

# Gastric Mucosal Changes and Frequency of *Helicobacter pylori* in Patients with Gastroenterostomy

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## Abstract

**Objective:** We investigated endoscopic and pathological changes in the gastric mucosa and the frequency of *Helicobacter pylori* (Hp) infection in patients undergoing gastroenterostomy surgery.

**Materials and Methods:** Patients who were admitted to our hospital between November 2009 and April 2010 and who had previously undergone gastroenterostomy surgery for any reason were included in the study. The control group consisted of patients without gastroenterostomy who underwent routine endoscopy.

**Results:** Hp was positive in 10 of 70 patients with gastroenterostomy (14.3%) and in 30 of 50 patients (60%) in the control group. The difference between the two groups was statistically significant ( $p<0.001$ ). Intestinal metaplasia was detected in 22 of 70 patients (31.4%) and in 8 of 50 patients (16%) in the gastroenterostomy and control groups, respectively ( $p=0.054$ ). Atrophic gastritis was detected in 42 of 70 patients (60%) and in 15 of 50 patients (30%). The difference was statistically significant ( $p<0.01$ ). Dysplasia and adenocarcinoma were detected in 4 (5.5%) patients (dysplasia in 1 patient, adenocarcinoma in 3 patients) in the gastroenterostomy group, but not in the control group ( $p<0.02$ ).

**Conclusion:** This study showed that the frequency of enterogastric reflux increased in patients who underwent gastroenterostomy and correspondingly decreased Hp's frequency. The incidence of atrophic gastritis and dysplasia from precancerous gastric lesions is significantly higher in patients who undergo gastroenterostomy. In light of these results, because enterogastric reflux and Hp have a synergistic damage effect on the gastric mucosa, we recommend that patients with gastroenterostomy should be tested for Hp, and if positive, they should be eradicated, and biopsies should be taken from the distal remnant gastric mucosa close to the stoma line.

**Keywords:** Aging, cell biology, geriatric care management, geriatric palliative care, geriatrics

## Introduction

Reflux of bile, pancreatic, and small intestinal secretions from the duodenum into the stomach is called enterogastric reflux. In general, these secretions are not normally found in the stomach. Insufficient pyloric function plays an important role in the reflux of duodenal contents into the stomach (1). Enterogastric reflux in the stomach increases by 30-100% after subtotal gastrectomy, pyloroplasty, and cholecystectomy (2,3). Billroth-I (B-I) is a gastroduodenostomy procedure that can be performed end-to-end or side-to-side. In a Billroth-II (B-II) operation, a side-to-side gastrojejunostomy is performed.

The decisive difference between B-I and B-II is that in B-I, the duodenal passage remains intact. Because of the nature of the anastomosis, antrectomy is typically performed in B-I as a rule. In cases requiring more extensive resection, B-II and Roux-en-Y (R-Y) surgery are preferred because of postoperative complications. In R-Y surgery, the afferent loop coming from the duodenum is connected more distally to the efferent jejunum segment anastomosed to the stomach. Therefore, bile reflux into the stomach is less common in R-Y surgery than in B-II surgery (4). If gastric emptying is not sufficient and delayed, gastric contents, including excess bile, remain for a prolonged time and have harmful effects on the gastric mucosa. Biliated duodenal

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content can cause damage to the gastric mucosa with local effects. Duodenal contents combine with gastric secretions in the stomach and cause mucosal damage (1). Histopathological evaluations of the gastric mucosa are graded as mild, moderate, and severe according to the modified Sydney classification based on chronic inflammation, neutrophil activity, glandular atrophy, intestinal metaplasia, and *Helicobacter pylori* (Hp) density (5).

The coexistence of enterogastric reflux and Hp infection is thought to increase damage to the gastric mucosa (6). In the long term, after gastric surgery, the reflux of bile back into the stomach is a factor in the development of stomach ulcers and stomach cancer. Chronic epithelial damage, particularly due to enterogastric reflux, may facilitate cancer development by increasing mucosal cell proliferation (7).

Although Hp infection is highly prevalent in our country and has been investigated in various conditions, it has not been adequately studied in patients who have undergone gastrectomy. In addition, it remains controversial whether eradication should be applied when Hp infection is detected after gastrectomies (8). We investigated the endoscopic and pathological findings in the gastric mucosa and the frequency of Hp infection in patients undergoing gastroenterostomy.

