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Esophageal Dysmotility in Patients with Gastroesophageal Reflux Disease

Amara Sadguna Rao [a++*], Preethi Mahalingam [a#], Priyansh Deven Bhayani [a++], K. R. Palaniswamy [a#], Ubal Dhus [a#] and Piramanayagam P. [a#]

[a] Department of Medical Gastroenterology, Apollo Main Hospitals, Chennai, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author PM raised the research question and wrote the protocol. Author ASR collected the data, performed the statistical analysis and wrote the first draft of the manuscript. Author PM corrected and finalized the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Gastroesophageal reflux disease (GERD) poses a spectrum of disorders characterized by heartburn and regurgitation. Diagnosis involves clinical assessments and Proton Pump Inhibitor (PPI) trials, but 24-hour pH impedance monitoring is the gold standard for objective evidence. Key diagnostic parameters include acid exposure time (AET) and nonacid bolus reflux episodes during impedance. GERD complications encompass reflux esophagitis, Barrett's esophagus, ulcers, hemorrhage, and peptic strictures. Notably, Ineffective Esophageal Motility (IEM) is linked to GERD, creating a cyclical relationship. This study aims to explore the correlation between esophageal dysmotility and GERD, shedding light on the controversial relationship.
Materials and Methods: This is a retrospective observational study Conducted from October 2010 to December 2021, which included 168 patients undergoing 24-hour pH impedance monitoring on and off PPI. Data collection involved clinical details and High-Resolution Manometry (HRM)

[++] DrNB Registrar;
[#] Consultant;
**Corresponding author: Email: sadguna.amara@gmail.com;*

findings. GERD was defined using the Demeester score and bolus reflux episodes, while IEM was diagnosed according to the Chicago 4.0 classification. The prevalence of IEM was compared between patients with and without GERD.

Results: Among the 168 patients (mean age: 44 years, 58.9% males, 41.1% females), 53.6% were on PPI during monitoring. IEM was present in 19% of patients, and objective evidence of GERD was found in 45.23%. Heartburn was significantly associated with GERD (67.1%). However, there was no statistically significant difference in regurgitation, chest pain, and extraesophageal symptoms between patients with and without GERD. IEM occurred in 22.4% of patients with GERD and 16.3% without, with no significant correlation (P=.316).

Conclusion: This study did not find a significant correlation between IEM and GERD. Nevertheless, these findings warrant validation through prospective studies to contribute to a comprehensive understanding of the relationship between esophageal dysmotility and GERD.

Keywords: Ineffective esophageal motility; 24-hour pH impedance monitoring; GERD; heartburn; regurgitation; chest pain; PPI.

ABBREVIATIONS

GERD : Gastro Esophageal Reflux Disease
IEM : Ineffective Esophageal Motility
PPI : Proton Pump Inhibitors
HRM : High-Resolution Manometry
SD : Standard Deviation
24hr : 24 hour
AET : Acid Exposure Time

1. INTRODUCTION

Gastro Esophageal Reflux Disease (GERD) is a spectrum of disorders that causes symptoms of heartburn and regurgitation. The spectrum contains Erosive reflux disease, non-erosive reflux disease, Reflux hypersensitivity and Functional heartburn [1]. It is defined as the reflux of gastric contents into the esophagus, resulting in symptoms and/or complications [2]. It is diagnosed by various methods like clinical questionnaires and PPI trials, but widely accepted and standardised objective evidence is by performing 24-hour pH impedance monitoring to diagnose and classify GERD [3]. Initially, the Demeester score was proposed to diagnose GERD. Still, Acid exposure time (AET) and computation of nonacid bolus reflux episodes during impedance are also equally important in the diagnosis of GERD [4].

GERD is complicated by reflux esophagitis, Barrett's esophagus, ulcers, hemorrhage and peptic strictures. In addition to the above, oesophagal motility disorders were also associated with GERD, especially Ineffective Esophageal Motility (IEM) [5]. Esophageal motility disorders are considered primary only after ruling out GERD as the secondary cause [6]. There is a vicious cycle between IEM and GERD as IEM causes decreased acid clearance from the esophagus, thereby increasing the exposure time to refluxate, which causes inflammation and further decreases contractility [7]. Some studies state that there is a positive correlation between the incidence of IEM and the severity of GERD [8]. There is a significant discrepancy in the studies on the incidence of postoperative dysphagia and improvement in already existing dysphagia after fundoplication for GERD between patients with preoperative IEM and normal oesophagal motility [9,10].

