

Primary bile reflux gastritis versus *Helicobacter pylori* gastritis: a comparative study

Enaase A.M.E. Barakat^a, Neven F. Abbas^b, Nashwa Y. El-Kholi^c

^aDepartment of Internal Medicine, Taibah University, Medina, Kingdom of Saudi Arabia,

^bDepartment of Internal Medicine, Faculty of Medicine, Mansoura University, Mansoura,

^cDepartment of Internal Medicine, Al-Azhar University, Cairo, Egypt

Correspondence to Enaase A.M.E. Barakat, MD, Department of Internal Medicine, Faculty of Medicine, University of Mansoura, Mansoura, 35516, Egypt. Tel: +20 100 582 6658; fax: +20 (50) 239733; e-mail: dr_enaas@hotmail.com

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Background

Bile reflux gastritis (BRG) is a common disorder, with few data on its pathophysiology and clinical course, whereas *Helicobacter pylori* is the well-known, commonest cause of chronic gastritis.

Aim

The aim of this study was to compare between BRG and *H. pylori*-related gastritis, as regards demographic data, comorbid conditions, and pattern of upper gastrointestinal involvement.

Patients and methods

It included 130 patients with endoscopic features of gastritis, subdivided into three groups: group A with BRG (56 patients); group B with *H. pylori* gastritis (58 patients); group C with gastritis in the presence of both *H. pylori* and bile reflux (16 patients). Statistical analysis was made to compare between the three groups as regards demographic data, history, and examination findings including endoscopic findings.

Results

BRG is more common among younger age (21–30 years) and elderly patients (71–80 years), whereas *H. pylori* gastritis is more common in patients in the middle age group (31–60 years), the female/male ratio was 1.5 : 1 in patients with BRG, 1 : 1 in *H. pylori* gastritis. Nausea was the commonest symptom in patients with BRG (69.6%), whereas epigastric pain/discomfort was the commonest symptom (77.6%) in *H. pylori* gastritis. Diabetes was found to be more common in patients with *H. pylori* gastritis (29.3%) followed by BRG (26.8%), whereas obesity was more common in patients with BRG (76.8%) followed by *H. pylori* gastritis (65.5%). Endoscopy showed antral gastritis in cases with BRG (57.1%), pangastritis in *H. pylori* and mixed etiology gastritis (60.3 and 68.8%, respectively), reflux esophagitis in both BRG and *H. pylori* gastritis (41.1 and 44.8%, respectively), higher than mixed etiology gastritis (25%). Endoscopic Barrett's mucosa was diagnosed in 10.7% of cases with BRG and 12.1% of cases with *H. pylori* gastritis. Duodenitis, duodenal erosions, or ulcerations were more common in cases with mixed etiology gastritis (62.5%), than in *H. pylori* gastritis (24.1%), followed by BRG (14.3%).

Conclusion

BRG is a common, underdiagnosed condition, with distinct clinical and endoscopic features from *H. pylori* gastritis.

Keywords:

bile reflux, diabetes mellitus, gastritis, *Helicobacter pylori*, obesity

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Introduction

Bile reflux gastritis (BRG) is caused by an excessive reflux of bile, pancreatic, and intestinal secretions into the stomach. It occurs in either: gastric resection and primary biliary reflux due to the failure of pylorus [1]. This can cause many complications such as peptic ulcer and antral gastritis [2]. The combination of bile reflux and *Helicobacter pylori* infection may cause progression to gastric cancer not by traditional stepwise: inflammation–atrophy–metaplasia [3].

The aim of this prospective study was to compare between BRG and *H. pylori* gastritis, as regards demographic data, comorbid conditions, and pattern

of upper gastrointestinal involvement during endoscopic diagnosis.

Patients and methods

This was a prospective comparative study including 130 patients with endoscopically diagnosed gastritis, who were subdivided into three groups:

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- (1) Group A having biliary reflux gastritis (endoscopic evidence of gastritis in the presence of excess bile in the stomach and negative rapid urease test for *H. pylori*, using gastric biopsy) included 56 patients.
- (2) Group B having *H. pylori* gastritis (endoscopic evidence of gastritis and positive rapid urease test for *H. pylori*, using gastric biopsy) included 58 patients.
- (3) Group C having gastritis, in the presence of both *H. pylori* and bile reflux, included 16 patients.

