

Gastroesophageal Reflux in Libyan Children with Respiratory Symptoms

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Abstract

Background: Epidemiological studies have shown an association between gastroesophageal reflux disease (GERD) and asthma, also that esophageal acid perfusion may cause bronchial constriction. Thus, this study was conducted to find out the correlation between GERD and respiratory symptoms as well as anti-reflux therapy and respiratory symptoms in Libyan children.

Methods: Pediatric patients admitted to respiratory clinic, pediatric department with different respiratory problems and clinically suspected GERD and underwent 24-hours pH monitoring by using Medtronic™ Ambulatory Reflex Testing were included in this study. Sixty-nine children aged between 48 days and 12 years with different respiratory symptoms were selected for 24-hour pH-IMP monitoring technique to confirm GERD diagnosis. Children detected to have GERD were advised to be on anti-reflux therapy and regular follow up. We investigated the underlying disease and main problems related to GERD of the patients, respiratory symptoms index, the correlation between the applied treatment and respiratory symptoms.

Results: The mean (\pm SD) age of 69 patients included in the study was 36.8 (\pm 43) months, ranged between 48 days to 12 years. 40% of the patients were infants (0 : 1 year) followed by 25% toddlers (1 : 3 years), 13% were preschool age children (3 : 6 years) and 19% were school age children (> 6 years) GERD was diagnosed in 37 (53.6%) patient, 20 were given anti-reflux therapy (intervention group), 8 patients required surgical intervention and were referred to pediatric surgery department and 9 patients who joined the study from other units to confirm the presence GERD were referred to their units and were dropped from the study. Eleven patients from the intervention group completed the study, 8 (72.7%) patients responded well and were symptom free by finishing anti-reflux therapy course, one patient (10.1%) showed little response and 2 patients (18.2%) did not respond.

Conclusions: This study supports that pH monitoring test is a reliable method for GERD diagnosis, GERD is a leading cause of respiratory disease (pneumonia, recurrent wheezy chest, chronic cough, uncontrolled asthma symptoms) and anti-reflux therapy can improve respiratory diseases in selected patients.

Keywords: Asthma; GERD; Anti-Reflux Therapy; pH Monitoring Test; Libya

Introduction

Gastroesophageal reflux (GER) is defined as an effortless passage of gastric contents in to the esophagus, it is considered as a normal physiological phenomenon experienced intermittently by most people, particularly after a meal, while gastroesophageal reflux disease (GERD) occurs when the amount of gastric juice that refluxes in to the esophagus exceeds the normal limit, causing symptoms with or without associated esophageal mucosal injury [1]. GER represents the most common gastrointestinal disease that leads to referral to a pediatric gastroenterologist during infancy. Although many infants have minor degrees of reflux, about 1 : 300 - 1 : 1,000 have significant reflux and associate complications [1]. It has been shown that in normal individuals reflux most commonly occurs as the child is swallowing and the lower esophageal sphincter (LES) is relaxing to allow the passage of food in to the stomach, during these brief `unguarded moments` ingested food and acid pass in to the lower esophagus, where a secondary peristaltic wave promptly clears the food back in to the stomach. If, however, esophageal peristalsis is deranged the content time of gastric acid on the esophageal mucosa will be prolonged. In a patient with very sever reflux, spontaneous relaxation of the LES occur throughout the day, leading to many more `unguarded moments` [2]. Although minor degrees of GER are noted in both children and adults, the degree and severity of reflux episodes are increased during infancy, with a peak at age 1 - 4 months. However, it can be seen in children of all ages, even healthy teenagers. Thus, GER represents a common physiological phenomenon in the first year of life. As many as 60 - 70% of infants experience emesis during at least one feeding

