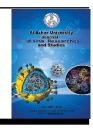


# Al-Azhar University Journal for Virus Research and Studies



Study of Postnasal Discharge Among Patients with GERD without Affection of Nose or Paranasal Sinuses and the Response to Treatment

Sahar Ahmed Saad<sup>1</sup>, Fatma Abd-Elkader Attia<sup>1</sup>, Fadila Mamdouh Elsayed<sup>2</sup>, Sammar Ahmed Kasim<sup>1</sup> and Ahmed Sobhi Abdelaal<sup>3</sup>

<sup>1</sup>Department of Internal Medicine, Faculty of Medicine for Girls, Al-Azhar University.

<sup>2</sup>Department of Diagnostic Radiology, Faculty of Medicine for Girls, Al-Azhar University.

<sup>3</sup>Department of Otolaryngology, Faculty of Medicine for Girls, Al-Azhar University.

\*E-mail: docsaharahmed18@gmail.com

## **Abstract**

Gastroesophageal reflux disease is a very common digestive disorder worldwide with an estimated prevalence of 18.1-27.8%. It is a condition with troublesome symptoms and complications that result from the reflux of stomach contents into the esophagus. To evaluate postnasal drip (PND) in patients with GERD without affection of nose or paranasal sinuses and to evaluate the role of PPI in the management of PND caused by GERD. The current study was conducted on forty patients with gastroesophageal reflux and postnasal drip, their ages range from 20-50 years old. In the current study, upper GI endoscopy was done to all the participants and it revealed that There were 12 patients with Esophagitis with incompetent cardia (30%), 10 patients with esophagitis (25%), 8 patients with Esophagitis with incompetent cardia and hiatus hernia (20%),3 patients with Esophagitis with hiatus hernia(7.5),2 patients with incompetent cardia (5%),2 patients with incompetent cardia with hiatus hernia (5%) and 3 patients with peptic ulcer (7.5%). Moreover, we found that there was a significant prevalence of GERD in males more than in females (60% to 40% prospectively) and the incidence is more common in the Middle Ages. Finally, our study shows that in the studied patients of GERD with PND after treatment with pantoprazole showing 29 patients (72.5%) improved and 11 patients (27.5%) not improved. PND is one of the common extra-esophageal manifestations of REFLUX. PND associated with GERD more common in males than females. PND has a higher incidence with typical symptoms of GERD than atypical symptoms. PPI is a good choice to manage PND associated with GERD.

**Keywords:** Gastroesophageal reflux disease, postnasal drip, proton pump inhibitor.

#### 1. Introduction

Gastroesophageal reflux disease (GERD) is a very common digestive disorder worldwide with an estimated prevalence of 18.1- 27.8%. It is a condition of troublesome symptoms and complications that result from the reflux of stomach contents into the esophagus Vakil et al., [1]. Risk factors for GERD include older age,

increased body mass index, smoking,

eating habits, anxiety/depression and less

physical activity Zheng et al., [2]. Gastroesophageal reflux is primarily a disorder of the lower esophageal sphincter (LES), but several factors may contribute to its development such as reduced lower esophageal sphincter (LES) pressure, hiatal hernias, impaired esophageal clearance, and delayed gastric emptying (Lin et al., [3]; Schubert, [4]. The classic and most common symptom of GERD is heartburn. GERD is a common cause of non-cardiac chest pain Bredenoord et al., [5]. Extra esophageal symptoms are more likely due to reflux into the larynx, resulting in throat clearing and hoarseness Lim et al., [6]. The most common diagnostic test used for the evaluation of GERD and its possible complications is the upper gastrointestinal endoscopy. The commonest benefit of endoscopy is to visualize the esophageal mucosa. This helps in the diagnosis of complications **GERD** of such esophagitis, strictures and Barrett's esophagus Garbin et al., [7]. Lifestyle changes remain the first line in the management of GERD with a primary goal of symptom reduction and improvement in quality of life. The only proven lifestyle modification for the management of GERD is head of bed (HOB) elevation Khan et al., [8]. In addition, factors contributing to the incidence of transient lower esophageal sphincter relaxations (TLESRs) should also be minimized or avoided DeVault et al., [9]. The primary acid-suppressive medications include H2 blockers and proton pump inhibitors. Schubert, [4]. Postnasal drip (PND) or catarrh is defined as the drainage of secretions from the nose or paranasal sinuses into the pharynx. Clinically, it is diagnosis is very vague, depending on history and examination and relies on the reporting of the patient of this sensation of something "dripping down the throat," rhinorrhoea and constant throat clearing. Nosendoscopy revealing rhinitis and mucopurulent secretions is suggestive but is not diagnostic (Cathcart and Wilson,

