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Prevalence and characterization of acute biliary pancreatitis-associated upper gastrointestinal mucosal lesions

Akut biliyer pankreatit'te üst gastrointestinal mukoza lezyonlarının yaygınlığı ve karakterizasyonu

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Background and Aims: *Acute pancreatitis can be associated with various upper gastrointestinal mucosal lesions. However, their pathogenesis and clinical significance have been discussed rarely. The aim of this study was to retrospectively investigate upper gastrointestinal mucosal lesions in relation to the prevalence of Helicobacter pylori infection in acute biliary pancreatitis.* ***Methods:*** *This study was carried out in 94 patients with acute biliary pancreatitis and 179 control dyspeptic patients with or without gallstone disease. In all research subjects, upper gastrointestinal endoscopy was performed, and two biopsy specimens were taken from the antrum and gastric body for histological examination and Helicobacter pylori detection.* ***Results:*** *71% of patients with acute biliary pancreatitis had evidence of upper gastrointestinal mucosal abnormalities. Esophagitis and peptic ulceration were more prevalent compared to the control groups (p<0.05). Peptic ulceration associated with pancreatitis showed lower Helicobacter pylori positivity compared to controls (p<0.05).* ***Conclusions:*** *Gastrointestinal mucosal lesions are common in the course of acute biliary pancreatitis. Peptic ulceration is less strongly associated with Helicobacter pylori.*

Key words: *Biliary pancreatitis, peptic ulcer disease, Helicobacter pylori*

Giriş ve Amaç: *Akut pankreatit'li olgularda akut pankreatite bağlı çeşitli üst gastrointestinal mukoza lezyonları görülebildiği ve akut pankreatitle ilişkili olduğu belirtilsede, bu ilişkinin patogenezi ve klinik önemi tam olarak araştırılmamış ve ortaya çıkarılmamıştır. Bu çalışmamızın amacı kliniğimizde akut biliyer pankreatit tanısı ile yatan olgularda üst gastrointestinal mukozal lezyonları saptamak ve bu lezyonlarda Helikobakter pilori prevalansını retrospektif olarak belirlemektir.* ***Gereç ve Yöntem:*** *Çalışmaya retrospektif olarak 94 akut biliyer pankreatitli ve toplam 179 safra taşı birlikteliği olan ve olmayan dispeptik olgu kontrol grubu olarak şdahil edilmiştir. Çalışmaya dahil edilen tüm vakalardan antrum ve korpustan hem Helikobakter pilori hemde mukozanın histolojik yapısını belirlemek için ikişer adet biyopsi alınmıştı.* ***Bulgular:*** *Akut biliyer pankreatitli olguların %71'inde üst gastrointestinal mukozal lezyon saptandı. Özofajit ve peptik ülser akut biliyer pankreatitli olgularda kontrol grubuna göre anlamlı olarak yüksek çıktı (p<0.05). Pankreatitli olgularda saptanan mide ülserli olgularda helikobakter pilori kontrol grubuna göre daha düşük saptanmıştır (p<0.05).* ***Sonuç:*** *Akut biliyer pankreatitli olgularda gastrointestinal mukozal lezyonlar sık görülsede mide ülseri olanda helikobakter pilori ilişkisi peptik ülserde düşük düzeydedir.*

Anahtar kelimeler: *Biliyer pankreatit, peptik ülser, Helikobakter pilori*

INTRODUCTION

Acute pancreatitis is an inflammatory disease of the pancreas and one of the leading gastrointestinal causes of hospitalization in the Western world (1). The majority of cases are caused by gallstone disease and alcohol abuse. Importantly, incidence is increasing in line with heavier alcohol consumption worldwide; survival rates are not improving with the advances in diagnosis and treatment (2).

