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The relationship between the numbers of reflux episodes with anatomic changes of the esophagus in children under one year with gastroesophageal reflux disease

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ABSTRACT

Gastroesophageal reflux is the most common gastrointestinal disorder in the neonatal period, and the main reason for it is the lack of development in the first months of an infant's digestive system and it gets improved with the aging of baby and development of the digestive system. Some studies have shown that there is a relationship between characteristics of anatomic and esophageal reflux. This study aimed to determine the relationship between the characteristics and frequency of reflux in infants under one year old with gastroesophageal reflux disease. This study is a cross-sectional study that was conducted in 2015 in the hospital of martyr Beheshti. In this study, a group of 120 children with reflux in three age groups less than one month, 1-6 months and 6-12 months were choses and the relationship between reflux episodes with esophagus anatomic characteristics, including distal esophagus distention, Hiss angle, internal angle and length of esophagus were examined. The data were analyzed using the SPSS software and the relationship between the characteristics was compared with the number of reflux in three groups. According to the results, the frequency of reflux and extent of distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and length of the esophagus, there was a statistically significant correlation (P <0.001). The correlation between reflux episodes and four parameters, are respectively, 0/95, 0/97, 0/71 and -0/79/. Also there was a direct relation between the frequency of reflux and extent of distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and an inverse relation with length of the esophagus. The correlation between the frequency of reflux and esophageal characteristics in separation between all three age groups showed a statistically significant relationship exists between anatomical esophageal characteristics and reflux frequency. Based on the results of this study it can be concluded that there is a direct relation between the frequency of reflux and extent of distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and an inverse relation with length of the esophagus. And the patient's age does not have a significant effect on the amount of correlation between reflux episodes and anatomical characteristic.

Keywords: infant reflux, distention of the distal esophagus, Hiss angle, internal angle, the length of the esophagus

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INTRODUCTION

Gastroesophageal reflux (GER), is the passage of gastric contents into the esophagus with or without nausea and vomiting, and it is a natural physiological process in healthy infants, while in case of symptoms or complications in passage of gastric contents into the esophagus or oropharyngeal is called GER or GERD [1]. Signs and symptoms associated with GER or GERD are considerably different, and the signs of disease can vary depending on the patient's age and health status. Gastroesophageal reflux until the ages of 8 and 12 months in the absence of respiratory symptoms or gastrointestinal is considered to be physiological.

[1]Gastroesophageal Reflux Disease refers to a condition associated with symptoms such as severe irritability and crying, lack of growth, reluctance to eat, sleep apnea and aspiration pneumonia. [2 and 3] GER in children under 4 months occurs about 61% and at ages 6 to 7 months accurs 21% [2 and 4].

Different risk factors are listed in the mechanism of GER. Impaired peristalsis is seen in about 50-40% of patients [3]. Impaired relaxation of the lower esophageal sphincter [4], anatomical abnormality of the diaphragm [5] and short length of abdominal esophagus [6] are some of the known causes of the incidence of GER.

However, medical history and physical examination is usually enough for reliable detection of pathological GER and results in the beginning of treatment in older children and adults. While diagnostic tests must be done when GERD remains uncertain and there are still questions. Since the description of subjective symptoms in infants and toddlers is unreliable and because many of these symptoms are non-specific several techniques have been used for the diagnosis of GERD, but no single test is sensitive and specific enough to diagnose. A Test is needed for children suspected of having GERD that is accurate and acceptable for non-invasive children.

GERD diagnosis is based on clinical symptoms and clinical studies such as barium swallow, esophageal pH and impedance monitoring and is endoscopy. [1] Due to inaccessibility and difficulty in diagnostic methods, in recent years several studies were done for the use of ultrasound as a non-invasive method to diagnose GERD. US of stomach is suggested as a convenient method, and the non-invasive with high sensitivity (with not so good quality), to provide morphological information. However, the role of the US in the GER in children is still being debated.