per 24 hours period by age 3 - 4 months, the distinction between this “physiologic” GER and “pathologic” GER reflux in infancy and childhood is determined, not merely by the number and severity of reflux episodes (when assessed by intraesophageal pH monitoring) but is most importantly determined by the presence of reflux-related complications, including failure to thrive, erosive esophagitis, esophageal stricture formation, and chronic respiratory disease [2,3]. Asthma is one of the chronic inflammatory airway diseases, it characterized by recurrent episodes, dyspnea, chest tightness wheeze and cough. These episodes are associated with variable airflow limitation which is usually reversible, either spontaneously, or through treatment as well as with increased airway responsiveness to various nonspecific stimuli [4]. There are many triggers and co morbid conditions that have been shown to increase asthma symptoms and/or precipitate asthma exacerbations [5]. One common, of-ten overlooked trigger is GER. The relationship between asthma and GERD has been recognized for many years, in 1892, Sir William Osler described “Severe paroxysms of asthma may be induced by overloading the stomach or by taking certain food”. He also stated that “attacks may be due to direct irritation of the bronchial mucosa or indirectly by reflux influences from stomach” [6]. The prevalence of gastro esophageal reflux disease in asthma patients varies from 30% to 90%, depending on the definition and methods used [7]. Gastro esophageal reflux disease is three times as prevalent in asthmatic patients compared to the general population [8]. Recent data suggest that treating GERD in selected asthmatics improves asthma symptoms and pulmonary function, and may decrease prednisone medication usage [9,10]. Gastro esophageal reflux disease is a potential trigger of asthma [11]. Acid GER in children at any age, could be the reason of various clinical manifestation (typical and atypical) of variable intensity, dependent on the range of reflux (high reflux, low reflux). On the basis of reflux symptoms, it is hardly possible to differentiate primary GER from GER secondary to allergy to cow milk protein and/or other food [12].

The reflux of gastric juice from the stomach in to the esophagus is prevented by some physiologic and anatomic factors including normal length of lower esophageal sphincter as well as normal pressure and normal number of episodes of transient relaxation [2,12]. In 85% of infants with GER, the condition is self-limited, disappearing between ages 6 and 12 months. Regurgitation may be reduced by offering small feedings at frequent intervals or by thickening feedings with rice cereal [13]. GER refers to immaturity of LES function, manifested by frequent transient lower esophageal relaxations (tLESRs) that results in retrograde flow of gastric contents into the esophagus. Esophageal clearance in infants is similar to that in adults, although evidence of reduced peristaltic activity in preterm infants has been reported [3]. In infants the volume ratio of meal-stomach-esophagus differs from adults. Reflux occurs when esophageal capacity is exceeded by refluxate, also decreased gastric compliance is believed to lead to LES relaxation at lower intragastric volumes in infants. This aspect, in conjunction with abdominal wall muscle contraction propels refluxate into the esophagus with subsequent regurgitation. There is also an association between GER and delayed gastric emptying. This is more common in premature infants [3,13]. Although usually a harmless condition of young infants, sever GER may cause weight loss or poor growth, esophagitis, hematemesis, occult blood loss, anemia, esophageal stricture and inflammatory esophageal polyp. Typical or atypical crying and/or irritability, Hiccups, sleep disturbances, apnea and/or bradycardia, poor appetite, apparent life-threatening event, Aspiration pneumonia, recurrent pneumonitis, sore throat, chronic cough, wheezing and asthma like attacks are reported [3,13].

To diagnose GERD, there are various investigations available which need to be considered in conjunction with the clinical picture. It includes; the ambulatory esophageal pH monitoring (which considered as gold standard for acid reflux), inspection of sputum for lipid-laden alveolar macrophages, scintigraphy monitoring, barium radiology, and the upper GI endoscopy with biopsy [2]. GERD is a prevalent disease with a tendency to further increase in most populations around the world. It has a significant impact on patient’s quality of life, and in subsets of patients, it leads to complications and may predispose to esophageal adenocarcinoma development. The recent global definition for GERD addresses the complexity of its clinical spectrum that ranges from typical esophageal symptoms and lesions to a series of atypical symptoms, including laryngeal and pulmonary symptoms [14]. The current strategies for management of GERD include a range of options. Over the years, patients with sporadic reflux symptoms have been reported to go for self-medication with drugs obtained over the counter. More troublesome and relapsing reflux symptoms are mainly taken care of by primary care medicine. For the initial management of severe GERD, and whenever complex therapies are needed in complicated GERD, specialists usually become involved [14,15].