[10]. The study aimed to evaluate the relationship between extraesophageal manifestations of gastroesophageal reflux (EER) and postnasal drip (PND) in patients complaining of (GERD) radiographic or endoscopic evidence of sinonasal inflammatory disease. To evaluate the efficacy of anti-reflux treatment in the improvement of patients with symptomatic postnasal drainage.

#### 2. Material and Methods

The current study is a prospective cohort one. it was conducted on forty patients (40) with gastroesophageal reflux (evidenced by upper endoscopy) with postnasal drip, radiographic or endoscopic without evidence of Sino nasal inflammatory disease who were allocated from the outpatient clinic of the internal medicine department and ENT department, Al-Zahraa University Hospital, Cairo, Egypt. Informed consent was obtained from each patient before enrollment to the study after explaining the content and implication of the study. The study was reviewed and approved by the ethical committee of the Faculty of Medicine for Girls, Al-Azhar University.

#### 2.1 Inclusion criteria

Patients with symptoms of GERD are associated with PND. Patients between the age of 20-50 years old (males and females). They received proton pump inhibitors (Pantoprazole 40mg) for three months then reevaluated again by nasal and para-nasal endoscopic examination to assess the effect of treatment.

#### 2.2 Exclusion criteria

Patients below 20 years or over 50 years. Cocomittent chronic diseases as diabetes or hypertension. Current infectious disease. Allergic disease or acute or chronic sinus disease. Patients with history of esophageal or gastric surgery. Chronic liver and kidney

diseases. Ischemic heart disease. pregnant females were excluded.

### 2.3 Methodology

All participants were subjected to the following: (1) Thorough medical history taking and physical examination which focused on Personal history (age, sex and smoking). Medical history of GERD symptoms and postnasal drip Laboratory investigations include Complete blood count. (2) Liver function test which includes (Albumin, bilirubin total and direct) and liver enzyme (ALT, AST). (3) Renal function test which includes (Blood urea, and serum creatinine). (4) Peripheral venous blood samples were collected under complete aseptic conditions. Upper gastrointestinal endoscopy. (5) An upper **GI** endoscopy is a procedure to diagnose and treat upper GI problems. Endoscopic examination of the nose and para nasal sinus in ENT office: Nasal endoscopy is a procedure to look at the nasal and sinus passages. Computed Tomography (CT)nose and para nasal sinus: We use TOSHIBA Aquilion PRIME 160 slice Device in our study. After the patients with postnasal discharge were diagnosed GERD with upper GIT

Table (1): Description of age and sex in all studied patients.

endoscope, the patients submitted to antiefflux treatment with pantoprazole 40 mg once daily for 3 months and subjective assessed after treatment.

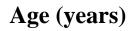
## 2.4 Statistical analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. Quantitative data were expressed as mean ±SD with minimum and maximum. Qualitative data were expressed as frequency and percentage. Mean (average): the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. Standard deviation (SD): is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicates that the values are spread out over a wider range.

#### 3. Results

The total number of patients in the study was 40, with 24 (60 %) of them being male and 16 (40%) being females. The patients ranged in age from 20 to 50 years old as shown in table 1 and figure 1 and 2.