Acute pancreatitis can lead to a clinical spectrum ranging from mild local manifestations to severe systemic complications. Local complications, such as gastritis, duodenitis, splenic vein thrombosis, and colonic necrosis, along with external compression of the common bile duct have been described in the course of pancreatitis (3). Previous studies have shown that mucosal lesions in the upper gastrointestinal tract complicate more than 50% of cases of acute pancreatitis (4-6). *Helicobacter pylori (H. pylori)* has been implicated as the major causative agent in cases of chronic gastritis and peptic ulceration worldwide, but its role in upper gastrointestinal mucosal lesions associated with acute pancreatitis is not known (7,8). Therefore, the aims of this study were to retrospectively investigate the characteristics of upper gastrointestinal mucosal lesions associated with acute gallstone pancreatitis and the relation with *H. pylori* infection.

MATERIALS AND METHODS

The study was conducted as a single-center, retrospective, cohort study. The patient records of the Gastroenterology Department, Celal Bayar University Hospital, Manisa, Turkey, from 2006 to 2010 were reviewed. Acute pancreatitis was diagnosed by the presence of two of the following three factors: typical upper abdominal pain, hyperamylasemia and/or hyperlipasemia of more than three times the upper limit of normal, as well as typical radiologic findings of pancreatitis during abdominal ultrasonography and/or computed tomography (CT). Acute biliary pancreatitis was diagnosed as visualization of a common bile duct stone by ultrasonography, CT or magnetic resonance cholangiopancreatography. Patients who had undergone upper gastrointestinal endoscopy during

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their hospitalization were included in the study. We routinely recommend upper gastrointestinal endoscopy to all hospitalized patients with the initial diagnosis of acute pancreatitis in order to rule out any other cause of abdominal pain or hyperlipasemia, unless this is contraindicated. Patients were excluded if they had a history of acid suppression therapy, antibiotic or non-steroidal anti-inflammatory drug treatment during the previous four weeks or any known peptic ulcer disease, chronic pancreatitis or pancreatitis from another etiology.

Data collected from the case notes were as follows: age, gender, comorbid risk factors and other possible etiologic factors such as alcohol consumption, and serum calcium and triglyceride levels. All patients with the initial diagnosis of acute pancreatitis underwent an abdominal CT to evaluate the severity of the acute pancreatitis, and were graded from A to E according to the scoring system established by Balthazar et al. (9). Ranson's criteria on admission were measured and recorded (10). Suspected and documented upper gastrointestinal bleeding was also searched from the patient files.

Our control group included patients with functional dyspepsia according to the Rome II criteria (11). They were divided into two subgroups according to the presence or absence of gallstones on ultrasound, as Group 1 and Group 2, respectively. Patients who had been receiving acid suppressive therapy or antibiotics and those who had a history of acute pancreatitis and cholangitis were excluded.

All groups of patients underwent endoscopy, and esophageal findings were assessed using the Los Angeles classification (12). Two biopsy specimens were taken from the antrum and gastric body for histological examination and detection of *H. pylori*. Biopsy specimens were fixed in formalin, embedded in paraffin, and stained with a modified toluidine blue for detection of *H. pylori*.

The study was carried out with the approval of the Institutional Review Board of Celal Bayar University Medical Center, Manisa, Turkey. The study protocol conformed to the ethical guidelines of the Declaration of Helsinki. Data were compared by χ^2 (SPSS 11.5 for Windows; SPSS Inc., Chicago, IL) or Fisher exact tests, as appropriate. Statistical significance was considered to be $p<0.05$.

RESULTS

One hundred and six patients with acute pancreatitis who had undergone upper gastrointestinal endoscopy during their hospitalization were identified. Twelve patients were excluded from the study (etiologic factors other than gallstone disease). The baseline characteristics of patients were similar in the acute biliary pancreatitis group and control groups (Table 1). Sixty-three patients were female and 31 were male. The mean age was 48.1±18 years (range: 21-87). One hundred and seventy-nine patients were identified as controls. Of those, 84 patients (Group 1) had gallstones and 95 patients (Group 2) did not. The mean ages for control Groups 1 and 2 were 51.3±18 and 50.2±18 years, respectively. Both control groups showed female predominance (73% and 61%).

