpur, Bihar, India

Received: 19-12-2024 / Revised: 15-01-2025 / Accepted: 27-02-2025

Corresponding Author: Dr. Siddhartha

Conflict of interest: Nil

Abstract:

Background: Gastroesophageal reflux (GER) is a condition in which stomach contents reflux into the esophagus, leading to symptoms such as cough, wheezing, and difficulty breathing. While GER is commonly associated with heartburn and regurgitation, its role in respiratory symptoms, particularly persistent cough and wheezing, is often overlooked in pediatric patients. Children with persistent cough and wheezing often present with a complex set of symptoms that can overlap with other respiratory conditions, making it difficult to diagnose the exact cause. This study aims to assess the prevalence of GER in children with persistent cough and wheezing and evaluate its potential contribution to respiratory symptoms.

Objective: The primary objective of this study is to determine the prevalence of gastroesophageal reflux in children with persistent cough and wheezing. Secondary objectives include investigating the relationship between GER and the severity of respiratory symptoms, and identifying possible risk factors for GER in this population.

Methods: This is a cross-sectional study conducted at Department of Pediatrics, RDJM Medical College and Hospital, Muzaffarpur, Bihar, India. The study included 120 children aged 1 to 12 years who presented with persistent cough and wheezing that lasted for at least 4 weeks. Participants were clinically evaluated, and a detailed medical history was taken, including data on the frequency and severity of respiratory symptoms, as well as any history of GER-related symptoms such as regurgitation, chest pain, or difficulty swallowing. Diagnosis of GER was confirmed using a combination of clinical evaluation, pH monitoring, and endoscopic findings. All subjects underwent a chest X-ray to rule out other causes of cough and wheezing, such as pneumonia or asthma.

Results: The study found that 45% of the children with persistent cough and wheezing had evidence of GER, as confirmed by diagnostic tests. Of these children, 55% had mild GER, while 35% had moderate GER, and 10% had severe GER. GER was more commonly observed in children with a history of recurrent respiratory infections, those with a family history of GERD, and those who were exposed to environmental tobacco smoke. The study also found a positive correlation between the severity of GER and the severity of respiratory symptoms.

Conclusion: This study suggests that gastroesophageal reflux may play a significant role in the pathogenesis of persistent cough and wheezing in children. Early identification and treatment of GER may help improve the management of respiratory symptoms in affected children. Clinicians should consider GER as a potential underlying cause in children with unexplained persistent cough and wheezing, particularly in those with other risk factors.

Keywords: Gastroesophageal reflux, persistent cough, wheezing, pediatric respiratory disorders, cross-sectional study, GERD.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Gastroesophageal reflux (GER) is a common condition where stomach contents, including acid, are regurgitated into the esophagus, causing a range of symptoms such as heartburn, regurgitation, and chest discomfort [1]. In children, GER can present with symptoms that differ from the classic signs seen in adults, often manifesting as respiratory

symptoms, including persistent cough, wheezing, and even asthma-like symptoms. The relationship between gastroesophageal reflux and respiratory symptoms has been a subject of growing interest in recent years, particularly regarding how GER may contribute to conditions like persistent cough and wheezing in pediatric patients [2].

Persistent cough and wheezing are among the most common reasons for pediatric consultations in outpatient settings. These symptoms are often associated with asthma, viral infections, or other respiratory conditions [3]. However, in some children, despite standard treatment for these conditions, symptoms may persist, suggesting an alternative or additional underlying cause. Gastroesophageal reflux has been increasingly recognized as a potential contributor to these unexplained respiratory symptoms, although its precise role remains debated [4].

GER can lead to respiratory symptoms through several mechanisms. The reflux of stomach contents can irritate the esophagus, leading to esophageal spasms and, in some cases, the aspiration of gastric contents into the airways [5]. This aspiration can cause bronchoconstriction, leading to wheezing and coughing. Furthermore, the acid in the stomach contents can trigger a reflex mechanism, causing laryngeal and bronchial hyperreactivity. This phenomenon is often seen in children with conditions like asthma, where the symptoms of GER may overlap with those of asthma, complicating diagnosis and treatment [6].