		Studied Patients. (N = 40)	
	Mean ±SD	35.9 ± 8.4	
Age (years)	Min - Max	20 – 50	
	Male	24	60%
Sex	Female	16	40%



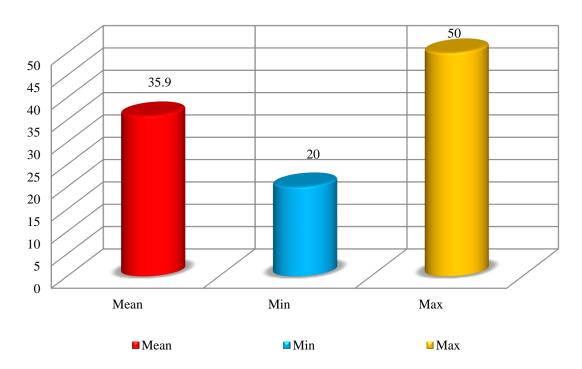


Figure 1: Methods of Percutaneous pinning.

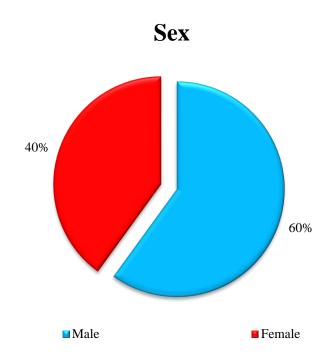


Figure 2: Description of sex in all studied patients.

The most common symptoms associated with PND in our studied patients were classic symptoms (heartburn or acid regurgitation) in 55%. atypical extraesophageal symptoms (hoarseness of voice, cough, sense of lump in the throat, dysphagia) with PND in 35 % and only PND in 15% as displayed in Table 2. The upper GIT endoscope of the studied patients with GERD revealed esophagitis in 82.5%, incompetent cardia in 60%, hiatus hernia in 32.5% and peptic ulcer in 7,5% as shown in Table 3. Anti-reflux treatment (pantoprazole 40 mg once daily) was administered to all the participants. Evaluating the severity of postnasal discharge visual analogue scale (VAS) in our studied patients before medical treatment shows: moderately severe PND in 8 patients (20%), severe in 27 patients

(67%) and moderate in 5 patients (13%). The (VAS) was assessed for 3 months postmedical treatment with pantoprazole,12 patients were cured (30%),12 patients were improved (55%) and 6 patients (15%) showed no improvement of their PND Table 4. When comparing the values of (VAS) at the time of diagnosis, to the values at the 3rd month after medical treatment with pantoprazole 20 mg twice daily, VAS scores were significantly lower at 3 months (M = 7.4 pre-medical treatment was changed into 1.7; p = 0.001) demonstrate a considerable improvement as shown in Table 5. The studied patients underlying upper GIT endoscope and proton pump inhibitors were subjected to complete laboratory investigations (CBC, liver function tests and renal function tests) as shown in Table 6.

**Table (2):** Distribution of the clinical presentation of the studied patients with PND.

			ed patients. N = 40)
Classic symptoms of GERD associated with PND	PND classic symptoms of GERD	22	55%
	PND with a typical symptom of GERD	2	30%
	Only PND	6	15%

PND: Postnasal discharge GERD: Gastroesophageal reflux

Table (3): Findings of upper GIT endoscopy of the studied patients of GERD with postnasal discharge.

	Count	%	
Upper GIT endoscope of the studied patients of GERD with postnasal discharge.	Esophagitis	10	25%
	esophagitis with incompetent cardia	12	30%
	Esophagitis with hiatus hernia	3	7.5%
	Esophagitis with incompetent cardia and hiatus hernia	8	20%
	Incompetent cardia with hiatus hernia	2	5%
	incompetent cardia	2	5%
	Peptic ulcer	3	7.5%

GITE: Gastrointestinal endoscope GERD: Gastroesophageal reflux

**Table (4):** The studied patients of GERD with PND before and after 3 months of treatment with pantoprazole according to VAS.