Conservative measures for management of GERD, includes upright positioning after feeding, elevating the head of the bed, prone positioning, and providing small, frequent feeds thickened with cereal [15,16]. In more severe cases, in addition to dietary management, pharmacological intervention is directed at reducing gastric acid secretion. Current guidelines from the North American Society for the

Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN), involve the use of "step-up" and "step-down" therapy, which should be instituted under the guidance of pediatric gastroenterologist [17,18]. Step-up therapy involves progression from diet and life style changes to H₂ receptor blockade medications as (ranitidine, nizatidine) to PPI as (omeprazole, lansoprazole) [19]. Both classes of acid antisecretory have proven safe and effective for both infants and children in reducing gastric acid output.

The goals of medical therapy are to decrease acid secretion thus, decrease acid content of the refluxate and, in many cases, to reduce gastric emptying time. However, other components of the refluxate as bile, pepsin and trypsin may also lead to esophageal- mucosal injury and exert damaging effect even under conditions of alkalization. Thus, some patients under antisecretory treatment may have normal pH probe studies yet continue to have GER symptoms [20,21].

In general, around 70% of patients with GERD may suffer from chronic or relapsing symptoms and they require long-term management by either intermittent, on demand or continuous acid suppressant therapy. A proportion of patients require continuous acid suppression with PPI, and selected cases may be suitable candidates for anti-reflux surgery [14,16]. When rigorous "step-up" therapy has failed, or when complications of GER pose a short or long term survival risk, the goal of surgical anti-reflux procedure is to tighten the region of the LES and, if possible, reduce hiatal herniation of the stomach which is occasionally seen in patients with GERD [3]. GER has been associated with significant respiratory symptoms in infants and children. The association between asthma and GERD has been debated for decades, and epidemiological studies have repeatedly shown this association in children and adults, in the way that GER is a complicating factor in asthma [3,22]. Thus, the Aim of study is to determine the percentage of GERD among children with respiratory symptoms and to study the impact of anti-reflux therapy in GERD management on respiratory symptoms.

Materials and Methods

A case series study was conducted by reviewing the medical records of pediatric patients admitted to Tripoli Medical Center, Respiratory clinic, pediatric department with different respiratory problems (chronic cough, wheezy chest, recurrent vomiting and choking attacks) with clinically suspected GERD and who underwent 24 hours pH monitoring by using Medtronic™ Ambulatory Reflex Testing. Sixty-nine files were reviewed which were belonged to children aged between (48 days - 12 years); 45 males and 24 females and which met the inclusion criteria of medical record of a pediatric age patient with respiratory symptoms and with 24 hours pH monitoring results. A performed work sheet used to collect the data from the records which includes age, sex, presenting complain, results of 24 hours pH monitoring and the outcome of anti-reflux therapy. The children were investigated by Digitrapper 24 hour's catheter pH monitoring device, following the Intraluminal impedance technique (IMP) to confirm GERD diagnosis on inpatients basis for 10 months. Calibration of the catheter was done by using buffer solution pH 7 and pH 1.07 and the catheter was inserted via nose to be around 3 - 5 cm above gastro-esophageal sphincter ($5 + 0.252$). The sensor position was confirmed by fluoroscopy control. Activities like eating, drinking were registered and other clinical findings were carefully noticed. It is said to be acidic GER if the reading is less than 4 and alkalotic GER if the reading is more than 7. GER with an esophageal pH in physiological range (pH 5 - 6.8) may represent many cases of clinically relevant GER. Children detected to have GERD were advised to be on anti-reflux therapy and regular follow up. The anti-reflux therapy was in the form of Non-pharmacological therapy which include elevation of bed head side, weight reduction especially if obese, low fat diet, avoidance of food and drugs that may reduce LES pressure, avoidance of eating before going to bed at least by three hours and feeding cereal-thickened formula in case of infants. Or in the form of Medical treatment by giving course of anti-reflux (H₂ blocking agents, proton pump inhibitors) treatment for a period between 3 - 12 months.

Results

In figure 1, sixty-nine patients were included in the study. Their mean (SD) age was 36.8 (\pm 43) months, ranged between 48 days to 12 years. 40% of the patients were infants (0 : 1 year), followed by 25% toddlers (1 : 3 years), 13% were preschool age children (3 : 6 years) and 19% were school age children (> 6 years). Frothy five patients were males (65%); 25 of them were positively diagnosed as GERD patients and 24 patients (35%) were female; 13 of them were diagnosed as having positive GERD. Using the 24 hours pH monitoring, 54% of the patients (n = 37) was found to have GERD and 46% (n = 32) showed negative results (Figure 2).

