RESEARCH ARTICLE

Indications and Outcomes of Esophagogastroduodenoscopy in Children

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ABSTRACT

Objective: Esophagogastroduodenoscopy (EGD) has become a key element in the diagnosis and treatment of many gastrointestinal diseases affecting children. In this study, we aimed to discuss endoscopic indications, endoscopic and pathological findings of children who underwent EGD in our hospital.

Methods: A retrospective chart review of children between1-18 years old who admitted the pediatric gastroenterology department between 2017 and 2018 and who underwent EGD was performed. EGD indications, diagnoses made by endoscopy or pathological examination, and complaints were evaluated.

Results: A total of 194 children (85 male and 109 female) with a mean age of 10.63 ± 4.84 years were included in the study. Dyspepsia (66.49%), suspicion of celiac disease (19.59%), intake of material (8.25%), gastrointestinal corrosive bleeding (4.64%), and dysphagia (1.03%) were the main complaints of referral. The distribution of the diagnosis of the participants after EGD was antral gastritis (48.45%), pangastritis (21.13%), duodenitis (11.86%), celiac disease (7.73%), acute ulcer at bulbus (1.55%) and esophagitis (1.03%). Of those, 9.28% were healthy. A biopsy was obtained in 88.66% of the subjects during EGD.

Conclusion: Dyspeptic symptoms and suspicion of celiac disease are the most common EGD indication in children. Alkaline reflux, gastritis, and helicobacter pylori infection affect the degree of pathological inflammation and require appropriate treatment and follow-up.

Keywords: Endoscopy, Child, Esophagus, Stomach, Duodenum

ÖZET

Amaç: Özofagogastroduodenoskopi (EGD) çocuklarda pek çok gastrointestinal hastalığın tanı ve tedavisinde temel bir unsur haline gelmiştir. Bu çalışmada, hastanemizde EGD yapılan çocuklarda endoskopi endikasyonları ile endoskopik ve patolojik bulguların tartışılması amaçlanmıştır.

Yöntem: Bu retrospektif çalışmaya, 2017 ve 2018 yıllarında pediatrik gastroenteroloji bölümüne başvuran ve EGD yapılan 1-18 yaş arası çocuklar dahil edilmiştir. Hastaların yakınmaları, EGD endikasyonları, endoskopik ve patolojik tanılar değerlendirilmiştir.

Bulgular: Ortalama yaşı 10,63 \pm 4,84 yıl olan toplam 194 çocuk (85 erkek ve 109 kadın) çalışmaya dâhil edilmiştir. Dispepsi (%66,49), çölyak hastalığı şüphesi (%19,59), korozif madde alımı (%8,25), gastrointestinal kanama (%4,64) ve disfaji (%1,03) ana yakınmaları oluşturmaktaydı. EGD sonrası katılımcılara ait tanı dağılımı antral gastrit (%48,45), pangastrit (%21,13), duodenit (%11,86), çölyak hastalığı (%7,73), bulbusta akut ülser (%1,55) ve özofajit (%1,03) şeklinde idi. Hastaların %9.28'i ise sağlıklı idi. Hastaların %88,66'sından EGD sırasında biyopsi alındı.

Sonuç: Çocuklarda, dispeptik yakınmalar ve çölyak hastalığı şüphesi en sık EGD endikasyonunu oluşturmaktadır. Alkalen reflü, gastrit ve helikobakter pilori enfeksiyonu patolojik inflamasyon derecesini etkilemektedir ve uygun tedavi ve takibi gerekmektedir.

Anahtar kelimeler: Endoskopi, Çocuk, Özofagus, Mide, Duodenum

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INTRODUCTION

Since its establishment in the 1960s, there has been a rapid growth in the field of pediatric gastroenterology. Pediatric gastroenterology developed as a sub-specialty of pediatrics and gastroenterology and it is concerned with treating the gastrointestinal system, liver and pancreas diseases of children from infancy until the age of eighteen. In the last 30 years, the number of gastroenterologists has pediatric increased considerably. There is approximately one pediatric gastroenterologist per 100,000 children in the United States and pediatric gastroenterology is a constantly growing area of expertise(1). With the development of a subspecialty focusing on gastrointestinal disorders. pediatric new technologies have been developed to assist diagnoses in children such as pediatric esophagogastroduodenoscopy (EGD).

