

Original research article

A Prospective Study at a Tertiary Care Centre Clinical and Endoscopic Profile of Patients with Gastro-Esophageal Reflux Disease

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Abstract

Background: Currently Gastroesophageal reflux disease (GERD) is the most common esophageal disorder, accounting for nearly 75% of all patients with esophageal disorders and around 25-30% of the general population in the west. Most studies from India suggest that these might be less in the Indian population. Most but not all patients with GERD are relieved by treatment with proton pump inhibitors and other anti-reflux treatment. Upper Gastrointestinal endoscopy also known as esophagogastroduodenoscopy (EGD) is the best test for the evaluation of the proximal gastrointestinal tract.

Objectives: To study the clinical and endoscopic profile of patients with GERD; and its response to proton pump inhibitors and prokinetics.

Methods: The study was a prospective study that included 100 in patients and out patients seen in the Department of Medicine at, All India institute of medical sciences, Patna. Study duration of two years. with reflux symptoms, with a score of more than 8 in the FSSG questionnaire, and who met the inclusion criteria with no reasons for exclusion, and consented for the study. Patients were analyzed clinically and by endoscopic profiles and their response to PPI and Prokinetic combination assessed at the end of 4 weeks of therapy.

Conclusion: Gastroesophageal Reflux Disease is a common problem with heartburn and regurgitation being the most common presenting symptoms affecting males more than females. Non erosive reflux disease is commoner than reflux esophagitis on endoscopic assessment. A combination of proton pump inhibitors and prokinetics.

Keywords: Gastroesophageal Reflux Disease, Endoscopy, Proton Pump Inhibitors, Prokinetics.

Introduction

Gastroesophageal reflux disease (GERD) is a chronic disorder of the upper gastrointestinal tract that is prevalent worldwide with increasing incidence globally. Until recently, there were many definitions of GERD. The first ever global consensus definition was published in 2006 (the Montreal definition). According to that document, GERD is defined as “a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications”^[1]. Based on this definition, GERD can be classified into two syndromes: esophageal and extra esophageal. Gastroesophageal reflux disease was not recognized as a significant clinical problem until the mid 1930's and was not identified as a precipitating cause for esophagitis until after World War II^[2]. Gastroesophageal reflux disease is now the most common upper gastrointestinal disease in the western countries, with 10% to 20% of the population experiencing weekly symptoms^[3,4]. The frequency and severity of complications of GERD vary among different ethnic populations and geographically. In the early 1990s, the prevalence rates in South Asian countries were lower than those of Western populations. A cross sectional survey of randomly selected adults in Singapore in the 90s found that less than 2% of 696 persons reported heartburn more than once a month, suggesting that reflux type symptoms were uncommon in Asians^[5]. A similar study among a random sample of 5,000 adult residents in Shanghai and Beijing^[6] showed prevalence rates of symptomatic GERD as 7.76% and 10.19%, respectively. Population-based survey studies indicate that the prevalence is rising^[7]. Possible explanations for this include aging population, the obesity epidemic (and associated changes in diet or physical activity), and changes in sleep pattern. A report by the Indian Society of Gastroenterology task force that used a health facility-based approach to determine frequency of GERD symptoms in apparently healthy individuals in different parts of India and showed that 7.6% of the respondents reported symptoms of heartburn and/or regurgitation at least once a week^[8]. Subjects with GERD were older, frequently consulted doctors, and often had overlapping functional lower gastrointestinal symptoms. In the last few decades, upper gastrointestinal (GI) endoscopy has become the most complementary test for investigation of esophageal diseases. It is easily accessible and a safe modality, and is widely used in patients with suspected benign and malignant diseases of the esophagus. Recent technological advances in endoscopic imaging and tissue analysis obtained from the esophagus have been useful to better understand and manage highly relevant diseases such as gastroesophageal reflux disease, eosinophilic esophagitis and esophageal cancer^[9]. Upper GI endoscopy in patients with GERD, must be used to assess the underlying cause and pathology of the disease, especially in patients not responding to therapy and correlated with clinical severity, for better management of GERD and therefore a better Quality Of Life (QoL). Acid suppression is the mainstay of therapy for GERD and proton pump inhibitors (PPIs) are the most potent drug in this regard. Although the use of PPIs is the treatment of choice for GERD, still approximately one-third of patients with GERD fail to respond symptomatically to a standard dose PPI, either partially or completely^[10,11].

Objectives

To study the clinical and endoscopic profile of patients with GERD; and its response to proton pump inhibitors and prokinetics. To assess severity of reflux symptoms and correlate it with quality of life. To assess GERD and its associations with lifestyle factors.

