

Fasting Gastric Acidity Evidential Effect on Esophageal Mucosal Damage

Achnes Pangaribuan¹, Iga Suryadarma², Wira Gotera²

pangaribuan2002@gmail.com

¹Internal Medicine Study Program, Faculty of Medicine, Udayana University/Sanglah Hospital
Denpasar, Indonesia

²Internal Medicine Department / KSM, Faculty of Medicine, Udayana University/Sanglah
Hospital Denpasar, Indonesia

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Abstract

Gastric substances that potentially increase the esophageal mucosal damage are gastric acid, pepsin, bile salts, and pancreatic enzymes. From all of these substances, the highest potential for reflux damage is gastric acid. Although the main cause of clinical symptoms of GERD is acid reflux, it has been known that there are subgroups with typical reflux symptoms that do not provide sufficient response or not responsive to PPI treatment. Despite the improvement of esophagitis, there are no clinical improvements in reflux symptoms of 30% of respondents. Therefore, this study was designed to determine fasting gastric acidity with endoscopic findings in patients with GERD. A comparative-analysis study, which determines the fasting gastric acidity from endoscopic findings in patients with GERD. Samples recruited using the consecutive sampling technique and divided into groups of esophagitis and non-esophagitis reflux. A total of 40 samples were involved in this study. The Mann-Whitney test was used for analyzing the difference between fasting gastric acidity from endoscopic findings of esophagitis lesions in a patient with GERD. The median value for fasting gastric acidity in the esophagitis reflux group was 1.88 (0.82-4.84), whereas the median value for fasting gastric acidity in the non-esophagitis reflux group was 2.49 (0.68-5.97). The Mann-Whitney test result was $p=0.298$ ($p>0.05$). This study shows that there is no significant difference in fasting gastric acidity from endoscopic findings between esophagitis and nonesophagitis reflux groups in patients with gastroesophageal reflux disease (GERD). This study shows that esophagitis lesions are not affected by gastric acidity.

Keywords: Gastroesophageal Reflux Disease (GERD), Esophagitis, Non-Esophagitis, Refluxat, Fasting Gastric Acidity

Introduction

The pathogenesis of GERD is very complex and multifactorial. GERD occurs due to an imbalance between the offensive and defensive factors of the esophageal mucosal defense systems and gastric reflux substances. Gastric substances that potentially increase the esophageal mucosal damage are gastric acid, pepsin, bile salts, and pancreatic enzymes. From all of these substances, the highest potential for reflux damage is gastric acid. A pH level less than 4 has been defined as a margin in which gastric reflux able to injure the esophagus. Ayazi et al., (2009) confirmed that there is a clear inverse relationship between fasting gastric acidity and esophageal acid exposure. There is an

inverse correlation between the escalation of fasting gastric pH and the total percentage of time esophageal pH less than 4.

In recent years, gastric acid has been shown to play a major role in GERD pathogenesis and proton pump inhibitors (PPIs) are the first choice treatment in GERD patients. Although the main cause of clinical symptoms of GERD is acid reflux, it has been known that there are subgroups with typical reflux symptoms that do not provide sufficient response or not responsive to PPIs treatment. Despite the improvement of esophagitis, there are no clinical improvements in reflux symptoms of 30% of respondents (Sifrim & Zerbib, 2012; Richter, 2009). This result shows that acid reflux is not a major cause of GERD. To test the hypothesis, we designed a study to determine fasting gastric acidity between esophagitis and non-esophagitis reflux from endoscopic findings.

Methods

This study was conducted using a comparative-analysis study. The sample population consisted of GERD patients who visited/came for control visits at the Gastroenterology Division of the Department of Internal Medicine of the Faculty of Medicine of the Udayana University/Sanglah Public Hospital from September 2019 until March 2020. A total of 40 GERD patients, which were confirmed with GERD questionnaire (GERD-Q) ≥ 8 and fulfilled inclusion and exclusion criteria, were recruited with consecutive sampling technique. Upper gastrointestinal endoscopy concomitant with measurement of fasting gastric acidity was performed after at least 24 hours without acid-suppressive medication. In view of the need for more diagnostic accuracy of esophageal mucosal damage, a high definition endoscopy coupled with narrow-band imaging (NBI) was performed. Furthermore, esophagitis reflux is classified according to the Los Angeles classification. The measurement of fasting gastric acidity is done with a digital pH meter (\square TRIMETER). Statistical analyzes were performed using SPSS 20. (Windows version; SPSS Inc, Chicago [IL], USA). The Mann-Whitney test was used for analyzing the difference between fasting gastric acidity from endoscopic findings of esophagitis lesions in patient with GERD.