Twenty patients were given anti-reflux therapy (intervention group), 8 patients required surgical intervention, and were referred to pediatric surgery department and 9 patients who joined the study from other units to confirm the presence GERD were referred to their units and were dropped from the study. The relation between the selected candidate's ages and the pH monitoring results (positive or

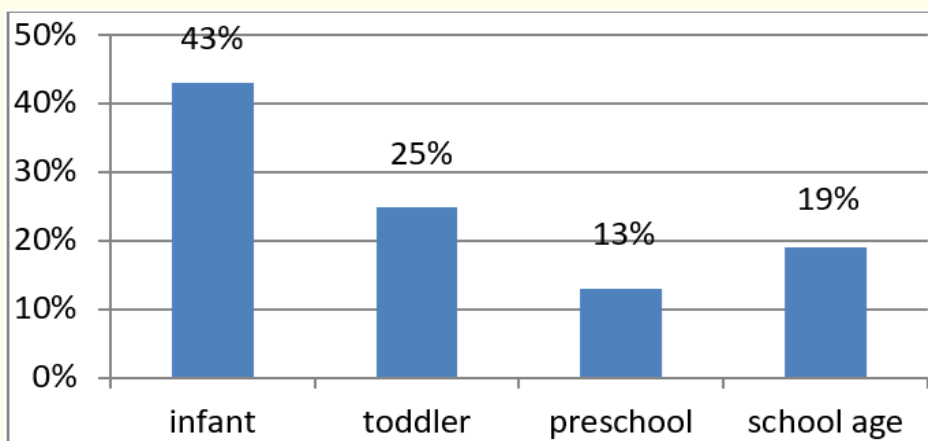


Figure 1: Age distribution of children underwent 24-hours pH monitoring.

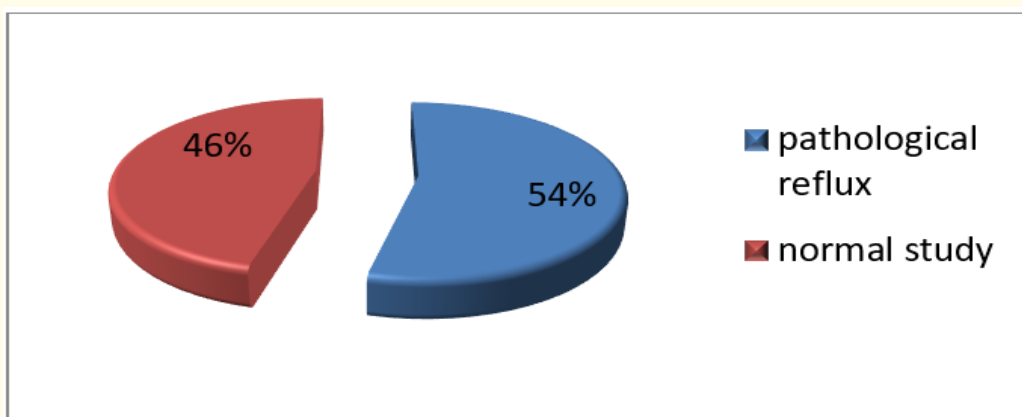


Figure 2: Percentage of GERD among children with respiratory symptoms.

negative) are shown in figure 3. It shows that most of the positive results that confirm GERD diagnosis were in the infant age, 42% followed by toddlers 32% while the preschool age group positive results were 11%, and in school age children were 16%.

