RESEARCH ARTICLE

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Increasing Frequency of *Helicobacter pylori* in Non Variceal Upper Gastrointestinal Bleeding

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Objective: Our aim in this study was to emphasize the increased frequency of *Helicobacter pylori* (*H. pylori*) infection in the non-variceal upper gastrointestinal bleeding patients and to draw attention to the fact that *H. pylori* infection is a condition, that merits substantial care.

Materials and Methods: Between January 01, 2019 and January 01, 2023, patients who were admitted to the emergency department of Fırat University with melena and hematemesis for the first time were investigated. Patients with non-variceal upper gastrointestinal bleeding were included in the study. The frequency of *H. pylori* infection was determined in patients who underwent biopsy according to Sydney protocol during endoscopy. As a control group, *H. pylori* infection was tested in healthy individuals without chronic disease who underwent upper endoscopy and gastric biopsies according to the Sydney protocol for dyspepsia.

Results: In 245 patients with non-variceal upper gastrointestinal bleeding, the main cause of the bleeding was peptic ulcer. *H. pylori* infection was positive in 204 (83.3%) and negative in 41 (16.7%) patients. In the control group, *H. pylori* infection was negative in 190 (54.4%) and positive in 159 (45.6%) patients. *H. pylori* positivity was significantly higher in the group with bleeding due to peptic ulcer compared to the control group (p<0.001). In the patient group, *H. pylori* was positive in 111 (83.45%) of 133 patients who were not using any drug and 88 (35.9%) patients were using NSAIDs including acetylsalicylic acid and 72 (81.8%) of them were positive for *H. pylori*.

Conclusion: *H. pylori* infection was positive in more than 80% of patients in both drug and non-medication groups in bleeding due to peptic ulcer. The frequency of *H. pylori* infection in non-variceal upper gastrointestinal bleeding was above normal. This showed that *H. pylori* infection alone constituted a very high risk for non-variceal upper gastrointestinal bleeding in our population.

Key Words: *Helicobacter pylori, peptic ulcer bleeding, non-variceal*

Varis Dışı Üst Gastrointestinal Kanamalarda Giderek Artan *Helicobacter pylori* Sıklığı

Amaç: Bu çalışmadaki amacımız *Helicobacter pylori* (*H. pylori*) enfeksiyonun toplumumuzda, varis dışı üst gastrointestinal sistem kanamalarının etyolojisinde sıklığının giderek arttığını ve *H. pylori* enfeksiyonun dikkat edilmesi gereken bir durum olduğuna dikkat çekmektir.

Gereç ve Yöntem: 01 Ocak 2019 yılı ile 01 Ocak 2023 yılı arasında, ilk kez melena ve hematemesis şikayetiyle Fırat üniversitesi acil servisine başvuran hastalar tarandı. Varis dışı üst gastrointestinal sistem kanaması olan hastalar çalışmaya dahil edildi. Kontrol grubu olarak da kronik hastalığı olmayan dispepsi nedeniyle üst endoskopisi yapılan ve Sydney protokolüne uygun gastrik biyopsiler alınan sağlıklı bireylerde *H.pylori* enfeksiyonu tarandı.

Bulgular: Varis dışı üst gastrointestinal sistem kanaması olan 245 hastada kanama nedeni peptik ülserdi. *H.pylori* enfeksiyonu 204 (%83.3) hastada pozitifdi ve 41 (%16.7) hastada negatifdi. Kontrol grubunda *H.pylori* enfeksiyonu 190 (%54.4) hastada negatifdi ve 159 (%45.6) hastada pozitifdi. Peptik ülsere bağlı kanaması olan grupta, kontrol grubuna göre *H. pylori* pozitifliği anlamlı derecede yüksek bulundu (p<0.001).

Sonuç: *H.pylori* enfeksiyonu, peptik ülsere bağlı kanamada ilaç kullanan ve kullanmayan grupta hastaların %80 den fazlasında pozitif geldi. *H.pylori* enfeksiyonu, varis dışı üst gastrointestinal kanamalarında ki sıklığı normalin üstündeydi. Buda toplumumuzda *H.pylori* enfeksiyonun varis dışı üst gastrointestinal kanamalarında tek başına çok yüksek bir risk oluşturduğu göstermekteydi.

