DOI: 10.5336/pediatr.2018-63316

# Is Gastroesophageal Reflux Disease a Common Complication in Infants with Congenital Heart Disease?

Konjenital Kalp Hastalığı Olan Bebeklerde Gastroözofageal Reflü Hastalığı Yaygın Bir Komplikasyon mudur?

**ABSTRACT Objective:** Gastroesophageal reflux disease (GERD) is believed to be one of the most common complications of congenital heart disease (CHD) in infants though the exact prevalence is not known. In this study, we aimed to investigate GERD symptoms in infants with CHD. **Material and Methods**: Infant Gastroesophageal Reflux Questionnaire Revised was applied twice for 109 infants with CHD and 81 healthy infants, both with a median age of 5 months, two months apart and data were analyzed. **Results**: Mean reflux score was 4.81±0.56 (0-23) and 5.1±5.71 (0-24) in the CHD and control groups, respectively (p=0.62). According to ROC curve analysis, we considered a score of 7 (95% CI=53%-76.6%) as being a cut-off value for GERD. Thirteen infants, 7 with CHD (6.42%) and 6 healthy infants (7.40%) had reflux score≥16 (p=0.79). **Conclusion:** GERD is not more common in CHD than in healthy babies. As the only difference in terms of individual symptom prevalence is in apnea and cyanosis, symptoms of CHD as well, it was concluded that there is a need for more objective methods and new questionnaires to be used for infants with CHD.

Keywords: Congenital heart disease; gastroesophageal reflux disease; infant, survey

ÖZET Amaç: Gastroözofageal reflü hastalığı (GÖRH), doğuştan kalp hastalığı olan bebeklerde en sık görülen komplikasyonlarından biri olduğuna inanılmakta olup, kesin prevalansı bilinmemektedir. Bu çalışmada, konjenital kalp hastalığı (KKH) olan bebeklerde GÖRH semptomlarını araştırmayı amaçladık. Gereç ve Yöntemler: Düzeltilmiş Gastroözofageal Reflü Anketi KKH olan 109 hasta ile 81 sağlıklı bebek üzerinde iki ay arayla uygulandı. Her bir sorunun cevabı hem KKH olan (siyano-tik ve asiyanotik) hem de sağlıklı gruplarda karşılaştırıldı. Her iki grubun medyan yaşı 5 ay olarak saptandı. Bulgular: Ortalama reflü skoru, KKH ve kontrol grubunda sırasıyla 4,81±0,56 (0-23) ve 5,1±5,71 (0-24) idi (p=0,62). ROC analizine göre, GÖRH için cut-off değerini 7 olarak (%95 CI=%53%76,6) kabul ettik. Yedisi KKH (‰6,42) ve altısı sağlıklı olmak üzere toplam 13 bebekte (‰7,40) reflü skoru ≥16 (p=0,79) idi. Sonuç: GÖRH, sağlıklı olan bebeklere göre KKH olanlarda daha yaygın değildir. Semptomlarını prevalansı açısından tek fark, KKH'nin da semptomları olan apne ve siya-noz olarak bulunmuştur. KKH'lı bebeklerde GÖRH açısından daha objektif yöntemlere ve yeni an-ketlere ihtiyaç olduğu sonucuna varılmıştır.

Anahtar Kelimeler: Konjenital kalp hastalığı; gastroözofageal reflü hastalığı; bebek, anket

Significant advances in surgical techniques and intensive care management have led to increased survival in children with congenital heart disease (CHD). However, a high number of those children suffer from feeding problems, malnutrition, and growth retardation.<sup>1,2</sup> Although gastroesophageal reflux disease (GERD) is believed to be one of the most common complications of CHD in infants and to cause recurrent pulmonary

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Received: 15.10.2018 Received in revised form: 10.01.2019 Accepted: 11.01.2019 Available online: 25.01.2019

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infections, and growth and development retardation, there is not any study investigating its prevalence among this group of patients.<sup>3,4</sup> Wide spectrum of GERD symptoms and invasive nature of diagnostic methods seem to be the obstacles for easy and reliable diagnosis. Some questionnaires have been developed so far for noninvasive diagnosis of GERD, among which is the revised Gastroesophageal Reflux Questionnaire (I-GERQ-R).<sup>5</sup>

The aim of our study was to determine the frequency of GERD in a group of infants with CHD using I-GERQ as a diagnostic tool.