In a study in 1995 that Di Mario and colleagues have implemented to check clearing time of the esophagus and hiatal hernia associated with the use of ultrasound and comparing the results with barium swallow, they reported ultrasound as a screening test to diagnose GERD is effective [7]. In a study of Jang and colleagues they examined the frequency of reflux within 15 minutes by color Doppler sonography and compare it with a 24-hour esophageal pH meter, and they know Color Doppler sonography is a sensitive and easy method to evaluate GERDthat had 81.5% agreement with the pH meter [8].

Farina and colleagues studied 120 children 1 to 24 months using color Doppler sonography with contrast, examined the movement of food from the stomach into the abdominal esophagus and the lower third of the thoracic esophagus. Compared with esophageal pH meter this method has high sensitivity (98%) [9]. Several studies have been conducted to evaluate the value of ultrasonography in the diagnosis of GERD and the role of ultrasonography in the diagnosis of gastroesophageal reflux disease has been confirmed that is even known as the standard method for diagnosis of GERD

Ultrasound compared with the pH meter is inexpensive, non-invasive and available and by using it the stomach and esophagus anatomical information can be easily achieved. Also, the diagnosis of short reflux compared with PH meter, has fewer false negatives. [9] Studies investigated the relationship between the length and thickness of the abdominal esophagus and esophageal reflux the relationship between shortness of abdominal esophagus, thickness of the lining of the esophagus and reflux [14, 16 and 19].

Alessandra and colleagues in a study reviewed 12 articles that used ultrasound to measure the features of the esophagus, and mentioned the angle of Hiss, the dilatation of the distal esophagus and the abdominal esophagus, as factors associated with reflux [20]. Given the lack of comprehensive studies of the anatomy of the esophagus in patients with gastroesophageal reflux disease we decided to measure these changes according to the number of reflux episodes to obtain more accurate criteria for the diagnosis of GERD and its intensity which can be helpful for faster diagnosis using ultrasound.

MATERIALS AND METHODS

This study is cross-sectional study that was conducted in 2015 in the hospital martyr Beheshti of Kashan. The study population consisted of children under 12 months who based on clinical diagnosis by pediatric gastroenterologist, endoscopy or barium desire, GER diagnosis is confirmed. The sample size required for this study using sample size formula for correlation studies and taking into account the confidence level of 95% (Z1-a / 2 = 1.96), Power of the test 80% (Z1-b = 0.84), the correlation between the length of abdominal esophagus and the number of reflux which amounted to 0/2 were considered, it was estimated for 113 people and in order to ensure further 120 children were studied.

Samples were collected and examined using a convenience sample of patients admitted to hospital martyr Beheshti in 2015. Of all children under 12 months based on clinical diagnosis by a gastroenterologist for children, endoscopy or barium diagnosis of GER was confirmed, and did not have the exclusion criteria in previous laboratory tests or

ultrasound, 120 patients in three groups of less than one month, one to six months, more than six months, and 40 patients in each group were selected. After obtaining informed consent to participate in the survey from parents and demographic information, these children were referred for ultrasound radiologist.

15 minutes after feeding children in were put Supin on the bed and using V20 medison unit 7.5 MHz linear probe and an angle of about 45 degrees below the area of Xiphoid number of reflux angle of His (external angle between the stomach and esophagus), the dilation of the distal esophagus (from serous to serous) abdominal esophagus length and angle of Internal Gastro esophageal were measured and the results were recorded in the Czech check list.

RESULTS

In this study, 120 children with gastroesophageal reflux were studied who 40 were less than one month, 40 were 1-6 months, and 40 were 6-12 months. The results associated with gastro-oesophageal reflux and its relationship with the anatomical characteristics is discussed in the following.

Average number of reflux in all patients studied, was 1/67 ± 3/28. The minimum and maximum number of reflux was respectively 1 to 7 times. Average number of reflux in the following three groups of less than one month, 1-6 months, and 6-12 months is respectively, 1/55 ± 3/18, 1/71 ± 3/43 and 1/78 ±3/ 25. According to ANOVA and Kruskal-Wallis test, the frequency of reflux in the three groups were not significantly different ($p = 0.79$). Based on the results, the frequency of reflux, in 42 patients was (35%) less than 3 times a day, in 75 patients (5/62%) between 6.3 times a day and in 3 patients (5/2%) 7 times and more.

