CHILDREN, GASTROESOPHAGEAL REFLUX AND ULTRASOUND

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Abstract- While a few studies have excluded ultrasound as a reliable diagnostic tool in screening for gastroesophageal reflux disease (GERD) in infant and children, others have referred to ultrasound as the screening test of choice in symptomatic patients and for patients follow-up. In this study, we evaluated the sensitivity and specificity of ultrasound in diagnosing GERD in children. This case-control study involved 56 patients and 50 controls. Inclusion criteria were age below 14 years, exhibiting GERD symptoms, having been chosen as a candidate for esophageal endoscopy and biopsy by a pediatric gastroenterology subspecialist, pathology or 24-hour pH-metry result suggestive of GERD, absence of obstructive gastrointestinal tract diseases, metabolic or other systemic diseases and having received no medications prior to the study. Ultrasound examination was performed for both patients and controls; endoscopy and 24-hour pH-metry were done for all patients and those in control group who had abnormal findings in ultrasound exam. Pediatric gastroenterologist's final judgment based on clinical and paraclinical findings constituted the gold standard. Sensitivity, specificity, positive predictive value and negative predictive value of ultrasound in diagnosing GERD were 76%, 100%, 100% and 79%, respectively. The mean length of subdiaphragmatic part of esophagus was 6.36 mm shorter in children with reflux than that in subjects without reflux and the difference was significant. Ultrasound can successfully be used as the first diagnostic approach in children with GERD.

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INTRODUCTION

The severity and scope of symptoms of gastroesophageal reflux disease (GERD) in children vary according to age (1, 2). GERD is the most common esophageal disorder and one of the most frequent diseases of the gastrointestinal tract in children and infants (3). GERD is the most costly gastrointestinal disease in adults and existing data suggest treatment costs in children is as high as adults (4).

One of the difficulties of GERD management in children is its diagnosis. While a few studies have excluded ultrasound as a reliable diagnostic tool in screening for GERD in infant and children (5, 7), others have referred to ultrasound as the screening test of choice in symptomatic patients and for patients follow-up (3, 8-10). Also, ultrasound has been highlighted as an effective and safe procedure, both in diagnosing and follow-up of young children with GERD (11-13) and successfully has been used as the first diagnostic approach in babies with

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persistent vomiting (14). Furthermore, ultrasound imaging of gastroesophageal junction has been shown as a valuable part of ultrasound diagnostics of reflux and helpful in establishing the etiology and choosing the treatment method (15). Westra *et al.* believe that ultrasonic evaluation of esophagus can serve as a reliable, simple and rapid method of screening for high-risk GERD patients and those with respiratory symptoms of reflux (16). Moreover, ultrasound has been applied successfully for assessment of hiatal hernia and morphological evaluation (8, 17), and as a safe and cheap alternative to scintigraphy for the assessment of gastric emptying (18, 19).

In this study, we evaluated the sensitivity and specificity of ultrasound in diagnosing GERD in children.

MATERIALS AND METHODS

This case-control study was conducted at the Gastroenterology Ward, Gastroenterology Clinic, Endsocopy Unit, Emergency Room and General Clinic of Children's Hospital Medical Center affiliated to Tehran University of Medical Sciences.

Cases were selected using the convenient methods. Criteria of inclusion in the study were as follow: 1) age below 14 years; 2) exhibiting GERD symptoms; 3) having been chosen as a candidate for esophageal endoscopy and biopsy by a pediatric gastroenterology subspecialist; 4) suggestive result for GERD in pathology or 24-hour pH-metry; 5) absence of obstructive gastrointestinal tract disease, metabolic or other systemic disease; and 6) having received no medications prior to the study.

Patient data were recorded through a questionnaire after obtaining parent's written consent. After history taking and physical examination, 24 hour pH-metry was performed for the patients the day after and they underwent endoscopy. Ultrasound examination was done two days later. Subjects meeting inclusion criteria remained in the study as established cases and received the required treatment. Diagnostic gold standard in our study constituted of patient's clinical picture; *i.e.* pediatric gastroenterologist's final judgment based on clinical and paraclinical findings.

Out of 69 healthy children presented in general clinic of the emergency department, 50 ones were chosen as controls. Control group were selected among children or siblings of children referred to general clinic or the emergency department with minor medical complaints such as common cold but without any GI symptoms. Children whose parents agreed with performing esophageal ultrasound examination, included in the study. Ultrasound was conducted in a complete state of health.

Patients with abnormal findings underwent 24–hour pH-metry and esophageal endoscopy and biopsy. Children whose parents did not consent to pH-metry or endoscopy were excluded.

Transabdominal esophageal ultrasound at the gastroesophageal junction was conducted longitudinally through the hepatic window using Aloka SSD-1700 ultrasound device with 7.5 MHz linear probe and 3.5 MHz curved probe if necessary. In order to diagnose esophagitis we considered esophageal biopsy as the gold standard. Ultrasonic mucosal thickness > 1.8 mm or esophageal wall thickness > 3.5 mm.