		Count	%
Pre-treatment severity of postnasal	moderately severe PND	8	20.0%
discharge (VAS)	severe PND	27	67.0%
	Moderate PND	5	13.0%
Post-treatment (VAS) after 3 months	Cured	12	30.0%
	Improved	22	55%
	Unchanged	6	15%

#### VAS: Visual analogue scale.

Table (5): Comparison of (VAS) premedical treatment at the time of diagnosis and after 3 months of medical treatment.

	Mean	Standard Deviation	Median	P value
Pre-treatment severity of PND (VAS)	7.40	1.39	7.92	
Post-treatment (VAS) after 3 months of pantoprazole 40 mg once daily treatment	1.70	2.17	1.00	< 0.001

VAS: Visual analogue scale, \*. The mean difference is significant at the 0.05 level.

 $\textbf{Table (6):} \ \ \textbf{Description of laboratory data in all studied patients}.$ 

(n = 40)	Minimum	Maximum	Mean	±SD
Hb	9.7	16.7	12.7	1.7
HCT	31	50	39.6	5.6
MCV	77	95	84.1	4.5
MCH	22	30	26.9	2.0
PLT	133	500	268.4	90.6
WBCs	4.2	13.2	8.4	2.8
Lymph	0.7	3.4	1.9	0.7
Neutrophil	1.6	11	6.1	2.8
Eosinophil	0	1.5	0.2	0.3
Basophil	0	0.3	0.0	0.1
ALB	3.5	4.5	4.0	0.3
Bilirubin	0.09	1.2	0.7	0.3
ALT	9	41	23.3	9.0
AST	17	48	32.2	7.7
Create	0.2	1.4	0.8	0.3
Urea	3	52	28.2	10.2

Hb: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, PLT: Platelet, WBCs: White blood cells Lymph: Lymphocyte, ALB: Albumin, ALT: alanine transaminase, AST: Aspartate transaminase.

## 4. Discussion

Gastroesophageal reflux disease (GERD) is defined as the presence of troublesome reflux or erosive complications in the esophagus due to retrograde reflux of gastric contents Vakil et al. [1]. While classically considered a disease of excess acid, up to 50% of patients with GERD experience little to no relief with pharmacologic acid suppression Ang et al., [11]. Gastroesophageal reflux disease (GERD) is a common clinical problem, affecting millions of people worldwide with an estimated prevalence of 18.1-27.8% in North America El-Serag et al., [12]. The current study is a prospective cohort one conducted on forty patients with gastroesophageal reflux (evidenced by upper endoscopy) with post-nasal drip, without radiographic or endoscopic evidence of Sino-nasal inflammatory disease. In the current study, forty patients complained of GERD symptoms (60% were males and 40% were females) and this result is in agreement with Eiko et al. [13] study which done over 1859 was participants and revealed that GERD prevalence in adult males was significantly higher than that in adult females (15.1% vs 9.4%, P < 0.001). On the other hand, Jorabar et al. [14] disagree with our study as the systemic review they done revealed that the prevalence of GERD according to gender was reported in 50 studies. The pooled prevalence of GERD in females (17.17% (95% CI 14.22%-120.33%)) was moderately higher than in CI (15.69% (95% 13.15% 118.42%)). Hashem [15] study which was performed on 803 patients stated that of the 803 participants, 60.5% (n= 486) were female, and 69.2% (n= 555) were younger than 50 years. Of those patients older than 50 years, 32.8% (n= 81) were female. Moreover, 31.0% (n= 249) of the patients had erosive esophagitis (ERD), and 69.0% (n= 254) had normal esophageal mucosa (NERD). The female-to-male ratio was

