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# Reliability Of Different Endoscopic Classification Systems In Predicting Pediatric Reflux Esophagitis

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#### Abstract

Aim: Retrospective in nature, this study was aimed at evaluating the reliability of four endoscopic classification systems in predicting histological reflux esophagitis in children undergoing esophagogastroduedenoscopy.

Materials and Methods: This retrospective study included 213 children (112 male, 101 female, average age  $8.4 \pm 4.8$  years, median age 9 years, range 2 months–18 years) who underwent diagnostic esophagogastroduodenoscopy between January 2002 and December 2004 and evaluated for the presence of reflux esophagitis. Data for age and gender, and detailed endoscopic and histopathological reports were retrieved from medical records. Los Angeles, Savary-Miller, Hetzel-Dent, and Tytgat endoscopic classification systems were used in the evaluation of patients with erosive distal esophagitis. The histological findings were classified according to Knuff & Leape. When reflux-related esophageal damage was identified as a result of the histological examination of endoscopic biopsy samples collected from distal esophagus, the patients were diagnosed with reflux esophagitis. The Statistical Package for the Social Sciences for Windows Release 12.0 (SPSS, Chicago, IL, USA) was used to analyse the statistical data.

### **Results:**

On the histological examination of esophageal mucosal biopsy specimens of 213 patients, 71 (33.3%) patients had normal (grade 0), 75 (35.2%) patients with only histologic changes of reflux (grade 1) without esophagitis and 67 (31.5%) patients were reflux esophagitis (grade 2–5) were detected. There were 49 (23%) patients with mild esophagitis (grade 2), 6 (3%) patients with moderate esophagitis (grade 3) and 12 (6%) patients with severe esophagitis 2 (1%) patients with grade 4 and 10 (5%) patients with grade 5) in 67 patients with reflux esophagitis. On the endoscopical examination of esophageal mucosal appearances of 213 patients, 36 (16.9%) patients, 36 (16.9%) patients, 100 (46.9%) patients and 90 (42.3%) patients were diagnosed with esophagitis according to the Los Angeles, Savary-Miller, Hetzel-Dent and Tytgat endoscopic classification systems, respectively. When the four different endoscopic classification systems evaluated in terms of score correlation with the histological diagnosis, the most linear relationship was found between LA endoscopic classification and Knuff & Leape histological classification (r = 0.544, p < 0.01).

#### **Conclusion:**

No significant strong association in the prevalence of reflux esophagitis between the endoscopic classification systems and Knuff & Leape histological classification. The Los Angeles endoscopic classification more compatible with Knuff & Leape histological classification than other endoscopic classification systems. Though not so safe, the Los Angeles endoscopic classification can be recommended in children as in adults.







Keywords: Gastroesophageal reflux disease, esophagitis, endoscopy, histopathology

# **INTRODUCTION**

Gastroesophageal reflux disease (GERD), the most common disease of the gastrointestinal tract in western countries (1-3). The prevalence of GERD symptoms ranged in 10% to 20% in Western Europe and North America. Prevalence, in Turkey (22.8%) similar to the levels with European countries (4, 5).

No clinical signs are considered the gold standard for diagnostic aspects of symptoms of GERD. Therefore, the incidence and prevalence of GERD is suggested to be more than known (6).

Endoscopy, particularly when supplemented by histology, is the most accurate method of demonstrating esophageal damage caused by reflux (7). For adult patients with reflux esophagitis based on the classification of the various classification systems have been developed for use in endoscopic appearance. Although there is no one actually fully adequate, these methods are important in terms of endoscopic assessments provide a standard comment (6, 8). Savary-Miller (SM), Hetzel-Dent (HD), Los Angeles (LA), and Tytgat endoscopic classification systems are widely used in adult patients (6, 8–10).

Retrospective in nature, this study was aimed at evaluating the reliability of four endoscopic classification systems in predicting histological reflux esophagitis in children undergoing esophagogastroduedenoscopy.

# MATERIALS AND METHODS

#### Patients

This retrospective study included 213 children (112 male, 101 female, average age  $8.4 \pm 4.8$  years, median age 9 years, range 2 months–18 years) who underwent diagnostic esophagogastroduodenoscopy between January 2002 and December 2004 and evaluated for the presence of reflux esophagitis. Data for age and gender, and detailed endoscopic and histopathological reports were retrieved from medical records. Endoscopic images of the patients and histopathological preparations were retrieved from computer archive and pathology archive, respectively. Images and histopathological preparations were re-examined for the purpose of this study.

None of the patients had upper gastrointestinal surgery, malignancy or esophageal varices. None had received antibiotics or bismuth during the last 6 months. Those using H2 blockers, proton pump inhibitors, alcohol, aspirin or non-steroidal anti-inflammatory drugs had discontinued such a treatment one week prior to the study. Patients with esophagitis due to causes other than reflux (e.g. eosinophilic esophagitis, infection) based on histological findings were not included.