## Materials and Methods

Patients who were admitted to the Gastroenterology Clinic of Türkiye Yüksek İhtisas Hospital between November 2009 and April 2010 and who had previously undergone gastroenterostomy surgery for any reason were included in the study. The control group consisted of patients without gastroenterostomy who underwent routine endoscopy. The study was designed as a single-center cross-sectional study. Written consent from each patient was obtained before entering the study. Patients with B-II, R-Y, and simple gastroenterostomy (SG) were included in the study. Patients who had previously undergone Hp eradication therapy and those who had been taking antibiotics and proton pump inhibitors (PPI) within the last 3 months were excluded from the study. The control group consisted of patients who had requested endoscopy for any reason, had not previously undergone Hp eradication therapy, and had not used antibiotics or PPIs in the last 3 months. All

endoscopic procedures were performed using video endoscopes with local throat anesthesia (xylocain 10%) following at least 12 h of fasting. The endoscopic appearance of dense bile and bile sludge on an edematous, hyperemic, and easily vulnerable mucosa was evaluated as endoscopic enterogastric reflux. In patients with gastroenterostomy, biopsy samples were obtained from four quadrants of the remnant mucosa close to the stoma and the proximal gastric remnant mucosa. In the control group, biopsies were obtained from all four quadrants of the antrum and corpus. All biopsies were evaluated using giemsa stain by a single pathologist. The Sydney classification was used to evaluate pathological findings. In addition, pathologically reactive gastropathy findings suggestive of enterogastric reflux (gland structures with cystic changes, hypercellularity in gastric pits, smooth muscle fibers between glands, foveolar hyperplasia, capillary congestion and vasodilation in superficial lamina propria) were examined. As a standard practice, the pathological evaluation of enterogastric reflux in patients undergoing gastric surgery was performed in the remnant gastric mucosa close to the stoma. Therefore, enterogastric reflux evaluation was not conducted in the proximal remnant mucosa. Endoscopic and pathologic findings of patients with or without previous gastric surgery were compared according to enterogastric reflux and Sydney classification Table 1 (5). The correlation between the endoscopic and pathological findings was evaluated. Ethical approval for the study was obtained from the clinical ethics committee of Türkiye Yüksek İhtisas Hospital (approval number: 242, date: 04.08.2010).

## Statistics

Statistical evaluation was performed using SPSS vs. 18.0 (SPSS Inc., IL, USA). Two-sample t-test when comparing different data, chi-square test when multiple variables need to be compared, Mann-Whitney U test when it is necessary to compare data whose distributions are shown not to be homogeneous; was used. In cases where p-values were less than 0.05, the result was considered statistically significant.

## Results

Seventy patients who underwent gastroenterostomy surgery and 50 control patients who underwent upper gastrointestinal

**Table 1. Modified Sydney classification**

	Histopatological grade		
	Mild	Moderate	Severe
Chronic inflammation	+	++	+++
Neutrophilic infiltrate	<1/3	1/3-2/3	>2/3
Atrophy	<1/3	1/3-2/3	>2/3
Intestinal metaplasia	+	++	+++
Hp density	+	++	+++

Hp: *Helicobacter pylori*

endoscopy for various reasons were included in the study. The distribution of the 70 patients with gastroenterostomy was as follows: 7 patients with R-Y anastomosis (10%), 18 patients with SG (25%), and 45 patients (64%) with B-II. The mean age was  $62.7 \pm 4.4$  years in patients with R-Y anastomosis,  $58.9 \pm 2.2$  years in SG patients,  $63 \pm 1.5$  years in B-II patients, and  $55.4 \pm 1.9$  years in the control group. There was no statistically significant difference in the mean age between the groups of gastroenterostomy patients. The mean time elapsed after the operation was  $10.4 \pm 2.5$  years in patients with R-Y anastomosis,  $18.1 \pm 2.3$  years in patients with SG, and  $14.7 \pm 2.1$  years in patients with B-II. The reason for gastroenterostomy was peptic ulcer in 50 of the 70 patients, adenocarcinoma in 19, and neuroendocrine tumor in one patient. When the groups were examined, 5 (71.4%) patients in the R-Y group were operated on for peptic ulcer and 2 (28.6%) patients for adenocarcinoma. In the SG group, all 18 (100%) patients underwent surgery for peptic ulcer, whereas in the B-II group, 27 (60%) patients underwent surgery for peptic ulcer, 17 (37.8%) for adenocarcinoma, and one patient for neuroendocrine tumor. Demographic characteristics and statistics are provided in Table 2.