At present, total fundoplication is not contraindicated in patients with IEM, and partial fundoplication may be preferred in patients with aperistalsis [10,11]. Still, there is a need for robust data on the correlation between IEM and GERD. Most of the studies excluded the data of a large number of patients who could not discontinue Proton Pump Inhibitors (PPI) at the time of 24-hour pH impedance monitoring. So, this study aims to assess this correlation in patients referred for 24-hour pH impedance monitoring to a tertiary care centre for various symptoms.

2. MATERIALS AND METHODS

2.1 Methodology

This is a single-centre retrospective study conducted at the Department of Medical Gastroenterology, Apollo Hospital, Chennai, from October 2020 to December 2021. This study included 173 patients who were referred for 24-hour pH impedance monitoring to the Department of Medical Gastroenterology after excluding the patients who underwent prior foregut surgery or those who were on prokinetics

at the time of testing. Out of them, 5 patients were excluded due to incomplete data. Demographic details like age and gender and clinical details like symptoms at presentation, HRM findings, and 24-hour pH impedance monitoring reports were collected.

In patients off PPI (patients who discontinued PPI for at least 7 days prior to the time of testing), acid reflux was defined as DeMeester score >14.7 and/or acid (pH less than 4) exposure time more than 4.2%. Nonacid bolus reflux was defined as the total number of reflux episodes of more than 73 in patients who did not meet the criteria for acid reflux. In patients on PPI (patients who have taken the last dose of PPI within 7 days before testing), acid reflux was defined as a DeMeester score >14.7 and /or acid exposure time of more than 1.3%. Nonacid bolus reflux was defined as the total number of reflux episodes of more than 48 in patients who did not meet the criteria for acid reflux. GERD group included patients with positive test results for both acid and nonacid bolus tested on and off PPI. No GERD group included patients who did not meet the criteria for acid or nonacid bolus reflux. The IEM group included patients with Ineffective oesophagal motility and Absent peristalsis as defined by Chicago 4.0 classification on High-Resolution Manometry (HRM) [12,13].

As most of the studies were done by defining patients with GERD, as those who are positive only for acid reflux, analysis of data was done by dividing the patients into the Acid reflux group and the No acid reflux group.

Subgroup analysis was also done between patients who were on PPI and those who were off PPI at the time of testing to look for the effect of PPI on the correlation between IEM and GERD at the time of testing.

2.2 Statistical Analysis

Descriptive statistics were presented with frequency (%) and mean (SD) for the categorical & and continuous factors, respectively. The normality of the data was checked by using the Shapiro-Wilk test. The students' t-test was used to determine the significant differences in a mean between the two groups. The chi-square test/Fisher's exact test was used to find out the association between two independent categorical factors. *P*-value < 0.05 is considered as statistical significance. All the analysis was done by using the statistical software SPSS (IBM, 28.0).

3. RESULTS

3.1 Demographic Data

A total of 168 patients were included in the study. The study population had a mean age of 44 years (Standard deviation SD = 14.5 years), and males were 58.9% (99), and females were 41.1% (69).

3.2 Clinical Characteristics

Heartburn was noted in 75% of the patients, regurgitation symptoms were seen in 75.6% of the patients, chest pain was seen in 38.1%, and extra oesophagal symptoms like chronic dry cough, asthma-like symptoms and laryngitis were seen in 3.5% of the patients. 53.6% of the patients were taking PPI at the time of 24-hour pH impedance monitoring.

3.3 Prevalence of IEM and GERD

Ineffective oesophagal motility, as defined earlier, was present in 32 patients (19%). Objective evidence of GERD was present in 76 patients (45.23%), and no objective evidence of GERD was present in 92 patients (54.76%).

3.4 Comparison between Patients with GERD and without GERD

There was no difference in mean age and sex distribution between the two groups of patients with (44.915.9 years, M=57.9%, F=42.1%) and without GERD (43.413.7 years, M=59.8%, F=40.2%).

Interestingly, in patients with GERD, heartburn was present in 67.1%, whereas in patients without GERD, heartburn was present in 81.5% (*P*=0.032). However, when the data was analyzed, there was no significant difference in the prevalence of heartburn between patients with acid reflux (78.1%) and those without acid reflux (74.3%). We could not explain the reason for such a finding.