Despite the increasing recognition of GER as a potential cause of respiratory symptoms, many cases go undiagnosed, as the link between GER and respiratory conditions such as wheezing and cough is often not considered in clinical practice [7]. Additionally, the diagnosis of GER in children with respiratory symptoms is complicated by the nonspecific nature of the presenting symptoms. Furthermore, diagnostic methods such as pH monitoring and endoscopy are not always accessible in every clinical setting, especially in developing countries or in rural areas, where most pediatric respiratory symptoms are treated empirically [8].

The prevalence of GER in children with persistent cough and wheezing is an area that has not been extensively studied in India, particularly in the pediatric population. Previous studies from Western countries have demonstrated that GER is present in a significant proportion of children with persistent respiratory symptoms. In a study conducted in the United States, it was found that up to 50% of children with asthma also had GER, and up to 30% of children with persistent cough were found to have GER as an underlying cause. These studies suggest that GER may be a common, yet often overlooked, condition in children presenting with chronic respiratory symptoms [9,10].

In India, where the prevalence of respiratory disorders such as asthma and viral infections is high, understanding the role of GER in contributing to these conditions could be crucial. As respiratory diseases often account for a substantial proportion of pediatric admissions, particularly in regions with

high rates of environmental pollution and malnutrition, exploring GER as an additional risk factor for persistent respiratory symptoms is essential. Children with GER may be misdiagnosed with asthma or other respiratory conditions, leading to inappropriate treatments and delayed resolution of symptoms.

The importance of identifying GER in children with persistent cough and wheezing lies in the potential for targeted treatments that could improve clinical outcomes. If GER is identified as a significant contributor to respiratory symptoms, interventions such as lifestyle changes, acid suppression therapy, and dietary modifications could be introduced. Early recognition and treatment of GER may not only reduce the frequency and severity of respiratory symptoms but also improve overall quality of life for affected children.

This study aims to bridge the gap in current literature by assessing the prevalence of GER in children with persistent cough and wheezing at a tertiary care hospital in India. By evaluating the relationship between GER and these respiratory symptoms, the study seeks to contribute to the understanding of this complex interplay and provide insights into the potential benefits of early identification and treatment of GER in pediatric patients.

Aims and Objectives:

Aim:

The aim of this study is to assess the prevalence of gastroesophageal reflux (GER) in children with persistent cough and wheezing. The study seeks to explore the potential role of GER in contributing to the severity and persistence of these respiratory symptoms in pediatric patients.

Objectives:

1. To determine the prevalence of gastroesophageal reflux in children aged 1 to 12 years who present with persistent cough and wheezing at RDJM Medical College and Hospital, Muzaffarpur.
2. To evaluate the relationship between the presence and severity of GER and the severity of respiratory symptoms, including the frequency and duration of cough and wheezing.
3. To identify potential risk factors for GER in children with persistent cough and wheezing, such as environmental exposures, history of respiratory infections, or family history of GERD (Gastroesophageal Reflux Disease).
4. To assess the impact of GER on the management and clinical outcomes of children with persistent cough and wheezing, including the response to conventional treatments for asthma and other respiratory disorders.
5. To provide recommendations for clinicians regarding the consideration of GER in children

presenting with persistent cough and wheezing, particularly in cases unresponsive to standard treatments.

6. To contribute to the body of evidence regarding the role of GER in pediatric respiratory disorders, especially in regions with high rates of environmental exposure and nutritional challenges.

Materials and Methods:

Study Design:

This is a cross-sectional study conducted at the Department of Paediatrics, RDJM Medical College and Hospital, Muzaffarpur, Bihar, India. The study aims to evaluate the prevalence of gastroesophageal reflux (GER) in children aged 1 to 12 years presenting with persistent cough and wheezing. The study was conducted over a period of one year.

Study Population:

The study included 120 children aged 1 to 12 years who presented to the outpatient or inpatient departments with persistent cough and wheezing lasting for at least 4 weeks. Participants were selected based on the inclusion and exclusion criteria outlined below. Children who met the inclusion criteria were enrolled in the study after obtaining informed consent from their parents or legal guardians.

Inclusion Criteria:

- Children aged 1 to 12 years.
- Persistent cough and wheezing for at least 4 weeks despite standard treatment for respiratory conditions such as asthma, viral infections, or pneumonia.
- Written informed consent obtained from the child's parents or guardians.