Anahtar Kelimeler: *Helicobacter pylori, peptik ülser kanaması, varisi olmayan*

Introduction

Patients with acute upper gastrointestinal bleeding (UGIB) usually present with hematemesis (vomiting of blood or coffee-ground-like material) or melena (black, tarry stools). UGIB is a very common condition in the emergency departments, particularly in the elderly and males with high mortality and morbidity (1-3). The hospitalization rate for acute upper gastrointestinal bleeding is approximately six times higher than that for lower gastrointestinal bleeding. The most common cause of UGIB is gastroduodenal ulcers (4-6).

The most common causes of gastroduodenal ulcers are *Helicobacter pylori* (*H. pylori*) infection, non-steroidal anti-inflammatory drugs (NSAIDs), physiologic stress and excessive gastric acid (7-9).

Helicobacter pylori is a gram-negative, flagellated bacterium. It is spread by fecal-oral or oral-oral transmission. *H. pylori* is considered the most common carcinogen causing gastroduodenal ulcers and gastric cancers. Although the frequency of people infected with *H. pylori* is decreasing in developed countries, it is still very common in developing countries (10-12). In developing countries, *H. pylori* starts to be seen in childhood, becomes chronic with getting older and is more common in the advanced age. Peptic ulcer-related bleeding (PUB) caused by *H. pylori* may cause death in 0.8-14% of patients. Upper endoscopy is of great importance in detecting the bleeding focus in the gastrointestinal tract and in the diagnosis of *H. pylori* infection (13-17).

Materials and Methods

Research and Publication Ethics: Our study was a retrospective single-center study. Approval was granted by the Non-Interventional Research Ethics Committee of Fırat University (Protocol no: 2024/11-04).

Patients with melena or hematemesis for the first time in their lives who presented to the Emergency Department of Fırat University Hospital between January 1, 2019 and January 1, 2023 were screened in the electronic registration system of our hospital.

Patients who presented to the emergency department with melena and hematemesis, who were 18 years of age or older, who had no previous history of UGIB, who underwent upper endoscopy within the first 12 hours after presentation to the emergency department, who had a non-variceal upper gastrointestinal bleeding focus on endoscopy, who had no history of antibiotic use in the last 6 months, who had not received *H. pylori* eradication treatment before, had not taken proton pump inhibitors in the last month and who underwent gastric biopsy in accordance with the Sydney protocol during the procedure were included. Patients' medication habits, chronic diseases and detailed anamnesis were obtained from the hospitals' electronic record system.

Patients who were 18 years of age or older, presented to the gastroenterology outpatient clinic between January 1, 2022 and January 1, 2024 due to dyspepsia, had no history of any chronic disease, had not received any antibiotics or *H. pylori* eradication therapy in the last 6 months, had not taken proton pump inhibitors in the last month, and had gastric biopsies taken in accordance with the Sydney protocol during upper endoscopy were selected as the control group.

The age, gender, and histologic *H. pylori* positive/negative results of gastric biopsies taken in accordance with the Sydney protocol in the endoscopic procedure were compared between the patients with non-variceal upper gastrointestinal bleeding and the control group.

The data were analyzed using the SPSS 22 package program. Continuous variables were expressed as mean ± standard deviation. Categorical variables were expressed as a percentage. Continuous variables were expressed as mean ± standard deviation. Student t test and Mann Whitney U tests were used for the comparison of groups.

Results

Between January 1, 2019 and January 1, 2023, 245 patients who met our criteria were admitted to the emergency department of Fırat University Hospital. In all patients with non-variceal upper gastrointestinal bleeding, the main cause of the bleeding was due to peptic ulcer. There were 86 (35.1%) female patients and 159 (64.9%) male patients with a mean age of 59.43 years. In the control group, there were 210 (60.2%) female patients and 139 (39.8%) male patients with a mean age of 50.11 years. In the patient group, 204 (83.3%) patients were *H. pylori* positive and 41 (16.7%) were *H. pylori* negative. In the control group, 190 (54.4%) patients were *H. pylori* negative and 159 (45.6%) were *H. pylori* positive.

H. pylori positivity was significantly higher in the group with bleeding due to peptic ulcer compared to the control group (p<0.001). In gastric biopsies taken in accordance with the Sydney protocol, chronic gastritis was seen in 200 (82.3%), metaplasia in 34 (14%) and low-grade dysplasia in 7 (2.9%) cases in the patient group. In the control group, chronic gastritis was seen in 332 (95.1%), metaplasia in 13 (3.7%) and low-grade dysplasia in 4 (1.1%). Metaplasia and low-grade dysplasia were more common in the group with non-variceal upper gastrointestinal bleeding (Table-1).

