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ABOUT COVER

Editorial Board Member of *World Journal of Clinical Pediatrics*, Tuna Kenar, MD, MSc, Assistant Professor, Department of Otolaryngology & Audiology, Private Denizli Cerrahi Hospital, Zeytinköy Ave. No:5 Pamukkale, Denizli, 20070, Türkiye. tuna.kenar@cerrahi.com.tr

AIMS AND SCOPE

The primary aim of the *World Journal of Clinical Pediatrics* (*WJCP*, *World J Clin Pediatr*) is to provide scholars and readers from various fields of pediatrics with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCP mainly publishes articles reporting research results and findings obtained in the field of pediatrics and covering a wide range of topics including anesthesiology, cardiology, endocrinology, gastroenterology, hematology, immunology, infections and infectious diseases, medical imaging, neonatology, nephrology, neurosurgery, nursing medicine, perinatology, pharmacology, respiratory medicine, and urology.

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ORIGINAL ARTICLE

Prospective Study

Prevalence of gastroesophageal reflux disease in children with extraesophageal manifestations using combined-video, multichannel intraluminal impedance-pH study

Sutha Eiamkulbutr, Termpong Dumrisilp, Anapat Sanpavat, Palittiya Sintusek

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Sutha Eiamkulbutr, Department of Pediatrics, King Chulalongkorn Memorial Hospital, Bangkok 10330, Thailand

Termpong Dumrisilp, Department of Pediatrics, Bhumibol Adulyadej Hospital, Bangkok 10220, Thailand

Anapat Sanpavat, Department of Pathology, Chulalongkorn University, Bangkok 10330, Thailand

Palittiya Sintusek, Thai Pediatric Gastroenterology, Hepatology and Immunology Research Unit, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand

Corresponding author: Palittiya Sintusek, MD, PhD, Associate Professor, Thai Pediatric Gastroenterology, Hepatology and Immunology Research Unit, King Chulalongkorn Memorial Hospital, Faculty of Medicine, Chulalongkorn University, 1873 Rama IV Road, Pathumwan, Bangkok 10330, Thailand. palittiya.s@chula.ac.th

Abstract

BACKGROUND

Gastroesophageal reflux disease (GERD) might be either a cause or comorbidity in children with extraesophageal problems especially as refractory respiratory symptoms, without any best methods or criterion for diagnosing it in children.

AIM

To evaluate the prevalence of extraesophageal GERD using conventional and combined-video, multichannel intraluminal impedance-pH (MII-pH), and to propose novel diagnostic parameters.

METHODS

The study was conducted among children suspected of extraesophageal GERD at King Chulalongkorn Memorial Hospital between 2019 and 2022. The children underwent conventional and/or combined-video MII-pH. The potential parameters were assessed and receiver operating characteristic was used for the significant parameters.

RESULTS

Of 51 patients (52.9% males), aged 2.24 years were recruited. The common problems were cough, recurrent pneumonia, and hypersecretion. Using MII-pH, 35.3% of the children were diagnosed with GERD by reflux index (31.4%), total reflux events (3.9%), and symptom indices (9.8%) with higher symptom recorded in the GERD group (94 *vs* 171, $P = 0.033$). In the video monitoring group ($n = 17$), there were more symptoms recorded (120 *vs* 220, $P = 0.062$) and more GERD (11.8% *vs* 29.4%, $P = 0.398$) by symptom indices. Longest reflux time and mean nocturnal baseline impedance were significant parameters for diagnosis with receiver operating characteristic areas of 0.907 ($P = 0.001$) and 0.726 ($P = 0.014$).

CONCLUSION

The prevalence of extraesophageal GERD in children was not high as expected. The diagnostic yield of symptom indices increased using video monitoring. Long reflux time and mean nocturnal baseline impedance are novel parameters that should be integrated into the GERD diagnostic criteria in children.

Key Words: Extraesophageal reflux; pH-impedance; Children; Gastroesophageal reflux; Mean nocturnal baseline impedance

Core Tip: This was a retrospective and cross-sectional study with 51 children suspected extraesophageal gastrointestinal esophageal reflux disease (GERD). This study found the prevalence of GERD in these pediatric patients was 35.3% by using combined-video, multichannel intraluminal impedance-pH study. Moreover, longest reflux time and mean nocturnal baseline impedance were depicted as the significant parameters for GERD diagnosis with satisfied diagnostic value in children.