## MATERIAL AND METHODS

The study was planned as a cross-sectional study in two separate groups in order to determine GERD frequency in 0-1 year old infants with CHD who were diagnosed with echocardiography and followed at the Pediatric Cardiology outpatient clinic. Infants included in the study were randomly selected among infants aged 0-1 who applied to İnönü University Turgut Özal Medical Center Pediatric Cardiology, Eco and general pediatric polyclinics between December 2016-2017. The group with congenital heart disease was divided into two main groups as cyanotic and acyanotic. In addition, the cyanotic decreased pulmonary blood flow, the cyanotic increased pulmonary blood flow; Acyanotic left-right shunt and Acyanotic obstructive were included in the study. Healthy infants were included as controls. Informed consent was obtained from the parents before entry into the study. The study protocol was approved by the Ethical Committee of the University (2016/178). The written authorization for the use of native language (Turkish) version of I-GERQ-R was taken from Pittsburg University Institute of Innovation (GSCC 130 Thackeray Avenue Pittsburgh, PA). In our study, the translation of the questionnaire into Turkish was used.

The questionnaire contains 13 questions. In the first 2 questions, the amount and number of regurgitation were asked to families. In the third question, the crying and restlessness due to regurgitation were asked. The fourth and fifth questions included refuse a feeding when the baby was hungry and to stop eating at the time of feeding. In the sixth question, families were asked about the excessive crying of infants after feeding. In the seventh question, we were asked about the state of crying and restlessness compared to the previous week. In the eighth question, we were asked about the duration of crying and restlessness of the infants during a 24 hour period. In the ninth question, the infants were asked about their hiccups during the past week. In the tenth question episodes of arching back; in the 11th and 12th questions, the families were asked questions of apnea/turned blue. In the thirteenth question, the parents were asked about the severity of GERD symptoms. Answers to each question in both CHD (cyanotic and acyanotic) and healthy groups, and the statistical comparisons were shown in (Table 1).

The questionnaire was initially applied to 30 infants (15 with CHD and 15 healthy) by two methods; first, the questionnaire was applied to the same baby twice by the same interviewer one week apart; second, it was applied to the same baby by two different interviewers at the same day. In both methods, similar reflux score results were found, which indicated the intra and inter rater reliability. I-GERQ-R score of 7 or greater (95% CI=53%-76.6%) had 61.3% and 83.8% sensitivity and specificity, respectively, according to ROC curve analysis and thus cut-off pathologic score for the 0-1 age group was accepted as≥7 in our study. Score of >16 was considered as the marker of GERD according to the study of Deal et al. who found the sensitivity and specificity as 95% and 74%, respectively.<sup>6</sup>

Infants with score ≥7 were followed up for a two-month period, then which the questionnaire was re-applied. During this period, it was planned to perform a 24-hour pHmeter/impedance analysis in those who would have additional symptoms including respiratory problems and growth faltering.

### STATISTICAL ANALYSIS

IBM SPSS Statistics 22.0 program was used for the statistical analysis. Normal distribution was evaluated by Shapiro-Wilk test. The Pearson chi-square test was used for the comparison of data. A value of p<0.05 was considered statistically significant.