Table 1. Histologic frequency of *Helicobacter pylori*

	Pepticulcer Bleeding *n (%)*	**Control** *n (%)*
Total	245	349
Male	159	139
Female	86	210
H.pylori positive	204 (83.3%)	159 (45.6%)
H.pylori negative	41 (16.7%)	190 (54.4%)
Normal gastric mucosa	2	0
Chronic gastritis	200	332
Metaplasia	34	13
Low-grade dysplasia	7	4

(p<0.001)

Table 2. Frequency of peptic ulcer bleeding in patients according to Forrest classification

Forrest	**n**	**%**
1a	2	0,81
1b	7	2,85
2a	22	8,97
2b	14	5,71
2c	26	10,61
3	174	71
Total	245	100

Table 3. Frequency of *Helicobacter pylori* infection by anatomic localization in peptic ulcers (p>0.5)

		ANTRUM	BULBUS	CARDİA	CORPUS	TOTAL
H.pylori negative	count	18	14	3	6	41
	%	43.9	34.1	7.3	14.6	100
H.pylori positive	count	77	93	9	25	204
	%	37.7	45.6	4.4	12.3	100

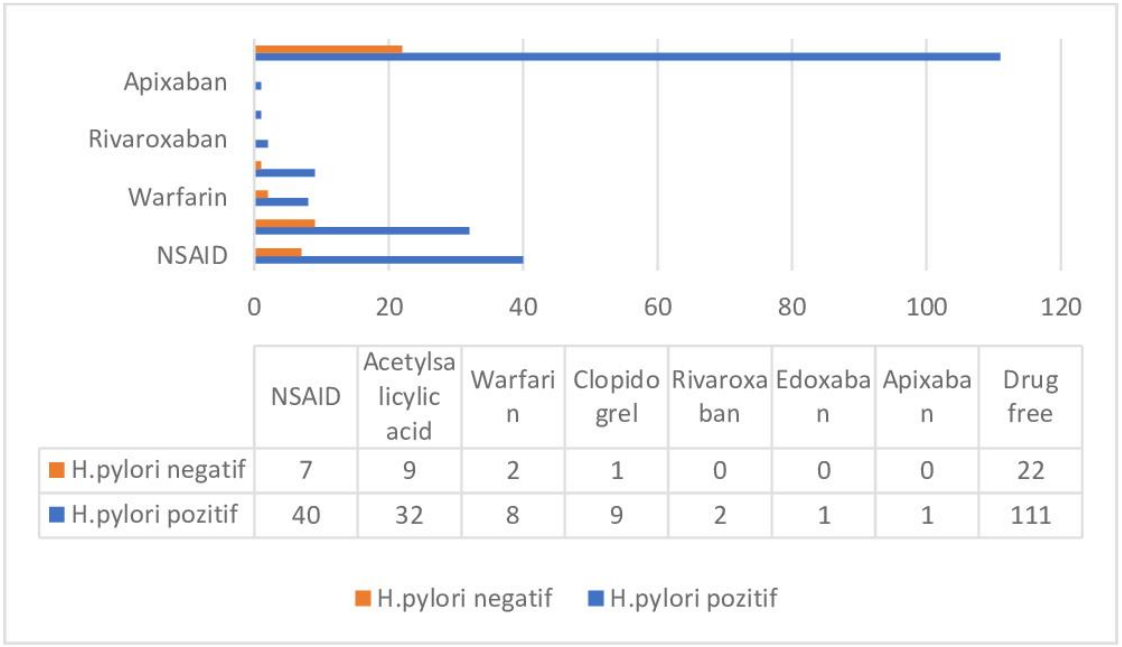

Figure 1. Prevalence of *H.pylori* inPUB patients with and without medication

In the peptic ulcer-related bleeding group, according to the endoscopic forrest classification, forrest-3 was most common in 174 (71%) patients and forrest-1a was least common in 2 (0.81%) patients (Table-2).

According to the endoscopic examination of the peptic ulcer bleeding group, the frequency of lesion localization was 12 (4.89%) in the cardia, 31 (12.65%) in the corpus, 95 (39.77%) in the antrum and 107 (43.67%) in the duodenum. *H. pylori* positivity and negativity were compared according to the anatomical localization of the ulcer, no statistically significant difference was found (p>0.5) (Table-3).