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INTRODUCTION

Gastroesophageal reflux (GER) is a physiologic process that commonly occurs in infants. Gastroesophageal reflux disease (GERD) occurs when the refluxates cause troublesome symptoms. The incidence of GERD has increased in children (0.84 per 1000 persons-year)[1]. Its manifestation varies. Hence, a high index of suspicion is necessary, especially for extraesophageal manifestations[2]. In clinical practice, respiratory problems that are refractory to the standard treatment might be from the disease itself or are extraesophageal manifestations of GERD. Moreover, GERD can be a serious comorbidity that worsens those respiratory conditions. Consequently, the development of a standard tool to diagnose extraesophageal GERD and its prompt management are crucial.

There are many diagnostic tools for extraesophageal GERD, including pH monitoring, combined multichannel intraluminal impedance and pH (MII-pH) study, esophagogastroduodenoscopy (EGD) with biopsies, and laryngoscopy[3]. According to clinical practice guidelines for GERD diagnosis and management in children (North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition), the MII-pH study is the best diagnostic method for esophageal manifestations of GERD[4]. Recent studies in adults also propose that additional parameters from the MII-pH study, mean nocturnal baseline impedance (MNBI), and post-reflux swallow-induced peristaltic wave (PSPW), increase the diagnostic value of this tool[5]. However, there is scarce evidence to support the best method for diagnosing extraesophageal GERD in children. Further evaluation is necessary. The main purpose of this study is to determine the prevalence of GERD in children with extraesophageal symptoms using conventional and combined-video MII-pH studies. The secondary aim is to assess the diagnostic usefulness of combined-video MII-pH studies for GERD and other diagnostic parameters.

MATERIALS AND METHODS

Patient selection

The present study is a retrospective and cross-sectional study in children and adolescents with respiratory symptoms and other extraesophageal manifestations suggestive of GERD. Participants were treated at King Chulalongkorn Memorial Hospital (KCMH) from February 2019 to December 2021. Patients who had extraesophageal symptoms (cough, apnea or brief resolved unexplained event, uncontrolled asthma, recurrent pneumonia, stridor, hoarseness, chronic sinusitis with unknown causes, allergic rhinitis with difficulty to treatment), and who were between 1 mo and 18 years old were included in the study. The exclusion criteria were patients who were on proton pump inhibitors or prokinetics during MII-pH monitoring, unwillingness to participate in the study, and patients who were already known the other causes that could explain those extraesophageal symptoms.

The Chulalongkorn University Institutional Review Board approved this study (IRB 029/64). Informed consents and assents were obtained from the patient's guardians and patients, respectively, before recruitment to the study.

MII-pH study and/or video monitoring

According to the protocol, patients had to fast for one to two hours before a nasal impedance catheter with a pH probe (Pediatric ZandorpH catheter with one antimony and six impedance sensors with 1.5 cm interval, Laborie, The Netherlands) was distributed throughout the esophagus. The Strobel formula [6] was used to calculate the proper position of the catheter. Chest X-ray was then used to confirm that the pH probe was located at 2–3 vertebral distance from the diaphragm. During the MII-pH monitoring, all patients had their regular meals. Video monitoring was conducted simultaneously with MII-pH monitoring in 17 patients. The total time of monitoring after excluding meal periods was at least 18 h. The number of reflux events, the reflux index (RI), the symptom index (SI)/symptom sensitivity index (SSI)/symptom association probability (SAP), longest reflux time (LRT), the MNBI, and PSPW were recorded.

Pathological reflux is defined according to the position statement by the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) Motility Working Group[6] as RI > 7% in children aged ≥ 1 year, and > 10% in children aged < 1 year, or if reflux episodes occur ≥ 70 times in children aged ≥ 1 year, and ≥ 100 times in children aged < 1 year or positive SI/SSI/SAP. Regarding symptom recoding, SI is calculated as (reflux-related symptom occurrences/total symptom events) × 100. SI is considered positive if the value is ≥ 50%. SSI is calculated as (number of symptom-associated reflux/total number of reflux episodes) × 100. If the percentage of SSI is ≥ 10%, it is considered positive. SAP is calculated by dividing the total measuring time into 2-min intervals, and creating a four-field contingency table: The number of intervals with and without GER symptoms, number of intervals with and without GER symptoms, number of intervals without GER and with the symptoms, and number of intervals without GER and symptoms. Fisher's exact test was performed for statistical examination of correlation. A percentage greater than 95% was considered positive.

