

# CORRELATION BETWEEN CLINICAL, ENDOSCOPIC AND HISTOLOGICAL FINDINGS AT ESOPHAGO-GASTRIC JUNCTION IN PATIENTS OF GASTROESOPHAGEAL REFLUX DISEASE

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## ABSTRACT

**Objective:** To determine the correlation between the clinical, endoscopic and histological findings in patients of GERD.

**Design:** An observational, cross-sectional study.

**Place and Duration of Study:** Lyari General Hospital, Dow University of Health Sciences from November 2003 to October 2004.

**Patients and Methods:** Patients complaining of heartburn and/or acid regurgitation at least twice per week for at least 3 months were inducted in the study. Presence of clinical symptoms of epigastric pain, retrosternal burning, and reflux were recorded. Patients were subjected to esophagogastroduodenoscopy and four biopsies were taken from esophago-gastric junction. Correlation/regression analysis was done on clinical, endoscopic and histological findings.

**Results:** A total of 196 patients were selected and endoscopically examined. Most common grade given by patients to epigastric pain was grade-4 (42.9%), retrosternal burning as grade-4 (41.8%) and reflux grade-5 (36.7%). There was significant correlation between the clinical severity of epigastric pain with endoscopic findings ( $p=0.002$ ) and reflux ( $p=0.0$ ) but no correlation was observed with histological findings ( $p=0.19$ ). Out of 109 (55.6%) patients who had normal mucosa on endoscopy but on histology 70 (35.7%) of them had inflammation. Grading of endoscopic and histological findings showed significant correlation with each other ( $p=0.0$ ).

**Conclusion:** Endoscopic negative GERD is common; severity of clinical symptoms correlated with endoscopic findings and reflux but did not correlated with histological findings.

**KEY WORDS:** Gastroesophageal reflux disease. Esophagitis. Endoscopic negative GERD. Endoscopy.

## INTRODUCTION

The gastroesophageal reflux disease (GERD) is defined by the presence of esophageal mucosal breaks or by the occurrence of reflux induced symptoms severe enough to impair quality of life.<sup>1</sup> The Genval Workshop defined GERD as "gastroesophageal reflux disease" (GERD, reflux disease) should be used to include all individuals who are exposed to the risk of physical complications from gastroesophageal reflux, or who experience clinically significant impairment of health related well-being (quality of life) due to reflux related symptoms, after adequate re-assurance of the benign nature of their symptoms.<sup>1,2</sup>

GERD has been the focus of dynamic research in the Asia Pacific region in the last few years. Previously the information from this area was scanty and GERD symptoms were uncommon in early 90's.<sup>3</sup> One study from Singapore reported very low prevalence in the region at 2% while another from China reported the prevalence at 6%.<sup>4</sup> These rates were lower than the Western populations where its prevalence has been reported at 25%.<sup>5</sup> There has been increase in the frequency of GERD in Asia. In a re-survey of community

residents, who

were interviewed in an earlier study in 1994,<sup>3</sup> there was more than 4-fold increase in the frequency of symptoms.<sup>6</sup> Similarly, there has been increase of endoscopic esophagitis from 1992 to 1999 while frequency of duodenal ulcer decreased during the same duration.<sup>7,8</sup>

Many patients of clinical diagnosis of GERD or having epigastric pain do not show any abnormality on endoscopic examination. These are labeled as endoscopic negative GERD. In such patients the histopathology could provide the diagnosis as it has been shown that esophageal biopsy is reasonably sensitive in diagnosing the reflux disease in the absence of endoscopic findings.<sup>9,10</sup>

The objectives of this study were to document the frequency of endoscopic and histological findings in patients with clinical diagnosis of gastroesophageal reflux disease and to determine the correlation between the clinical, endoscopic and histological findings.

## PATIENTS AND METHODS

It was a cross-sectional study conducted at Medical Ward, Lyari General Hospital, Karachi, affiliated to Dow University of Health Sciences as its Medical Unit VI from November 2003 to October 2004. All patients with clinical diagnosis of GERD undergoing endoscopic examination in the unit in the said

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duration were included using convenience sampling technique. Patients complaining of heartburn and/or acid regurgitation at least twice per week for at least 3 months were inducted.<sup>11</sup>

Patients who had taken proton pump inhibitors during the last 4 weeks and those with peptic ulcers or malignancy were excluded but patients on H<sub>2</sub> receptor antagonist or antacids were not excluded.