Endoscopic examination and biopsy

The indications for endoscopy and the number of patients who had them were as follows: prediagnosis of celiac disease in 60 patients (28.2%), dyspepsia in 37 patients (17.4%), epigastric pain in 29 patients (13.6%), burning sensation in the retrosternal area in 27 patients (12.7%), regurgitation in 20 patients (9.4%), asthma in 11 patients (5.2%), recurrent pneumoniae in nine patients (4.2%), routine evaluation of gastrointestinal system before kidney transplantation in eight patients (3.8%), chronic cough in seven patients (3.3%), routine evaluation for portal hypertension in four patients (1.9%), suspected enteropathy of infancy in one patient (0.5%). Endoscopic examinations had been carried out by one of the two experienced endoscopists in the department. All the endoscopic examinations were performed using Fujinon EG-250PE (infants 0–1 year or <10 kg) or EG-250HR (children >1 year or >10 kg) model video







endoscopes (Fuji Photo Optical Company Ltd, Tokyo, Japan). LA classification system had been used for the evaluation of patients with erosive distal esophagitis during the initial examination procedure. For the purpose of this study, each patient was classified using SM, Tytgat, and HD classification systems using endoscopy reports and computer images.

At the end of each endoscopic procedure, four fragments had been collected from the distal esophagus, at least 3 cm above the gastroesophageal mucosal junction, using biopsy forceps that remove samples sized between 2 and 2.5 mm. The specimens had been submitted to routine histological processing, embedded in paraffin and sectioned perpendicular to the mucosal surface. Slices of 5-6  $\mu$ m thickness had been mounted on slides and then stained with haematoxylin & eosin (HE). For the purpose of this study, preparations were re-examined using a conventional binocular optical microscope of Olympus BH2 model (Olympus Company, Tokyo, Japan). If the eosinophil count was lower than 15 per high power field, histological reflux-related changes could be distinguished from eosinophilic esophagitis (12). The findings were classified according to Knuff & Leape as recommended by the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (13, 14). A score equal to or greater than 2 was considered reflux esophagitis.

#### Statistical analysis

The Statistical Package for the Social Sciences for Windows Release 12.0 (SPSS, Chicago, IL, USA) was used to analyse the statistical data. Results are expressed as mean values and standard deviation (SD). For each classification system, the sensitivity, specificity, positive and negative predictive values for the detection of reflex esophagitis are calculated and compared. Correlations between the scores of different classification system were examined using Pearson's correlation analysis. A p value <0.05 was considered an indication of statistical significance.

#### RESULTS

On the histological examination of esophageal mucosal biopsy specimens of 213 patients, 71 (33.3%) patients had normal (grade 0), 75 (35.2%) patients with only histologic changes of reflux (grade 1) without esophagitis and 67 (31.5%) patients were reflux esophagitis (grade 2–5) were detected. There were 49 (23%) patients with mild esophagitis (grade 2), 6 (3%) patients with moderate esophagitis (grade 3) and 12 (6%) patients with severe esophagitis 2 (1%) patients with grade 4 and 10 (5%) patients with grade 5) in 67 patients with reflux esophagitis. Demographic characteristics were similar in patients with and without esophagitis; however, presence of GERD symptoms was more frequent in the group of patients with histologically confirmed reflux esophagitis (Table 1).

On the endoscopical examination of esophageal mucosal appearances of 213 patients, 36 (16.9%) patients, 36 (16.9%) patients, 100 (46.9%) patients and 90 (42.3%) patients were diagnosed with esophagitis according to the LA, SM, HD and Tytgat endoscopic classification systems, respectively.

Diagnostic value of each endoscopic classification system for the diagnosis of reflux esophagitis is shown in Table 2. All diagnostic parameters were similar for SM and LA classifications. The sensitivities of HD and Tytgat classifications for the prediction of histologically confirmed reflux esophagitis were significantly better than both SM and LA classifications (SM vs. HD, p=0.001; SM vs. Tytgat, p=0.006; LA vs. HD, p=0.001; LA vs. Tytgat, p=0.006). However, HD and Tytgat classifications did not differ with regard to sensitivity (p=0.594).

With regard to specificity, SM and LA classifications had better specificities when compared to both HD and Tytgat classifications (p<0.001 for all comparisons). On the other hand, Savary-









Miller had similar specificity with LA (p=1.00); and HD and Tytgat had similar specificities (p=0.395).

Among the four different endoscopic classification systems, the most consistent relation was found between the scores of LA and SM classification systems (r=0.989, p<0.001). When the four different endoscopic classification systems evaluated in terms of score correlation with the histological diagnosis, the most linear relationship was found between LA endoscopic classification and Knuff & Leape histological classification (r = 0.544, p < 0.01). Table 3 shows the correlations of the scores of the different classification systems.