Regarding the new parameters, MNBI was measured from the most distal impedance channel during sleep, with three 10-min time intervals that did not interfere with swallowing. The mean of these three values was then calculated. PSPW was defined as an antegrade 50% drop in impedance originating in the proximal esophagus within 30 s after the end of a reflux event and reaching the distal lumen. The PSPW index was calculated by the number of PSPW divided by the total number of refluxes[5,7].

Esophageal gross and histopathology finding

Within three months of the MII-pH study esophagogastroduodenoscopy with biopsy was performed on selected patients from recruitment according to decisions by the doctors in charge. The Los Angeles (LA) Classification[8] was routinely used to record endoscopic findings. The esophageal histopathology finding was reported by a pathologist using the modified Esohisto criteria as described in our previous study[8]. In short, a calculated severity score of 0–0.25 was considered normal and a score of ≥ 0.5 was regarded as esophagitis.

Statistical analysis

Data of categorical variables were expressed as percentages or proportions, and continuous variables as median [interquartile range (IQR)]. These variables were compared using Fisher's exact test and Wilcoxon signed ranks test as appropriate. Univariable and multivariable analyses were used to assess the independent factors of extraesophageal GERD from demographic variables and parameters from MII-pH analysis. Statistical significance was defined as P value < 0.05. Receiver operating characteristic analysis with calculation of the area under the curve was used to assess the diagnostic yield of the potential parameters of extraesophageal GERD. Statistical analysis was performed using SPSS software version 24.0.0 (SPSS Inc., Chicago, IL, United States) and Stata version 15.1 (Stata Corp, LLC, College Station, TX, United States).

RESULTS

Baseline characteristics of children with suspected extraesophageal GERD

There were 83 children with suspected extraesophageal GERD at KCMH from February 2019 to July 2022. Thirty-two participants were excluded from the present study because they received proton pump inhibitors/prokinetics during the MII-pH study (n = 21), had unwilling guardians (n = 3), and because they had known causes of respiratory symptoms (n = 8). Consequently, a total of 51 children were recruited and 17 of them underwent both the MII-pH study and video monitoring. Twenty-five children underwent upper endoscopy, while 22 underwent esophageal biopsy for histopathology. The median age of these 51 participants was 2.24 (1.11, 7.67) years and 27 (52.9%) participants were males. Their underlying diseases were multiple anomalies (47%), respiratory disorders (35.3%), and neurological disorders (17.7%). The most common extraesophageal symptoms indicated in the MII-pH study were cough (41.2%), recurrent pneumonia (25.5%), and hypersecretion (11.8%). However, 16 (31.4%) participants also had concurrent gastrointestinal symptoms. The median duration of MII-pH recording was 22.09 (20.20, 23.41) h. Only 265 symptoms were recorded by guardians, including cough (n = 109, 41.1%), irritability (n = 54, 20.4%), apparent secretion (n = 24, 9.1%), vomiting (n = 34, 12.8%), and heartburn (n = 44, 16.6%). In total, 18 (35.3%) participants were diagnosed with GERD using the MII-pH study. In the subgroup of children who underwent upper endoscopy (n = 25) and 22 of them had received esophageal tissue biopsy, 18 (72%) and 16 (72.7%), respectively, were diagnosed with GERD using the LA classification and modified Esohisto, respectively (Figure 1).

MII-pH study

According to the diagnostic criteria by the BSPGHAN Motility Working Group[6], 18 participants had parameters that were compatible with GERD. A comparison between the GERD and non-GERD groups did not reveal any statistical difference in the baseline characteristics. Besides the parameters from the MII-pH study that were used for diagnosing GERD (total reflux event, reflux index, and symptom index), total symptom record (94 *vs* 171 times, P = 0.033), LRT (1.3 (0, 4.3) *vs* 17.2 (9.43, 38.55), P < 0.001), and MNBI (1897.69 (806.89) *vs* 1300.48 (600.31) ohms, P = 0.008), were significantly different between the non-GERD and GERD groups, respectively. Meanwhile, PSPW, another novel metric, did not show a significant difference between the groups [53.57 (27.59) *vs* 56.11 (15.7), P = 0.721]. In the multivariable analysis, LRT and MNBI were the independent parameters that were significantly differences in participants diagnosed with GERD (P < 0.05) (Table 1).