Informed consent was taken from all the selected patients. Presence of clinical symptoms of epigastric pain, retrosternal burning, and reflux were recorded. Patients were also asked to fill out the proforma grading the severity of symptoms of epigastric pain, retrosternal burning and reflux on a scale of 0-5; where 0 = no symptoms and 5 = maximum symptoms according to patients' perception. Patients who were unable to fill the form themselves were helped by a resident/medical officer.

Patients were subjected to esophagogastroduodenoscopy (EGD) observing standard procedure. Presence of esophagitis was recorded and grading was done according to the Los Angeles Classification System for endoscopic assessment of esophagitis.<sup>12,13</sup> Four biopsies were taken from the esophagogastric junction (EGJ); biopsies were transferred to histopathologist within 24 hours in 10% buffered formalin. EGD findings were not known to the histopathologist and he was asked to comment on the presence of inflammation or otherwise, apart from the routine histological reporting.

Correlations between different variables were calculated using Spearman's rank correlation.<sup>14</sup> Difference in means of continuous variables was assessed by Student's 't' test and Chi-square test was also used where applicable. Significance level was at <0.05. Statistical analysis was done using SPSS version 13.0.

## RESULTS

During the study period, a total of 196 patients of GERD underwent endoscopic examination. Mean age of the patients was 35.5 ±14.9 years. Gender distribution was males 97 (49.5%) and females 99 (50.5%). Mean age ± SD of males was 36.3 ±15.2 years and that of females 34.7 ±14.6 years.

Clinically most common grading of epigastric pain, as done by patients was grade-4 (42.9%) and least common was grade-1 (4.6%). Details are given in Table I. Most patients graded the

**Table I:** Clinical grading of symptoms done by patients.

Grade	Epigastric pain	Retrosternal burning	Reflux
0	0	0	0
1	9 (4.6%)	10 (5.1%)	6 (3.1%)
2	16 (8.2%)	29 (14.8%)	16 (8.2%)
3	53 (27.0%)	42 (21.4%)	35 (17.9%)
4	84 (42.9%)	82 (41.8%)	67 (34.2%)
5	34 (17.3%)	33 (16.8%)	72 (36.7%)

**Table II:** Endoscopic findings in patients presenting with GERD and mean age according to findings.

Endoscopic findings	Mean age ± SD	Total	Males	Females
Normal	30.3 ±12.4 yr	109 (55.6%)	49 (25.0%)	60 (30.6%)
Esophagitis Grade-A	38.6 ±12.3 yr	20 (10.2%)	12 (6.1%)	08 (4.1%)
Esophagitis Grade-B	40.9 ±17.4 yr	38 (19.4%)	20 (10.2%)	18 (9.2%)
Esophagitis Grade-C	41.2 ±14.5 yr	18 (9.2%)	10 (5.1%)	08 (4.1%)
Esophagitis Grade-D	52.8 ±7.8 yr	11 (5.6%)	06 (3.1%)	05 (2.6%)

symptom of retrosternal burning as grade-4 (41.8%) while that of reflux as grade-5 (36.7%) (Table II). The endoscopic examination revealed that 109 (55.6%) patients had normal mucosa while 87 (44.4%) patients had various grades of inflammation; details are given in Table II. Severity of esophagitis increased with increasing age. Mean age of patients with grade-A esophagitis was 38.6, grade-B was 40.9 years, grade-C was 41.2 years and that of grade-D was 52.8 years.

Out of 109 patients of endoscopic negative GERD; the histological examination revealed presence of inflammation in 70 (64.2%) patients while 39 (35.8%) had normal histology which was significant statistically (p= 0.0; df 8).

Increasing age related significantly with the ranking of endoscopic findings, histologic inflammation, epigastric pain and to the presence of reflux. No significant correlation was observed with gender and retrosternal burning (Table III).

Endoscopic findings were found to correlate with presence of histologic inflammation and ranking of epigastric pain and presence of reflux. It did not have correlation with gender and symptom of retrosternal burning.

Presence of histologic inflammation related significantly with increasing age, endoscopic findings and presence of reflux.