Table 1. Characteristics of patients with and without GERD

Parameters	Group, n (%)		Total, (n=168)	*P*-value
	GERD, (n=76)	NO GERD, (n=92)		
Age (In years)				0.512
Mean ± SD	44.9 ± 15.9	43.4 ± 13.7	44 ± 14.5	
Gender				0.804
Male	44 (57.9)	55 (59.8)	99 (58.9)	
Female	32 (42.1)	37 (40.2)	69 (41.1)	
Heart Burn	51 (67.1)	75 (81.5)	126 (75)	**0.032**
Regurgitation	60 (78.9)	67 (72.8)	127 (75.6)	0.359
Chest pain	27 (35.5)	37 (40.2)	64 (38.1)	0.532
Extraesophageal symptoms	1 (1)	5 (5.4)	6 (3.5)	0.118
IEM	17 (22.4)	15 (16.3)	32 (19)	0.316
PPI	54 (71.1)	36 (39.1)	90 (53.6)	**<0.001**

Table 2. Characteristics of patients with and without acid reflux

Parameters	Group, n (%)		Total, (n=168)	*P*-value
	Acid Reflux, (n=32)	No Acid Reflux, (n=136)		
Age (In years)				0.324
Mean ± SD	41.8 ± 14	44.6 ± 14.5	44 ± 14.5	
Gender				0.955
Male	19 (59.4)	80 (58.8)	99 (58.9)	
Female	13 (40.6)	56 (41.2)	69 (41.1)	
Heart Burn	25 (78.1)	101 (74.3)	126 (75)	0.655
Regurgitation	25 (78.1)	102 (75)	127 (75.6)	0.713
Chest pain	12 (37.5)	52 (38.2)	64 (38.1)	0.942
Extraesophageal symptoms	0	6 (4.4)	6 (3.6)	-
IEM	5 (15.6)	27 (19.9)	32 (19.1)	0.577
PPI	19 (59.4)	71 (52.2)	90 (53.6)	0.463

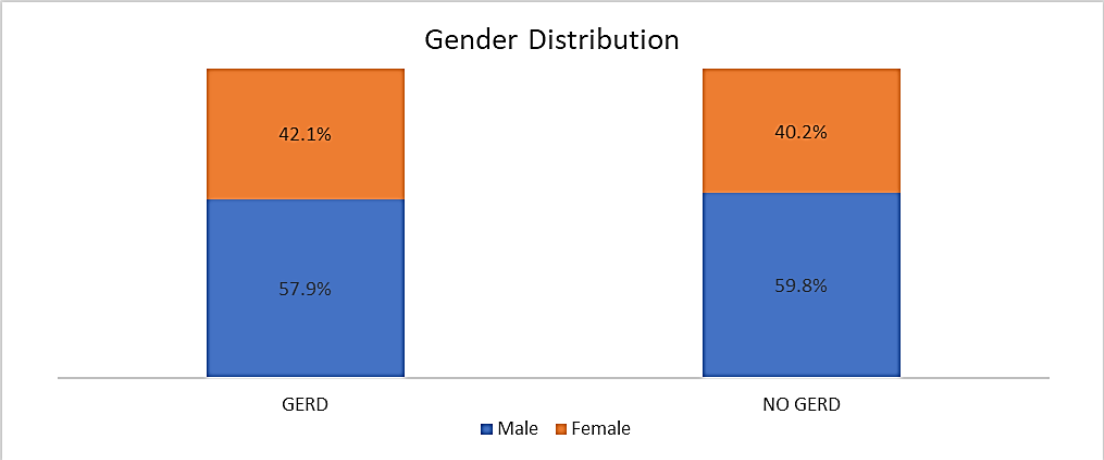

Fig. 1. Sex distribution

Table 3. Analysis of patients on and off PPI

IEM	On PPI (n=90), n (%)			Off PPI (n=90), n (%)		
	GERD	**NO GERD**	***P*-value**	**GERD**	**NO GERD**	***P*-value**
IEM	14 (25.9)	6 (16.7)	0.301	3 (13.6)	9 (16.1)	>0.99
NO IEM	40 (74.1)	30 (83.3)		19 (86.4)	47 (83.9)	
Total	54	36		22	56	

It was observed that there was no statistically significant difference in symptoms of regurgitation (78.9% vs. 72.8%), chest pain (35.5% vs. 40.2%) and extra oesophagal symptoms (1% vs. 5.4%) between patients with and without GERD.