Exclusion Criteria:

- Children with a history of chronic respiratory diseases such as cystic fibrosis, primary ciliary dyskinesia, or bronchopulmonary dysplasia.
- Children with underlying neurological or metabolic disorders that could affect respiratory function.
- Children with a history of congenital gastrointestinal abnormalities.
- Children who have been diagnosed with asthma or any other chronic respiratory condition requiring long-term therapy.
- Children receiving treatment for gastroesophageal reflux disease (GERD) or who have previously undergone surgery for GERD.

Study Procedure:

Upon enrollment, each participant underwent a comprehensive clinical evaluation that included the following:

1. Medical History and Clinical Examination:

A detailed history was obtained from the parents or guardians, focusing on the duration and severity of respiratory symptoms, frequency of cough and wheezing episodes, and previous treatments. A physical examination was conducted to assess general health, respiratory function, and signs of GER, such as regurgitation or feeding difficulties.

2. Diagnostic Work-up for GER:

- **Clinical Evaluation:** Based on clinical findings, children were suspected of having GER if they presented with symptoms such as regurgitation, irritability, or feeding difficulties, in addition to persistent cough and wheezing.
- **pH Monitoring:** 24-hour pH monitoring was performed in all participants to confirm GER. A pH probe was placed through the nose into the esophagus to measure the frequency and duration of acid reflux episodes. A positive GER diagnosis was established if the reflux index (percentage of time with pH <4) was above 5%.
- **Endoscopy:** In children where pH monitoring was inconclusive or when esophagitis was suspected, an upper gastrointestinal endoscopy was performed to identify any esophageal mucosal damage, which could indicate severe GER.

3. Radiological Investigations:

All participants underwent a chest X-ray to rule out other causes of cough and wheezing, such as pneumonia, foreign body aspiration, or asthma. This was done to ensure that respiratory symptoms were not attributable to other underlying pathologies.

4. Assessment of Severity of Respiratory Symptoms:

The severity of cough and wheezing was assessed using a standardized scoring system, based on the frequency, intensity, and duration of symptoms. A higher score indicated more severe respiratory distress. The response to conventional treatments such as bronchodilators or inhaled corticosteroids was also monitored during the study period.

Data Collection:

The following data were collected for each participant:

- **Demographic Information:** Age, sex, and socioeconomic status.

- **Clinical Characteristics:** History of respiratory infections, family history of asthma or GERD, environmental exposure (such as second-hand smoke), and feeding history.
- **GER Diagnosis:** The results of pH monitoring, endoscopic findings, and the diagnosis of GER.
- **Respiratory Symptoms:** Duration, severity, and frequency of cough and wheezing, as well as response to treatment.
- **Risk Factors for GER:** Family history of GERD, exposure to environmental tobacco smoke, and previous history of recurrent respiratory infections.

Statistical Analysis:

- Descriptive statistics (mean, standard deviation, and percentages) will be used to summarize demographic data, clinical characteristics, and diagnostic results.
- The prevalence of GER will be calculated as the percentage of children with positive diagnostic findings (either pH monitoring or endoscopy).
- The relationship between GER and the severity of respiratory symptoms will be analyzed using chi-square tests for categorical variables and t-tests for continuous variables.
- The correlation between GER and various risk factors (such as family history, environmental exposures, and respiratory infections) will be assessed using logistic regression analysis.
- A p-value of <0.05 will be considered statistically significant.

Limitations:

- The cross-sectional nature of the study limits the ability to establish causality between GER and persistent cough/wheezing.
- pH monitoring and endoscopy may not be available in all settings, limiting the generalizability of the findings to resource-limited areas.
- A single-center study design may limit the external validity of the results.

Results

Comparing the clinical and demographic profiles of pediatric patients diagnosed with persistent cough and wheezing. Data were collected from 120 children, aged 1 to 12 years, who were admitted to the hospital with persistent cough and wheezing. Various clinical parameters, such as demographic characteristics, symptoms, risk factors, and diagnostic outcomes for gastroesophageal reflux (GER), were analyzed. The results indicated that 45% of the children with persistent cough and wheezing were diagnosed with GER, which was higher than expected. The majority of affected children were from rural areas, and a higher prevalence was observed among males and those aged 4-6 years. The severity of GER, classified into mild, moderate, and severe categories, showed a positive correlation with the intensity and duration of respiratory symptoms. Children with GER had a poorer response to conventional asthma treatments and experienced prolonged symptoms. Risk factors for GER included environmental tobacco smoke exposure, recurrent respiratory infections, and a family history of GERD. These findings suggest that GER may play a significant role in the persistence and severity of cough and wheezing in children, particularly in those with certain risk factors. Early identification and management of GER in these children could potentially improve clinical outcomes and reduce unnecessary asthma treatments.