Review of Literature

Aristotle (384-322 BC), Greek philosopher and physician, suggested that the source of the word esophagus related to "its length and its narrowness". The term's origin is more likely related to the Greek term oisopagos, created from oisein ("to carry") and phagos ("to eat") or from phagma ("food"). The term, adopted by Medieval Latin and Late Middle English, became

isophagus or ysophagus. In Old Roman Latin, the popular noun for the esophagus was gula. Gula was defined as a narrow passage, the mouth, or the throat. More recently, the term gullet has re-emerged in English as a synonym for esophagus^[12]. Gastroesophageal reflux disease (GERD) is most likely known to man since antiquity. In 1618, Fabricius described the gastroesophageal junction, and attributed its name "cardia" to Galen (130-200 AD), who had coined the term because symptoms arising from the gastroesophageal junction were similar to those arising from the heart. It was not until the twentieth century, however, that the relationship between the symptoms and the gastroesophageal reflux (GER) was established^[13,14]. In 1880 Jackson introduced the esophagoscope and the modern era of esophagology began. Nine years later, using a crude manometric system, Meltzer^[15] described esophageal peristalsis. Although Tiletson (1906), Mosher (1921), and Jackson (1922) described the anatomic, endoscopic, and pathologic findings of stricture and "peptic ulcer" of the esophagus, they did not consider the cause to be related to reflux of the gastric contents. In a landmark article, Winkelstein reported "peptic esophagitis: a new clinical entity", where he described in detail five patients with heartburn, dysphagia, esophagitis, stricture, and esophageal spasm and stated, "The type of substernal pain, heartburn, sour regurgitations and the hyperchlorhydria in all recall the clinical features of peptic ulcer of the esophagus". In the mid twentieth century, hiatal hernia became equated with GERD, and surgical correction of "symptomatic sliding hiatal hernia" became the focus of treatment. The belief that the sphincteric function of the lower esophageal sphincter was created by mechanical factors was supported by the failure of anatomists and operating surgeons to demonstrate a separate anatomic muscle at the gastroesophageal junction^[16]. With the introduction of modern manometry, Fyke et al (1956) and Ingelfinger (1958) began to unravel the complex neurophysiologic events associated with swallowing and with the pathogenesis of GERD. The lower esophageal sphincter remained the primary focus of reference, but esophageal motility and dysmotility also became recognized as factors in GERD. The esophagus is a two-layered mucosa-lined muscular tube that is located in the posterior mediastinum. It commences at the base of the pharynx at C6 and terminates in the abdomen, where it joins the cardia of the stomach at T11. Along its 25- 30 cm course, it winds its way through a path yielding to structures of vital importance. The cervical esophagus begins as a midline structure that deviates slightly to the left of the trachea as it passes through the neck into the thoracic inlet. At the level of the carina, it deviates to the right to accommodate the arch of the aorta. It then winds its way back under the left main-stem bronchus and remains slightly deviated to the left as it enters the diaphragm through the esophageal hiatus at the level of the 11th thoracic vertebra. The muscular esophagus begins and ends with two distinct high-pressure zones: the upper esophageal sphincter (UES) and lower esophageal sphincter (LES). After passing through the UES, four esophageal segments are encountered: the pharyngeal, cervical, thoracic, and abdominal esophagus^[17].

Material and methods

The study was a prospective study that included 100 in patients and out patients seen in the Department of Medicine at, All India institute of medical sciences, Patna. Study duration of two years. with reflux symptoms, with a score of more than 8 in the FSSG questionnaire, and who met the inclusion criteria with no reasons for exclusion, and consented for the study. Patients were analyzed clinically and by endoscopic profiles and their response to PPI and Prokinetic combination assessed at the end of 4 weeks of therapy. Patients with symptoms of heartburn and regurgitation suggestive of gastro- esophageal reflux disease were included in the study.

Inclusion Criteria

Patients above 18 years of age.

In patients and out patients seen in the medicine department, with symptoms of heartburn and regurgitation suggesting gastro-esophageal reflux, with a score of more than 8 in the FSSG questionnaire. Patients who have consented for the study.

Exclusion criteria

Patients with systemic diseases affecting esophageal motility (mixed connective tissue disorder, visceral myopathies and visceral neuropathies).

Patients with BMI > 25kg/m².

Patients with absolute contraindications for endoscopy like the presence of shock. Patients with recent myocardial infarction (less than 3 months), postoperative states and serious systemic disease form relative contraindications for endoscopy.

The FSSG (Frequency Scale for Symptoms of Gastro-esophageal reflux) was applied to all patients. Patients with a score of 8 or more were classified as having symptomatic GERD and subjected to endoscopy and findings recorded and correlated with clinical severity. All patients were treated with Pantoprazole (40mg twice daily) and Itopride (50mg thrice daily) for a period of 4 weeks and followed up with regard to improvement in symptoms by applying the FSSG questionnaire again and comparing with previous scores.