PPIs could not be discontinued at the time of testing in a higher proportion(*P*=<0.001) of patients with GERD (71.1%) compared to the patients without GERD (39.1%).

3.5 Correlation of IEM with GERD

IEM was present in 22.4% of patients with GERD (17/76) compared to 16.3% of patients without GERD (15/92), but the difference was not statistically significant. Even when the data was reanalyzed by separating the groups as patients with and without acid reflux, the difference in IEM was found insignificant (15.6%vs19.9%) between the groups. This implies that there is no significant correlation between GERD and IEM in this group of patients.

3.6 Correlation of IEM and GERD in patients on and off PPI

The prevalence of IEM was not different between patients with and without GERD, whether patients were on or off PPIs.

4. DISCUSSION

By consensus, gastroesophageal reflux disease (GERD) has been defined as the effortless movement of stomach contents into the esophagus or mouth causing troublesome symptoms or complications. It is associated with both esophageal and extraesophageal symptoms [14]. Esophageal symptoms like heartburn, regurgitation are more common than extraesophageal symptoms like cough, hoarseness of voice and globus sensation.

Dent J et al showed that only 49% of the patients with GERD has problematic symptoms like heartburn and regurgitation. Our study showed that the prevalence of heartburn or regurgitation was about 75%. But these symptom frequencies, except for extraesophageal symptoms, are in concordance with some studies [15]. The prevalence of extraesophageal manifestations like chronic cough, asthma-like symptoms, and laryngitis was much lower than in other studies [16]. Jaspersen D et al showed a prevalence of 32.8% of extraesophageal symptoms in patients with GERD [17]. Cesario et al described a prevalence of 20-60% of extraesophageal symptoms in patients with GERD [18].

The prevalence of objective GERD in patients who were referred for refractory symptoms was

lower in this study (45.23%) compared to the Diamond study (66%). However, the cut-off value for acid exposure time was less in this study (4.2%) compared to the Diamond study (5.5%). This might be because of differences in criteria used to refer for 24-hour pH impedance monitoring by physicians, gastroenterologists, and surgeons. But this study population has a higher prevalence of heartburn (75%) and regurgitation (75.6%) compared to the Diamond study (49%). So, the threshold to refer the patients for 24-hour pH impedance monitoring was higher in this study, which was also represented by the inability to discontinue PPI in 53.6% of the study group.

In North America and in Europe, there is no association between sex and symptoms of GERD, but in South America and in the Middle East, women are approximately 40% more likely to report GERD symptoms than men [19]. There is no clear association between sex and esophageal stricture. However, men are at greater risk than women for erosive esophagitis. Also men are at greater risk for Barrett's esophagus and for esophageal adenocarcinoma than women [20]. In our study, there is no statistically significant difference between sex in both the groups of GERD and No GERD.

Ineffective esophageal motility is the most common motility disorder of esophagus in patients with GERD. GERD was described as a pathophysiologic factor for ineffective esophageal motility. Ineffective esophageal acid clearance was described as a risk factor for GERD. When there is severe defect in esophageal clearance, surgical correction of GERD (fundoplication) will be partial rather than complete wrap. But this correlation was not proven in high quality studies. Mittal R et al and Shetler et al showed a correlation between IEM and GERD [21,22]. But our study showed that, 22.4% of patients with GERD has IEM, but 16.3% of the patients without GERD also had IEM and the difference is not significant. This indicates that there is no significant correlation between IEM and GERD in our study population which was referred to 24hr pH impedance monitoring at tertiary care center. This difference was the same even when the analysis was done between the groups with patients on PPI and patients off PPI. This does not correlate with many of the existing studies [21,22]. This study included a good number of patients and is novel because strict criteria were used to define GERD as per the spectrum of disorders included in it. It also included patients tested on PPI. This negative correlation might be because of the design of the study (retrospective, single-centered) and referral bias. Further prospective, probably blinded, randomised controlled studies are needed to prove the correlation and causative association between GERD and IEM.

5. CONCLUSION

This retrospective study concluded that there was no statistically significant correlation between GERD and IEM, which is contrary to the previous studies, and this correlation needs to be confirmed by further studies.

ETHICAL APPROVAL AND CONSENT

Informed consent was taken under the institutional consent form to use the medical records and data for research purposes. Institutional Ethics Committee clearance was obtained for the study (EC/NEW/INST/2022/TN/0195).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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