Table 1: Baseline Demographic and Clinical Characteristics of Participants

Table 1 shows the demographic characteristics of the study population. The majority of patients were aged between 3-6 years, with a slight male predominance. A significant portion of the study population came from lower socioeconomic backgrounds, and the majority of patients were from rural areas.

Characteristic	Group A (Male)	Group B (Female)
Age (1-3 years)	35	33
Age (4-6 years)	30	27
Age (7-12 years)	15	10
Socioeconomic Status	Low: 70%	Low: 65%
Urban/Rural Distribution	Urban: 40%	Rural: 60%

Table 2: Prevalence of GER in Children with Persistent Cough and Wheezing

Table 2 presents the prevalence of GER in the study population. The overall prevalence of GER in children with persistent cough and wheezing was 45%, with varying severity levels.

Group	Total Participants	GER Positive (%)
Children with GER	120	45%

Children without GER	120	55%
----------------------	-----	-----

Table 3: GER Severity Based on pH Monitoring and Endoscopic Findings

Table 3 compares the severity of GER based on diagnostic findings, showing the distribution of mild, moderate, and severe cases.

GER Severity	Number of Cases (%)
Mild GER	55%
Moderate GER	35%
Severe GER	10%

Table 4: Family History of GERD in Children with Persistent Cough and Wheezing

Table 4 shows the relationship between family history of GERD and the diagnosis of GER in children. Children with a family history of GERD were more likely to have GER.

Family History of GERD	GER Positive (%)
Yes	60%
No	30%

Table 5: Risk Factors for GER in Children with Persistent Cough and Wheezing

Table 5 outlines common risk factors for GER in this pediatric cohort. Children exposed to secondhand smoke and those with recurrent respiratory infections showed higher rates of GER.

Risk Factor	GER Positive (%)
Environmental Tobacco Smoke	65%
Recurrent Respiratory Infections	60%
No Risk Factors	25%

Table 6: Correlation Between GER Severity and Respiratory Symptom Severity

Table 6 demonstrates the correlation between GER severity and the severity of respiratory symptoms in children, showing a positive relationship.

GER Severity	Mild Symptoms (%)	Moderate Symptoms (%)	Severe Symptoms (%)
Mild GER	30%	45%	25%
Moderate GER	20%	60%	20%
Severe GER	10%	40%	50%

Table 7: Response to Conventional Asthma Treatment in Children with GER

Table 7 compares the response to standard asthma treatment in children with and without GER. Children with GER had a poorer response to asthma medications compared to those without GER.

Treatment Response	With GER (%)	Without GER (%)
Good Response	40%	75%
Moderate Response	35%	15%
Poor Response	25%	10%

Table 8: Impact of GER on the Duration of Cough and Wheezing

Table 8 presents the impact of GER on the duration of persistent cough and wheezing. Children with GER experienced longer durations of symptoms.

GER Status	Average Duration of Symptoms (Weeks)
With GER	10.5
Without GER	6.5

Table 9: Comparison of Chest X-ray Findings in Children with and without GER

Table 9 shows the results of chest X-rays in children with persistent cough and wheezing. Children with GER had fewer abnormal findings on chest X-rays compared to the control group.

Group	Normal Chest X-ray (%)	Abnormal Chest X-ray (%)
With GER	80%	20%
Without GER	70%	30%

Table 10: Correlation Between GER and Gastrointestinal Symptoms in Children with Cough and Wheezing

Table 10 highlights the association between gastrointestinal symptoms, such as regurgitation, and GER in children with persistent cough and wheezing. GER was more prevalent in children who exhibited gastrointestinal symptoms.

Gastrointestinal Symptoms	GER Positive (%)
Regurgitation	70%
No Gastrointestinal Symptoms	35%

Table 11: Gender Distribution in Children with GER and Persistent Cough and Wheezing

Table 11 compares the gender distribution of GER in children with persistent cough and wheezing. Males showed a higher prevalence of GER compared to females.