#### Distal gastric biopsy examinations in patients with gastroenterostomy

Hp was positive in 10 of 70 patients with gastroenterostomy (14.3%) and in 30 of 50 patients (60%) in the control group. The difference between the two groups was statistically significant ( $p < 0.001$ ). Intestinal metaplasia was detected in 22 of 70 patients (31.4%) and in 8 of 50 patients (16%) in the gastroenterostomy and control groups, respectively ( $p = 0.054$ ).

Pathologic activity according to Sydney classification was positive in 32 of 70 patients (48.6%) and in 25 of 50 (25%) patients. No significant difference was found ( $p = 0.6$ ). Chronic inflammation was positive in 58 of 70 patients (82.9%) and in 46 of 50 patients (92%) in the gastroenterostomy and control groups, respectively. No significant difference was found ( $p = 0.1$ ). Atrophic gastritis was found in 42 of 70 patients (60%) and 15 of 50 patients (30%). The difference was significant ( $p < 0.01$ ). Dysplasia and adenocarcinoma were detected in 4 (5.5%) patients (dysplasia in 1 patient, adenocarcinoma in 3 patients) in the gastroenterostomy group but not in the control group. A comparison of distal gastric biopsy samples from gastroenterostomy patients and control group patients is provided in Table 3.

#### Proximal gastric biopsy examinations in patients with gastroenterostomy

In the gastroenterostomy and control groups, 14 of 70 patients (20%) and 31 of 50 patients (62%) were positive for Hp. The difference between the two groups was significant ( $p < 0.001$ ). The rate of intestinal metaplasia was detected in 13 of 70 patients (18.6%) and in 7 of 50 patients (14%) ( $p = 0.5$ ). Atrophic gastritis was detected in 31 of 70 patients (44.3%) and in 12 of 50 (24%) patients. The difference was statistically significant ( $p < 0.02$ ). Activity was positive in 34 of 70 patients (48.6%) and in 25 of 50 (50%) patients. There was no statistically significant difference ( $p = 0.8$ ). Chronic inflammation was detected in 61 of 70 patients (88.4%) and in 44 of 50 patients (88%). There was no statistically significant difference ( $p = 0.9$ ). Proximal gastric biopsies of patients with gastroenterostomy revealed

**Table 2. Demographic characteristics of patients**

Patients undergoing gastroenterostomy	70 (n)	R-Y	7 (10%)
		B-II	45 (65%)
		SG	18 (25%)
Control group	50 (n)		
Age	Gastroenterostomy	R-Y	62.7±4.4
		B-II	63±1.5
		SG	58.9±2.2
	Control	55.4±1.9	
Duration of time after gastroenterostomy	R-Y		10.4±2.5 (year)
	SG		18.1±2.3 (year)
	B-II		14.7±2.1 (year)
Reason for the gastroenterostomy procedure	R-Y	Peptic ulcer	5 (71.4%)
		Adenocarcinoma	2 (28.6%)
	SG	Peptic ulcer	18 (100%)
	B-II	Peptic ulcer	27 (60%)
		Adenocarcinoma	17 (37.8%)
		Neuroendocrine tumor	1 (2.2%)
R-Y: Roux-en-Y, B-II: Billroth-II, SG: Simple gastroenterostomy			

neuroendocrine tumors in one patient (1.4%) and dysplasia in one patient (2%) in the control group. The difference was not statistically significant ( $p=0.6$ ). As a rule, pathologic evaluation of enterogastric reflux in patients with gastroenterostomy was performed on the remnant gastric mucosa close to the stoma; therefore, enterogastric reflux evaluation was not performed on the proximal remnant mucosa. A comparison of proximal gastric biopsy samples of gastroenterostomy patients and control group patients is given in Table 4.

## Discussion

Hp is responsible for the etiology of gastric cancer (9,10). Cell damage and Hp infection are influential in the development of malignancy in patients undergoing gastroenterostomy (11). Therefore, Hp eradication is important in patients undergoing gastroenterostomy. The prevalence of Hp was 38% in patients who underwent gastroenterostomy for peptic ulcers and 60% ( $p=0.015$ ) in the control group (12). In our country, Hp's frequency in patients undergoing gastroenterostomy has not been sufficiently studied. In our study, we detected Hp positivity rates of 14% and 20% in distal and proximal gastric biopsy specimens in gastroenterostomy patients, respectively, and 60% and 62% in distal and proximal gastric biopsy specimens in the control group ( $p<0.01$ ). The lower rates of Hp in gastroenterostomy patients are probably related to the higher pH values of the gastric milieu due to alkaline reflux. Previous studies have pointed out that the risk of developing carcinoma in remnant gastric tissue is related to the fact that gastrectomy is performed before the age of 40 years and to the patients' advanced age (13). In our cases who underwent

