



Endoscopic and Histopathological Study of Gastro Esophageal Reflux Disease(GERD)

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ABSTRACT

Introduction: The study was conducted to evaluate the endoscopic and histomorphological features of GERD.

Methods: A total of 79 patients were evaluated prospectively, in a cross sectional study, in the endoscopic unit of Gastroenterology department for symptoms compatible with GERD. In all cases, routine endoscopy and Los Angeles grading of GERD were performed. In each subject biopsy was taken and assessed histologically.

Results: 5/79 (6.3%) patients had NERD on endoscopy. Los Angeles Grade A was present in 25/79 (31.6%) patients, Grade B in 10/79(12.6%) patients and none had Grade C or D. The most important histological findings of GERD were basal cell hyperplasia(67%), elongation of lamina propria papillae(60%) and dilatation of intercellular spaces(70.9%).

Conclusion: The endoscopic and histopathological features of GERD were assessed in detail.

KEYWORDS : Gastroesophageal reflux disease; Histopathology; Endoscopy

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common condition with a variety of clinical manifestations and potentially serious complications. The prevalence of GERD in India is now higher than previous estimates and seems to be between 8-19%. This appears to be similar to that of the western countries.^{1,4}

In 2006, the Montreal International Consensus defined GERD as a condition that develops when the reflux of stomach contents causes troublesome reflux-associated symptoms and/or complications.⁵ The Montreal International Consensus defined Nonerosive reflux disease (NERD) as the presence of these symptoms in the absence of esophageal mucosal breaks.⁵

Early diagnosis of GERD is crucial because chronic reflux esophagitis is a key factor for the development of Barrett's esophagus, which is a precursor lesion for esophageal adenocarcinoma.^{6,7} However, there is no gold standard method for the diagnosis of GERD.⁸ This is because of the heterogeneity in the clinical manifestations.⁹ Hence the diagnosis of GERD is based on a combination of clinical symptoms, endoscopic findings and histological changes.⁸ In patients with normal or near normal endoscopic finding (nonerosive reflux disease) the major diagnostic burden lies with the histology.

OBJECTIVE

To evaluate the endoscopic and histomorphological features of GERD.

MATERIALS AND METHODS

This was a cross sectional study lasting from December 2011 to October 2013 carried out in the Departments of Pathology and Department of Gastroenterology of Sree Gokulam Medical College. A total of 79 patients were evaluated prospectively in the endoscopic unit of Gastroenterology department for symptoms compatible with GERD.

Cases were selected based on a validated questionnaire which included demographic features, risk factors and clinical features. Non-cooperative patients, patients with history of gastric surgeries, patients

with esophageal varices and sick patients were excluded from the study. Patients gave their informed consent to be a part of the study.

A routine endoscopy was performed by the same gastroenterologist on all patients. GERD was graded in accordance with the Los Angeles classification.¹⁰ Endoscopic pictures and reports were evaluated to know the macroscopic features. In each subject biopsy was taken from the mucosa 3cm above the squamocolumnar junction.

The biopsy specimens were fixed in 10% formalin and embedded in paraffin wax. Sections were stained using H&E and assessed histologically for features of GERD. The main histological features of GERD assessed include basal cell hyperplasia, elongation of lamina propria papillae, dilatation of intercellular spaces and increased intraepithelial inflammation including eosinophils, neutrophils & lymphocytes¹¹.

Basal cell hyperplasia is defined as the expansion of the basal zone of the squamous epithelium to more than 15% of the epithelial thickness.¹¹ The upper limit of the basal layer is defined as the level where the nuclei of epithelial cells are separated by a distance greater than their diameter. Basal cell hyperplasia was graded as mild (<30% of the total epithelial thickness) and severe (>30%).¹²

Elongation of lamina propria papillae is defined as lengthening of the subepithelial lamina propria to more than two thirds the thickness of the squamous epithelium.¹¹ Upper limit of papillae is the upper limit of vessels running along its axis. Papillae elongation was graded as mild (<75% of the total epithelial thickness) and severe (>75%).¹² Dilatation of intercellular spaces is defined as irregular dilatations of intercellular spaces detectable at light microscopy as optically empty bubbles or ladders.¹¹ This feature can be graded as small or large (less than or more than diameter of a small lymphocyte).¹² The principal intraepithelial inflammatory cells include neutrophils, eosinophils and lymphocytes.¹¹

STATISTICAL ANALYSIS

Data, entered in Microsoft excel, was filtered and coded. Data was analysed using SPSS version 16 (SPSS “C Statistical Package for Social Sciences). Simple proportions and chi square values with level of significance were evaluated and interpreted.

