

Prevalence and Epidemiological Characteristics of Endoscopically Proven Reflux Esophagitis in Children in Korea

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Purpose: The prevalence of reflux esophagitis (RE) has increased recently in Korea. Little is known concerning the prevalence and characteristics of RE in pediatric patients. This study investigated the prevalence and influence of risk factors in endoscopically proven RE in Korea in pediatric patients over a period of 14 years.

Methods: A retrospective chart review of all patients between the ages of 1 month and 20 years who underwent esophagogastroduodenoscopy at Samsung Medical Center between 2001 and 2014 was carried out. Univariate and multivariate analyses were conducted to identify independent risk factors for RE.

Results: The prevalence rate of endoscopically proven RE in this study was 28.7% (978/3,413). The prevalence of RE increased from 11.8% from 2001 to 2007 to 37.7% from 2008 to 2014. Multivariate logistic regression analysis revealed that residency in the Greater Gangnam area (odds ratio [OR], 1.21; 95% confidence interval [CI], 1.02-1.44) and age (OR, 1.13; 95% CI, 1.11-1.15) were significant predictive factors for the presence of RE.

Conclusion: The prevalence rate of endoscopically proven pediatric RE has increased over the past 14 years. Residency and older age are more important independent risk factors for pediatric RE in Korea.

Key Words: Gastroesophageal reflux, Prevalence, Risk factors, Endoscopy, gastrointestinal, Pediatrics

INTRODUCTION

Gastro-oesophageal reflux disease (GERD) is an esophageal mucosal injury or regurgitation that occurs secondary to abnormal reflux of gastric contents into the esophagus. GERD is common in infants, children, and adolescents [1]. Characteristic specific

symptoms include heartburn and acid regurgitation [2], but symptoms in pediatric patients vary with age [3,4]. Although GERD can be diagnosed by typical history and physical examination findings [5], it is difficult to define due to its extensive heterogeneity.

Pediatric patients with pathologic reflux may be more prone to complications of GERD than those

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with physiologic GER [3]. Esophagogastroduodenoscopy (EGD) with biopsy is recommended to confirm the diagnosis of reflux esophagitis (RE) and to screen for other upper gastrointestinal (GI) disorders whose symptoms may mimic those of GERD in children [3].

Epidemiologic data has indicated an increased prevalence of RE in recent decades in Asia [6]. Time trend studies in adults have also indicated an increased prevalence in symptom based-GERD and endoscopic RE [7]. These increases may be due to multiple factors, such as Westernized diet and lifestyle [8]. In addition, risk factors include older age, male sex, race, family history, higher socioeconomic status (SES), increased body mass index (BMI), and smoking [9]. While GERD has been amply studied in adults, there is very limited literature on the characteristics and incidence of RE in children. Time trends of endoscopically proven RE in pediatric patients are unclear.

The objective of this study was to identify time trends in the incidence and the influence of risk factors on the prevalence of endoscopically proven RE in children in Korea.

MATERIALS AND METHODS

Patients and study design

This retrospective study was conducted in patients between 1 month and 20 years of age who had undergone EGD at the Department of Pediatrics, Samsung Medical Center between January 2001 and December 2014. Patients with a history of foreign body ingestion or GI surgery or repeated upper endoscopies on already-included subjects were excluded. Patients with confounding factors known to increase the risk of developing GERD, such as neuromuscular disorders, hemato-oncological diseases, Down syndrome, and chronic pulmonary conditions were also excluded. Data regarding age, gender, weight, height, indication for EGD, presence of RE, and the location of residency were obtained from electronic charts. Endoscopic diagnosis and grading of RE was based on the Los Angeles (LA) classification [10]. Weight

and height were used to calculate BMI percentiles. Age- and gender-specific scores for weight and BMI were calculated. Location of residency was divided into two regions: Greater Gangnam area (Gangnam, Seocho, Songpa district) and other regions (rural and Capital except Greater Gangnam area). Comparison of characteristics was performed between groups divided according to the presence and absence of RE and possible risk factors associated with the occurrence of RE were investigated.