surgery for adenocarcinoma, two patients showed recurrence at the 2<sup>nd</sup> and 4<sup>th</sup> years. Two of our patients with dysplasia had a history of surgery due to peptic ulcers 30 and 45 years ago. Although the number of cases is insufficient, it shows that the risk of developing malignancy in the late period increases in those who underwent surgery for ulcers. Adenocarcinoma should be evaluated for malignancy in the early period because of local recurrence. Hp positivity was lower in gastroenterostomy patients than in non-gastroenterostomy patients. It was concluded that Hp may play an important role in the development of gastric lesions in patients undergoing gastroenterostomy (14). Dysplasia and adenocarcinoma were significantly more common in gastroenterostomy patients than in the control group (5.5%-0) ( $p<0.02$ ). In the distal biopsy samples, dysplasia and adenocarcinoma were detected in four patients with gastroenterostomy, but none in the control group. The more frequent occurrence of dysplasia and adenocarcinoma in distal biopsy specimens can be explained by their proximity to the primary operation site and increased exposure to enterogastric reflux. Although there was no significant difference between the distal and proximal gastric biopsy samples of patients with gastroenterostomy and the control group in terms of the frequency of intestinal metaplasia, it was concluded that a significant increase in the incidence of intestinal metaplasia could be detected with a larger sample size ( $p=0.054$  vs.  $p=0.5$ ).

Distal and proximal gastric biopsy specimens showed a high rate of atrophic gastritis compared with the control group ( $p<0.01$ ). We did not find a significant difference between patients with gastroenterostomy and control group in terms of

**Table 3. Comparison of distal gastric biopsy samples of gastroenterostomy and control group patients**

	Gastroenterostomy	Control	p-value
<i>Helicobacter pylori</i>	10 (14.3%)	30 (60%)	<0.001
Intestinal metaplasia	22 (31.4%)	8 (16%)	0.054
Activity	32 (48.6%)	25 (50%)	0.6
Chronic inflammation	58 (82.9%)	46 (92%)	0.1
Atrophic gastritis	42 (60%)	15 (30%)	0.01
Dysplasia-adenocarcinoma	4 (5.5%)	0	0.02

**Table 4. Comparison of proximal gastric biopsy samples from gastroenterostomy patients and control group**

	Gastroenterostomy	Control	p-value
<i>Helicobacter pylori</i>	14 (20%)	31 (62%)	0.001
Intestinal metaplasia	13 (18.6%)	7 (14%)	0.5
Activity	31 (44.3%)	12 (24%)	0.02
Chronic inflammation	34 (48.6%)	25 (50%)	0.8
Atrophic gastritis	61 (88.4%)	44 (88%)	0.9
Dysplasia	1 (1.4%)*	1 (2%)	0.6

\*: Neuroendocrine tumor

chronic inflammation and activity values. In our study, the small number of patients with R-Y was a limiting factor in comparison among patients who underwent gastroenterostomy. However, in our study, the pathologic examination of patients with gastroenterostomy separately for both distal and proximal gastric mucosa made it possible to evaluate in detail this group of patients with increased frequency of precancerous lesions.

### Study Limitations

We think that increasing the number of patients with gastroenterostomy and duration of time after surgery will show us more powerful and correct numbers in accordance with risk factors for gastric malignancies and premalignancies.

### Conclusion

This study showed that the frequency of enterogastric reflux increased in patients who underwent gastroenterostomy and, correspondingly, decreased Hp's frequency. The incidence of atrophic gastritis and dysplasia, which are precancerous gastric lesions, is significantly higher in patients undergoing gastroenterostomy. In addition, the frequency of intestinal metaplasia in the distal gastric mucosa is increasing although the difference is not statistically significant.

Considering these results, because enterogastric reflux and Hp have a synergistic damaging effect on the gastric mucosa, we recommend that patients with gastroenterostomy should be tested for Hp, and if they test positive, they should undergo eradication treatment. In addition, biopsies should be taken from the distal remnant gastric mucosa close to the stoma line.

### Ethics

**Ethics Committee Approval:** Ethical approval for the study was obtained from the clinical ethics committee of Türkiye Yüksek İhtisas Hospital (approval number: 242, date: 04.08.2010).

**Informed Consent:** Informed consent was obtained.

### Authorship Contributions

Surgical and Medical Practices: S.S., B.Ö., Concept: S.S., B.Ö., Design: S.S., B.Ö., Data Collection or Processing: S.S., Analysis or Interpretation: S.S., B.Ö., Literature Search: S.S., Writing: S.S.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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