All patients included in the study were above 18 years old (adults), of both sexes and were selected by the gastroenterologist among patients with upper gastrointestinal dyspeptic symptoms (e.g. nausea, epigastric discomfort, or pain) attending the inpatient and outpatient clinics of the Gastroenterology and Hepatology Unit at the Internal Medicine Department, Riyadh National Hospital, between July 2010 and June 2014. All the patients provided written informed consent. The Institutional Review Board (IRB) of Riyadh National Hospital approved the study.

Patients were excluded from the study if they have hiatal hernia diagnosed by endoscopy (to exclude the contributing factor to reflux esophagitis). Patients with prior upper gastrointestinal surgery causing abnormal emptying mechanisms of the stomach (e.g. gastric bypass surgery) and patients unfit or are nonwilling to do gastrointestinal endoscopy were also excluded from this study.

The patients' demographic data, history, and examination findings including endoscopic findings were recorded. In diagnostic upper gastrointestinal endoscopy, the presence of bile into the stomach, erythema of the gastric mucosa with or without erosions, mucosal ulcerations were recognized, and *H. pylori* test (rapid urease test) results were obtained.

SPSS, version 18 (SPSS Inc., Chicago, Illinois, USA) was used to conduct all the analysis. Independent *t*-test and one-way analysis of variance test were used to compare between different groups.

Results

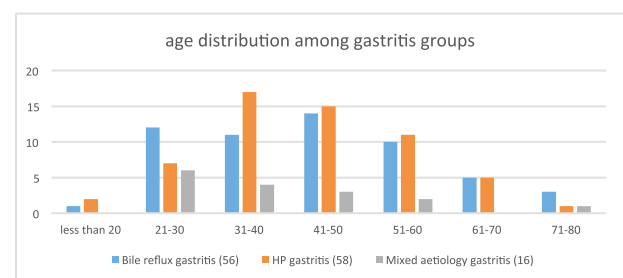
Over a 4-year period we investigated the distinctive features of BRG from *H. pylori* gastritis, the mean age of patients with BRG was 45.03±14.4 years, patients with *H. pylori* gastritis was 43.62±13.1 years, whereas the mean age of patients with mixed etiology gastritis was 38.25±14.1 years. There was no significant difference on comparing different groups ($P=0.22$) (Table 1).

Age distribution of patients with BRG showed a bimodal pattern where it was more common among younger age groups (21–30 years) and elderly patients (71–80 years), whereas *H. pylori* gastritis was more common among patients in the middle age group (31–60 years) (Fig. 1).

Female patients were more common in the BRG group, with a ratio of 1.5 : 1. In patients with mixed etiology gastritis men predominate (ratio of 2 : 1), whereas patients with *H. pylori* gastritis showed equal sex distribution (1 : 1) (Table 1).

Nausea was the most commonly reported symptom in patients with BRG followed by epigastric pain/discomfort (69.6 and 58.9%, respectively), whereas in patients with *H. pylori* gastritis, epigastric pain/discomfort was the most commonly reported symptom followed by heartburn (77.6 and 36.2%, respectively). Epigastric pain/discomfort was also the most commonly reported symptom in patients with mixed etiology gastritis, followed by nausea (81.2 and

Figure 1



Age distribution of patients in different gastritis groups. HP, *Helicobacter pylori*.

Table 1 Age and sex distribution of different gastritis groups

	Bile reflux gastritis (n=56) [n (%)]	<i>Helicobacter pylori</i> gastritis (n=58) [n (%)]	Mixed etiology gastritis (n=16) [n (%)]	P
Age	45.03±14.4	43.62±13.1	38.25±14.1	0.22
Sex				
Male	22 (39.3)	29 (50)	11 (68.8)	
Female	34 (60.7)	29 (50)	5 (31.2)	

56.3%, respectively). Heartburn was found to be present in patients with either BRG or *H. pylori* gastritis with comparable frequency (33.9% in BRG vs. 36.2% in *H. pylori* gastritis), whereas it was less common in patients with mixed etiology gastritis (18.8%).

Hematemesis was more common in patients with mixed etiology gastritis (12.5%) than *H. pylori* gastritis (8.6%), followed by BRG (3.6%) (Table 2).