**Table III:** Spearman rank correlation test.

		Age	EGD findings	Histologic inflammation	Gender	Epigastric pain	Retrosternal burning	Reflux
Age	CCoE	1.000	.428(**)	-.289(**)	.052	-.262(**)	-.110	-.170(*)
	P-value	.	.000	.000	.467	.000	.126	.017
EGD findings	CCoE	.428(**)	1.000	-.883(**)	.091	-.219(**)	-.133	-.427(**)
	P-value	.000	.	.000	.206	.002	.063	.000
Histologic inflammation	CCoE	-.289(**)	-.883(**)	1.000	-.014	.092	.137	.308(**)
	P-value	.000	.000	.	.841	.198	.055	.000
Gender	CCoE	.052	.091	-.014	1.000	.326(**)	.380(**)	-.255(**)
	P-value	.467	.206	.841	.	.000	.000	.000
Epigastric pain	CCoE	-.262(**)	-.219(**)	.092	.326(**)	1.000	.678(**)	.525(**)
	P-value	.000	.002	.198	.000	.	.000	.000
Retrosternal burning	CCoE	-.110	-.133	.137	.380(**)	.678(**)	1.000	.374(**)
	P-value	.126	.063	.055	.000	.000	.	.000
Reflux	CCoE	-.170(*)	-.427(**)	.308(**)	-.255(**)	.525(**)	.374(**)	1.000
	P-value	.017	.000	.000	.000	.000	.000	.

\*\*Correlation is significant at the 0.01 level (2-tailed); \*Correlation is significant at the 0.05 level (2-tailed); CCoE = Correlation coefficient.

No statistically significant correlation was found with gender, epigastric pain and retrosternal burning.

Gender was significantly related to epigastric pain, retrosternal burning and reflux while no significant correlation was found with age, EGD findings and histologic inflammation. The grades of epigastric pain correlated significantly with all the variables except histologic inflammation.

Retrosternal burning correlated significantly with gender, epigastric pain and reflux, while it did not correlate significantly with age, EGD findings and histologic inflammation.

Reflux correlated significantly with all the variables.

## DISCUSSION

GERD continues to intrigue both clinicians and researchers alike because of its varied presentation, changing epidemiology, lack of gold standard for diagnosis and evolving treatment. It affects the major adult population of Western World and recent studies suggest that the prevalence in the Asia is increasing. It may be due to more frequent recognition by the clinicians after improved diagnosis or lifestyle change in dietary fat and increases intake of carbonated drinks. The prevalence of GERD from Asian Pacific region in early 90's was reported at 2-6 % which is very low as compared to the western countries.<sup>4,7,15</sup> In resurvey of same population after few years a four-fold increase in the prevalence was documented.<sup>16</sup> This is also the case in our population although no serial assessment of prevalence has been done. In this study, we aimed at correlating clinical diagnosis with endoscopic and histological findings.

Upto 70% of patients with typical symptoms of gastroesophageal reflux disease (GERD) neither have definite endoscopic esophageal breaks nor Barrett's esophagus at upper GI endoscopy. These patients suffer from non-erosive reflux disease (NERD), also termed endoscopic negative reflux disease (ENRD).<sup>17</sup> The frequency of ENRD was 55.6% with female preponderance. They belonged to the younger age group as compared to the patients with erosive esophagitis. In our study, majority of the individuals with ENRD experienced epigastric pain and retrosternal burning of grade-4 intensity despite the absence of any endoscopic evidence. Similarly, individuals with erosive esophagitis principally complained of epigastric pain of grade-4 intensity. Endoscopic negative patients have symptom severities comparable to those with erosive disease and which significantly impair their quality of life. Contrary to our observation a recent study showed that individuals without GERD evidence experience mild GERD symptoms.<sup>18</sup> Since ENRD has approached as a milder end of the spectrum and Barrett's esophagus at the other end, suggesting that the patient's disease may progress over time along this spectrum. Another current study conducted on a cohort of ENRD has shown that after a median time of 10 years following the original diagnosis, majority of the patients have developed reflux esophagitis.<sup>19</sup> It was also observed in the patients with normal endoscopy that majority of them rated the reflux symptom as grade-5 as compared to the individuals with erosive esophagitis. Another study suggested that ENRD is a disease of excessive gastroesophageal reflux.<sup>20</sup>

## CONCLUSION

ENRD is a disorder in its own right that shares symptoms with other GERD groups. Absence of endoscopic esophagitis at presentation does not represent the prognostic factor. It is needed that the natural history be better defined to improve the treatment of this disorder.

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