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Helicobacter Pylori Might be a Contributing Factor in Gallbladder Polyps or Gallstones: A Single Center Case-Control Matching Study of Turkish Individuals

Cenk Ozkan[1], Serhan Yilmaz [2], Emre Bozdag[1], Osman Sibic[3], Erkan Somuncu[1]

[1] University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, General Surgery, Istanbul, Turkey

[2] University of Health Sciences, Ankara Bilkent City Hospital, General Surgery, Ankara, Turkey

[3] Ministry of Health, Derik State Hospital, General Surgery, Mardin, Turkey

Cenk OZKAN
0000-0001-6801-7704
Serhan YILMAZ
0000-0002-5612-5932
Emre BOZDAG
0000-0002-2729-1667
Osman SIBIC
0000-0002-7600-9154
Erkan SOMUNCU
0000-0002-5622-1983

Correspondence: Cenk Ozkan
University of Health Sciences, Kanuni Sultan Suleyman Training and Research Hospital, General Surgery, Istanbul, Turkey
Phone: +90 541 260 95 11
E-mail: cenkozkann@hotmail.com

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ABSTRACT

Background/Purpose: In recent studies, Helicobacter pylori (Hp) infection has been shown to be associated with diseases such as obesity, diabetes, chronic obstructive pulmonary disease and kidney failure. In our study, we aimed to examine the relationships between Hp infection and gallstones or gallbladder polyps.

Methods: Patients who underwent elective cholecystectomy between January 2017 and December 2021 were retrospectively examined. Patients were divided into those with only polyps in the gallbladder (Group P), those with polyps and stones together (Group SP), and those with only stones (Group S). The control group consisted of patients who underwent gastroscopy due to dyspeptic complaints (Group No). The groups were screened for the presence of Helicobacter pylori. Demographic data, comorbidities, the presence of hepatosteatosis and laboratory values were recorded and compared.

Results: A total of 244 patients were included in the study. HP was positive in 141 (57.8%) of the patients and negative in 103 (42.2%). There were 58 (23.8%) patients in Group P, 22 (9%) in Group SP, 90 (36.9%) in Group S, and 74 (30.3%) in Group No. There was a significant difference in age between Group P and Group No (P = 0.012). Female sex was significantly more common in Group S (P=0.009). The Helicobacter pylori positivity rate was significantly greater in Group P and Group SP (P = 0.012).

Conclusion: HP infection may be associated with gallbladder polyps. We recommend that prospective randomized controlled studies be supported by large sample data.

Keywords: Case-control study, gallstones, gallbladder polyp, gallbladder disease, Helicobacter pylori

ÖZET

Giriş/Amaç: Son yıllarda yapılan çalışmalarda Helicobacter pylori (Hp) enfeksiyonu; Obezite, diyabet, kronik obstrüktif akciğer hastalığı ve böbrek yetmezliği gibi hastalıklarla ilişkili olabileceği belirtildi. Çalışmamızda Hp enfeksiyonu ile safra taşı ve safra kesesi polipleri arasındaki ilişkiyi incelemeyi amaçladık.

Yöntem: Ocak 2017 ile Aralık 2021 tarihleri arasında elektif kolesistektomi yapılan hastalar retrospektif olarak incelendi. Hastalar safra kesesinde sadece polip olanlar (Grup P), polip ve taşı birlikte olanlar (Grup SP) ve sadece taş olanlar (Grup S) olarak ayrıldı. Kontrol grubunu hazımsızlık şikayeti nedeniyle gastroskopi yapılan hastalardan oluşturdu (Grup No). Gruplar Helicobacter pylori varlığı açısından tarandı. Demografik veriler, komorbiditeler, hepatosteatoz varlığı ve laboratuvar değerleri kaydedilip karşılaştırıldı.

Bulgular: Çalışmaya 244 hasta dahil edildi. Hastaların 141›inde (%57,8) HP pozitif, 103›ünde (%42,2) negatifti. Grup P›de 58 (%23,8), Grup SP›de 22 (%9), Grup S›de 90 (%36,9), Grup No›da 74 (%30,3) hasta vardı. Grup P arasında yaş farkı anlamlıydı. ve Grup No (P = 0,012). Kadın cinsiyet Grup S›de anlamlı derecede yüksekti (P=0.009). Helicobacter pylori pozitiflik oranı Grup P ve Grup SP›de anlamlı derecede yüksekti (P=0,012).

Sonuç: HP enfeksiyonu safra kesesi polipleri ile ilişkili olabilir. Prospektif randomize kontrollü çalışmaların geniş örneklem verileriyle desteklenmesini öneriyoruz.

Anahtar Kelimeler: Helicobacter pylori, safra taşı, safra kesesi polipi, safra kesesi hastalığı, vaka kontrol çalışması

Helicobacter pylori (H. pylori) infection affects more than 50% of the world's population, and its close relationship with gastric diseases is well known (1). In our country, although this rate is not clear, in a study conducted in 2003 in which the 13C urea breath test was applied, the general prevalence was found to be positive in 82.5% of the participants (2). In recent years, an increasing number of studies have reported that this infection may also be associated with obesity (3), diabetes (4), chronic obstructive pulmonary disease and renal failure (5).

The incidence of gallbladder polyps has been reported to be 6% in cholecystectomy series (6). Similarly, this rate is 3-7% on ultrasonographic imaging of the gallbladder (7). Gallbladder polyps are usually clinically asymptomatic. There are studies in the literature indicating that they may carry a malignancy risk of approximately 2%. For this reason, some approaches have been adopted in the treatment of gallbladder polyps by evaluating their characteristics, such as size and number (8). The prevalence of gallstones in the community varies between 10% and 15%, and features such as age, sex, genetic factors, hypercholesterolemia, diabetes, and alcohol use are responsible for the formation of gallstones (9).