Combined MII-pH study with video monitoring

The MII-pH study with video monitoring was performed in 17 participants. By the novel combined video-MII-pH study is different from the conventional MII-pH study. The video-MII-pH study had conducted simultaneously with MII-pH monitoring and given the clinical symptoms recorded by the investigator that can make more accurate of symptoms in children who cannot even report their symptoms. Then we compared the symptoms that were recorded by the participants' guardians (conventional study) to the symptoms that were recorded by the video monitoring which is the same participants.

The total number of symptoms recorded from video by an investigator who simultaneously viewed throughout the recording, was detected higher than from participants' guardians even though there's no statistical significance (220 *vs* 120, P = 0.062. This led to an increase in the number of participants who were diagnosed with GERD by using symptom association indices (SI/SSI/SAP) (n = 2, 11.8% *vs* n = 5, 29.4%, P = 0.398) (Table 2).

Diagnostic value of the novel parameters from MII-pH study

When using the significant parameters from multivariable analysis to identify GERD, longest reflux duration and MNBI yielded an area under the curve (AUC) of 0.907 (95%CI: 0.802–1) and 0.726 (95%CI: 0.581–0.870), correspondingly. Combining these two parameters yielded an AUC of 0.914 (95%CI: 0.819–1) (Figure 2). A cutoff value of eight minutes for longest reflux duration had a sensitivity of 83.33% and a specificity of 90.91%. A cutoff value of 1466 ohm for MNBI had a sensitivity of 50.0% and a specificity of 33.33%.

DISCUSSION

The prevalence of extraesophageal GERD was 35.3% by using the MII-pH study in this study. Interestingly, 31.4% of children who had extraesophageal manifestations of GERD also had gastrointestinal symptoms. Total symptom record, LRT, and MNBI were the parameters that were significantly different between the GERD and non-GERD groups. LRT and MNBI were the independent parameters from multivariable analysis. Using video monitoring during MII-pH study to depict more symptom record increases the diagnostic yield of extraesophageal GERD.

Table 1 Demographic characteristics and parameters from Multichannel intraluminal impedance-pH study in children diagnosed with extraesophageal gastroesophageal reflux disease and no extraesophageal gastroesophageal reflux disease, *n*, (%)

Characteristics	No extraesophageal GERD (*n* = 33)	Diagnosed extraesophageal GERD by MII-pH study (*n* = 18)	*P* value	
			Univariable analysis	Multivariable analysis
Age (yr) (median, IQR)	1.67 (0.91, 3.38)	4.58 (1.70, 13.15)	0.174	
Age < 1 yr	10 (30.3)	2 (11.1)		
Age ≥ 1 yr	23 (69.7)	16 (88.9)		
Sex, male	17 (51.5)	10 (55.6)	1	
Underlying diseases			0.441	
Respiratory disorder				
Bronchiectasis	1 (3.03)	0		
Chronic lung disease	7 (21.21)	2 (11.11)		
Congenital hypoventilation syndrome	0	2 (11.11)		
Subglottic stenosis	0	1 (5.56)		
Tracheobronchomalacia	1 (3.03)	0		
Laryngomalacia	1 (3.03)	0		
BRUE	1 (3.03)	0		
Chronic cough	1 (3.03)	0		
Neurological disorder				
Swallowing dysfunction	2 (6.06)	1 (5.56)		
Spastic cerebral palsy	2 (6.06)	3 (16.67)		
Infantile spasm	1 (3.03)	0		
Multiple anomalies				
Syndromic disorder	6 (18.18)	2 (11.11)		
Non-syndromic disorder	9 (27.27)	7 (38.89)		
Indication for evaluation				
Extraesophageal symptoms			0.679	
Recurrent pneumonia	9 (27.3)	4 (22.2)		
Hypersecretion	4 (12.1)	2 (11.1)		
Cough	11 (33.3)	10 (55.6)		
Glossoptosis	1 (3.0)	0		
Tracheobronchomalacia	1 (3.0)	0		
Stridor	1 (3.0)	0		
Choking	4 (12.1)	1 (5.6)		
Chronic rhinosinusitis	0	1 (5.6)		
BRUEs	1 (3.0)	0		
Apnea	1 (3.0)	0		
Esophageal symptoms			0.293	
Vomiting	8 (24.2)	6 (38.9)		
Heartburn	1 (3.0)	1 (5.6)		
None	24 (72.7)	11 (61.1)		
Total recorded symptoms	94	171	0.033	0.064