65% of children less than one month, 5/67% children 1-6 months and 55% of children 6-12 months, had reflux 3-6 times a day. Fisher's exact tests on the data showed no significant differences in the frequency of reflux by age group $p = 0.58$. Average distention of the distal esophagus in all patients studied, 6/88±1/79 with 4/5-10/6mm.

The average in three age groups less than one month 1-6 months and 6-12 months, was respectively, 68/1 ± 79/6, 87/1 ± 06/7 and 85/1 ± 72/6 mm. According to the results obtained, the mean distal esophagus distention in children with reflux less than 3 times a day was5/12±0/49 in children with reflux episodes 6-3 times a day 1/45±7/68 and in children with reflux 7 times and more, 0/06± 10/53and based on one-way analysis of variance, the mean distal esophagus distention in terms of reflux episodes was significantly different ($p <0.001$).

Mean of angle of Hiss in all patients studied, was 15/04 ± 122/23with the range of 102-159 degrees. This angel in three age groups less than one month 1-6 months and 6-12 months was respectively, 13/16/13 ± 119/4, 15/52/ ± 123/9 and 16/22 ± 123/4. According to the results obtained, the mean of the angle in children with reflux less than 3 times a day was 49/0±12/5 in children with reflux episodes 6-3 times a day 3/88 ± 108/528 and in children with reflux 7 times and more, 5/12± 47/128 and based on one-way analysis of variance, the average angle of hiss in terms of reflux episodes is significantly different ($p <0.001$).

Mean of internal angle in all patients studied, was 8/91±8106/89 with the range of 89-134 degrees. This angel in three age groups less than one month 1-6 months and 6-12 months was respectively, 103/3±6/25, 106/93±8/96and 110/35±9/87.

According to the results obtained, the mean of the angle in children with reflux less than 3 times a day was101/33±4/84in children with reflux episodes 6-3 times a day 109/03±8/4and in children with reflux 7 times and more, 130± 3/46 and based on one-way analysis of variance, the average internal angle in terms of reflux episodes is significantly different ($p <0.001$).

Mean of length of abdominal esophagus in all patients studied, was 1/23 ± 15/2 with the range of 5/12-9/18 mm.

This angel in three age groups less than one month 1-6 months and 6-12 months was respectively, 14/51±1/12, 15/18±1/04and15/9±1/12.According to the results obtained, the mean of the angle in children with reflux less than 3 times a day was 0/88±16/29 in children with reflux episodes 6-3 times a day 14/66 ± 0/93 and in children with reflux 7 times and more, 13/3± 0/52 and based on one-way analysis of variance, the average length of abdominal esophagus in terms of reflux episodes is significantly different ($p <0.001$).

Based on Spearman correlation between the amount of reflux episodes in the distal esophageal distention, Hiss angle, the angle of the esophagus and the stomach and abdominal esophagus length there was a statistically significant correlation ($P <0.001$). The correlation between reflux episodes and four parameters, was respectively, 0/95, 0/97/0, 0/71 and -0/79. Also there was a direct relation between the frequency of reflux and extent of

distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and an inverse relation with length of the esophagus. On the other hand between each parameter of the distal esophageal distention, Hiss angle, the angle of the esophagus and the length of abdominal esophagus, there was a statistically significant relationship.

Table 1: Correlation between reflux episodes and characteristics of esophageal by Spearman correlation test

		The number of reflux	Distention of the distal esophageal	Hiss angle	Internal angle	Length of esophagea
The number of reflux	Correlation amount	1	0/95	0/97	0/71	-0/79
	P	*	<0/001	<0/001	<0/001	<0/001
Distention of the distal esophageal	Correlation amount	0/95	0/99	0/93	0/7	-0/76
	P	<0/001	<0/001	<0/001	<0/001	<0/001
Hiss angle	Correlation amount	0/97	0/93	0/99	0/78	-0/72
	P	<0/001	<0/001	<0/001	<0/001	<0/001
Internal angle	Correlation amount	0/72	0/7	0/78	0/99	-0/4
	P	<0/001	<0/001	<0/001	<0/001	<0/001
Length of esophagea	Correlation amount	-0/79	-0/76	-0/72	-0/4	0/99
	P	<0/001	<0/001	<0/001	<0/001	<0/001

According to Spearman correlation test, between all specifications of esophageal and number of reflux there was a statistically significant relationship. Also according to table the lowest correlation was between number of reflux and internal angel in children under 6 months 0/49, and highest correlation for the distention of the distal esophagus in two age groups under a month and 1-6 month with the amount of 0/98.