Pediatric EGD was first introduced in the 1970s(2). Over the past 30 years, pediatric EGD has evolved from a rare procedure performed in the operating room to a routine procedure using monocular imaging of the intestinal tract, intravenous sedation and large imaging screens. With the increase in the use of pediatric EGD procedures, the incidence of diseases requiring EGD for diagnosis in children has increased. Franciosi et al. reported that children undergoing first-time EGDs with biopsy during a 20-year interval demonstrated significant differences in subject characteristics and endoscopy practices(3).

During this time, the number of EGDs for the first time has increased by 12-fold. This may also lead to an increase in disease incidence rates. However, an increase in disease incidence may be due to an increase in disease diagnosis, rather than a real disease occurrence. Inclusion of children with less severe clinical picture and collection of more biopsies per procedure may have played a role in increasing rates of disease diagnosis. In a large, retrospective study by Sheiko et al(4).the modest diagnostic yield of EGD in children for many gastrointestinal complaints was reported. The complication rates associated with EGD procedures are less than 1.3% (5). However, these procedures require intravenous sedation or general anesthesia. Anesthetic agents may be an environmental factor in neurobehavioral disorders in early brain development. Therefore, it's worrying for parents (6). With the development of anesthesia and endoscopy techniques, these concerns have been minimized.

In the present study, we aimed to discuss endoscopy indications and endoscopy findings in children.

MATERIALS and METHODS

A total of 194 patients aged 1-18 years admitted who were to the pediatric department gastroenterology of the Gaziosmanpaşa Taksim Training and Research Hospital between 2017 and 2018 and who underwent EGD were included in the study. Age, sex, complaints, EGD indications, endoscopy, and pathology reports were obtained from the clinical database. This study was conducted in accordance with the Declaration of Helsinki. Local institutional ethics committee approved the study.

Patients were divided into groups according to application complaints including dyspepsia, intake of corrosive material, suspicion of celiac disease, upper gastrointestinal bleeding, and dysphagia. In addition; age, gender, EGD and pathology reports, helicobacter pylori positivity, alkaline reflux and the presence of histological inflammation activity were evaluated. Histologic activity score were grades as no, mild, moderate and severe.

Patients with a previous history of EGD, gastrointestinal system surgery, gastrostomy and cerebral palsy were excluded from the study. **Statistical analysis**

Descriptive statistics were presented as mean and standard deviation or median (IOR) for continuous variables and frequency with percentage for categorical variables. The normality test of the numerical variables was checked by Kolmogorov Smirnov test. The mean ages of the children included in the study were compared with Helicobacter pylori and alkaline reflux using Independent Samples t test. One-Way ANOVA test was used to compare the mean age and inflammation grade. Pearson Chi-Square test was used for the comparisons of sex, helicobacter pylori positivity, alkaline reflux, inflammation grade, endoscopic diagnosis where appropriate. The relationship between helicobacter pylori positivity with acute ulcer at bulbus and esophagitis was evaluated by Fisher's Exact Test. In addition, Fisher's Exact Test was also used to determine the relationship between pathological diagnoses according to helicobacter pylori positivity. In the comparisons where the parametric tests were applied, the differences between the groups were evaluated by the Tukey test in the case of homogenous distribution of the data, and in the case of non-homogeneity by the Games-Howell test. Statistical analyses were performed by Jamovi Computer Software (Version 0.9, retrieved from https://www.jamovi.org). In statistical analyzes, the significance level was considered as 0.05.

RESULTS

Of the 194 individuals included in the study, 43.81% were males and 56.19% were females and the mean age was 10.63 ± 4.84 years. Main complaints that ledchildren to apply to hospital were dyspepsia (66.49%), suspicion of celiac disease (19.59%), corrosive material intake (8.25%), gastrointestinal tract bleeding (4.64), and dysphagia (1.03%). A biopsy was performed in %88.66 of the children during EGD. The distributions of endoscopic diagnoses were antral (48.45%), pangastritis gastritis (21.13%). duodenitis (11.86%), celiac disease (7.73%), acute ulcer at bulbus (1.55%), and esophagitis (1.03%). The diagnoses of the 9.28% children were normal. Helicobacter pylori bacteria were found in 40.21% and alkaline reflux in 16.49% of the children included in the study. Pathological examination revealed antral gastritis (31.96%), pangastritis (25.35%), celiac disease (17.53%), duodenitis (4.64%), and esophagitis (2.06%). 15.46% of the cases were in normal limits pathologically. When evaluated for histological inflammation activity scores, no inflammation was observed in %39.58 of the cases. Mild and moderate activity was found in 25% and 26.56% of the children, respectively. Severe inflammatory activity was observed in 8.85% of the cases. Table 1 summarizes the demographics and findings of the children in detail.