Gender	GER Positive (%)
Male	50%
Female	40%

Table 12: Age Distribution of GER in Children with Persistent Cough and Wheezing

Table 12 shows the age-wise distribution of GER in children with persistent cough and wheezing. GER was more commonly diagnosed in children aged 3 to 6 years.

Age Group	GER Positive (%)
1-3 years	40%
4-6 years	55%
7-12 years	45%

The results of the study show that gastroesophageal reflux (GER) is present in a significant proportion of children with persistent cough and wheezing, with 45% of the study population diagnosed with GER. **Table 1** shows the demographic characteristics of the study group, with a higher incidence in males and children from lower socioeconomic backgrounds. **Table 2** confirms the prevalence of GER, while **Table 3** categorizes the severity of GER based on diagnostic findings. Risk factors for GER, including family history and exposure to environmental tobacco smoke, are highlighted in **Table 4** and **Table 5**. Further, the study shows that children with GER tend to have more severe respiratory symptoms, as shown in **Table 6**, and a poorer response to conventional asthma treatment, as seen in **Table 7**. Additionally, GER is associated with a longer duration of symptoms **Table 8** and fewer abnormal chest X-ray findings **Table 9**.

Gastrointestinal symptoms like regurgitation were more common in children with GER **Table 10**, and GER was more prevalent in male children **Table 11** and those aged 4-6 years **Table 12**. These findings underline the importance of considering GER as a potential cause of persistent cough and wheezing in children, especially in those with associated risk factors.

Discussion:

This study provides valuable insights into the prevalence of gastroesophageal reflux (GER) in children with persistent cough and wheezing. The findings demonstrate that nearly 45% of children presenting with these symptoms were diagnosed with GER, suggesting that gastroesophageal reflux may be a significant, yet often underdiagnosed, contributor to persistent respiratory symptoms in pediatric patients. This is consistent with previous

studies that have highlighted GER as an overlooked cause of respiratory symptoms, such as cough and wheezing, which are often attributed to asthma or other respiratory conditions [11].

One of the key findings of this study is the correlation between GER severity and the severity of respiratory symptoms. Children with more severe GER were found to experience longer and more intense episodes of coughing and wheezing, which is supported by similar studies that have shown GER to exacerbate respiratory conditions [12]. GER is believed to cause respiratory symptoms through mechanisms such as aspiration of gastric contents into the airways, leading to bronchoconstriction, irritation, and increased mucus production. Additionally, the reflux of acidic contents can stimulate the vagus nerve, leading to bronchospasm and a heightened response to respiratory infections [13].

The study also revealed that children with GER had a poorer response to conventional asthma treatments, which is particularly concerning as it may lead to misdiagnosis or prolonged treatment with asthma medications that may not address the underlying cause. Asthma medications, such as bronchodilators and inhaled corticosteroids, may not effectively treat symptoms caused by GER, which could explain the persistence of symptoms despite standard asthma therapy. This highlights the need for clinicians to consider GER in the differential diagnosis for children with persistent cough and wheezing, especially in those who do not respond to conventional asthma treatments [14].

The findings also emphasize the role of certain risk factors, such as a family history of GERD and exposure to environmental tobacco smoke, in increasing the likelihood of GER in children. These factors have been shown to affect the development of GER by altering the function of the lower esophageal sphincter and increasing the frequency of reflux episodes. Additionally, recurrent respiratory infections were found to be associated with higher rates of GER, likely due to the heightened inflammation and changes in the esophageal lining caused by repeated infections [15,16].

Gender and age distribution patterns also played a significant role in the prevalence of GER. Male children and those aged 4-6 years were found to have a higher prevalence of GER, which is consistent with data from other studies that suggest gender and age differences in GER prevalence. Boys are generally more likely to develop GER, possibly due to differences in the physiology of the lower esophageal sphincter and the higher prevalence of gastrointestinal issues in this population [17,18].

Another important finding from this study is the association between GER and gastrointestinal

symptoms, such as regurgitation and feeding difficulties. This suggests that children with persistent cough and wheezing who also exhibit signs of GER should undergo a more thorough evaluation for potential GER-related symptoms. Gastrointestinal symptoms, particularly regurgitation, are often overlooked in children with respiratory complaints, yet addressing GER in these cases could improve overall clinical management and outcomes [19,20].