(times, %)				
Cough	43 (45.75)	66 (38.60)	0.404	
Irritability	32 (34.04)	22 (12.86)	0.754	
Apparent secretion	7 (7.44)	17 (9.94)	0.346	
GI symptoms (vomiting or heartburn)	12 (12.77)	66 (38.60)	0.081	
Impedance parameters (median, IQR)				
Total time (hours)	22.12 (20.34, 24.04)	21.34 (19.97, 22.62)	0.391	
Reflux index[1]	0.40 (0, 1.45)	8.4 (4.43, 14.20)	0.001	
Longest reflux time (min)	1.3 (0, 4.30)	17.2 (9.43, 38.55)	0.001	
Total reflux events[1]	12 (5.00, 37.50)	28 (18.50, 45.50)	0.032	0.012
Weakly acid reflux events				
Acid reflux events	9 (2.50, 27.00)	10 (3.75, 21.75)	0.79	
Nonacid reflux events	1 (0, 4.50)	15.5 (8.75, 25.25)	0.001	
Symptom indices	0 (0, 4.00)	0 (0,1.00)	0.381	0.212
Symptom index[1]	0 (0, 0.00)	0 (0, 12.73)	0.208	
Symptom sensitivity index[1]	0 (0, 0.00)	0 (0, 1.40)	0.32	
Symptom associated index[1]	0 (0, 0.00)	0 (0, 85.63)	0.168	
MNBI (ohms) (mean, SD)	1897.69 (806.89)	1300.48 (600.31)	0.008	
PSPW (%) (mean, SD)	53.57 (27.59)	56.11 (15.70)	0.721	
Diagnosis GERD				
Gross finding (n = 25)	8/12 (66.7)	10/13 (76.9)	0.673	
Histopathology (n = 22)	6/11 (54.5)	10/11 (90.9)	0.149	

[1]Significant factors in univariable analysis were not included in the multivariable analysis because of collinearity with criteria diagnosis gastroesophageal reflux disease using the MII-pH study.

BRUE: Brief resolved unexplained event; MNBI: Mean nocturnal baseline impedance; PSPW: Post-reflux swallow-induced peristaltic wave index; GERD: Gastroesophageal reflux disease; MII-pH: Multichannel intraluminal impedance-pH; IQR: Interquartile range.

Table 2 Comparing symptoms recorded by conventional and combined visual data object -monitoring in children who underwent multichannel intraluminal impedance-pH study (n = 17), n, (%)

Characteristics	Conventional MII-pH study	Combined video-MII-pH study	*P* value
Total recorded symptoms	120	220	0.062
Cough	31 (25.83)	46 (20.90)	0.259
Irritability	38 (31.67)	101 (45.90)	0.114
Apparent secretion	3 (2.50)	43 (19.55)	0.02
GI symptoms (vomiting or heartburn)	48 (40.00)	33 (15.00)	0.339
Symptom indices (median, IQR)			
Symptom index	0 (0–5.00)	0 (0–11.65)	0.306
Symptom sensitivity index	0 (0–2.65)	0 (0–5.80)	0.306
Symptom associated index	0 (0–37.60)	0 (0–93.15)	0.306
Diagnosis GERD using symptom indices	2 (11.76)	5 (29.41)	0.398

GI: Gastrointestinal; GERD: Gastroesophageal reflux disease; MII-pH: Multichannel intraluminal impedance-pH; IQR Interquartile range.