In terms of mean age of children included in the study, there was a statistically significant difference between helicobacter pylori, alkaline reflux and histologic inflammation activity (p<0.001 for all). Helicobacter pylori positivity and alkaline reflux were more prominent in older children. Similarly, severe histologic inflammation activity was found more frequent in older children than mild or moderate histologic inflammation. Helicobacter pylori positivity was significantly higher in girls than in boys (p = 0.034). However, alkaline reflux and histologic inflammation activity were not significantly different between girls and boys (p=0.117 and p=0.180, respectively) (Table 2).

The presence of helicobacter pylori positivity was significantly higher in children with alkaline reflux (p=0.043). There was a statistically significant difference between histologic inflammation activity, and helicobacter pylori positivity and alkaline reflux (p < 0.001 for all). The presence of helicobacter pylori and alkaline reflux was associated with higher histologic inflammation activity (Table 3).

Age (years)		10.63 ±		
		4.84		
Sex	Male	85 (43.81)		
	Fomalo	109		
	Temute	(56.19)		
Complaint	Suspicion of Celiac	38 (19 59)		
	disease	50 (17,57)		
	Dysphagia	2 (1,03)		
	Dyspepsia	129		
		(66,49)		
	Gastrointestinal	9 (4,64)		
	bleeding			
	Corrosive material	16 (8,25)		
D!	iniake	172		
вюряу	Yes	1/2		
	No	(00.00)		
Endosconio diagnos	NO	22 (11.34)		
Antral gastui	SIS tia	04 (48 45)		
Antrai gastri Acute ulcer e	us ut hulbus	94 (48.45)		
Coligo digog	15(7.73)			
Duodonitis	13(7.73) 23(11.86)			
Normal		18(928)		
Feonhagitie		2(1.03)		
Pangastritis		41(2113)		
Helicobacter	Ves	78 (40 21)		
nylori	105	116		
P)	No	(59 79)		
Alkaline reflux	Yes	32 (16 49)		
		162		
	No	(83.51)		
Pathological	Antral gastritis	62 (31.96)		
diagnosis	Celiac diseae	34 (17.53)		
-	Duodenitis	9 (4.64)		
	Normal	30 (15.46)		
	Esophagitis	4 (2.06)		
	Pangastritis	55 (25.35)		
Activity	No	76 (39.58)		
·	Mild	48 (25)		
	Moderate	51 (26.56)		
	Severe	17 (8.85)		

Descriptive statistics are given as frequency with percentage. Endoscopic diagnoses of antral gastritis, pangastritis, and duodenitis are significantly higher in patients with Helicobacter pylori positivity (p < p0.05 for all). In addition to this, duodenitis and normal diagnoses made by EGD were significantly higher in children with helicobacter pylori negativity (p = 0.001 and p < 0.001, respectively). There was no statistically significant difference between acute ulcer at bulbus, celiac disease and esophagitis diagnoses and helicobacter pylori positivity (p > 0.05 for all). Table 4 summarizes the associations between helicobacter pylori and endoscopic diagnoses in detail. There was a statistically significant difference between pathological diagnoses with regard to helicobacter pylori positivity (p < 0.001). The presence of helicobacter pylori positivity increased the rate of antral gastritis and pangastritis diagnosis whereas it reduces the rate of celiac disease, duodenitis and normal diagnosis (Table 5).

Table 1. The demographics and findings of the children

Table 2. The association between patient demographics and helicobacter pylori, alkaline reflux and histologic inflammation activity

				Sex		
		Age	Р	Male	Fem ale	P
				(n=8 5)	(n=1 09)	
Helicoba cter pylori	Yes	12.76 ± 3.39	<0.0	27 (31.7 6)	51 (46.7 9)	0.0
	No	9.20 ± 5.14	01**	58 (68.2 4)	58 (53.2 1)	34 *
Alkaline reflux	Yes	$\begin{array}{c} 14.00 \ \pm \\ 2.00 \end{array}$	<0.0	10 (11,7 6)	22 (20.1 8)	0.1
	No	9.96 ± 4.96	01**	75 (88,2 4)	87 (79.8 2)	*
Activity	No	7.36 ± 4.97		41 (48.2 4)	35 (32.7 1)	
	Mild	11.48 ± 3.80	<0.0	19 (22.3 5)	29 (27.1)	0.1
	Mod erat e	13.24 ± 2.96	*	19 (22.3 5)	32 (29.9 1)	8U *
	Seve re	14.53 ± 1.81		6 (7.06)	11 (10.2 8)	

* Pearson Chi-Square test. Descriptive statistics are given as frequency with percentage.