Data collected via questionnaires and procedures for all patients and controls, were analyzed using SPSS and the results were compared with chi square and *t* test. $P < 0.05$ was considered significant.

RESULTS

A total of 56 cases out of 113 cases who had referred to pediatric gastroenterology subspecialists with symptoms of GERD and 50 controls were enrolled in the study with the mean age of 4.7 ± 3.4 and 4.7 ± 3.7 years, respectively, with no significant difference; 38.56 of cases (67%) and 24.50 of controls (48%) were male and the distribution of sex between two groups was significantly different ($P = 0.04$). As it is shown in table 1, the following GERD manifestation were significantly more frequent among cases compared to control: iron deficiency anemia, loss of appetite, vomiting, weight loss, chronic cough, wheezing or dyspnea and history of aspiration pneumonia (Table 1). Frequency of clinical features of 2 groups is shown in table 1. Mean esophageal diameter, mean esophageal wall

Table 1. Frequency of clinical feature in cases*

Parameters	Cases
Loss of appetitie	36 (64)
Vomiting	40 (71)
Past history of gastrointestinal bleeding	4 (8)
Esophageal stricture	5 (9)
Past history of weight loss	31 (54)
Chronic cough, wheezing or dyspnea	36 (64)
Past history of aspiration pneumonia	16 (29)
Past history of apnea	2 (4)
Iron deficiency anemia	33 (58)
Sandifer syndrome	5 (8)

*Data are given as number (percent).

thickness, mean esophageal mucosa thickness and mean hiatal diameter all significantly were larger in case group compared to control group (Table 2). Moreover, the mean length of subdiaphragmatic part of esophagus was 6.36 mm shorter in children with reflux than those without reflux and the difference was significant. Then, all ultrasonic measures revealed GER presence in cases.

Mean and standard deviation of ultrasonic features of GER in 2 groups are shown in table 2. GER was detected by ultrasound in 43.56 of case group and none of the control group. The sensitivity and specificity, positive predictive value and negative predicative value of ultrasound in diagnosing GER were 76% 100%, 100% and 79%, respectively (Table 3). Different diagnostic characteristics of ultrasound in children with gastroesophageal disease are also shown in table 3.

DISCUSSION

Distention of the esophagus and shortening of subdiaphragmatic part of esophagus may occur during GER and could play a role in the causation of esophageal symptoms (15, 17, 20). In our study, all ultrasonic esophageal measurements were in favor of esophageal distention and GER in cases. Sonographic measurement of the abdominal esophagus length is highly diagnostic for GERD in neonates and infants (21). The mean difference of abdominal esophagus between cases and controls in our study (6.36 mm) was greater than that in similar studies - 4.4 mm in Halkiewicz study (15) and form 3.4 to 4.8 mm in Koumanidou study (21). Ultrasonographic assessment of GERD in the control group yielded completely normal results. On the other hand, normal results were reported only for 13 in 56 patients, indicating no false positive ultrasound results with only 24% false negative, hence positive ultrasound results seem to be of value. In 2002, Fallahi *et al.* has reported the following results for ultrasonic detection of GERD in children; false positive: 26% false negative: 6% sensitivity: 90%, specificity: 35%, positive predictive value: 67%, negative predictive value: 70% (22). In another study, the positive and negative predictive value of ultrasonic versus the result of continuous 24 hour pH-monitoring was 80% and 50%, respectively (5).

In Riccabona *et al.* study, specificity of ultrasonic diagnosis of GERD was 87.5% and the sensitivity was 100% (14). Tani *et al.* has revealed ultrasonic sensitivity of 79% to 87% and specificity of 76.5% to 81% in different age groups (9). Also, a sensitivity of 68% and specificity of 84.6% was reported by Lucio-Villegas (23).

As it was expected, most of the manifestation of GERD were significantly more frequent among cases than controls and the patient's clinical picture (pediatric gastroenterologist's final judgment based on clinical and paraclinical findings) constituted the gold standard in our study, whereas in the study conducted by Fallahi *et al.* in 2002, pH-metry was

Table 2. Mean and standard deviation of ultrasonic features of gastroesophageal reflux in 2 groups

Parameters	Cases	Controls	*P* value
Esophageal diameter	11.97 (± 2.67)	10.11(± 2.01)	$P < 0.001$
Esophageal wall thickness	5.06 (± 2.06)	3.83 (± 1.17)	$P < 0.001$
Esophageal mucosa thickness	2.84 (± 1.22)	2.02 (± 1.11)	$P = 0.001$
Hiatal diameter	13.86 (± 3.8)	12.4 (± 3.1)	$P = 0.007$
Length of subdiaphragmatic segment	15.89 (± 7.8)	21.53 (± 9)	$P = 0.001$
Gastric wall thickness	3.04 (± 1.4)	2.79 (± 1.02)	$P = 0.07$