RESULTS

The mean age of the patients was 46.1± 12.2 years. Among the 79 patients included in the study group 72.2% were males. 29.1% of the subjects were smokers and 40.5% were alcoholics. 73.4% of subjects consumed tea for 4-7 days per week. 51.9% took fried foods, 49.4% took spicy foods and 29.1% took coffee for 4-7 days per week. Only 13.9% took citrus fruits and 1.3% chocolates for the same period. Majority of the patients presented with complaints of heart burn(84.8%) and regurgitation (75.9%).

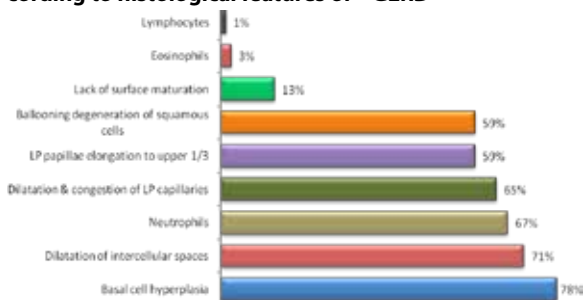
Nonerosive reflux disease was present in only 5/79 (6.3%) patients. All of these patients with NERD were having histological features of GERD. Endoscopic findings of GERD were graded according to Los Angeles classification as A, B, C and D. 25/79 (31.6%) patients had Grade A, 10/79(12.6%) had Grade B. None of the patients had Grade C or D. Majority of the subjects with endoscopic finding of GERD were also having histological finding of GERD. 28 subjects had findings of Barrett’s esophagus and 11 of them presented miscellaneous findings [Table 1].

Table 1: Distribution of patients according to endoscopic findings

Endoscopic Feature	Number of patients	Percentage
Normal	5	6.3%
GERD- Grade A	25	31.6%
GERD- Grade B	10	12.6%
GERD- Grade C	0	0%
GERD- Grade D	0	0%
Barrett’s esophagus	28	35.4%
Others	11	13.9%

Most common histological feature of GERD in our study was basal cell hyperplasia (78.5%) [Figure 1]. We observed that majority(58.2%) of our patients had only mild basal cell hyperplasia. Another important feature observed in the study was lamina propria papillae elongation to upper one third, which was seen in 60.3% of subjects. Most (49.4%) of our patients had only mild (<75%) elongation Dilatation of intercellular spaces was observed in 70.9% of subjects. Majority (58.2%) of our subjects had only small dilatation of intercellular spaces. Intraepithelial neutrophilic infiltration was observed in 67.9% cases, eosinophilic infiltration in 2.5%, lymphocytic infiltration in 1.3%.

Figure 1: Percentage (%) distribution of the sample according to histological features of GERD



DISCUSSION

The aim of our study was to evaluate the endoscopic and histomorphological features of GERD. On endoscopy, the prevalence of NERD was 5/79 (6.3%). This rate is lower when compared to study done by Zuberi et al¹³ (55.6%), Gatopoulou et al¹⁴ (58%) and Jonaitis et al¹⁵ (49%). All of these patients with NERD in our study were having histological features of GERD.

Los Angeles Grade A was present in 25/79 (31.6%) patients and Grade B in 10/79(12.6%) patients. This rate is comparable to study done

by Gatopoulou et al¹⁴ (Grade A: 26% and Grade B: 12%). However, this rate of Grade A is higher and Grade B is lower when compared to study done by Zuberi et al¹³ (Grade A: 10.2% and Grade B: 19.4%) and Jonaitis et al¹⁵ (Grade A: 15% and Grade B: 25.9%). None of our patients had Los Angeles Grade C or D while Zuberi et al¹³ had 9.2% cases of Grade C and 5.6% cases of Grade D, Gatopoulou et al¹⁴ had 4% cases of Grade C and none with Grade D and Jonaitis et al¹⁵ had 3.8% cases of Grade C and 0.9% cases of Grade D. Majority of the subjects in our study with endoscopic finding of GERD were also having histological features of GERD.

The most common histological feature of GERD in our study was basal cell hyperplasia. In our study the cut off value for basal cell hyperplasia was taken as 15% of the total thickness of stratified squamous epithelium and majority(58.2%) of the patients had only mild(<30% of the total epithelial thickness) basal cell hyperplasia.