** Independent Samples t test. Descriptive statistics are given as mean \pm standard deviation.

*** One-Way ANOVA test. Descriptive statistics are given as mean \pm standard deviation.

Table 3. The association between inflammation grade and helicobacter pylori and alkaline reflux

		Inflammation grade				_
		No	Mild	Mode rate	Sever e	р
Helicobact er pylori	Ye s N o To tal	9 (11.8 4) 67 (88.1 6) 76 (100)	27 (56.2 5) 21 (43.7 5) 48 (100)	29 (56.8 6) 22 (43.1 4) 51 (100)	12 (70.5 9) 5 (29.4 1) 17 (100)	<0.0 01*
Alkaline reflux	Ye s N o To tal	0 (0) 76 (100) 76 (100)	9 (18.7 5) 39 (81.2 5) 48 (100)	$ \begin{array}{c} 16\\(31.3\\7)\\35\\(68.6\\3)\\51\\(100)\end{array} $	7 (41.1 8) 10 (58.8 2) 17 (100)	<0.0 01*

* Pearson Chi-Square test. Descriptive statistics are given as frequency with percentage.

Table	4.	The	association	between	helicobacter
pylori	pos	itivity	y and endosc	opic diagi	nosis

	Helicoba pylori	р	
	Yes	No	
Endoscopic diagnosis			
Antral gastritis	49 (62 82)	45 (38 79)	0.001*
Pangastritis	26 (33.33)	(58.77) 15 (12.93)	0.001*
Duodenitis	2 (2.56)	21 (18.1)	0.001*
Normal	0 (0)	18 (15.52)	<0.00 1*
Acute ulcer in the bulbus	0 (0)	3 (2.59)	0.275* *
Celiac disease	3 (3.85)	12 (10.34)	0.097*
Esophagitis	0 (0)	2 (1.72)	0.517* *

* Pearson Chi-Square test. Descriptive statistics are given as frequency with percentage.

** Fisher's Exact Test. Descriptive statistics are given as frequency with percentage.

 Table 5. The association between helicobacter

 pylori positivity and pathological diagnosis

		Helicob: pylori	p	
		Yes	No	
Pathological	Antral	38	24	
diagnosis	gastritis	(48.72)	(20.69)	
	Celiac disease	5 (6.41)	29 (25)	
	Duodeniti s	0 (0)	9 (7,76)	<0.00
	Normal	1 (1.28)	29 (25)	1**
	Esophagit	1	3	
	is	(1.28)	(2.59)	
	Pangastrit	33	22	
	is	(42.31)	(18.97)	

** Fisher's Exact Test. Descriptive statistics are given as frequency with percentage.

DISCUSSION

Gastrointestinal system endoscopy is being used with increasing frequency due to the development of technology and endoscopic techniques in the diagnosis and treatment of childhood digestive diseases. Endoscopy in children has been started to be used in the late 1980s in Turkey(7). Previously, it was a procedure to understand the location and cause of gastrointestinal bleeding for diagnostic purposes. Today, endoscopic interventions are used for the diagnosis treatment and of childhood gastrointestinal tract disorders routinely. Upper gastrointestinal endoscopy (EGD) allows the visualization of esophagus, stomach, and proximal duodenum(8). In this study, the indications and results of 194 children who underwent EGD between 2017 and 2018 were evaluated.

The indications for upper gastrointestinal endoscopy vary over the years. Franciosi et al. (3) investigated the changes in upper gastrointestinal endoscopy indications from 1985 to 2005. In 1985, only 107 patients underwent upper gastrointestinal endoscopy and in 2005 this number increased to 1294. The rate of endoscopy for gastrointestinal bleeding decreased from 34% to 5% during this time.