1/1.06 and 1.94/1 in ERD and NERD patients, respectively. Hiatal hernia was more prevalent in females than in males. In our study,24 of the studied patients (60%) were males while 16 of them (40%) were females. This mismatch between our study and others may be due to the higher incidence of heavy smoking, unhealthy food style and stressful conditions among males in our society than in females. The fact that patients with GERD with ENT signs and symptoms deny the presence of GERD symptoms such as heartburn or regurgitation makes it difficult to establish a relationship between the two. Because pH monitoring and UGIE are not routinely used as first-line investigations of these conditions, formal diagnosis is dependent on history and subjective mechanisms. Our research revealed PND as extra esophageal symptoms with the other classic symptoms and with other extraesophageal symptoms occurred more with esophagitis in 82.5% as revealed with upper GIT endoscope. This the finding correlated with retrospective and more recent prospective studies that demonstrate that asthma as eosophageal extra manifestation prevalent in patients with GERD in 30-90%.12. The current study shows a significant incidence of classic symptoms of GERD associated with PND more than atypical symptoms as the distribution of the clinical presentation of the studied patients (GERD with PND)., classic symptoms of GERD with PND were in 22 patients (55%), Atypical symptoms of GERD with PND in 14patients (35%) and only PND in 6 patients (15%.). According to the Marlina et al. [16] study, the most common complaint was heartburn (27.8%), followed by a lump in the throat (12%). (22.2) percent). It is based on a study by Mallikarjunappa and Deshpande [17], who found that 93.9 percent of people suffer from heartburn symptoms. Heartburn was most common symptom also the encountered by LPR patients, according to

another study conducted by Mishra et al. [18] (38 percent). In a study done by Patigaroo et al. [19] the most common symptoms of laryngopharyngeal reflux were foreign body sensation in 74% followed by frequent throat clearing 64%. After 16 weeks of PPI foreign body sensation and frequent throat clearing dropped to 6.5, this coincides with our study in which the post-nasal drip was improved in 72.5 of patients after 3 months (12 weeks) of PPI. This study is similar to other studies done by Belfasky and Postma [20] and Bilgen and Ogut [21]. The most utilized diagnostic test for the evaluation of GERD and its possible complications is the gastrointestinal endoscopy, esophago gastro duodenoscopy (EGD). The primary benefit of endoscopy is direct visualization of the esophageal mucosa. the diagnosis This assists in of complications of **GERD** such as esophagitis, strictures and Barrett's esophagus Garbin et al., [7]. This coincides with our study where we evaluated the GERD by upper GIT endoscopy, and found esophagitis in 82.5 %, incompetent cardia 60%, hiatus hernia 32.5%, and peptic ulcer in 7.5%. In the current study, upper GI endoscopy was done to all the participants and it revealed that There were 12 patients with Esophagitis with incompetent cardia (30%), 10 patients with esophagitis (25%), patients with **Esophagitis** incompetent cardia and hiatus hernia (20%),3 patients with Esophagitis with patients hiatus hernia (7.5),2incompetent cardia (5%), 2 patients with incompetent cardia with hiatus hernia (5%) and 3 patients with peptic ulcer (7.5%). Our findings were consistent with those of Johan et al. [22], who studied 405 ENT patients with suspected GERD and 545 typical GERD patients and found that the prevalence of erosive esophagitis (52.3 percent vs 38.4 percent; p 0.05), primarily grade 1 (31.9 percent vs 22.7 percent; p 0.05), and peptic ulcer (8.4 percent vs 4.3 percent; p 0.05) was significantly higher. Kamel et al. [23], was the first to utilize a PPI, and he used omeprazole. PPIs, which are more potent acid-suppressive drugs, have been employed in recent trials. We in our study PPI which pantoprazole. Since the introduction of PPI in the early 1990s, they have become the gold standard in the treatment of GERD due to their efficacy and relatively low risk of side effects Carter and Dickman, [24]. The current study shows that the studied patients of GERD with PND after treatment with pantoprazole showing 29 patients (72.5%) improved and 11 patients (27.5%) not improve. Due to a lack of unanimity, most research used PPIs at varied doses and for different lengths of time. In the majority of studies, PPIs are administered before meals. To better regulate both nighttime and daytime for esophageal acid exposure, a twice-daily dosage is commonly used. This correlates with our study, the PPI was used daily with the same measures. In the study done by Patigaroo et al. [19] did not come across any PPI-resistant individuals, this does not correlate with our study where 27.5% of patients did not improve. Even though resistance has been recorded in a considerable percentage of patients, Amin. employed according to We pantoprazole 40 mg once daily and the improvement in significant portion. Our study is consistent with Marlina et al. [16],18 patients were included, and they revealed that the mean RSI (reflux score index) score before therapy in this study was 16.78 with a standard deviation of 2.102. After 14 days of therapy with lansoprazole twice a day before meals, there was a decrease in the mean RSI score to 9.94 with a standard deviation of 2.155. It is according to the research conducted by Febriyanti [25], where there was a significant difference in mean, 18.47 with a standard deviation of 4.35 at the start of the assessment and 10.94 with a standard deviation of 3.90 after two weeks of therapy with omeprazole 20 mg twice. the day before meals (p < 0.05). Another study conducted by Lee et al. [26], also stated a significant change in the RSI score after