# DISCUSSION

**GERD** symptoms to diagnosis in paediatric patients after 8 years of age be evaluated as a more reliable (4, 11). Because of not apply to the treatment of GERD in infants Barrett's esophagus and esophageal adenocarcinoma later in life, such as the possible complications of GERD may occur (14). Inadequate weight gain or intermittent torticollis due to Sandifer syndrome should be considered in the paediatric GERD symptoms (7, 11, 15, 16). Unlike adults in the paediatric patients the correlation between the presence of GERD symptoms and esophagitis is not good enough (11, 17, 18). In a multicenter study carried out by Lombardi and colleagues in the 136 paediatric patients with GERD symptoms was not a good relationship with histological esophagitis (19).

According to the definition of GERD is present when reflux of gastric contents causes troublesome symptoms and/or complications. The same consensus also admits that histology has limited use in establishing or excluding a diagnosis of GERD. Reflux esophagitis could be interpreted as a marker for GERD (11). Since in the children neither the GERD symptoms nor the endoscopic findings are not sufficiently reliable for the diagnosis of GERD, during endoscopic examination esophageal mucosal biopsy is proposed as a routine practice (7).

### CONCLUSION

There is no significant strong association in the prevalence of reflux esophagitis between the endoscopic classification systems and Knuff & Leape histological classification. The LA endoscopic classification more compatible with Knuff & Leape histological classification than other endoscopic classification systems. Though not so safe, the LA endoscopic classification can be recommended in children as in adults.

#### **References**

*Moayyedi P, Talley N. Gastro-oesophageal reflux disease. Lancet 2006; 367: 2086 – 100.* 

- 2 Locke GR, Talley NJ, Fett SL, et al. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. Gastroenterology 1997; 112: 1448 – 56.
- *3* Shaheen N, Ransohoff DF. Gastroesophageal reflux, Barrett esophagus, and esophageal cancer: scientific review. JAMA 2002; 287: 1972 81.
- 4 Vakil N, Zanten SV, Kahrilas P, et al. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence based consensus. Am J Gastroenterol 2006; 101: 1900 20.
- 5 Bor S, Mandıracıoğlu A, Kitapçıoğlu G, et al. Gastroesophageal reflux in a low income region in Turkey. Am J Gastroenterol 2005; 100: 759 – 65.
- 6 Vandenplas Y. Gastroesophageal reflux. In: Guandalini S, Dhawan A, Branski D (eds). Textbook of Pediatric Gastroenterology, Hepatology and Nutrition. Switzerland: Springer, 2016, 104 – 30.
- 7 Rudolph CD, Mazur LJ, Liptak GS, Baker RD, Boyle JT, Colletti RB, et al. North American Society for Pediatric Gastroenterology and Nutrition. Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American













Society for Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr. 2001;32 Suppl 2:S1 – 31.

- 8 Lundell LR, Dent J, Bennett JR, et al. Endoscopic assessment of oesophagitis: clinical and functional correlates and further validation of the Los Angeles classification. Gut 1999; 45: 172 80.
- 9 *Richter JE. Diagnostic tests for gastroesophageal reflux disease. Am J Med Sci 2003; 326: 300* - 8.
- 10 Vieira MC, Pisani JC, Mulinari RA. Diagnosis of reflux esophagitis in infants: histology of the distal esophagus must complement upper gastrointestinal endoscopy. J Pediatr (Rio J) 2004; 80: 197 202.
- 11 Sherman PM, Hassall E, Fagundes-Neto U, et al. A global, evidence-based consensus on the definition of gastroesophageal reflux disease in the pediatric population. Am J Gastroenterol 2009; 104: 1278 95.
- 12 Vandenplas Y. Reflux esophagitis in infants and children: a report from the Working Group on Gastroesophageal Reflux Disease of the European Society of Paediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr 1994; 18: 413 – 22.
- 13 Thomson M. Esophagitis. In: Walker WA, Goulet O, Kleinman RE, Sherman PM, Shneider BL, Sanderson IR, eds. Pediatric gastrointestinal disease. 4 th ed. Hamilton: BC Decker Inc, 2004; 400 – 23.
- 14 Gold BD. Is gastroesophageal reflux disease really a life-long disease: do babies who regurtitate grow up to be adults with GERD complications? Am J Gastroenterol 2006; 101: 641 4.
- 15 Werlin SL, D'Souza BJ, Hogan WJ, et al. Sandifer syndrome: an unappreciated clinical entity. Dev Med Child Neurol 1980; 22. 374 – 8.
- 16 Gorrotxategi P, Reguilon MJ, Arana J, et al. Gastroesophageal reflux in association with the Sandifer syndrome. Eur J Pediatr Surg 1995; 5: 203 5.
- 17 Biller JA, Winter HS, Grand RJ, et al. Are endoscopic changes predictive of histologic esophagitis in children? J Pediatr 1983; 103: 215 8.
- 18 Wenner J, Hall M, Höglund P, Johansson J, Johnsson F, Oberg S. Wireless pH recording immediately above the squamocolumnar junction improves the diagnostic performance of esophageal pH studies. Am J Gastroenterol. 2008; 103: 2977 – 85.
- 19 Lombardi G, de'Angelis G, Rutigliano V, et al. Digestive and Liver Disease 2007; 39: 864–71.