		Acyanotic CHD	Cyanotic CHD	Healthy					
Symptoms	CHD N=109	N=95	N=14	N=81	P1	P2	P3	P4	P5
Regurgitation frequency									
Less than once	76.1% (n=83)	77.9% (n=74)	64.3% (n=9)	69.1% (n=56)	0.07	0.15	0.5	0.058	0.50
1 to 3 times	8.3% (n=9)	7.4% (n=7)	14.3% (n= 2)	21% (n=17)					
4 to 6 times	12.8% (n=14)	11.6% (n=11)	21.4% (n=3)	8.6% (n=7)					
More than 6 times	2.8% (n=3)	3.2% (n=3)	0% (n=0)	1.2% (n=1)					
Regurgitation volume									
Did not spit up	76.1% (n=83)	77.9% (n=74)	64.3% (n=9)	69.1% (n=56)	0.231	0.506	0.602	0.223	0.83
< 1 tablespoonful	10.1% (n=11)	7.4% (n=9)	14.3% (n=2)	17.3% (n=14)					
1-2 tablespoonful	11% (n=12)	10.5% (n=10)	14.3% (n=2)	7.4% (=6)					
> 2 ounces to half the feeding	2.8% (n=3)	2.1% (n=2)	7.1% (n=1)	3.7% (n=3)					
More than half the feeding	0% (n=0)	0% (n=0)	0% (n=0)	2.5% (n=2)					
Regurgitation discomfort									
Never	73.4% (n=80)	75.8% (n=72)	57.1% (n=8)	72.8% (n=59)	0.717	0.300	0.101	0.559	0.36
Rarely	7.4% (n=8)	4.2% (n=4)	21.4% (n=3)	7.4% (n=6)					
Sometimes	12.8% ( n=14)	13.7% ( n=13)	14.3% (n=2)	9.9% (n=8)					
Often	6.4% (n=7)	6.3% (n=6)	7.1% (n=1)	9.9% (n=8)					
Always	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)					
Refuse feed when hungry									
Never	81.7% (n=89)	82.1% (n=78)	78.6% (n=11)	82.7% (n=67)	0.786	0.500	0.249	0.738	0.3
Rarely	9.2% (n=10)	7.4% (n=7)	21.4% (n=3)	8.6% (n=7)					
Sometimes	7.3% ( n=8)	8.4% ( n=8)	0% (n=0)	4.9% ( n=4)					
Often	1.8% (n=2)	2.3% (n=2)	0% (n=0)	3.7% (n=3)					
Always	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)					
Stop feed when hungry									
Never	82.6% (n=90)	82.1% (n=78)	85.7% (n=12)	86.4% (n=70)	0.42	0.111	0.504	0.029	0.86
Rarely	6.4% (n=7)	5.3% (n=5)	14.3% (n=2)	9.9% (n=8)					
Sometimes	9.2% (n=10)	10.5% (n=10)	0% (n=0)	0% (=0)					
Often	0.9% (n=1)	1.1% (n=1)	0% (n=0)	2.5% (n=2)					
Always	0.9% (n=1)	1.1% (n=1)	0% (n=0)	1.2% (n=1)					
Cry during/after feed	. ,	. ,	. ,	. ,					
Never	76.1% (n=83)	78.9% (n=75)	57.1% (n=8)	63.0% (n=51)	0.219	0.184	0.233	0.121	0.54
Rarely	10.1% (n=11)	8.4% (n=8)	21.4% (n=3)	18.5% (n=15)					
Sometimes	11% (n=12)	10.5% (n=10)	14.3% (n=2)	17.3% (=14)					
Often	1.8% (n=2)	1.1% (n=1)	7.1% (n=1)	1.2% (n=1)					
Always	0.9% (n=1)	1.1% (n=1)	0% (n=0)	0% (n=0)					
Cry greater than usual				. ,					
Never	56.5% (n=61)	62.8% (n=59)	28.6% (n=4)	61.7% (n=50)	0.711	0.367	0.097	0.840	0.14
Rarely	28.7% (n=31)	23.4% (n=22)	50% (n=7)	21.0% (n=17)					
Sometimes	11.1% (n=12)	10.6% (n=10)	14.3% (n=2)	12.3% (=10)					
Often	3.7% (n=4)	3.2% (n=3)	7.1% (n=1)	3.7% (n=3)					
Always	0% (n=0)	0 % (n=0)	0% (n=0)	1.2% (n=1)					
Cry duration									
Less than 10 minutes	62.4% (n=68)	64.8% (n=62)	52.4% (n=6)	51.9% (n=42)	0.057	0.058	0.108	0.016	0.87
10 minutes to 1 hour	23.9% (n=26)	23.2% (n=22)	28.6% (n=4)	21% (n=17)	0.001	0.000	0.100	0.010	5.01
1 -3 hour	11% (n=12)	8.4% (n=8)	28.6% (n=4)	25.9% (n=21)					
i o noui	11/0 (11=12)	0.470 (11-0)	20.0 /0 (11-4)	20.0 /0 (11=21)					