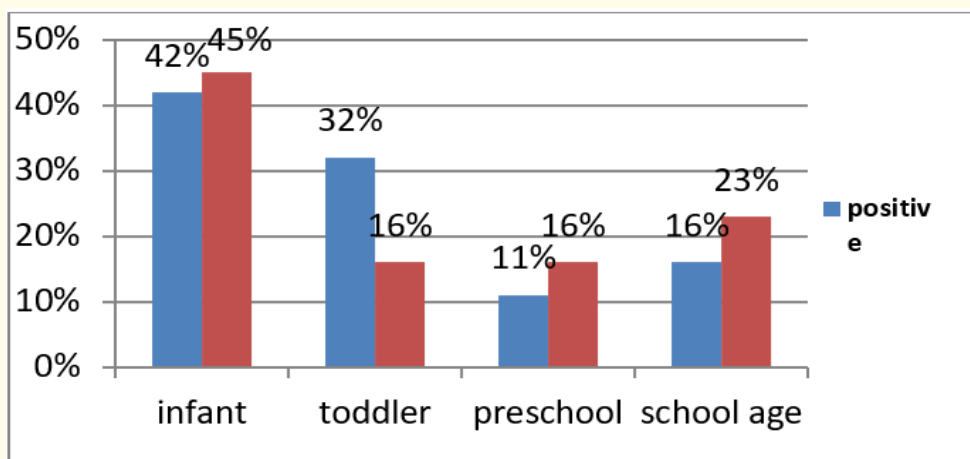


Figure 3: Distribution of positive and negative results in relation to age.

All patients were presented with one or more GERD symptoms; including vomiting, cough, chocking, wheezy chest, chest infection, failure to thrive as shown in figure 4. The usual course of anti-reflux treatment was from 3 - 12 months period, and as expected the response was variable from patient to patient. Of the total GERD positive patients (37), anti-reflux therapy was started for 20 patients and the results showed that only 11 patients were followed up regularly; 8 patients (72.7%) were responded well and were symptom free by finishing the anti-reflux therapy course (3 months - 1 year) as shown in figure 5, while the other 2 patients (18.2%) did not respond to the treatment and only one patient showed little improvement and needed reevaluation and a longer course of anti-reflux therapy.

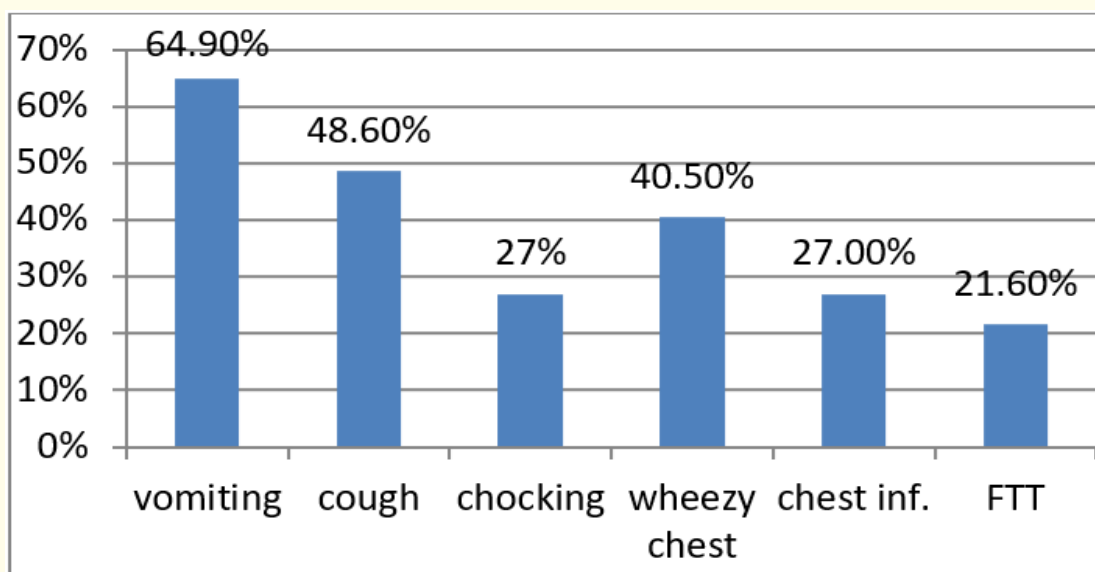


Figure 4: Percentage of presenting symptoms in children with GERD.