Statistical analyses

Wilcoxon signed rank sum test was used for the comparison of continuous variables, and chi-square (χ^2) test for the comparison of categorical variables between groups. Univariate analysis was performed to assess the effect of each variable. Multivariate logistic regression analysis was used to identify each correlations related with RE risk, which were expressed as the odds ratio (OR) and 95% confidence interval (CI). Using the backward stepwise selection procedure, variables with a p -value < 0.05 were included in the multivariate logistic regression models. p -values < 0.05 were considered statistically significant. Statistical analyses were performed using SAS ver. 9.4 (SAS Institute, Cary, NC, USA).

Ethics statement

This retrospective study was undertaken after approval by the institutional review board of the Samsung Medical Center (IRB no. 04-159) and the requirement for informed consent from individual patients was waived.

RESULTS

Baseline characteristics of patients

A total of 3,413 patients were included in this study, of whom, 978 (28.7%) had been diagnosed with RE by EGD. The age of the subjects was 10.5 ± 5.1 years, and 51.8% (1,768/3,413) were male. Comparison of baseline characteristics between the two groups revealed significant differences in age, BMI, and residency (Table 1; all $p < 0.0001$).

Table 1. Baseline Characteristics between Subjects with and without Endoscopically Proven Reflux Esophagitis

Variable	Reflux esophagitis		Total (n=3,413)	p-value
	Present (n=978)	Absent (n=2,435)		
Gender				0.3887
Male	518 (53.0)	1,250 (51.3)	1,768 (51.8)	
Female	460 (47.0)	1,185 (48.7)	1,645 (48.2)	
Age (y)	12.5±4.4	9.7±5.2	10.5±5.1	<0.0001*
Body mass index (kg/m ²)	19.0±3.8	18.3±3.8	18.5±3.8	<0.0001*
Residency				<0.0001*
Rural and capital (without Greater Gangnam area)	660 (67.5)	1,807 (74.2)	2,467 (72.3)	
Greater Gangnam area (Gangnam, Seocho, Songpa district)	318 (32.5)	628 (25.8)	946 (27.7)	

Values are presented as number (%) or mean±standard deviation.

**p*<0.05.

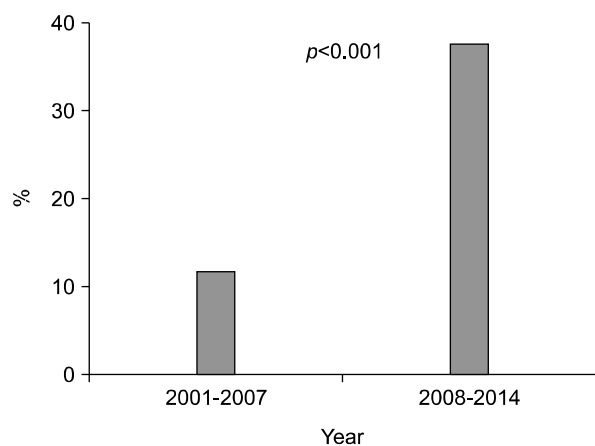


Fig. 1. Percentage of reflux esophagitis (RE) in two 7-year periods. It shows a significant increase in patients with RE from 11.8% in 2001-2007 to 37.7% in 2008-2014 (*p*<0.001).

Prevalence and grade of reflux esophagitis

The percentage of patients with RE was significantly higher during 2008-2014 (37.7%) compared to the period of 2001-2007 (11.8%, *p*<0.001; Fig. 1). The composition of RE according to LA classification was 83%, 12%, 5%, and 0.1% for LA-A, B, C, and D, respectively.

Indications for upper gastrointestinal endoscopy

The indications for EGD in patients are listed in Table 2. The most common indication for upper GI endoscopy was recurrent abdominal pain (RAP) reported in 1,008 (29.5%) patients, followed by epi-

gastric pain in 980 (28.7%) and GI symptoms including recurrent vomiting, nausea, regurgitation, and dyspepsia in 482 (14.1%). Except for GI bleeding (*p*=0.102), other indications for EGD such as RAP, epigastric pain, heartburn, and vomiting (all *p*<0.0001) were significantly associated with endoscopically proven RE.