		TABLE	1: Continued.						
		Acyanotic CHD	Cyanotic CHD	Healthy					
Symptoms	CHD N=109	N=95	N=14	N=81	P1	P2	P3	P4	P5
Hiccups									
Never	53.2% (n=58)	53.7% (n=51)	50% (n=7)	46.9% (n=38)	0.394	0.665	0.665	0.475	0.71
Rarely	22.9% (n=25)	21.1% (n=20)	35.7% (n=5)	23.5% (n=19)					
Sometimes	22% (n=24)	22.3% (n=22)	14.1% (n=2)	22.2% (=18)					
Often	1.8% (n=2)	2.1% (n=2)	0% (n=0)	6.2% (n=5)					
Always	0% (n=0)	0% (n=0)	0% (n=0)	1.2% (n=1)					
Arching									
Never	85.3% (n=93)	88.6% (n=83)	76.2% (n=10)	81.5% (n=66)	0.594	0.031	0.046	0.363	0.18
Rarely	5.5% (n=6)	4.2% (n=4)	14.3% (n=2)	11.1% (n=9)					
Sometimes	6.4% (n=7)	6.3% (n=6)	7.1% (n=1)	6.2% (n=5)					
Often	1.8% (n=2)	2.1% (n=1)	0% (n=0)	1.2% (n=1)					
Always	0.9% (n=1)	0% (n=0)	7.1% (n=1)	0% (n=0)					
Apnea (awake/struggle)									
no	90.8% (n=99)	93.7% (n=89)	71.4% (n=10)	98.8% (n=80)	0.020	0.001	0.007	0.086	0.00
yes	9.2% (n=10)	6.3% (n=6)	28.6% (n=4)	1.2% (n=1)					
Turned blue									
no	92.7% (n=101)	93.7% (n=89)	85.7% (n=12)	100% (n=81)	0.013	0.017	0.286	0.021	0.00
yes	7.3% (n=8)	6.3% (n=6)	14.3% (n=2)	0% (n=0)					
Overall severity									
No symptoms	62.4% (n=68)	65.3% (n=62)	42.9% (n=6)	63.0% (n=51)	0.894	0.727	0.341	0.787	0.63
Very mild	19.3% (n=21)	16.8% (n=16)	35.7% (n=5)	19.8% (n=16)					
Mild	14.7% (n=16)	14.7% (n=14)	14.3% (n=2)	11.1% (=9)					
Moderate	2.8% (n=3)	2.1% (n=2)	7.1% (n=1)	4.9% (n=4)					
Severe	1.1% (n=1)	1.1% (n=1)	0% (n=0)	1.2% (n=1)					
Very severe	0% (n=0)	0% (n=0)	0% (n=0)	0% (n=0)					

P1: CHD-Healthy; P2: Acyanotic-Cyanotic-Healthy; P3: Acyanotic-Cyanotic; P4: Acyanotic-Healthy; P5: Cyanotic-Healthy.

# RESULTS

One hundred and nine infants with CHD (46.8% girls and 53.2% boys), 95 of whom were acyanotic and 14 were cyanotic and 81 (45.7% girls and 54.3% boys) healthy infants were included. There was no significant difference in gender between the patient and healthy groups (p=0.879). Median age was 5 months in both groups (p=0.169). Mean body weight in the healthy and CHD group was  $6.90\pm2.0$  kg and  $6.1\pm1.7$  kg, respectively (p=0.02). It was found that 11.9% of CHD group and 2.5% of healthy group had body weight percentile below <3p (p=1).

While ventricular septal defect (VSD) was the most common diagnosis in the acyanotic group, Fallot tetralogy (FT) was at the top of the list in the cyanotic group. Etiologic distribution of the CHD was shown in (Figure 1).

Reflux score of  $\geq$ 7 was found in 48 (25.2%) of all infants. It was  $\geq$ 7 in 29 babies (60.4%) among CHD group and in 19 babies (39.6%) among healthy group (p=0.376). We also found a reflux score of  $\geq$ 16 in thirteen infants in this group of 48 babies. Thirteen infants, 7 with CHD and 6 healthy infants had reflux score $\geq$  16 (p=0.79) (Table 2). There was no significant difference in gender between the patient and healthy groups who had reflux score $\geq$  7 (p=0.376). Mean reflux score was 4.81±0.56 (0-23) and 5.1±5.71 (0-24) in the CHD and control groups, respectively (p=0.62).