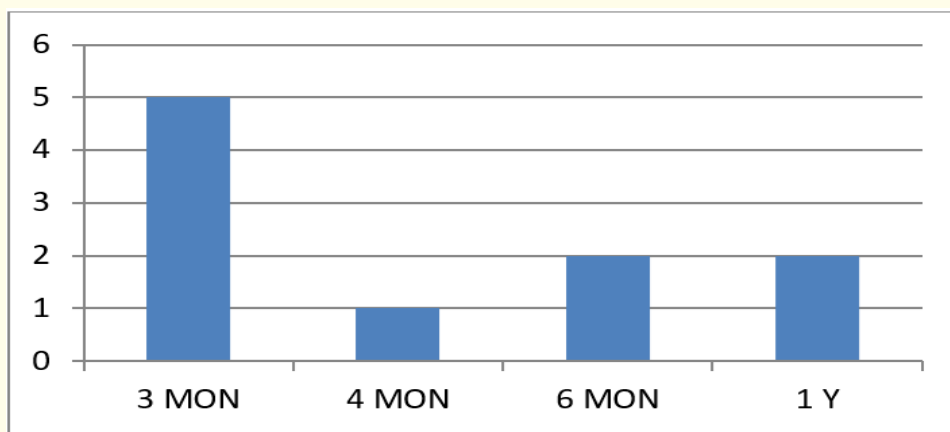


Figure 5: Variable responses to anti-reflux therapy among Children with GERD

Discussion

Using the 24 hours pH monitoring test the results of this study showed that 54% of the patients complained of respiratory symptoms were having GERD. This finding is compatible with the previous studies which shows that the prevalence of GERD in children with extra esophageal symptoms (including respiratory symptoms), varies from 19.3% - 65%, depending on the definition and methods used [23]. Tolia., *et al.* used a systematic review of studies that assessed the prevalence or incidence of extra-esophageal symptoms in children

with GERD, the results of 15 articles and studies were investigated and it revealed that the reported prevalence of GERD in children with asthma had a wide variation. This wide variation in prevalence estimates most likely reflects the small sample sizes, the differing definitions of asthma and GERD used in those studies, the fact whether asthma symptoms were present during the investigations, the variety of age groups studied, and the differing techniques used to make a diagnosis [23].

Extra-esophageal symptoms are thought to be common, atypical symptoms of GERD in children [23]. Many previous studies reported that, there are possible associations exist between GERD and asthma, pneumonia, bronchiectasis, laryngotracheitis. Data from well-selected retrospective and prospective observational studies suggest an association between GERD and asthma in children, and further possible associations with pneumonia and bronchiectasis [23]. It was also reported by EL-Serag, et al. that GERD in children without neurological defects is associated with a several fold increase in the risk of sinusitis, laryngitis, asthma, pneumonia, and bronchiectasis [24]. In another study, the prevalence of symptoms associated with GERD was increased in children with asthma and in overweight children. Overweight and asthma were independently associated with GERD symptoms, and overweight did not explain the higher frequency of GERD in asthma patient [25]. Our results also concur with those of other studies that used a GERD diagnostic tests other than 24 hours pH monitoring test in patients with respiratory diseases as in Chopra, *et al.* study when eighty children with bronchial asthma and ten control cases underwent radionuclide gastroesophagography for the detection of gastroesophageal reflux [26]. The result of that study shows that 39% of asthmatic children demonstrated esophageal reflux on scintiscanning.

According to Jason and coworkers study the association between GERD symptoms and emergency department visits and inhaled medication use were stronger among children with asthma who reported daily GERD symptoms [27]. The prevalence of GERD symptoms was greater in adolescents with current asthma than in those without asthma. In addition, the presence of at least weekly GERD symptoms was strongly associated with greater asthma morbidity and the use of asthma medications.

The impact of the anti-reflux therapy used in this study and the time needed for the resolving of GERD patients were compatible with previous studies. It shows that 72% of the patients treated with antisecretory therapy were responded well and were symptom free by finishing the course of treatment (3 months - 1 year). Also it shows that 50% of the patients were symptom free after 6 months, which is compatible with the retrospective review study of Tolia V, *et al.* that involve 341 infants presenting with symptoms suggestive of GERD, and underwent extended pH monitoring for one or more of the same symptoms that are indicated in our study and stated that the majority of infants with symptoms suggestive of GERD resolve their symptoms within 3 - 6 months of initiating treatment [28].

Conclusion

Twenty four hours pH monitoring test is a reliable method for GERD diagnosis. GERD can be a leading cause of respiratory diseases (pneumonia, recurrent wheezy chest, chronic cough and uncontrolled asthma symptoms). Anti-reflux therapy can improve respiratory diseases in selected patients. We recommend that health education to improve the knowledge of parents especially new mothers is needed. In addition, increase the awareness of pediatric doctors to GERD and its relation to respiratory diseases, and to emphasize on the inclusion of the pH monitoring test as one of the routine investigations of children with recurrent respiratory symptoms.

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