Basal cell hyperplasia was present in 78.5% of subjects which was comparable to the study done by Gatopoulou et al¹⁴ (more than 90%) and Zentilin et al⁹ (72% at 2cm above Z line and 88% at Z line). However, this rate is higher when compared to study done by Keisslich et al¹⁶ (44%) and Bove et al¹⁷ (22.1%). Bowrey et al¹⁸ observed basal cell hyperplasia in 51% of patients with nonerosive reflux disease and 60% of patients with mucosal breaks.

Another important feature, lamina propria papillae elongation to upper one third, was observed in 60.3% of subjects which was comparable to the study by Gatopoulou et al¹⁴ (66%) and Johnson et al¹⁹ (67%) and was higher when compared to study done by Zentilin et al⁹ (32% at 2cm above Z line and 58% at Z line), Keisslich et al¹⁶ (42%) and Schindlbeck et al²⁰ (25%). Bowrey et al¹⁸ observed papillae elongation in 21% of patients with nonerosive disease and 29% of those with mucosal breaks. Most(49.4%) of our patients had only mild elongation.

Dilatation of intercellular spaces, yet another important feature, was observed in 70.9% of subjects which was comparable to the study by Solcia E et al²¹ (68% of patients with nonerosive reflux disease and 90% with mucosal breaks) and Zentilin et al⁹ (67% at 2cm above Z line and 72% at Z line). This feature was graded as small or large (less than or more than diameter of a small lymphocyte) in our study. Majority (58.2%) of our subjects had small dilatation of intercellular spaces.

The predominant intraepithelial inflammatory infiltrate in this study was neutrophils (67.9%) whereas Gatopoulou A et al¹⁴ and Zentilin et al⁹ observed eosinophils and lymphocytes as the predominant inflammatory infiltrate. Lymphocytes were the predominant inflammatory infiltrate in the studies conducted by Keisslich et al¹⁶, Veith et al²² and Ismail Beigi et al²³.

Zentilin et al⁹ studied biopsies from multiple sites at gastroesophageal junction. A major limitation of our study was that a single biopsy from 3cm above the squamocolumnar junction was studied to avoid inconvenience to the patients. Also we were not able to exclude patients on acid suppressive therapy. In fact most of our patients were on acid suppressive therapy. This may be the reason why we got only mild basal cell hyperplasia, mild papillae elongation and only small dilatation of intercellular spaces. However, in spite of all these limitations most of our results were similar to several other studies.^{9,14}

GERD continues to intrigue both clinicians and researchers alike because of its varied presentations, changing epidemiology, lack of gold standard diagnosis and evolving treatment.¹³ Recent studies suggest that prevalence of GERD in India is now higher and it appears to be similar to that of the western countries.¹⁻⁴ Hence it is important to reemphasize the different diagnostic methods of GERD as at present, there are no methods that can be taken as the gold standard.

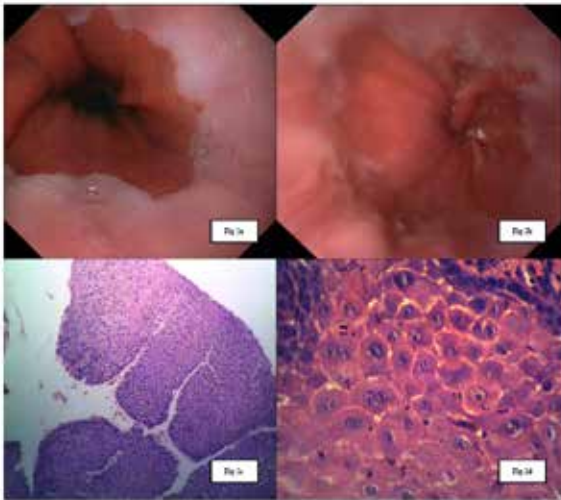
The histological diagnosis of GERD is generally believed to be a tool of limited value.^{20,24,25} The sensitivity and specificity of histological GERD diagnosis are generally believed to be low.²⁰ Several recent studies have, however, demonstrated that histology, if systematically applied, may render important diagnostic clues.

CONCLUSION

The endoscopic and histopathological features of GERD were assessed in detail in patients with symptoms compatible with GERD. Majority of the patients were having endoscopic finding of Los Angeles Grade A(31.6%) or B(12.6%). The most important histological findings of GERD were basal cell hyperplasia(67%), elongation of lamina propria papillae(60%) and dilatation of intercellular spaces(70.9%) [Figure 2] .

Figure 2: (a) Los Angeles grade A GERD (b) Los Angeles grade B GERD

(c) Stratified squamous epithelium showing basal cell hyperplasia and lamina propria papillae elongation. (H&E) (10X10) (d) Stratified squamous epithelium showing dilatation of intercellular spaces and intraepithelial inflammation (H&E) (40X10)



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