Back arching during feeding was more common in cyanotic infants compared to acyanotic ones (p=0.03). When we evaluated the respira

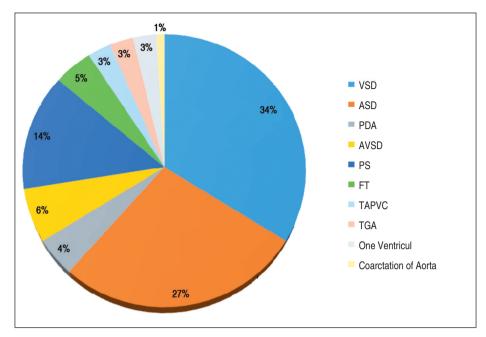


FIGURE 1: Etiologic distribution of congenital heart disease.

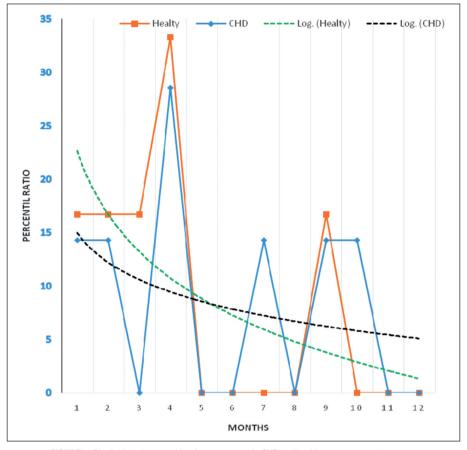
VSD: Ventricular septal defect; ASD: Atrial septal defect; PDA: Patent ductus arteriosus; AVSD: Atrioventricular septal defect; FT: Tetralogy of Fallot; TGA: Transposition of the Great Arteries; TAPVC: Total anomalous pulmonary venous return.

	TABLE 2: Gend	er distribution of p	atients accor	ding to reflux sco	res in CHD and con	trol groups.			
		Reflux score ≥ 7			Reflux score ≥ 16				
			Gender			Gender			
Grou	ps	Male	Female	Total	Male	Female	Total		
CHD	Number	13	16	29	4	3	7		
	For groups %	%44.8	%55.2	%100.0	%57.1	%42.9	%100.0		
	For genders %	%54.2	%66.7	%60.4	%57.1	%50	%53.8		
HEALTY	Number	11	8	19	3	3	6		
	For groups %	%57.9	%42.1	%100.0	%50	%50	%100.0		
	For genders %	%45.8	%33.3	%39.6	%42.9	%50	%46.2		
Toplam	Number	24	24	48	7	6	13		
	%	%50.0	%50.0	%100.0	%53.8	%46.2	%100.0		
	р	0.376			0.56				

tory symptoms such as apnea and turning blue/purple within the last one week, we found increased frequency in the cyanotic group, as expected (p<0.001).

Median age was 4 months for both CHD and control groups who had a reflux score  $\geq$ 7. It was found that reflux score reached a peak value at the 4th month and decreased towards the 1st year of life in CHD group. Similarly, in healthy group, reflux score  $\geq$ 7 rate was highest (26.3%; n=5) at the 4th month. Furthermore, 2 patients with CHD (28.6%) and 2 infants (33.3%) from healthy group had a reflux score  $\geq 16$  while they were 4 months old. Surprisingly, we found that reflux score peaked at 4 months in the group who had reflux score  $\geq 16$ . Reflux score and age relationship was shown in (Figure 2).

In our study, 27.3%, 40%, 20%, and 12.9% of patients with secundum atrial septal defect (ASD), patent ductus arteriosis (PDA), pulmonary steno-



**FIGURE 2:** Distribution of cases with reflux score  $\geq$  16 in CHD and healthy groups according to age. CHD: Congenital heart disease.

sis, and VSD, respectively, had reflux score  $\geq$ 7 (p=0.424). It was found that type of CHD had no effect on reflux in CHD patients with reflux score  $\geq$ 16 (p=0.91), either.

