Original Research Article

ESOPHAGEAL DYSMOTILITY IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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, with 24-hour pH impedance monitoring being 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) 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.

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. 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).

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 AND DISCUSSION

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%). The prevalence of GERD in patients with suspected GERD 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. The prevalence of extraesophageal manifestations like chronic cough, asthma-like symptoms, and laryngitis was much lower than in other studies. [14] But these symptom frequencies, except for extraesophageal symptoms, are in concordance with some studies.[15]

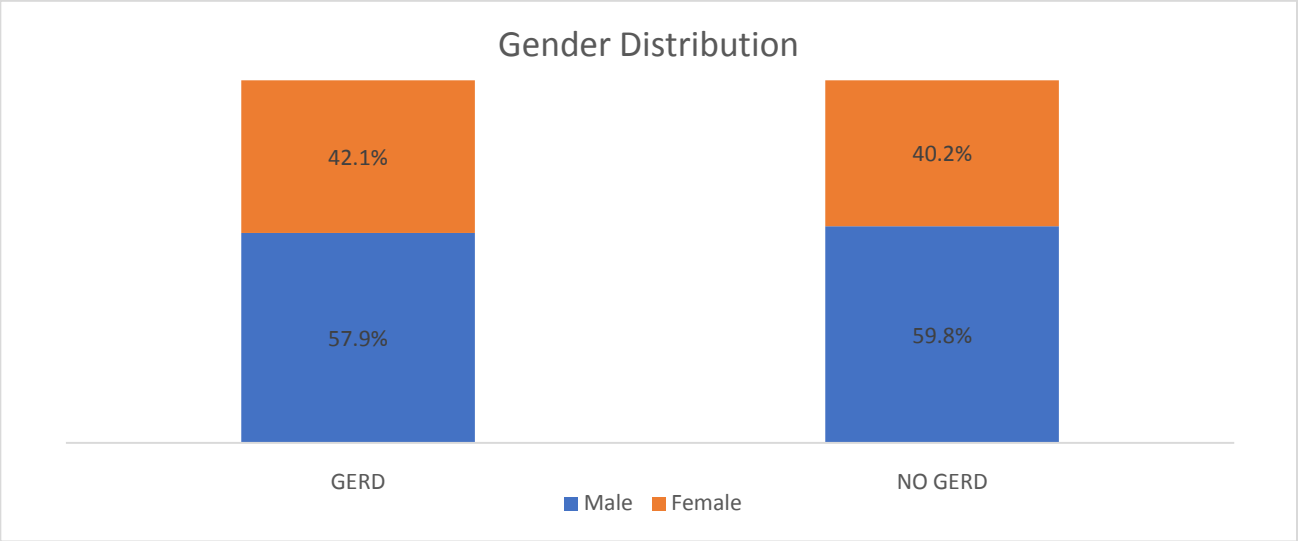
Table 1: Characteristics of patients with and without GERD

Parameters	**Group, n (%)**		**Total, (n=168)**	***P*-value**
	GERD, (n=76)	**NO GERD, (n=92)**		
Age (In years) Mean ± SD	44.9 ± 15.9	43.4 ± 13.7	44 ± 14.5	0.512
Gender				
Male	44 (57.9)	55 (59.8)	99 (58.9)	0.804
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
Chestpain	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**

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%).

Figure 1: Sex distribution



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 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) Mean ± SD	41.8 ± 14	44.6 ± 14.5	44 ± 14.5	0.324
Gender				
Male	19 (59.4)	80 (58.8)	99 (58.9)	0.955
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
Chestpain	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

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.

This inference does not correlate with many of the existing studies.[16,17]. 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.

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

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	

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

4. 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.

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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