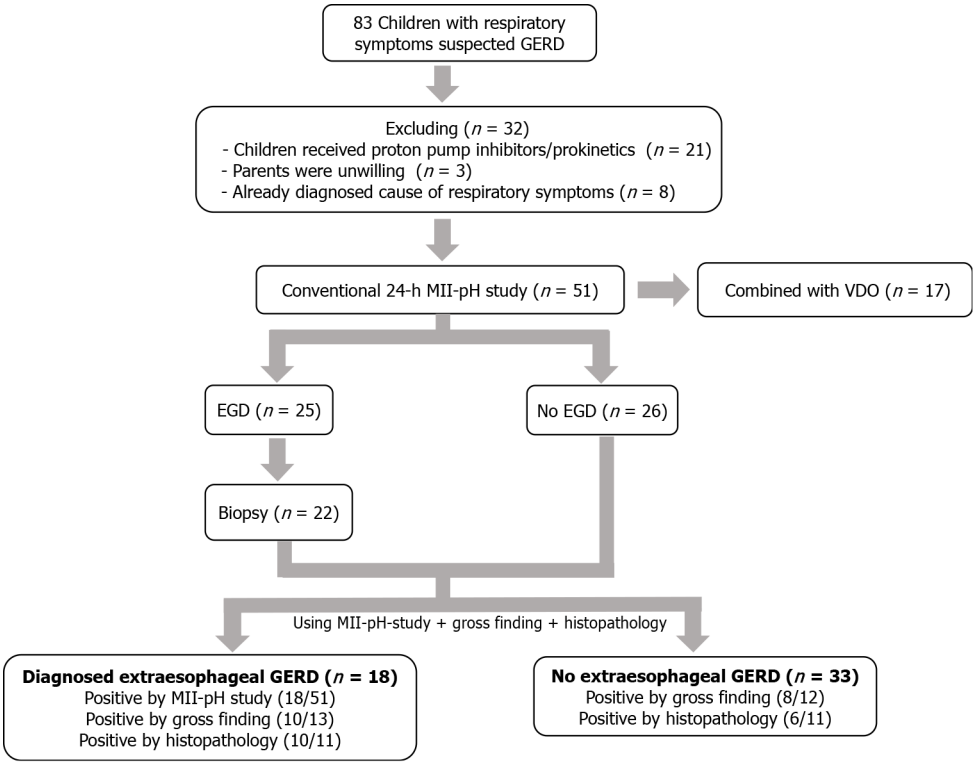

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Figure 1 Recruitment of children with respiratory symptoms suggestive of gastroesophageal reflux disease. EGD: Esophagogastroduodenoscopy; GERD: Gastroesophageal reflux disease; MII-Ph: multichannel intraluminal impedance and pH.

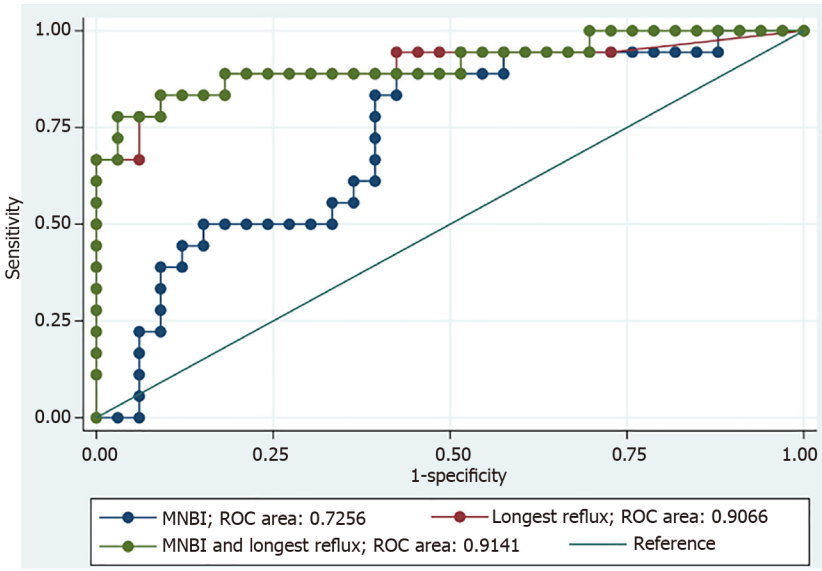

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Figure 2 Area under the receiver operating characteristic curve of the novel parameters to diagnose extraesophageal gastroesophageal reflux disease. MNBI: Mean nocturnal baseline impedance; ROC: Receiver operating characteristic curve; GERD: Gastroesophageal reflux disease.