Patients with CHD whose reflux score  $\ge 7$  were followed and reevaluated after 2 months using the same questionnaire. Considering the possibility of physiological reflux, the questionnaire was re-applied in this period due to the situation of spontaneous recovery. Twenty three of them (23/29) could be assessed; three patients were already dead, remaining could not be contacted. Mean reflux score was found as  $5.30\pm0.48$  in the second evaluation (1-9; p=0.03) and only two CHD patients had reflux score  $\ge 7$  (8.7%). Of all, 6.4% (n=7) had reflux score  $\ge 16$ ; 5 of these CHD patients were in acyanotic, 2 of them were in the cyanotic group. Although pH meter/impedance analysis was planned for those infants, parents did not accept the procedure. Third I- GERQ-R, which was performed one month after the  $2^{nd}$  evaluation revealed lower scores (<7).

We evaluated the probable risk factors which might have increased the reflux score ( $\geq$ 7) in infants with CHD including age, gender, weight percentile, and type of CHD and found that cyanotic CHD group had a 3.72 times higher risk (a confidence rate of 1.08-14.2) than acyanotic left-right shunt infants (Table 3). Multiple regression analysis was also planned for the group who had reflux score  $\geq$  16, however it could not be performed due to insufficient number of patients.

### DISCUSSION

It is envisaged that 11,500 children with CHD are born every year in our country and 3500-4000 of these children require medical, interventional or surgical treatment.<sup>7,8</sup> Although life expectancy has

<b>TABLE 3:</b> Assessment of risk factors affecting reflux score in CHD.						
			Odds ratio at 95% CI			
Risk Factors	p value	Odds Ratio	Lower	Upper		
Age (month)	0,748	0,968	0,796	1,178		
Gender	0,191	1,853	0,736	4,666		
<3p	0,854					
3-90p	0,574	1,504	0,362	6,253		
>90p	0,999	0,000	0,000			
Acyanotic Left-Right Shunt	0,185					
Acyanotic Obstructive	0,688	0,751	0,186	3,038		
CHD with decreased pulmonary blood flow	0,393	2,378	0,326	17,324		
CHD with increased pulmonary blood flow	0,035	3,727	1,016	19,169		
Constant	1,298	0,273				

<3p: Under 3 percentileges; 3-90p: Beetwen 3-90 percentileges; >90p: Upper 90 percentileges; Legends. CHD: Congenital hearth disease; CI: Confidence interval.

increased over time as a result of prenatal diagnosis and treatment, and surgical advances; these children are still at risk of infection, malnutrition, anemia, growth and developmental retardation.<sup>9,10</sup> In theoretical base, presence of hepatomegaly or ascites in CHD might cause delayed gastric emptying which subsequently results in GERD.

Gastroesophageal reflux is not rare in infants and the diagnosis is often based on symptoms though it is not always easy due to age-related nonspecific symptoms and findings.<sup>11</sup> Questionnaires for symptoms are based on the parents' perception and have been developed to increase the reliability of story rather than to diagnose.<sup>12</sup> It is widely recommended that I-GERQ-R developed by Orenstein et al. and GSQ-I and GSQ-YC by Deal et al. could be used in follow-up of infants with GERD.<sup>5,6,13</sup>

Despite their noninvasive and easy to perform characteristics, no questionnaire-based study has been performed in CHD infants so far. In this study, we aimed to investigate GERD in CHD infants using this method. We found that GERD prevalence according to I-GERQ-R in healthy and CHD infants was 7.40% and 6.42%, respectively (p=0.79). Mean reflux score was not different in CHD and healthy infants (4.81±5.06 vs.  $5.1\pm5.71$ ; p=0.62), either. Van Howe and Storms reported mean I-GERQ-R score gradually decreasing from 11.7 to 6.97 in 1-6 months old healthy infants.<sup>14</sup> This rates are compatible with our mean score of 0-1 year old infants with a median age of 4 months.

Tanrıverdi et al. found the rate of GERD as 14% among 0-2 year-old infants in the Aegean region of our country in a survey-based study.<sup>15</sup> In our study, we found the prevalence of GERD in healthy infants as 7.4%; it was lower than that of Tanrıverdi probably due to narrow age distribution and regional differences.<sup>15</sup>

It is widely accepted that there is a strong relationship between age and GER and that reflux symptoms appear in the first months of life, peaking at about 4<sup>th</sup> month.<sup>16</sup> The age at which reflux made a peak was 4th month in both groups in our study and it was also observed that GERD rate decreased towards to 1 year old.