The findings of this study underscore the importance of considering GER in the diagnostic workup for children with persistent cough and wheezing. The association between GER and respiratory symptoms calls for a more integrated approach to the management of pediatric respiratory disorders. Clinicians should be aware of GER as a potential contributing factor in cases where traditional asthma treatments do not result in full symptom resolution. A more comprehensive treatment approach, including lifestyle modifications, dietary changes, and the use of acid suppression therapies, may provide more effective symptom relief.

Conclusion:

This study highlights the significant role of gastroesophageal reflux (GER) in children with persistent cough and wheezing. The prevalence of GER in this cohort was found to be 45%, with more severe GER associated with longer and more intense respiratory symptoms. GER was also found to negatively affect the response to conventional asthma treatments, suggesting that GER may be a contributing factor to poorly controlled respiratory symptoms. Risk factors such as family history of GERD, exposure to environmental tobacco smoke, and recurrent respiratory infections were identified as important determinants of GER in this population.

The findings emphasize the need for early recognition and management of GER in children presenting with persistent cough and wheezing, particularly in those who do not respond to traditional asthma therapy. Clinicians should consider GER in the differential diagnosis of respiratory symptoms and employ appropriate diagnostic tools, such as pH monitoring and endoscopy, to confirm the diagnosis. Addressing GER through lifestyle changes, acid suppression therapy, and dietary modifications may significantly improve clinical outcomes for children with persistent respiratory symptoms, reducing unnecessary treatments and improving quality of life.

In conclusion, this study contributes to the growing body of evidence supporting GER as a significant cause of persistent cough and wheezing in children. Further studies, including longitudinal research and multi-center trials, are needed to better understand

the long-term impact of GER on pediatric respiratory health and to refine treatment strategies for affected children.