Table 2: Correlation between reflux frequency and characteristics of esophageal, divided by age group based Spearman correlation test

characteristics of esophageal	Less than 1 month		1-6 months		6-12months	
	Correlation amount	P	Correlation amount	P	Correlation amount	P
Distention of distal esophageal	0/98	<0/001	0/98	<0/001	0/90	<0/001
Hiss angle	0/98	<0/001	0/98	<0/001	0/95	<0/001
Internal angle	0/49	<0/001	0/82	<0/001	0/89	<0/001
Length of esophagea	-0/96	<0/001	-0/90	<0/001	-0/93	<0/001

Notably, based on linear regression (GLM) age of patients had no significant effect on the amount of correlation between the frequency of reflux and the anatomical characteristics of esophagus (P> 0.05).

DISCUSSION AND CONCLUSION

Gastroesophageal reflux is the most common digestive disease in the neonatal period and in form of pathology can cause serious complications and secondary diseases of infants, therefore, detection and treatment of this condition is necessary and essential. Also to identify factors affecting the incidence of reflux in babies, can be effective in the prevention and treatment of reflux. Some studies have shown anatomical characteristics of esophagus including the distal esophagus distention; Hiss angle and internal angle and length of abdominal esophagus are effective on reflux frequency. But on the impact of these factors there is no unified theory and so far there is no consensus in the studies. Considering the high prevalence of infant reflux, this study aimed to determine the relationship between reflux frequency and anatomic changes of esophagus in children less than one year with gastroesophageal reflux disease.

Based on results of our study of the four anatomical characteristics mentioned, the variables of internal angle and length of abdominal esophagus in three age groups less than one month, 1-6 months and 6-12 months had a significant difference, while the number of reflux in the three age groups was not different. Based on the results of this study there is a direct relation between the frequency of reflux and extent of distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and an inverse relation with length of the esophagus. The patient's age does not have a significant effect on the amount of correlation between reflux episodes and anatomical characteristic. The correlation was significant in all three age groups. In a study conducted by Dehtashi and colleagues in 2007, a significant inverse correlation between the frequency of reflux and length of esophagus and the results of this study are in line with the results of our study [14]. In study of Nemati and colleagues in2013 the thickness and length of esophagus and the frequency of reflux had a significant relationship in infants less than one year [19].

Pezzati et al in 2007 reported that there is a significant correlation between gastric reflux and some anatomical features of esophagus in infants under one year [12]. Of course, as already mentioned, several factors affect the incidence of reflux in babies that anatomical features and lack of development of digestive system a in infancy are some of these factors. Other factors such as food allergies, the feeding, the milk into the baby's stomach also effect the severity and frequency of reflux. And therefore it is necessary to first identify the type of reflux (physiological or pathological) in infants and in cases of physiological reflux primarily a reforming of how to feed the baby must be done and pathological cases should be investigated and treated.

Based on results there is a direct relation between the frequency of reflux and extent of distention of the distal esophageal, Hiss angle, Internal Gastro esophageal angle and an inverse relation with length of the esophagus in children under 1 year old. And the patient's age does not have a significant effect on the amount of correlation between reflux episodes and anatomical characteristic. Given the significant relationship between the number of reflux with esophagus anatomical changes it is recommended that, this study is conducted with larger sample sizes and more broadly to determine the cut of point and Anatomic markers according to the number of reflux to identify the severity of reflux on ultrasound.

In a study of the role of environmental factors and the incidence of reflux in infants should be compared and studied. The results of this study should be considered in future research. The results of this study be given to the radiologists of children and babies.

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