The study performed by Deal et al. in 2005 revealed that the most frequent symptom was regurgitation/vomiting (90%) and the least frequent was feeding refusal (42%) among 0-11 month old infants with GERD.<sup>6</sup> In our study we found feeding refusal rate as 18.3% (n=20) in the CHD group and 17.3% (n=14) in the healthy group. There are a number of studies trying to figure out whether crying episodes and restlessness are meaningful findings for GERD in infants. Vandenplas et al. found that crying attacks and fussiness showed a poor correlation with GERD in their study.<sup>17</sup> One of the rare studies that supports discomfort is related to reflux episodes is the Feranchack's.<sup>18</sup> Orenstein et al. reported crying and restlessness as 66% in their study in 1996. In our study, crying and restlessness rates at any time was 43.5% in CHD group and was 38.3% in the control group (p=0.36).<sup>19</sup>

Animasahun et al reported in their study that cyanosis was the most common presentation of CHD. As symptoms of cyanosis and apnea are seen at high rates in CHD, we evaluated the data of acyanotic and cyanotic groups separately with the concern that cyanosis due to CHD might have decreased the reliability of the scoring system.<sup>20</sup> In our study, 1.2% (n=1), 6.3% (n=4), and 28.6% (n=6) of infants from control, acyanotic, and cyanotic CHD groups had apnea or turning blue/purple (p<0.0001). Thus it was concluded that apnea and cyanosis in favor of cyanotic CHD could be attributed to CHD itself, not to GERD. Crying time was shorter in cyanotic CHD infants compared to healthy group probably due fatigue and weakness. It is surprising that the total score and the frequency of GERD is lower (not statistically) in CHD infants. This can partially be attributed to over reporting of mothers of healthy infants compared to others who have more serious health problem experiences so far.

The mean GERD score and GERD frequency at baseline and follow-up of our study were not statistically different between CHD and healthy infant groups. The only difference in terms of individual symptoms between CHD and control group was found in apnea and cyanosis rates. The higher score that was found in cyanotic CHD patients seems to be due to cyanosis, which is the essential symptom of the heart disease. The fact that we have fewer patients compared to the studies in the literature is one of our most important shortcomings of our study. In addition, answers to some questions in the surveys we used that may include symptoms is also seen in the congenital heart disease, was another inhibiting factor in our study.

# CONCLUSION

The mean GERD score and GERD frequency at baseline and follow-up of our study were not statistically different between CHD and healthy infant groups. For more reliable results there is a need for more objective methods such as pH-meter/impedance analysis in CHD. It seems that there is also a need for new questionnaires to be used for infants with CHD, especially for cyanotic CHD infants.

#### Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

#### Authorship Contributions

Idea/Concept: Ayşe Selimoğlu, Mehmet Semih Demirtaş, Cemşit Karakurt; Design: Ayşe Selimoğlu, Cemşit Karakurt; Control/Supervision: Ayşe Selimoğlu, Cemşit Karakurt; Data Collection and/or Processing: Mehmet Semih Demirtaş, Harika Gözde Gözükara Bağ; Analysis and/or Interpretation: Ayşe Selimoğlu, Cemşit Karakurt; Literature Review: Mehmet Semih Demirtaş, Cemşit Karakurt; Writing the Article: Mehmet Semih Demirtaş, Ayşe Selimoğlu; Critical Review: Cemşit Karakurt, Ayşe Selimoğlu; References and Fundings: Mehmet Semih Demirtaş; Materials: Mehmet Semih Demirtaş.