Results and Discussion

A total of 40 subjects recruited in this study, which were divided into esophagitis reflux and non-esophagitis reflux. In addition, there were higher number of females participants than males, with the percentage 72,5% (29 subjects) and 27,5% (11 subjects) respectively, while the average age of both gender was 42.85 ± 15.84 years. As seen from the endoscopic result, we found more subjects without hiatal hernia compared to participants with hiatal hernia, with around 80% (12 subjects) and 20% (8 subjects) respectively. The median value for fasting gastric pH in patient with GERD was 2.06 (0.68-5.97). Moreover, there were 32 (80%) subjects with gastric pH < 4 and 8 (20%) with gastric pH ≥ 4 . In esophagitis reflux group, there were 17 (85%) subjects with gastric pH < 4 with the median value of fasting gastric pH 1.88 (0.82-4.84), whereas in non-esophagitis group there were 15 (75%) subjects with gastric pH < 4 with the median value for fasting gastric pH 2.49 (0.68-5.97). As a result, the demography characteristic of fasting gastric pH and esophageal mucosal damage from endoscopic findings can be seen in tabel 1 and table 2 below.

Table 1. Characteristics variables patient with GERD

Variable	n = 40
Sex, n (%)	
Male	11 (27.5%)

Female	29 (72.5%)
Age (years), mean \pm SD	42.85 \pm 15.84
BMI, mean \pm SD	22.36 \pm 3.45
Underweight (BMI < 18.5)	5 (12.5%)
Normal (BMI 18.5-24.9)	29 (72.5%)
Overweight (BMI 25-29.9)	5 (12.5%)
Obese (BMI \geq 30)	1 (2.5%)
GERDQ score, mean \pm SD	10.68 \pm 1.34
Hernia hiatal	
Present	8 (20%)
Absent	32 (80%)
Fasting gastric pH, median (min-max)	2.06 (0.68-5.97)

Table 2. Differences in characteristics between ERD dan NERD group

Variable	ERD	NERD	p value
Sex			0,723
Male	5 (25%)	6 (30%)	
Female	15 (75%)	14 (70%)	
BMI, mean \pm SD	22,07 \pm 2,97	22,42 \pm 3,77	0,706
Underweight (BMI < 18,5)	3 (15%)	2 (10%)	
Normal (BMI 18,5-24,9)	14 (70%)	15 (75%)	
Overweight (BMI 25-29,9)	3 (15%)	2 (10%)	
Obese (BMI \geq 30)	0 (0%)	1 (5%)	
GERDQ score, mean \pm SD	11,05 \pm 1,05	10,30 \pm 1,52	
Hernia hiatal			0,114
Present	6 (30%)	2 (10%)	
Absent	14 (70%)	18 (90%)	
Gastric pH, median (min-max)	1.88 (0.82-4.84)	2,49 (0,68-5,97)	
Gastric pH < 4 / pH \geq 4	17/3	15/5	0,429

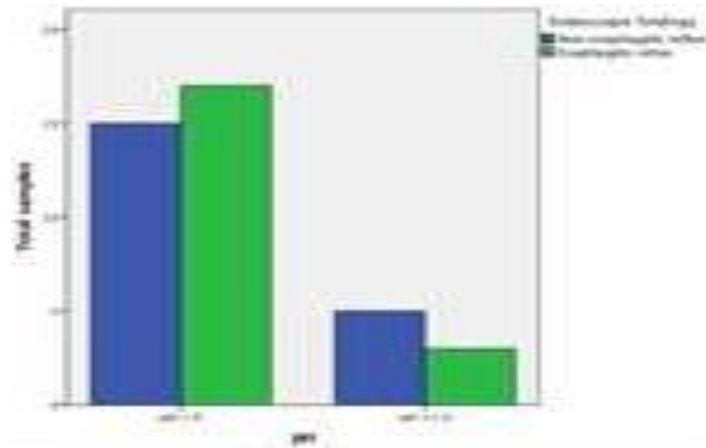


Figure 1. Frequency of fasting gastric pH determine by $\text{pH} < 4$ or $\text{pH} \geq 4$ and endoscopic findings in patient with GERD.