receiving PPI therapy for four weeks, from 13.15 with a standard deviation of 8.68 to 10.03 with a standard deviation of 8.97 (p. <0.01). It is also in line with a study conducted by Silva et al. [27], which showed a significant decrease in the RSI score after PPI administration, from the mean initial score before treatment of 16.0 to 10.5 after being given therapy (p <0.001).

## 5. Conclusion

## References

- 1- Vakil N, van Zanten SV, Kahrilas K, et al. (2006): The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. Am. J. Gastroenterol. 101: 1900–1920.
- 2- Zheng Z, Nordenstedt H, Pedersen NL, Lagergren J, Ye W (2007): Lifestyle factors and risk for symptomatic gastroesophageal reflux in monozygotic twins. Gastroenterology. 132:87–95.
- 3- Lin S, Li H, Fang X (2019): Esophageal motor dysfunctions in gastroesophageal reflux disease and therapeutic perspectives. Journal of neurogastroenterology and motility, 25(4): 499.
- 4- Schubert ML (2004): Gastric secretion. Current opinion in gastroenterology, 20(6): 519-525.
- 5- Bredenoord AJ, Weusten BL, Curvers WL, Timmer R, Smout AJ (2006): Determinants of perception of heartburn and regurgitation. Gut; 55:313-318.
- 6- Lim KG, Morgenthaler TI, Katzka DA (2018): Sleep and nocturnal gastroesophageal reflux: an update. Chest, 154(4): 963-971.
- 7- Garbin N, Mamunes AP, Sohn D, Hawkins RW, Valdastri P, Obstein KL (2019): Evaluation of a novel low-cost disposable endoscope for visual assessment

PND is one of the common extraesophageal manifestations of REFLUX. PND associated with GERD is more common in males than females. PND has a higher incidence with typical symptoms of GERD than atypical symptoms. PPI is a good choice to manage PND associated with GERD.

**Funding Sources:** There was no support for this study from any governmental, private, or non-profit Organization.

**Conflicts of interest:** No competing interests.

- of the esophagus and stomach in an ex-vivo phantom model. Endoscopy international open, 7(09): E1175-E1183.
- 8- Khan BA, Sodhi JS, Zargar SA, Javid G, Yattoo GN, Shah A, et al. (2012): Effect of bed head elevation during sleep in symptomatic patients of nocturnal gastroesophageal reflux. J Gastroenterol Hepatol. 27:1078–1082.
- 9- DeVault KR, Castell DO American College of Gastroenterology (2005): Updated guidelines for the diagnosis and treatment of gastroesophageal reflux disease. Am J Gastroenterol. 100:190–200.
- 10-Cathcart RA and Wilson JA (2011): "Should chronic catarrh patients seen in primary care be referred for further investigations?" International Journal of Clinical Practice, 49(4): 387–391.
- 11-Ang D, How CH, Ang TL (2016): Persistent gastro-oesophageal reflux symptoms despite proton pump inhibitor therapy. Singapore Med. J. 57: 546–551.
- 12-El-Serag HB, Sweet S, Winchester CC, Dent J (2014): Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. Gut 63:871-880.
- 13-Eiko O, Ishimura N, Morito Y, Mikami H, Shimura S, Uno G, Tamagawa Y, Aimi M, Oshima N, Kawashima K, Kazumori H