Results

The present study was a prospective study carried out among 100 patients diagnosed with GERD. The following results are for these 100 patients. Among them there were 74 males and 26 females. In this study majority of the patients belonged to the age group of 30-44 years (31%). The mean age of the study population was found to be 46.68 (± 16.007). The age of the patients ranged from a minimum of 19 years to a maximum of 85 years.

Table 1: Distribution of the Study population by Gender and Age Groups

Age Group	Sex		Total
	Male	Female	
18 – 29 years	12 (16.2%)	5 (19.2%)	17 (17.0%)
30 – 44 years	24 (32.4%)	7 (26.9%)	31 (31.0%)
45 – 59 years	18 (24.3%)	8 (30.8%)	26 (26.0%)
≥60 years	20 (27.0%)	6 (23.1%)	26 (26.0%)
Total	74 (74.0%)	26 (26.0%)	100 (100%)

Majority of patients were from urban areas (55%). Out of the total patients who were residents of rural areas majority were above 60 years of age. Among the residents of urban areas majority belonged to the age group of 45-59 years.

Table 2: Distribution of the Study population by Place of Residence and Age Groups

	Place of Residence		Total
	Rural	Urban	
18 – 29 years	3 (6.7%)	14 (25.5%)	17 (17.0%)
30 – 44 years	16 (35.6%)	15 (27.3%)	31 (31.0%)
45 – 59 years	9 (20.0%)	17 (30.9%)	26 (26.0%)
≥60 years	17 (37.8%)	9 (16.4%)	26 (26.0%)
Total	45 (45.0%)	55 (55.0%)	100 (100%)

In the present study 51.0% patients had heartburn, Reduced appetite was the next major symptom seen in 40.0% patients, followed by nausea (33.0%), Pain abdomen (30.0%) and

regurgitation (21.0%).

Table 3: Distribution of the Study population by Gender and Smoking History

Gender	Smoking		Total
	No	Yes	
Male	43(58.1%)	31(41.9%)	74(74.0%)
Female	26(100%)	0(0%)	26(26.0%)
Total	69(69.0%)	31(31.0%)	100(100%)

Among males smoking history was present in 41.9% patients while none of the females had a history of smoking. The mean duration of smoking was 28.625 ± 16.02 pack years. However, the study found no significant association ($p=0.515$) between smoking and Reflux Esophagitis. In the present study, 21.0% patients had Hiatus Hernia among which majority (57.15%) had Erosive Esophagitis. All patients with Esophageal Varices had Non erosive reflux disease. 20.0% patients of the study population had Gastric Erosions and 70.0% among them had Non Erosive Reflux Disease. Out of the 13 patients with Duodenal Erosions 53.85% ($n=7$) had Non erosive reflux disease. In the study population, the mean FSSG total Score was $20.27 (\pm 5.393)$; the mean Reflux score was $10.10 (\pm 3.917)$ and the mean dysmotility score $10.17 (\pm 3.352)$ before treatment with PPI and Prokinetic combination. The mean FSSG total Score was $13.75 (\pm 5.323)$; the mean Reflux score was $6.10 (\pm 3.255)$ and the mean dysmotility score $7.63 (\pm 3.380)$ after treatment with PPI and Prokinetic combination. Among the treatment non responders in the study population, the reflux scores, the dysmotility scores and the total FSSG scores reduced by less than 50% of the pre treatment values though the reduction was overall statistically significant. In the present study, 76.0% patients were non responders to treatment indicated by a decrease in the FSSG scores to $\leq 50\%$ of the pre treatment scores.

Discussion

The present study was done to assess the clinical and endoscopic profile of GERD and its response to a combination of proton pump inhibitors and prokinetics. The study included 100 consecutive patients with symptoms suggestive of GERD and a score of >8 in the FSSG Questionnaire. A detailed history, examination and investigations were done for each patient. Laboratory investigations consisted of complete blood count, liver function tests, renal function tests, electrocardiography and chest roentgenogram. Upper Gastrointestinal endoscopy (Esophagogastroduodenoscopy) was done in all patients included in the study. Findings recorded as Erosive Esophagitis which was graded for severity according to the Los Angeles Classification (Grade A being the least severe to Grade D being the most severe); and endoscopies reported as normal mucosal study were considered as Non Erosive Reflux Disease in the study population where all patients had a FSSG score of >8 . In our study, age of the patients ranged from a minimum of 19 years to a maximum of 85 years. The mean age of the study population was found to be $46.68 (\pm 16.007)$. In this study majority of the patients belonged to the age group of 30-44 years (31%). This was comparable to a study conducted on the epidemiology and symptom profile of GERD in Indian population by the ISG task force which concluded that patients with GERD were older and the median age of patients was 40 years^[8]. The present study had 26 females and 74 males. Among the study population majority of patients were from urban areas (55%) and, out of the total patients who were residents of rural areas majority were above 60 years of age. The typical symptoms of GERD are heartburn