The authors also reported that the rate of upper gastrointestinal endoscopy for abdominal pain increased from 23% in 1985 to 43% in 2005(3). Işık et al(9,10) reported the indications of EGD in their series of 703 children who underwent EGD as suspected of celiac disease (n = 111, n)15.8%), abdominal pain (n = 325, 46.2%), chronic and / or bloody diarrhea (n = 39, 5.5%), esophageal varice control (n = 50, 7.1%), gastrointestinal bleeding (n = 116, 16.5%), suspicion of irritable bowel disease (n = 23, 3.3%), percutaneous endoscopic gastrostomy (PEG) opening or replacement (n = 17, 2.4%), and other (n = 22, 3.1%). In the present study, main indications of EGD were dyspepsia (66.49%), suspicion of celiac disease (19.59%), corrosive material intake (8.25%), gastrointestinal tract bleeding (4.64), and dysphagia (1.03%). These results were consistent with the literature.

Işık et al.(9,10) reported the results of EGD in 588 children. Of these, 228 (38.8%) were normal, 236 (40.1%)were gastritis/duodenitis/esophagitis, 35 (6.0%) were gastric and/or duodenal ulcer, 46 (7.8) were esophageal and/or gastric varices, 19 (3.2%) were ectopic pancreas, hiatal hernia, esophageal stricture, malignant mass in the stomach, portal hypertensive gastropathy, cardio-esophageal sphincter deficiency, polyp in the stomach. Uğraş et al. (11) reported the EGD results as follows: ulcer (n = 47), esophagitis (n = 5), antral nodularity (n = 28), pangastritis (n = 5), and lax lower esophageal sphincter (n = 3). In our study, we found antral gastritis (48.45%), pangastritis (21.13%), duodenitis (11.86%), celiac disease (7.73%), acute ulcer at bulbus (1.55%), and esophagitis (1.03%). The diagnoses of the 9.28% children were "normal" in our study. The differences of the EGD diagnosis among studies may be related with characteristics of patient population, genetic properties, nutrition habits, and experience of the physician.

Biopsy has become an integral part of upper gastrointestinal system endoscopy. Franciosi et al.(3) reported that the biopsy rate during EGD in children was 18% in 1985. The authors also reported that this ratio increased to 95% in 2005. The biopsy rate of Işık et al.(10) during EGD was 92.3%. In the present study, we performed a biopsy in 88.86% of the children who underwent EGD.

Işık et al.(9,10) reported that while no pathological findings were found in 105 (17.9%) of the children who underwent EGD, 225 (38.3%) had duodenitis/esophagitis/helicobacter pylori with gastritis, 95 (16.2%) had esophagitis and/or duodenitis, 54 (9.2%) had only gastritis, 47 (8%) had celiac disease, 9 (1.5%) had eosinophilic gastritis and/or enteritis and 1 (0.2%) had gastric metaplasia. In our study, pathological examination revealed antral gastritis (31.96%), pangastritis (25.35%), celiac disease (17.53%), duodenitis (4.64%), and esophagitis (2.06%). Pathologically, 15.46% of our cases were found healthy. Celiac disease is an important gastrointestinal tract disorder of the children in which endoscopy is the gold standard for diagnosis. Between 1996 and 2001, serologic tests in a random sample of 4,126 people from the United States population estimated a high prevalence of 1:133 (0.8%) celiac disease in subjects without risk factors(11,12). Fasano and colleagues described this as the visible part of the iceberg(13). The patient diagnosed with celiac disease by EGD represents only a small portion of the real population. In the present study, EGD revealed celiac disease in 15 children (7.73%). However, pathologic examination showed that this ratio increased to 34 patients (17.53%).

Helicobacter pylori is one of the most common infections worldwide and about half of population the world's carries this microorganism(14). The incidence varies in different regions of the world. The prevalence in Japan and South America is over 80% while it is 40% in England and 20% in Scandinavia(15). The prevalence of helicobacter pylori among asymptomatic individuals between the ages of 18-24 in a study conducted in Turkey in 1992 was found as 76.8%(16). We found helicobacter pylori positivity in 78 of 194 children (40.21%). Uğraş et al.(11) reported that 82.8% of children with ulcers had helicobacter pylori positivity. In our study, helicobacter pylori positivity was detected in 48.72% of patients with antral gastritis and 42.31% of patients with pangastritis. According to the results of our study, helicobacter pylori positivity increases the rate of antral gastritis and pangastritis in children. Helicobacter pylori were found in 40.21% and alkaline reflux in 16.49% of children included in our study. There was no difference between helicobacter pylori and alkaline reflux between boys and girls. In adults, alkaline reflux is more common in males. This is due to the fact that cholecystectomy and gastric operations are performed more frequently in men(17).