Firstly, the correlation between acute biliary pancreatitis and gastrointestinal mucosal lesions was investigated. Seventy-one percent (n=66) of patients with acute gallstone pancreatitis were found to have abnormal findings during upper gastrointestinal endoscopy, including esophagitis, gastritis and peptic ulcer, and the rates were significantly higher when compared to both control groups. The incidence of esophagitis was significantly higher in patients with acute biliary pancreatitis than the control groups ($p<0.05$). There was a significant rise in the incidence of gastric and duodenal ulcer in the pancreatitis group ($p<0.01$) compared to controls. The anatomic localization of gastrointestinal mucosal lesions is illustrated in Table 2. No patient was reported to have upper gastrointestinal bleeding. There was no significant difference in the CT grading and Ranson's scoring between patients with normal endoscopic findings and gastrointestinal mucosal lesions (Table 3).

The histological analysis of biopsy samples from the gastric antrum and corpus revealed no difference in the prevalence of *H. pylori* infection between groups. However, patients with

Table 1. Baseline characteristics of the patient and control population

	Pancreatitis n (%)	Dyspepsia and Gallstone n(%)	Dyspepsia n (%)	p
Age	48.1±18	51.3±18	50.2±18	NA
Male	31 (33%)	22 (27%)	37 (39%)	NA
Female	63 (67%)	62 (73%)	58 (61%)	NA
Hemoglobin	11.8±1.2	13.8±0.2	12.8±0.8	NA
Hematocrit	34±2.8	36±1.7	35±0.9	NA
ALT	148±16	34±11	21±0.8	<0.05
AST	126±14	36±12	28±7	<0.05
GGT	72±7	41±4	34±2	<0.05
ALP	234±28	80±18	72±12	<0.05

Table 2. Endoscopic and histological assessment of the patient and control groups

Upper GI endoscopy	Pancreatitis (1) n (%)	Dyspepsia and Gallstone (2) n (%)	Dyspepsia (3) n (%)	P (1-2)	P (1-3)
Normal	28 (29%)	53 (63%)	74 (79%)	<0.05	<0.05
Esophagitis	18 (19%)	10 (13%)	2 (2%)	<0.05	<0.05
Erythematous antral gastritis	14 (15%)	10 (13%)	8 (8%)	NA	NA
Endoscopic pan-gastritis	14 (15%)	5 (4%)	4 (4%)	<0.05	<0.05
Antral ulcer	14 (15%)	6 (7%)	6 (6%)	<0.05	<0.05
Bulbar ulcer	6 (7%)	0	1 (1%)	<0.05	<0.05

Table 3. Assessment of pancreatitis severity by radiological and clinical scores

	Endoscopic mucosal lesions	Normal endoscopic findings	p
Ranson 1-3	37 (56%)	18 (63%)	NA
Ranson 4-8	29 (44%)	10 (36%)	NA
Balthazar A	17 (26%)	7 (27%)	NA
Balthazar B	30 (45%)	11 (36%)	NA
Balthazar C	16 (24%)	7 (27%)	NA
Balthazar D	3 (5%)	3 (1%)	NA
Balthazar E	0	0	NA

Table 4. Histological evaluation of H. pylori in patient and control groups

Upper GI endoscopy	Pancreatitis (1) n (%)	Dyspepsia and Gallstone (2) n (%)	Dyspepsia (3) n (%)	P (1-2)	P (1-3)
Normal	22 (36%)	29 (54%)	48 (78%)	NA	NA
Esophagitis	7 (40%)	9 (50%)	1 (50%)	NA	NA
Erythematous antral gastritis	10 (75%)	6 (60%)	5 (66%)	NA	NA
Endoscopic pan-gastritis	9 (71%)	3 (66%)	3 (75%)	NA	NA
Antral ulcer	7 (50%)	6 (100%)	5 (80%)	<0.05	<0.05
Bulbar ulcer	5 (75%)	0	1 (100%)	<0.05	<0.05

pancreatitis who had peptic ulceration at endoscopy showed significantly lower *H. pylori* positivity than controls. The *H. pylori* prevalence in patients with gastrointestinal mucosal lesions is summarized in Table 4.