The study investigated the association of gastritis with diabetes mellitus (DM) and obesity. Diabetes was found to be more common in patients with *H. pylori* gastritis (29.3%), followed by BRG (26.8%) and gastritis of mixed etiology (12.5%), whereas obesity was more frequent in patients with BRG (76.8%) followed by *H. pylori* gastritis (65.5%) and gastritis of mixed etiology (56.3%). The mean of BMI was compared in the three groups and there was no significant difference among them ($P: 0.35$) (Table 3).

Endoscopic findings were reported in the three groups; antral gastritis was the commonest endoscopic finding in cases with BRG (57.1%), whereas pangastritis was the commonest in *H. pylori* and mixed etiology gastritis (60.3 and 68.8%, respectively).

Reflux esophagitis was found in both BRG and *H. pylori* gastritis (41.1 and 44.8%, respectively) and in each was higher than mixed etiology gastritis (25%). Endoscopic Barrett's mucosa was diagnosed in 10.7% of cases with BRG, 12.1% of cases with *H. pylori* gastritis, where none of the cases with mixed etiology gastritis showed Barrett's mucosa (Table 4).

Duodenal involvement (as duodenitis, erosions, or ulcerations) was much more prominent in cases with mixed etiology gastritis (62.5%), than *H. pylori* gastritis (24.1%), followed finally by BRG where it was found in only 14.3% of patients (Table 4).

Table 2 Clinical presentation of patients of different gastritis groups

	Bile reflux gastritis (n=56) [n (%)]	<i>Helicobacter pylori</i> gastritis (n=58) [n (%)]	Mixed etiology gastritis (n=16) [n (%)]
Epigastric pain/discomfort	33 (58.9)	45 (77.6)	13 (81.2)
Heartburn	19 (33.9)	21 (36.2)	3 (18.8)
Nausea	39 (69.6)	11 (19)	9 (56.3)
Vomiting	11 (19.6)	5 (8.6)	5 (31.3)
Hematemesis	2 (3.6)	5 (8.6)	2 (12.5)

Discussion

BRG is a kind of gastritis which is caused by reflux of bile contents through the duodenum on the stomach [4]. It is a common disorder which usually occurs after stomach surgeries in which the pyloric sphincter is damaged (secondary BRG) [1,5]. Sometimes it can occur spontaneously without earlier surgeries (primary BRG) [1]. Many studies described secondary BRG; however, primary BRG and its relation to *H. pylori* gastritis were not extensively studied previously. The aim of this study was to compare between primary BRG and *H. pylori*-related gastritis as regards demographic data, comorbid conditions, and pattern of upper gastrointestinal involvement during endoscopic diagnosis.

Age distribution of patients with BRG showed a bimodal pattern which was more common among younger age groups (21–30 years) and elderly patients (71–80 years), whereas *H. pylori* gastritis was more common among patients in the middle age group (31–60 years). This was agreed upon by Vere *et al.* [1], who found that the BRG was more frequent at older ages, with incidence being higher between 51 and 80 years. Another study on *H. pylori* has confirmed that *H. pylori*-associated nonatrophic gastritis and antral atrophic gastritis peak at the age of

Table 3 Prevalence of diabetes mellitus and obesity in patients in different groups

	Bile reflux gastritis (n=56) [n (%)]	<i>Helicobacter pylori</i> gastritis (n=58) [n (%)]	Mixed etiology gastritis (n=16) [n (%)]
Diabetes mellitus	15 (26.8)	17 (29.3)	2 (12.5)
Obesity	43 (76.8)	38 (65.5)	9 (56.3)
Mild	25 (44.6)	20 (34.5)	6 (37.5)
Moderate	16 (28.6)	12 (20.7)	3 (18.8)
Severe	2 (3.6)	2 (3.4)	0 (0)
Morbid	0 (0)	4 (6.9)	0 (0)
BMI*	27.9±4.3	28.32±7.9	25.75± 5.1

*There was nonsignificant difference in BMI among the three groups ($P=0.35$).