There are several debates over clinical symptoms of extraesophageal reflux disease in children because of heterogeneity, non-specificity, and unreliability. Moreover, the prevalence of extraesophageal GERD reflects the real burden and depends on the modalities for diagnosis. Hence, finding the best diagnostic tool for extraesophageal GERD is crucial. Many proposed diagnostic tools, such as oropharyngeal pH monitoring/salivary pepsin, have been studied with unsatisfactory results[9-11]. As a result, the present study was designed using MII-pH study and histopathology—which are the gold standard for diagnosing esophageal GERD—to be the gold standard diagnosis for extraesophageal GERD. Moreover, combined-video monitoring was performed in 17 participants. The present study

found that video monitoring increased the value of symptom-reflux association in extraesophageal GERD. This is congruent with our previous study which depicted a trend of symptom-reflux association with particular symptoms of GERD in children diagnosed with esophageal atresia[12]. The real-time video captured in MII-pH monitoring with physician symptom recordings had higher symptom indices. There were more symptoms recorded including cough, hypersecretion, irritability, and vomiting. There were also more GERD diagnoses secondary to the symptoms that were more trustworthy than conventional methods. These studies highlight that symptom recording by video monitoring in children increases the value of symptom association for GERD diagnosis.

Although identifying extraesophageal manifestation of GERD is challenging and needs evaluation regarding whether it represents true GERD or a mimicker, the present study found concomitant gastrointestinal symptoms or signs in a majority of these children. Moreover, esophagitis was also detected in a majority of children with extraesophageal symptoms in the present study. This might explain the gastrointestinal symptoms they experienced. The reflex theory is a possible explanation regarding why children with extraesophageal GERD also had gastrointestinal involvement. The theory suggests that reflux stimulates the vagus nerve in the esophagus leading to cough, bronchoconstriction, or other extraesophageal symptoms *via* vagally mediated reflexes[13,14]. However, previous studies demonstrated a lower prevalence of esophagitis in patients with extraesophageal GERD. A positive reflux-laryngitis varies from 5% up to 31%[15-18]. Routine upper endoscopy in all children with solely extraesophageal symptoms might be avoided. This invasive procedure should be preserved for patients who have both extraesophageal and esophageal manifestations of GERD. To increase the reliability of symptom assessment, we encourage the physician to have the dedicated history taking or possible video recording of symptoms during MII-pH study simultaneously with the routine symptom recorded by patients or their guardians. Upper endoscopy with biopsy is necessary and could increase the yield of GERD diagnosis in these selected children.

Besides using symptom association to diagnose extraesophageal GERD, we found that acid reflux was mainly present in the present study in accordance with Borrelli *et al*'s work. Borrelli *et al*[19] found that 66% of cough bursts were related to acid reflux episodes. However, different results were demonstrated by Zenzeri *et al*[20] who found predominantly weak acid and nonacid reflux in children with respiratory problems. Because of the lack of standardized protocol and children's conditions in previous studies, a large multicenter study regarding children with different manifestations is necessary to extend the knowledge and narrow the specific treatment for them. In the present study, a majority of children had complicated underlying diseases (multiple anomalies, respiratory disease, or neurological deficit) that increased the risk of esophageal motility disorder and reflux. This could explain the high predominance of acid reflux.

The pathogenesis of GERD is complex and multifactorial. Though abnormal transient esophageal relaxation is the main pathogenesis, other factors such as-esophageal mucosal disease, esophageal dysmotility, gastroparesis, and anatomical defect (hiatal hernia, short segment of abdominal esophagus)-must be considered as aggravated risk factors of GERD[21]. Children with multiple comorbidities, especially neurological deficit, usually have sedentary lifestyles or are bedridden, and this affects gastrointestinal motility. We found that the LRT had statistically significant discriminate GERD and non-GERD children, reflexes the impairment of esophageal volume clearance as one of the pathogenesis of GERD[22,23]. However, there was no impairment of chemical clearance as shown by the insignificant difference in PSPW in both groups. MNBI is another parameter that can discriminate GERD from non-GERD children. MNBI represents esophageal integrity[5] and has a reasonably low value in GERD. To the best of our knowledge, PSPW and MNBI are the new impedance-pH parameters which are integral in the Lyon Consensus criteria for diagnosing GERD in adults[24]. The impact of PSPW and MNBI on increasing the yield of GERD diagnosis in children is rare. There is only one study concerning the impact of MNBI in children with GERD by Rosado-Arias *et al*[25]. That study found that a low MNBI is associated with a pathological AET. Our study is compatible with the study by Rosado-Arias *et al*[25] and confirmed the role of a low MNBI in helping the diagnostic yield of GERD. To the best of our knowledge, the present study is the first study to evaluate the PSPW parameter between GERD and non-GERD children. A previous study by Park *et al*[26] showed impairment of PSPW in adults with laryngopharyngeal reflux and esophageal GERD, but our study is incongruent with same. It is possible that the chemical clearance is important for the pathogenesis of extraesophageal GERD in adults *vs* in children. Further studies from multicenter or with the higher number of participants about PSPW and MNBI parameters, are crucial in aiding the diagnosis of GERD in children.