DISCUSSION

In this study, we evaluated the prevalence of upper gastrointestinal mucosal lesions and their characteristics in acute biliary pancreatitis. The clinical significance of these lesions was also investigated retrospectively. We found a significant association between upper gastrointestinal mucosal abnormalities and acute biliary pancreatitis, with 71% of patients having these abnormalities. Previous studies have also shown that more than half of the patients with acute pancreatitis were complicated with upper gastrointestinal mucosal lesions (4,5). Our study population with acute biliary pancreatitis was predominantly female (67%). Amongst the global population, there is a higher prevalence of gallstone disease in women. It can therefore be seen that the risk of development of acute pancreatitis is greater in females, especially in the low alcohol-consuming population.

Upper gastrointestinal endoscopies revealed that esophagitis was significantly more common in the acute biliary pancreatitis group than the dyspepsia group. Most patients with acute pancreatitis develop some level of nausea and vomiting, which may partially explain why we observed more esophageal lesions in patients with pancreatitis. It is also well known that the nasogastric tubes themselves may lead to mucosal lesions in the esophagus and/or stomach. Peptic ulcer has also been found to be associated with pancreatitis. Duodenal ulcer is the prevailing endoscopic finding in patients with alcoholic chronic pancreatitis and acute pancreatitis (13); similarly, we encountered a duodenal ulcer in five patients of the study population. In addition, we also observed a high incidence of antral ulcers in the biliary pancreatitis group, which has not been observed previously (6).

There was no association between the presence of upper gastrointestinal mucosal lesions and the severity of pancreatitis

according to the two severity scores, which shows consistency with the previous studies (4,5). However, a recent study by Lee and colleagues (6) reported the clinical association of peptic ulcers with APACHE scores in acute pancreatitis patients. This can be explained by application of endoscopy at different time points of the disease course. We usually perform upper gastrointestinal endoscopy during the first two days of abdominal pain rather than just before beginning oral feeding. In our study, none of the patients suffered complications such as bleeding. This can be explained by either a relatively small research population or routine prophylaxis with H2 receptor blockers and proton pump inhibitors.

By histological examination, the prevalence of *H. pylori* infection was found as 64% and 55% in the pancreatitis and control groups, respectively. Khan et al. (14) reported a 20% incidence of *H. pylori* in alcohol-induced acute pancreatitis, which was similar to the control groups. Manes et al. (15) found that the prevalence of *H. pylori* infection in patients with chronic pancreatitis was similar to that of patients with alcoholic liver cirrhosis and healthy subjects. Our results indicated a higher *H. pylori* positivity in all subgroups, correlating with the higher prevalence of *H. pylori* in Turkey. *H. pylori* infection is strongly associated with peptic ulceration of the duodenum and stomach. In our study, almost all peptic ulcers in the dyspepsia group were associated with *H. pylori* infection, probably due to the exclusion of non-steroidal anti-inflammatory drug users. However, *H. pylori* prevalence was significantly lower in patients with peptic ulcers and pancreatitis and similar to the non-ulcer dyspeptic population. Whether the lower incidence of *H. pylori* infection in this patient group can be partly explained with stress ulcer, the pathogenesis remains unclear. The pathogenesis of these lesions is not completely understood, but gastric acid secretion, mucosal ischemia and reflux of upper gastrointestinal contents into the stomach may have a role in this process, similar to stress ulcers (16-18). Regarding the ulcer localization and *H. pylori* status of the patients, these lesions should be defined as pancreatitis-associated peptic ulcers rather than stress-associated mucosal damage.

In conclusion, esophagitis and antral and duodenal ulcers are common endoscopic findings in acute biliary pancreatitis, although they are not correlated with the severity of pancreatitis. *H. pylori* is less strongly associated with upper gastrointestinal mucosal lesions in acute biliary pancreatitis.

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