47 (19.18%) of the patients were using NSAIDs other than acetylsalicylic acid, 40 (85.11%) of these patients were *H. pylori* positive and 7 were *H. pylori* negative. Of 41 (16.73%) patients using acetylsalicylic acid, 32 (78.05%) were *H. pylori* positive. Including acetylsalicylic acid, 88 (35.9%) patients were using NSAIDs and 72 (81.8%) of them were *H. pylori* positive. Among other drugs, 8 of 10 patients on warfarin, 9 of 10 on clopidogrel, 2 on rivoraxaban, 1 on apixaban and 1 on edoxaban were positive for *H. pylori* In the patient group, *H. pylori* was positive in 111 (83.45%) of 133 patients who did not use drugs (Figure-1).

Discussion

Helicobacter pylori is a gram-negative, spiral and microaerophilic bacterium that causes mucosal damage and gastric peptic ulcer by infecting the gastric mucosa and decreasing the defense of the mucosa against acid, and histologic examination of samples taken during endoscopy is of great importance in its diagnosis (18, 19). NSAIDs may cause peptic ulcers with both systemic prostaglandin inhibition and local effects. NSAID-induced peptic ulcers usually have an asymptomatic course and may rarely lead to complications (20, 21)

Pilotto et al. (22) showed that NSAID use caused a higher risk of upper gastrointestinal bleeding than *H. pylori* infection. In this respect, our study was different from theirs, in that more than 80% of our patients with bleeding due to peptic ulcer were *H. pylori* positive, both NSAID users and nonusers. This may be explained by the fact that we are a developing country and *H. pylori* is more common in the developing countries than in the developed countries.

In the study by Ramsoekh et al. (23), only 61% of 361 peptic ulcer bleeding patients were tested for *H. pylori* and one fourth of the patients were not associated with *H. pylori* and NSAIDs.

Aalykke et al. (24) found that patients infected with *H. pylori* and using NSAIDs were twice as likely to bleed from peptic ulcer than *H. pylori* negative patients using NSAIDs.

Labenz et al. (25) showed that *H. pylori* eradication therapy reduced the risk of rebleeding in *H. pylori*-positive patients with duodenal and gastric ulcers. According to Sostres et al. (26), *H. pylori* and NSAID use were independent risk factors for peptic ulcer bleeding.

In our study, the bleeding focus was related to the peptic ulcer in all patients with non-variceal upper gastrointestinal bleeding. When we compared *H. pylori* positivity with the control group, *H. pylori* positivity was significantly higher in the patient group (p<0.001). In our study, 204 of 245 patients were *H. pylori* positive, only 41 were *H. pylori* negative.

In the patient group, 88 (35.9%) patients were using NSAIDs, including acetylsalicylic acid, and 72 (81.8%) of them were *H. pylori* positive. *H. pylori* was positive in 111 (83.45%) of 133 patients with PUB who were not using drugs. More than 80% of our patients with NSAID-induced PUB were *H. pylori* positive, suggesting that *H. pylori* infection has a synergistic effect on peptic ulcer bleeding in NSAID users.

In this respect, our study showed similar results with many previous studies. In our study, the number of patients infected with *H. pylori* in PUB was very high and *H. pylori* positivity was the most common independent risk factor for peptic ulcer bleeding. Bleeding ulcers were most commonly seen in the duodenum, which is similar to the results of other studies.

The shortcomings of our study were that there was no NSAID use in the healthy control group. This prevented us from comparing the effect of NSAIDs with *H. pylori* infection in the etiology of PUB. In many studies, it is still debated that *H. pylori* infection alone is the most common independent factor in the etiology of PUB and the high risk of bleeding due to peptic ulcer in NSAID users. Therefore, further and detailed studies are needed to understand the increased risk of *H. pylori* infection in the etiology of PUB.

In conclusion, in all patients who underwent upper endoscopy for non-variceal upper gastrointestinal bleeding, the main cause of upper gastrointestinal bleeding was peptic ulcer. *H. pylori* positivity was significantly higher in the group with peptic ulcer bleeding than in the group of healthy individuals without chronic disease (p<0.001). In the patient group, 83.45% of non-medication users and 81.8% of NSAID users were *H. pylori* positive.

This shows that *H. pylori* infection is the most common independent factor in the etiology of peptic ulcer bleeding in the geographical region where we live and its prevalence is gradually increasing; it also contributes to peptic ulcer bleeding by creating a synergistic effect in NSAID users.

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