Risk factors of reflux esophagitis

Univariate analysis revealed that age, location of residency, and BMI were significantly associated with the occurrence of RE (Table 3). According to multivariate analysis with stepwise selection, age (OR, 1.13; 95% CI, 1.11-1.15; *p*<0.0001) and residency in the Greater Gangnam area (OR, 1.21; 95% CI, 1.02-1.44; *p*=0.0266) were significantly associated with RE. Receiver operating characteristic curve of age for predicting reflux esophagitis is displayed in Supplementary Fig. 1.

DISCUSSION

The results of our study demonstrate that the prevalence of endoscopically proven RE in children during a recent 14-year period has significantly increased when divided into two time periods. Our findings correspond with previous data from Korea which show an increase in the prevalence of erosive esophagitis from 5.7% in 1992 to 19.9% in 2008 among children with upper abdominal pain [11-13].

Table 2. Association between Indications for Esophagogastroduodenoscopy and Reflux Esophagitis

Variable	Reflux esophagitis		Total (n=3,413)	OR	95% CI	p-value
	Present (n=978)	Absent (n=2,435)				
Indications						
Recurrent abdominal pain	233 (6.8)	775 (22.7)	1,008 (29.5)	1.00		<0.0001
Epigastric pain	425 (12.5)	555 (16.3)	980 (28.7)	2.54	2.09-3.08	<0.0001
Heartburn (chest pain, discomfort)	33 (1.0)	34 (1.0)	67 (2.0)	3.22	1.95-5.31	<0.0001
Vomiting, nausea regurgitation, dyspepsia	192 (5.6)	290 (8.5)	482 (14.1)	2.20	1.74-2.77	<0.0001
Anemia, iron deficiency anemia	13 (0.4)	91 (2.7)	104 (3.0)	0.49	0.27-0.89	0.0198
Gastrointestinal bleeding	55 (1.6)	241 (7.1)	296 (8.7)	0.76	0.55-1.06	0.102
Dysphagia	10 (0.3)	7 (0.2)	17 (0.5)	5.12	1.67-15.73	0.0044
Work up for other disease*	17 (0.5)	442 (13.0)	459 (13.4)	0.50	0.17-1.71	0.065

Values are presented as number (%).

OR: odds ratio, CI: confidence interval.

*These include Behcet's disease, protein losing enteropathy, Peutz-Jeghers syndrome, familial adenomatous polyposis, trichobezoar, esophageal varix, liver cirrhosis.

Table 3. Univariate and Multivariate Analyses of Risk Factors for Patients with Endoscopically Proven Reflux Esophagitis

Variable	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender (male)	1.07	0.92-1.24	0.3887			
Age	1.13	1.11-1.15	<0.0001	1.13	1.11-1.15	<0.0001
Residency			<0.0001			0.0266
Rural and capital (without Greater Gangnam area)	1.00			1.00		
Greater Gangnam area (Gangnam, Seocho, Songpa district)	1.39	1.18-1.63		1.21	1.02-1.44	
BMI	1.05	1.03-1.07	<0.0001	0.99	0.96-1.01	0.1156

OR: odds ratio, CI: confidence interval, BMI: body mass index.

The calculation of multiple logistic regression analysis with stepwise selection was performed by using the factors of age, residency, and BMI. OR calculated in comparison to patients in a rural area.

Our study also reveals significant associations of age and residency with RE.

The prevalence of RE in adults reportedly varies from 14% to 31% [12-15]. However, the prevalence of pediatric esophagitis is still unclear and there are few data on the prevalence of RE in children. The prevalence rate of endoscopically proven RE in our study throughout the study period was 28.7%, which was higher than previous studies. Gilger et al. [16] reported a 12.4% prevalence of erosive esophagitis in a population of 888 pediatric patients referred to one institution. This difference might be due to several reasons. First, the time period of investigation in the study of Gilger et al. [16] was 1999 to 2002, which was shorter compared to our study.

However, our results showed a similar prevalence of 11.8% in the earlier group of patients from 2001 to 2007. Second, Gilger et al. [16] involved a more randomized population based subjects, which produced a lower prevalence rate than the present result.