Table 3. Different diagnostic characteristics of ultrasound in children with gastroesophageal disease referred to center of children diseases, 2004-2005

Ultrasound procedure	Sensitivity	Specificity	PPV	NPV	Accuracy
Diagnosis of reflux	76%	100%	100%	79%	88%
esophagitis base on thickness > 3.5 mm	79%	52%	80%	76%	68%
esophagitis base on thickness > 1.88 mm	77%	65%	66%	80%	72%

Abbreviations: PPV, positive predictive value; NPV, negative predictive value.

the gold standard (22). However, because of the high prevalence of nonerosive gastroesophageal reflux disease and functional heartburn associated with normal esophageal pH-metry, the value of pH-metry as a gold standard has been questioned (24, 25) and in many recent articles, prime value has been added to the clinical picture or the combination of clinical and paraclinical findings (26, 27), especially given that the new diagnostic and treatment questionnaires are currently the focus of attention. (28–30). If possible, the combination of 24- pH-metry and intraluminal impedance test is considered as gold standard (31-33), however, conducting both is difficult and expensive.

Higher accuracy of the gold standard in our study (compared to the Fallahi's study) can explain the lower sensitivity and higher specificity of ultrasound. It is reasonable to assume that reflux detected by ultrasound to be the ′true′ type, and is unlikely to be mistaken for other conditions; although the acid, basic or neutral nature of reflux remains to debate.

Nonetheless, the patient who is actually suffering form GERD might not exhibit an episode of reflux during the ultrasound procedure, or the sonographist might fail to detect the condition. Apparently, comparison of the results of pH-metry and ultrasound is liable to be misinterpreted because the two procedures have been performed at different times. But, the pH-metry procedure itself is prone to problems. For example, pH-metry dose not detect non–acid reflux (32). In a study conducted by Milcocco, pH-metry detected 72.5% of reflux cases (5) while ultrasound detected 76% in our study and 78% in Westra's study (16). In studies which consider pH-metry as the gold standard, ultrasound specificity levels below 100% are due to non–acid reflux. For instance, the Fallahi's study (22) has reported 35% specificity for ultrasound; this may indicate that only 35% of reflux cases in that study were acidic and the rest were basic or neutral (pH > 4) or pH-metry may not have been done under optimal conditions (anti-reflux medications may not have been discontinued at the right time, etc). In addition, GER patients do not always present with vomiting, and pH-metry is a difficult test of low value below one year of age, when reflux is highly prevalent. Also, reflux detected by ultrasound is unlikely to have been mistaken for other conditions. Hence, ultrasound combined with the clinical picture assist the diagnosis of GERD, while it can be used as the first step in paraclinical diagnosis of this disease and can serve as a good tool to justify the administration of somewhat risky medications such as cisapride or metoclopramide.

The children in our study were on average two years younger than in the Fallahi's study and if we assume thickness of the mucosal layer to be less than 1.8 mm, diagnostic sensitivity will be higher than figures mentioned above. This may account for the difference between this study and the Fallahi's study.

If we take into account the esophageal wall thickness below 3.5 mm as normal, based on a study conducted by Mahdizadeh and colleagues (34), the following results will be obtained: sensitivity: 79% specificity: 53% positive predictive value: 80% negative predictive value: 76%, diagnostic accuracy. 68%. Then, the lower age of subjects in our study may have somewhat contributed to the lower sensitivity of ultrasound. Also, many of the cases previously labeled as mild esophagitis may have been reported as normal, thanks to the long experience of gastroenterologist and pathologist.

Worthy of nothing esophageal wall thickness in subjects of Mahdizadeh study (34) is considerably greater than expected; this may provide some explanation as to the difference between the studies. In the later study, esophageal thickness was even greater than in studies conducted by Mahdizadeh, which involved adult subjects (34).

It must be emphasized that the ultrasound procedure should be performed accurately with the suitable device by a skilled sonographist and under no time constraints. Our patients may have been referral cases with higher degrees of reflux (reflux index = 32.32 ± 21) and the skilled sonographist may have performed the procedure based on his/her insight. Ultrasound may gain greater importance in areas where endoscopy and biopsy, pH-metry, and video fluoroscopy are not available for children. We need to note that ultrasound currently lacks standardized measurements.

In the next stage, especially in evaluation for esophagitis, endoscopic and pathological assessments supersede ultrasound in value. However, ultrasound can be used to screen patients with suspected esophagitis, follow up patients with established esophagitis, and evaluate response to treatment. Although many recent studies have used endosonography to this end, under the present condition, when pediatric endosonography is unavailable and pediatric endoscopy can be performed in very few centers in Iran. We may be able to use ultrasound to follow up esophagitis in established cases of the disease. Furthermore, ultrasound is the only diagnostic test for reflux which can be repeated several times a day; i.e. before, during and after eating, etc.

Conflict of interests

We have no conflict of interests.

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