The Mann-Whitney was used to determine fasting gastric acidity between esophagitis and non-esophagitis reflux. The Mann-Whitney test result showed no significant difference, with $p=0.298$ ($p>0.05$).

Tabel 3. Association between fasting gastric pH in esophagitis and non-esophagitis reflux from endoscopic findings

		n	pH	p value
Endoscopic findings	NERD	20	2.495 (0.68-5.97)	p = 0.298
	ERD	20	1.88 (0.82-4.84)	

Mann-Whitney test

In this study we found that the median value for fasting gastric pH in the esophagitis reflux group was 1.88 (0.82-4.84), whereas the median value for fasting gastric acidity in the non-esophagitis reflux group was 2.49 (0.68-5.97). The Mann-Whitney test result was $p=0.298$ ($p>0.05$). The result from this study shows that there is no significant difference of fasting gastric pH between esophagitis and non esophagitis reflux groups (GERD) from endoscopic findings. This study shows that esophagitis lesions are not affected by fasting gastric pH. Therefore, this result was similar with several previous studies.

Boeckxstaens & Smout. (2010) a metaanalysis study suggested that the proportions of reflux episodes are acidic ($\text{pH} < 4$), weak acidic ($\text{pH} 4-7$) and weak alkaline ($\text{pH} > 7$) in adult patients with GERD, in order to evaluate their correlation with symptoms, this study stated that the proportion of acid reflux episodes did not differ between patients without reflux esophagitis and those who had reflux esophagitis. The same result was obtained by Bredenoord et al., (2006) comparing the characteristics of reflux episodes from the control group, NERD and patients with varying degrees of oesophagitis and Barrett's esophagus, also stated that the proportion of total reflux episodes that were acidic, weak and alkaline were similar in each group and only had slight variation between controls, NERD, reflux esophagitis and Barrett's esophagus.

Hirschowitz (1991) stated that there was no significant increase in gastric basal acid output (BAO), stimulated gastric acid secretion and maximum gastric acid secretion (MAO) against esophagitis lesions. Zhu et al. (1998) assessed the relationship between BAO and esophagitis lesions in patients with GERD, only esophagitis and reflux esophagitis with duodenal ulcer proved that there is no parallel relationship between BAO and the severity of esophagitis reflux with or without duodenal ulcer, suggesting that BAO is not a major pathogenetic factor in GERD.

The pathogenesis of GERD is very complex and not fully understood. The mechanism when reflux episodes become clinically manifested is determined by duration and volume of the reflux, the ability of the esophagus to neutralize refluxat with bicarbonate from saliva, and the degree of acid reflux Tack & Pandolfino, 2018). However, some important questions remain unanswered. For instance, in some patients with reflux esophagitis (ERD) do not have severe clinical manifestations compared with non-esophagitis (NERD), reflux with normal pH can cause clinical manifestations in patients with NERD and some patients with ERD experienced remission spontaneously with placebo while in some other patients do not show improvement in esophagitis lesions even after received optimal PPIs therapy.

Because the severity of esophageal damage cannot be predicted based on the amount of time acid contacts the esophageal mucosa, nor can the pH of esophageal refluxate predict the severity of symptoms, researchers have proposed that factors other than the acidity of refluxate or the amount and duration of exposure to refluxate might determine esophageal damage. Several studies demonstrate mucosal resistance, inflammation, and free radical damage are major determinants in the progression of reflux esophagitis (Patrick, 2011). In studies with animal models, oxidative stress has more relevant role than acid exposure in the pathogenesis of esophageal ulceration. This study stated that the administration of ethanol extracted from artemisia asiatica as an antioxidant is more effective to prevent the erosion of esophagus compared to ranitidine (Oh et al., 2001). Therefore, it explains that immunologic response played a bigger role than caustic injury.

Conclusion

Finally, the result of this study provides a strong evidence that esophageal mucosal damage is not affected by gastric acidity.

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