GERD is a multifactorial disease that is affected by age, BMI, hiatal hernia, lifestyle, and gender [17-19]. In recent decades, GERD in adults is prevalent and increasing in Western countries and in Asia, which is thought to be caused by multiple factors that include increased gastric acid secretion due to the westernization of dietary habits, decreased *Helicobacter pylori* infection rate, and increased obesity rate [20,21]. Unlike adults, risk factors of RE in children are

unclear. Of those that are known, risk factors in severe GERD during childhood include neurological disorders, such as spastic quadriplegia and cerebral palsy [22], congenital malformations including esophageal atresia and tracheoesophageal fistula [23], chronic lung disease [24], and extraesophageal disease [25]. Although obesity and overweight have been reported as independent risk factors for GERD and endoscopy-proven esophageal erosions in adult studies [26-28], it is controversial in the pediatric population. In addition, the previous reported pediatric study showing no significant association between BMI and RE supports the results of our study [29]. The reason behind BMI losing its significance in multivariate analysis while showing a certain degree of significance in univariate analysis could be due to age acting as a confounding variable, considering that a large proportion of adolescents were included in our study. Thus, as we were not able to control and exclude these confounding variables described above, it would be hard to conclude that BMI is not a risk factor.

Our study reported that the risk ratio for RE was found to increase with age, and several studies of adults also showed a stronger association to RE with aging [17,18,30]. These results of adults are thought to be related to decreases in esophageal defense mechanisms with aging [31,32]. However, the linear relationship between aging and RE in children has not yet been investigated. Thus, further detailed research on risk factors of RE including aging is needed in children.

Meanwhile the association between RE and residence location is not well known in pediatrics, while few studies in adults have reported a positive correlation between high SES and urban residency with RE [33,34]. We were unable to evaluate the SES of subjects according to well-known indices including the Hollingshead index [35]. Thus, we sought to indirectly investigate the SES of subjects by investigation the location of residency, which was divided into two regions; Greater Gangnam area and other regions. The Greater Gangnam area, which is regarded as the most segregated region in Korea for

high income and education, consists of three districts (Gangnam-gu, Songpa-gu, and Seocho-gu) [36,37]. Therefore, we assumed that the Greater Gangnam area may represent high SES in Korea. With the view of RE as a part of psychosomatic disorder, it is conceivable that children living in the Greater Gangnam area can be more exposed to many stressful educational environments than children living in other areas. Accordingly, higher prevalence of RE in Greater Gangnam area may reflect indirect effects of emotional stress on RE as reported in previous studies [38,39].

The most common indication for endoscopy and symptom of RE was RAP throughout the study period. In previous studies, up to 25% of children and adolescents are reported to have RAP, whereas the most common symptoms of RE in adults are heartburn and regurgitation [1,40]. In addition, it should be noted that symptoms of RE in children can be various including RAP, unlike adults, which manifests mainly as heartburn.

This retrospective study has several limitations. The study lacked information regarding the use of medications including proton pump inhibitors and antibiotics prior to EGD. As this study investigated children who underwent EGD for indication only, there was a possibility of selection bias towards those with more severe GI symptoms. Therefore there is a chance that those children examined were actually more likely to have endoscopic pathology than children with abdominal pain in whom physicians choose not to perform invasive testing. Moreover, the increased prevalence rate of endoscopically proven RE may be related to overall increases in EGD rates. As previously stated, the inability to evaluate the SES of subjects according to quantitative indices is another limitation.

Despite these limitations, our study included a large population of 3,413 subjects, the largest number of subjects in the pediatric studies to date. It is also notable that this new result of children living in higher socioeconomic areas showing a higher prevalence of RE. In addition, these findings are meaningful as they provide clues regarding the prevalence

of RE and risk factors in Korean pediatric patients.

Given the recent increasing trend of RE, fuller understanding of risk factors will be helpful for early detection and treatment to prevent progression of complications like Barrett esophagus.

In conclusion, the prevalence rate of RE in Korean pediatric patients has significantly increased in 2008 to 2014 compared to 2001 to 2007. Older age and residence in the Greater Gangnam region were associated factors of the development of RE. Further studies are required in order to more definitely delineate the development and risk factors for RE in the pediatric population.

SUPPLEMENTARY DATA

Supplementary data can be found with this article online at <http://www.pghn.org> and at <https://doi.org/10.5223/pghn.2017.20.3.160>.

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