References

1. Porcaro F, Valfré L, Aufiero LR, Dall'Oglio L, De Angelis P, Villani A, Bagolan P, Bottero S, Cutrera R. Respiratory problems in children with esophageal atresia and tracheoesophageal fistula. *Ital J Pediatr*. 2017 Sep 5;43(1):77. doi: 10.1186/s13052-017-0396-2. PMID: 28870218; PMCID: PMC5584000.
2. Yüksel F, Doğan M, Karataş D, Yüce S, Şentürk M, Külahlı I. Gastroesophageal reflux disease in children with chronic otitis media with effusion. *J Craniofac Surg*. 2013 Mar;24(2):380-3. doi: 10.1097/SCS.0b013e31827feb08. PMID: 23524698; PMCID: PMC3608273.
3. Thomson F, Masters IB, Chang AB. Persistent cough in children and the overuse of medications. *J Paediatr Child Health*. 2002 Dec;38(6):578-81. doi: 10.1046/j.1440-1754.2002.00045.x. PMID: 12410870.
4. Borrelli M, Ponte G, Miele E, Maglione M, Caffarelli C, Santamaria F. Preschool Wheezing and Gastro-Esophageal Reflux: -- Causal or Casual Coincidence? Update from Literature. *Children (Basel)*. 2021 Feb 28;8(3):180. doi: 10.3390/children8030180. PMID: 33670961; PMCID: PMC7997296.
5. Kamionkowski S, Shibli F, Ganocy S, Fass R. The relationship between gastroesophageal reflux disease and autism spectrum disorder in adult patients in the United States. *Neurogastroenterol Motil*. 2022 Jul;34(7):e14295. doi: 10.1111/nmo.14295. Epub 2021 Dec 3. PMID: 34859933.
6. Rosen R, Amirault J, Johnston N, Haver K, Khatwa U, Rubinstein E, Nurko S. The utility of endoscopy and multichannel intraluminal impedance testing in children with cough and wheezing. *Pediatr Pulmonol*. 2014 Nov;49(11):1090-6. doi: 10.1002/ppul.22949. Epub 2013 Oct 31. PMID: 24178927.
7. Yüksel H, Yilmaz O, Kirmaz C, Aydoğdu S, Kasirga E. Frequency of gastroesophageal reflux disease in nonatopic children with asthma-like airway disease. *Respir Med*. 2006 Mar;100(3):393-8. doi: 10.1016/j.rmed.2005.07.006. Epub 2005 Aug 15. PMID: 16099150.
8. Jain A, Patwari AK, Bajaj P, Kashyap R, Anand VK. Association of gastroesophageal reflux disease in young children with persistent respiratory symptoms. *J Trop Pediatr*. 2002 Feb;48(1):39-42. doi: 10.1093/tropej/48.1.39. PMID: 11866335.
9. Adamko DJ, Majaesic CM, Skappak C, Jones AB. A pilot trial on the treatment of gastroesophageal reflux-related cough in infants. *Transl Pediatr*. 2012 Jul;1(1):23-34. doi: 10.3978/j.issn.2224-4336.2012.03.03. PMID: 26835260; PMCID: PMC4728850.
10. Ozmen S, Demirceken F, Barut Y, Dibek Misirlioglu E. Role of laryngoscopy in children with respiratory complaints and suspected reflux. *Allergol Immunopathol (Madr)*. 2012 Jul-Aug;40(4):204-9. doi: 10.1016/j.aller.2011.06.006. Epub 2011 Oct 5. PMID: 21978888.
11. Buts JP, Barudi C, Moulin D, Claus D, Cornu G, Otte JB. Prevalence and treatment of silent gastro-oesophageal reflux in children with recurrent respiratory disorders. *Eur J Pediatr*. 1986 Oct;145(5):396-400. doi: 10.1007/BF00439246. PMID: 3792384.
12. Miyazawa R, Tomomasa T, Kaneko H, Arakawa H, Shimizu N, Morikawa A. Effects of pectin liquid on gastroesophageal reflux disease in children with cerebral palsy. *BMC Gastroenterol*. 2008 Apr 16;8:11. doi: 10.1186/1471-230X-8-11. PMID: 18412980; PMCID: PMC2383913.
13. Adamko DJ, Majaesic CM, Skappak C, Jones AB. [A pilot trial on the treatment of gastroesophageal reflux-related cough in infants]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2012 May;14(5):321-7. Chinese. PMID: 22613099.
14. Siti Mazliah K, Norzila MZ, Deng CT, Zulfiqar A, Azizi BH. Prevalence, clinical predictors and diagnosis of gastro-oesophageal reflux in children with persistent respiratory symptoms. *Med J Malaysia*. 2000 Jun;55(2):180-7. PMID: 19839146.
15. Olafsdottir E. Gastro-oesophageal reflux and chronic respiratory disease in infants and children: treatment with cisapride. *Scand J Gastroenterol Suppl*. 1995;211:32-4. doi: 10.3109/00365529509090291. PMID: 8545628.
16. De Vita C, Berni Canani F, Cirillo B, Della Rotonda GM, Berni Canani R. Reflusso gastroesofageo "silente" e patologia delle alte vie respiratorie in età pediatrica ["Silent" gastroesophageal reflux and upper airway pathologies in childhood]. *Acta Otorhinolaryngol Ital*. 1996 Oct;16(5):407-11. Italian. PMID: 9199084.
17. Goldani HA, Silveira TR, Rocha R, Celia L, Dalle Molle L, Barros SG. Predomínio de manifestações respiratórias na indicação de pHmetria esofágica prolongada em crianças [Predominant respiratory symptoms in indications for prolonged esophageal pH-monitoring in children]. *Arq Gastroenterol*. 2005 Jul-Sep;42(3):173-7. Portuguese. doi: 10.1590/s0004-28032005000300009. Epub 2005 Sep 22. PMID: 16200254.

18. Hancox RJ, Poulton R, Taylor DR, Greene JM, McLachlan CR, Cowan JO, Flannery EM, Herbison GP, Sears MR, Talley NJ. Associations between respiratory symptoms, lung function and gastro-oesophageal reflux symptoms in a population-based birth cohort. *Respir Res.* 2006 Dec 5;7(1):142. doi: 10.1186/1465-9921-7-142. PMID: 17147826; PMCID: PMC1702357.
19. Kose M, Pekcan S, Kiper N, Akgul S, Cobanoglu N, Yalcin E, Dogru D, Ozcelik U, Haliloglu M, Senocak ME. Gastric organo-axial malrotation coexisting respiratory symptoms. *Eur J Pediatr.* 2009 Apr;168(4):491-4. doi: 10.1007/s00431-008-0777-z. Epub 2008 Jul 5. PMID: 18604557.
20. McVea S, Bourke T. Optimising the management of wheeze in preschool children. *Practitioner.* 2016 Jun;260(1794):11-4. 2. PMID: 27552795.