The certain strength of our study is that we integrated video monitoring into MII-pH study for diagnosing extraesophageal GERD in children. Moreover, the novel parameters (PSPW and MNBI) were evaluated to increase the yield of GERD diagnosis. However, there are some limitations. Firstly, it was a small number of children in a single center study. Therefore, the results are specific to the particular comorbidities that were present and cannot be extrapolated to children with previously healthy or less comorbidities. Secondly, because of the coronavirus disease 2019 pandemic, upper endoscopy was not performed in all children. Given this, there is the potential for selective bias and a high prevalence of children with extraesophageal GERD having esophagitis.

CONCLUSION

In conclusion, the prevalence of GERD was not as high as expected. Employing video monitoring into conventional MII-pH study increases the diagnostic yield of symptom indices. LRT and MNBI are novel parameters that should be integrated into the diagnostic criteria for GERD.

ARTICLE HIGHLIGHTS

Research background

Gastroesophageal reflux disease (GERD) might be either a cause or comorbidity in children with extraesophageal problems especially as refractory respiratory symptoms, without any best methods or criterion for diagnosing it in children.

Research motivation

Recent studies in adults also propose that additional parameters from the multichannel intraluminal impedance (MII)-pH study, mean nocturnal baseline impedance (MNBI), and post-reflux swallow-induced peristaltic wave, increase the diagnostic value of this tool. However, there has been scarce evidence to support the best method for diagnosing extraesophageal GERD in children.

Research objectives

To study the prevalence of extraesophageal GERD, especially in children who presented with refractory respiratory problems by using combined video-MII-pH study. Furthermore, to identify other parameters from MII-pH study that can help the diagnosis of extraesophageal GERD.

Research methods

Children with respiratory symptoms and other extraesophageal manifestations suggestive of GERD were enrolled to participate in the present study. MII-pH study and/or video monitoring and/or upper endoscopy with esophageal histopathology were performed. The prevalence of extraesophageal GERD and the novel diagnostic parameters to diagnose extraesophageal GERD were analyzed.

Research results

The prevalence of extraesophageal GERD was 35.3% by using the MII-pH study and 31.4% of children who had extraesophageal manifestations of GERD also had gastrointestinal symptoms. Total symptom record, longest reflux time (LRT), and MNBI were the parameters that were significantly different between the GERD and non-GERD groups. LRT and MNBI were the independent parameters from multivariable analysis. Using video monitoring during MII-pH study to depict more symptom record increases the diagnostic yield of extraesophageal GERD.

Research conclusions

In conclusion, the prevalence of GERD was not as high as expected. Employing video monitoring into conventional MII-pH study increases the diagnostic yield of symptom indices. LRT and MNBI are novel parameters that should be integrated into the diagnostic criteria for GERD.

Research perspectives

The diagnostic test for extraesophageal GERD in children is limited and there have been a few data support the favorable treatment outcome in these children. Hence, the extensive investigations in these difficult cases are needed and other mimic causes should be ruled out. Further study in aspect of esophageal manometry combined with video-MII-pH study and histopathology in various presentations of GERD should be initiated to extend the knowledge about the pathogenesis of GERD and hopefully, could tailor therapy for these patients.

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FOOTNOTES

Author contributions: Eiamkulbutr S, Dumrisilp T and Sintusek P performed the upper endoscopy and MII-pH study; Eiamkulbutr S, Dumrisilp T collected all the data; Sanpavat A analyzed and interpreted the histopathological data; Eiamkulbutr S recorded all symptoms from video recording; Eiamkulbutr S and Sintusek P analyzed and interpreted the MII-pH study and wrote the manuscript; Sintusek P was responsible for designing, editing, and revising the manuscript; Sintusek P edited the intellectual content in the manuscript; all approved for the final version of the manuscript.

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ORCID number: Termpong Dumrisilp 0000-0001-7110-0664; Anapat Sanpavat 0000-0002-6425-3379; Palittiya Sintusek 0000-0003-4441-0151.

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