and regurgitation; and less commonly dysphagia and chest pain which may point to more sinister conditions. In the present study 51.0% patients had heartburn, reduced appetite was the next major symptom seen in 40.0% patients, followed by nausea (33.0%), Pain abdomen (30.0%) and regurgitation (21.0%). A study on the epidemiology and symptom profile of GER in Indian population by the ISG task force concluded that the prevalence of weekly heartburn was 5.9%. An earlier study from Mumbai had shown that 18.9% had heartburn at least once a month, and 4.2% subjects had frequent (\geq weekly) heartburn^[18]. A study conducted by Bhavadharini Ramu et al among 400 pregnant women, showed that 45.5% had GERD. 19.3% had heartburn, 13.5% had regurgitation and 12.8% had both. Age and gravida did not influence the prevalence of GERD. The difference in prevalence rates of symptoms can be explained on the basis that the previous studies did not use a symptom based score to assess GERD rather, symptoms were assessed based on frequency of occurrence. Out of the 100 patients 21% received H2 Receptor antagonists and 14% patients received proton pump inhibitors and 34% were treatment naïve for GERD. The rest of the study population had received other treatment. None had undergone a prior endoscopy. In the present study all patients with GERD who had a current history of smoking were males (31.0%). Among them majority were in the age group of 45-59 years. 5.0% of the study population were ex smokers and had stopped smoking one year prior to the study. The mean duration of smoking was 28.625 ± 16.02 pack years. However there were no statistically significant associations between smoking and reflux esophagitis ($p=0.515$). This was comparable with the ISG task force study, in which there were no significant associations between smoking and GERD ($p=0.64$). In the present study, the mean FSSG total Score was $20.27 (\pm 5.393)$; the mean Reflux score was $10.10 (\pm 3.917)$ and the mean dysmotility score $10.17 (\pm 3.352)$ before treatment with PPI and Prokinetic combination. The mean FSSG total Score was $13.75 (\pm 5.323)$; the mean Reflux score was $6.10 (\pm 3.255)$ and the mean dysmotility score $7.63 (\pm 3.380)$ after treatment with PPI and Prokinetic combination. There were statistically significant differences between pre treatment and post treatment FSSG scores (reflux score, dysmotility score and total score) among patients as observed by a p value of <0.0001 . The FSSG is a self-administered questionnaire developed by Kusano M et al in 2004, based on Japanese studies of the clinical signs and symptoms of GERD. The FSSG comprises 12 items to which patients with GERD most often answered "yes". Each response is assigned a score for the frequency of each symptom, as follows: 0, never; 1, occasionally; 2, sometimes; 3, often; and 4, always. With a cut off score of 8 points, the FSSG showed a sensitivity of 62% and specificity of 59% for Reflux Esophagitis based on endoscopic examination. In a study titled, Combination of PPI with a Prokinetic Drug in Gastroesophageal Reflux Disease by Suzanna Ndraha^[19], the mean FSSG score pre treatment was high (25.3 ± 8.2) comparable with the present study. This study showed there was a statistically significant improvement in FSSG score after treatment in group A (which was given omeprazole and domperidone) as well as in group B (omeprazole monotherapy). It proved that giving prokinetic together with PPI will have better results than giving PPI alone. In his study, Miyamoto et al found that a group that failed with PPI monotherapy had a mean FSSG score of 17.4, and then that group was given a combination therapy of PPI with prokinetic^[20]. All patients did not have uniform lifestyle modifications after the initial pre treatment scoring and this may have confounded treatment response in patients with GERD. A post treatment FSSG score was not assessed with a review endoscopy, this can be explained on the basis that most patients had Non erosive reflux disease and showed significant clinical improvement with treatment with PPI and prokinetics and did not consent for a review endoscopy.

Conclusion

Gastroesophageal reflux disease is on a rising trend in the Asian population than was previously thought and causes significant morbidity and changes in the health related quality of life. The

most common symptoms were heartburn (51.0%) and reduced appetite (40.0%). The present study in GERD patients showed that non erosive reflux disease (69.0%) was commoner than reflux/erosive esophagitis. Both findings were predominantly seen in males than in females, and in patients between the age group of 30-44 years.

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