- (2015): Prevalence of gastroesophageal reflux disease in children, adults, and elderly in the same community. Journal of gastroenterology and hepatology. 30(7):1140-6.
- 14-Jorabar NS, Hasan SS, Conway BR, Ghori MU (2020): Global prevalence and risk factors of gastro-oesophageal reflux disease (GORD): systematic review with meta-analysis. Scientific reports. 10(1):1-4.
- 15-Hashem YF (2017): Gender is a risk factor in patients with gastroesophageal reflux disease. Medical journal of the Islamic Republic of Iran. 31:58.
- 16-Marlina L, Poluan FH, Zebua RL (2021): Improvement of the life quality for laryngopharyngeal reflux patients after receiving proton pump inhibitor (ppi) therapy at the ent-kl polyclinic of uki hospital January 2021-february 2021. International Journal of Research-Granthaalayah. 9(4):281-96.
- 17-Mallikarjunappa AM, Deshpande GA (2020): Comparison of Reflux Symptom Index (RSI) with Reflux Finding Score (RFS) and Its Effectiveness in Diagnosis of Laryngopharyngeal Reflux Disease (LPRD). Indian Journal of Otolaryngology and Head & Neck Surgery. 1-5.
- 18-Mishra P, Agrawal D, Artham P (2020): Screening Test for LPRD: History Versus Video Laryngoscopy. Indian Journal of Otolaryngology & Head & Neck Surgery. 72(4).
- 19-Patigaroo SA, Hashmi SF, Hasan SA, Ajmal MR, Mehfooz N (2011): Clinical manifestations and role of proton pump inhibitors in the management of laryngopharyngeal reflux. Indian Journal of Otolaryngology and Head & Neck Surgery. 63(2):182-9.

- 20-Belfasky PC and Postma GN (2001): The validity and reliability of reflux finding score. The laryngoscope. 111:1313–1317.
- 21-Bilgen C and Ogut F (2003): The comparison of empiric proton pump inhibitor trial versus 24-hour double probe Ph monitoring in laryngopharyngeal reflux. J Laryngo Otol. 117:386–390.
- 22-Johan P, Feenstra L, Demedts I, Rutgeerts P, Tack J (2004): The yield of upper gastrointestinal endoscopy in patients with suspected reflux-related chronic ear, nose, and throat symptoms. Official journal of the American College of Gastroenterology ACG. 99(8):1419-26.
- 23-Kamel PL, Hanson D, Kahrilas PJ (1994): Omeprazole for the treatment of posterior laryngitis. Am J Med. 96:321–6.
- 24- Carter D and Dickman R (2018): Practice styles, knowledge and attitudes of general practitioners and gastroenterology specialists who treat gastroesophageal reflux disease. Medicine (Baltimore): 97 (52): e13781.
- 25- Febriyanti R (2014): Perbedaan Kualitas Hidup Pada Penderita Refluks Laringofaring Sebelum dan. Tesis), 1–106.
- 26- Lee JS, Lee YC, Kim SW, Kwon KH, Eun YG (2014): Changes in the quality of life of patients with laryngopharyngeal reflux after treatment. Journal of Voice, 28(4): 487–491.
- 27- Silva ÁS, Duprat AC, Machado SR, Melo DN, Ribeiro DK (2021): Evaluation of the reflux symptom index and the endolaryngeal findings scale after treatment in individuals with laryngopharyngeal reflux. International Archives of Otorhinolaryngology. 25:115-22