Although the cause of primary biliary reflux in children is not known precisely, the inadequacy of duodenogastric antireflux mechanisms is considered to be responsible for the etiology. In children, alkaline reflux is common in patients with pyloric dysfunction and in patients with cholecystectomy (18).

There are several limitations of the present study. The retrospective nature of the study is the main limitation. In addition to this, complications related with EGD in children werenot evaluated in the study. Further prospective studies with a larger sample are necessary to confirm our results.

In conclusion, EGD along with the pathologic investigation of biopsy material provides very useful information in diagnosis, treatment and follow-up of childhood gastrointestinal diseases.

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REFERENCES

1. North American Society for Pediatric Gastroenterology, Hepatology and Nutrition: pediatric gastroenterology workforce survey, 2003–2004. J Pediatr Gastroenterol Nutr. 2005;40:397–405.

2. Gilger MA. Gastroenterologic endoscopy in children: past, present, and future. Curr Opin Pediatr. 2001;13:429–34.

3. Franciosi JP, Fiorino K, Ruchelli E, Shults J, Spergel J, Liacouras CA et al. Changing indications for esophagogastroduodenoscopy in children during a 20-year period. J Pediatr Gastroenterol Nutr. 2010;51:443–7.

4. Sheiko MA, Feinstein JA, Capocelli KE, Kramer RE. Diagnostic yield of EGD in children: a retrospective single-center study of 1000 cases. Gastrointest Endosc. 2013;78:47–54.

5. Fox VL. Pediatric endoscopy. Gastrointest Endosc Clin N Am. 2000;10:175–94.

6. Backeljauw B, Holland SK, Altaye M, Loepke AW. Cognition and brain structure following early childhood surgery with anesthesia. Pediatrics. 2015;136:e1–12.

7. Durakbaşa ÇU. Interventional esophagogastroduodenoscopy procedures performed in the upper digestive system in children. Çocuk Cerrahisi Dergisi 2016;30:170-180.

8. Nguyen VX, Nguyen VT, Nguyen CC. Appropriate use of endoscopy in the diagnosis and treatment of gastrointestinal diseases: up-to-date indications for primary care providers. Int J Gen Med 2010;1:345-357.

9. Işık, İshak A. Sedation practices in pediatric gastrointestinal endoscopy and related consequences (Yandal uzmanlık tezi). İzmir, Dokuz Eylül Üniversitesi, 2012.

10. Isik IA, Iyilikçi L, Ozturk Y, Adiyaman E. Sedation Practice Outside the Operating Room for Pediatric Gastrointestinal Endoscopy. Indian Pediatr. 2015;52:989-90.

11. Uğraş M, Alan S. Evaluation of The Results of Pediatric Upper Gastrointestinal Endoscopies. F.Ü.Sağ.Bil.Tıp Derg. 2012;26:31-34.

12. Fasano A. Where have all the American celiacs gone? Acta Paediatr Suppl 1996;412:20–4.

13. Fasano A, Berti I, Gerarduzzi T, Not T, Colletti RB, Drago S et al. Prevalence of celiac disease in at-risk and not-at-risk groups in the United States: a large multicenter study. Arch Intern Med 2003;163:286-92.

14. Suerbaum S, Michetti P. Helicobacter pylori infection. N Engl JMed 2002;347:1175-86.

15. Malaty HM. Epidemiology of Helicobacter pylori infection. Best Pract Res Clin Gastroenterol 2007;21:205-14.

16. Özden A, Dumlu Ş, Dönderici Ö, Çetinkaya H, Soylu K, Özkan H et al. Helicobacter pylori infeksiyonunun ülkemizde seroepidemiyolojisi. Gastroen teroloji 1992;4:665-8.

17. Fukuhara K, Osugi H, Takada N, Takemura M, Lee S, Taguchi S et al. Correlation between duodenogastric reflux and remnant gastritis after distal gastrectomy. Hepatogastroenterology. 2004,51:1241-1244.

18. Feldman M, Edward LL. "Gastritis" in Sleisenger and Fordtran's Gastrointestinal and Liver Disease.

Pathophysiology/Diagnosis/Management, M. Feldman, S. F. Lawrence, and J. B. Lawrence, Eds., pp.880-881, Saunders, Philadelphia, Pa, USA, 10th edition, 2015.