Table 4 Endoscopic findings in patients of different groups

	Bile reflux gastritis (n=56) [n (%)]	<i>Helicobacter pylori</i> gastritis (n=58) [n (%)]	Mixed etiology gastritis (n=16) [n (%)]
Reflux±Barrett's mucosa	23 (41.1)	26 (44.8)	4 (25)
Barrett's mucosa	6 (10.7)	7 (12.1)	0 (0)
Antral gastritis	32 (57.1)	23 (39.7)	5 (31.3)
Pangastritis	23 (41.1)	35 (60.3)	11 (68.8)
Duodenitis/duodenal ulcer	8 (14.3)	14 (24.1)	10 (62.5)

41–50 years, with a decline thereafter [6]. This can be explained by the need of shorter time to develop *H. pylori*-related gastritis than bile reflux – alkaline gastritis which has later presentation, whereas in the very young age group (21–30 years) of BRG, functional bowel disorders predominate and usually are more severe in this age group.

Female patients were more common in the BRG group, with a ratio of 1.5 : 1. In patients with mixed etiology gastritis men predominate (ratio of 2 : 1), whereas patients with *H. pylori* gastritis showed equal sex distribution (1 : 1); to our knowledge, no previous studies compared sex predominance in BRG compared with *H. pylori* gastritis, but individual studies on each showed similar results of female predominance in primary BRG [7–12], whereas men predominate in *H. pylori* infection [13,14]. However, in another study, sex and age were not significantly different in *H. pylori* infection [15]. This can be explained by the underlying functional pathophysiology of primary BRG which is frequent in female patients, contrary to the infection by *H. pylori* with similar exposure rates in either sex.

The study investigated the association of gastritis with DM and obesity as both may be considered as risk factors for primary BRG as it affects gastric motility and emptying. DM was found to be more common in patients with *H. pylori* gastritis (29.3%) followed by BRG (26.8%) and gastritis of mixed etiology (12.5%). The association between *H. pylori* and DM was first explored by Simon *et al.* [16], whereas the increased prevalence of reactive gastritis (which includes both BRG and NSAID-related gastritis) in diabetic patients was reported in another study [17]. Immunosuppression in DM was hypothesized to be a predisposing factor for *H. pylori* infection [18,19], which can explain the increased prevalence of DM in patients with *H. pylori* gastritis in our study.

Obesity was more frequent in patients with BRG (76.8%) followed by *H. pylori* gastritis (65.5%) and gastritis of mixed etiology (56.3%). The mean of BMI was compared in the three groups and there was no significant difference among them ($P=0.35$). To our knowledge, none of the earlier studies investigated the role of obesity in BRG. Wolter *et al.* [20] have found that gastritis was the commonest endoscopic finding in obese patients during endoscopic evaluation before bariatric surgery, but they did not clarify the etiopathogenesis of gastritis. However, the association of obesity with other functional disorders like gastroesophageal reflux disease (GERD) was studied and confirmed [21–23]. The association of obesity with

primary BRG in our study can be explained as obesity may affect the gastroduodenal reflux in a similar way as in gastroesophageal reflux.

Barrett's esophagus (BE) is a premalignant condition which develops as a consequence of GERD [24–26]. In our study, reflux esophagitis was observed in both BRG and *H. pylori* gastritis (41.1 and 44.8%, respectively) and in each was higher than mixed etiology gastritis (25%). Endoscopic Barrett's mucosa was diagnosed in 10.7% of cases with BRG, 12.1% of cases with *H. pylori* gastritis, where none of the cases with mixed etiology gastritis showed Barrett's mucosa.

There is much recent evidence pointing to a role for duodenogastric bile reflux and bile acids in the pathogenesis of BE [27–30]. Patients with BE have more evidence of BRG than subjects with uncomplicated GERD or nonulcer dyspepsia in the esophagus [31], as bile acids could be the source of carcinogens which act on the metaplastic mucosa to produce neoplasia [32]. As regards *H. pylori* infection, it could pose a risk for the onset of GERD, which could in turn trigger BE [33]. The combined effect of both BRG and *H. pylori* infection for the development of GERD and BE is an important area for further research.

Conclusion

BRG is a common problem with different presentation and risk factors, which may need specific management than *H. pylori* gastritis.

Recommendations

BRG is a new area of research, and more studies are needed on a larger scale to study its pathogenesis as a primary functional gastrointestinal disorder, its risk factors and complications.

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Conflicts of interest

There are no conflicts of interest.

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