- Costello CL, Gellatly M, Daniel J, Justo RN, Weir K. Growth restriction in infants and young children with congenital heart disease. Congenit Heart Dis. 2015;10(5):447-56. [Crossref] [PubMed]
- Medoff-Cooper B, Ravishankar C. Nutrition and growth in congenital heart disease: a challenge in children. Curr Opin Cardiol. 2013; 28(2):122-9. [Crossref] [PubMed]
- Indramohan G, Pedigo TP, Rostoker N, Cambarec M, Grogan T, Federman MD. Identification of risk factors for poor feeding in infants with congenital heart disease and a novel approach to improve oral feeding. J Pediatr Nurs. 2017;35:149-54. [Crossref] [PubMed] [PMC]
- Weesner KM, Rosenthal A. Gastroesophageal reflux in association with congenital heart disease. Clin Pediatr (Phila). 1983;22(6):424-6. [Crossref] [PubMed]
- Orenstein SR, Cohn JF, Shalaby TM, Kartan R. Reliability and validity of an infant gastroesophageal reflux questionnaire. Clin Pediatr (Phila). 1993;32(8):472-84. [Crossref] [PubMed]
- Deal L, Gold BD, Gremse DA, Winter HS, Peters SB, Fraga PD, et al. Age-specific questionnaires distinguish GERD symptom frequency and severity in infants and young children: development and initial validation. J Pediatr Gastroenterol Nutr. 2005;41(2):178-85. [Crossref] [PubMed]
- Lightdale JR, Gremse DA; Section on Gastroenterology, Hepatology, and Nutrition. Gastroesophageal reflux: management guidance for the pediatrician. Pediatrics. 2013; 131(5):e1684-95. [Crossref] [PubMed]

### REFERENCES

- Loccoh EC, Yu S, Donohue J, Lowery R, Butcher J, Pasquali SK, et al. Prevalence and risk factors associated with non-attendance in neurodevelopmental follow-up clinic among infants with CHD. Cardiol Young. 2018;28(4): 554-60. [Crossref] [PubMed]
- Kuwata S, Iwamoto Y, Ishido H, Taketadu M, Tamura M, Senzaki H. Duodenal tube feeding: an alternative approach for effectively promoting weight gain in children with gastroesophageal reflux and congenital heart disease. Gastroenterol Res Pract. 2013;2013: 181604. [Crossref] [PubMed] [PMC]
- Naef N, Liamlahi R, Beck I, Bernet V, Dave H, Knirsch W, et al. Neurodevelopmental profiles of children with congenital heart disease at school age. J Pediatr. 2017;188:75-81. [Crossref] [PubMed]
- Kleinman L, Revicki DA, Flood E. Validation issues in questionnaires for diagnosis and monitoring of gastroesophageal reflux disease in children. Curr Gastroenterol Rep. 2006;8(3):230-6. [Crossref] [PubMed]
- Rosen R, Vandenplas Y, Singendonk M, Cabana M, DiLorenzo C, Gottrand F, et al. Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018;66(3):516-54. [Crossref] [PubMed]
- Kleinman L, Rothman M, Strauss R, Orenstein SR, Nelson S, Vandenplas Y, et al. The infant gastroesophageal reflux questionnaire re-

vised: development and validation as an evaluative instrument. Clin Gastroenterol Hepatol. 2006;4(5):588-96. [Crossref] [PubMed]

- Van Howe RS, Storms MR. Gastroesophageal reflux symptoms in infants in a rural population: longitudinal data over the first six months. BMC Pediatr. 2010;11(10):7. [Crossref] [PubMed] [PMC]
- Tanriverdi S. [Scoring of gastroesophageal reflux symptoms and the prevalence of gastroesophageal reflux among 0-6 year old children in Menderes region]. İzmir: Doctorate thesis; 2010. [Link]
- Mousa H, Hassan M. Gastroesophageal reflux disease. Pediatr Clin North Am. 2017;64(3):487-505. [Crossref] [PubMed]
- Vandenplas Y, Salvatore S, Hauser B. The diagnosis and management of gastrooesophageal reflux in infants. Early Hum Dev. 2005;81(12):1011-24. [Crossref] [PubMed]
- Feranchak AP, Orenstein SR, Cohn JF. Behaviors associated with onset of gastroesophageal reflux episodes in infants. Prospective study using split-screen video and pH probe. Clin Pediatr (Phila). 1994;33(11): 654-62. [Crossref] [PubMed]
- Orenstein SR, Shalaby TM, Cohn JF. Reflux symptoms in 100 normal infants: diagnostic validity of the infant gastroesophageal reflux questionnaire. Clin Pediatr. 1996;35(12):607-14. [Crossref] [PubMed]
- Animasahun BA, Madise-Wobo AD, Kusimo OY. Cyanotic congenital heart diseases among Nigerian children. Cardiovasc Diagn Ther. 2017;7(4):389-96. [Crossref] [PubMed] [PMC]