There are few studies in the literature investigating the relationships between H.pylori infection and gallbladder polyps and stones. In this study, we aimed to investigate the relationships between H.pylori infection and gallbladder polyps and stones.

Methods

Patients who underwent elective cholecystectomy at the general surgery clinic between January 2017 and December 2021 were retrospectively reviewed. Patients who underwent gastroscopy for dyspeptic complaints and whose pathology slides revealed gallstones or polyps in the gallbladder were included in the study. The control group consisted of patients who did not have luminal or mural pathology in the gallbladder on ultrasonography (USG) due to dyspeptic complaints or who underwent gastroscopy for screening purposes.

Patients younger than 18 years of age, patients who had undergone Helicobacter pylori eradication therapy, pregnant or breastfeeding patients, patients with a history of malignancy, patients without abdominal USG data and patients with missing data were excluded.

Patients were divided into those with only polyps in the gallbladder (Group P), those with polyps and stones (Group SP), and those with only stones (Group S) in the cholecystectomy slides. The control group was named Group No.

Biopsies of the groups taken under gastroscopy were screened for the presence of Helicobacter pylori according to the Sydney classification by hematoxylin and eosin (H&E) and modified Giemsa methods under light microscopy.

Demographic data (age, sex, BMI (body mass index)), comorbidities (no comorbidity, 1 comorbidity, 2 or more comorbidities), presence of hepatosteatosis according to USG measurement, alanine aminotransferase (ALT), aspartate aminotransferase (AST), low-density lipoprotein (LDL), triglyceride levels (normal or high), and high-density lipoprotein (HDL) levels (normal or low) were recorded.

Ethical approval for the study was granted by the hospital in which the procedures were performed (IRB No:KAEK/2024.04.73).

Statistical Analysis

The Shapiro-Wilk test was used to assess whether the variables followed a normal distribution or not. Continuous variables are presented as median (minimum:maximum) and mean±standard deviation values. Categorical variables are reported as n(%). According to the normality test results, the Kruskal- Wallis test or ANOVA test was used if the number of groups was greater than two. Multiple comparison procedures were performed via the Dunn-Bonferroni approach to identify different groups or groups after the Kruskal-Wallis test. Pearson's chi-square test and Fisher's Freeman-Halton test were used to compare categorical variables. SPSS (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY: IBM Corp.) was used for statistical analysis and a p value <0.05 was considered to indicate statistical significance.

Results

The study included 244 patients. The mean age was 49.7 ± 12.52 years and the male/female ratio was 144 (59%)/100 (41%).

HP was positive in 141 (57.8%) patients and negative in 103 (42.2%) patients. Demographic data (Table 1) and laboratory data (Table 2) are given below.

Table 1: Demographic data	
Age (mean±SD)	49.7±12.52
Sex (n/%)	
Female	144 (59%)
Male	100 (41%)
BMI (mean±SD)	27.27±5.09
Comorbidity (n/%)	
None	142 (58.2%)
<2	49 (20.1%)
≥2	53 (21.7%)
Hepatosteatosis (n/%)	
No	160 (65.6%)
Yes	84 (34.4%)
SD: Standard deviation	

Table 2: Laboratory data	
ALT (n/%)	
Normal	234 (95.9%)
High	10 (4.1%)
AST (n/%)	
Normal	229 (93.9%)
High	15 (6.1%)
TG (n/%)	
Normal	142 (58.2%)
High	102 (41.8%)
LDL (n/%)	
Normal	221 (90.6%)
High	23 (9.4%)
HDL (n/%)	
Normal	216 (88.5%)
Low	28 (11.5%)

There were 58 (23.8%) patients in Group P, 22 (9%) in Group SP, 90 (36.9%) in Group S and 74 (30.3%) in Group No.

When the groups were compared, a significant difference was found between Group P and Group No in terms of age (P=0.012). The proportion of females was significantly greater in Group S (P=0.009) (Table 3).

Table 3: Comparison of groups					
	Group P 58 (23.8%)	Group SP 22 (9%)	Group S 90 (36.9%)	Group No 74 (30.3%)	P value
Age (mean±SD)	46.06±11.73	52.27±10.71	49.15±11.75	52.74±13.82	**0.015**
Sex (n/%)					
Female	33 (56.9%)	10 (45.55)	65 (72.2%)	36 (48.6%)	**0.009**
Male	25 (43.1%)	12 (54.5%)	25 (27.8%)	38 (51.4%)	
BMI (mean±SD)	28.03±4.74	27.95±4.40	27.13±5.41	26.63±5.13	0.443
Comorbidity (n/%)					
None	35 (60.3%)	10 (45.5%)	55 (61.1%)	42 (56.8%)	0.349
<2	8 (13.8%)	4 (18.2%)	21 (23.3%)	16 (21.6%)	
≥2	15 (25.9%)	8 (36.4%)	14 (15.6%)	16 (21.6%)	
Hepatosteatosis (n/%)					
No	41 (70.7%)	15 (68.2%)	57 (63.3%)	47 (63.5%)	0.779
Yes	17 (29.3%)	7 (31.8%)	33 (36.7%)	27 (36.5%)	
SD: Standard deviation					

There were no significant differences between the groups in terms of ALT (P=0.212), AST (P=0.802), TG (P=0.289), LDL (P=0.442) or HDL (P=0.343) levels.

The Helicobacter pylori positivity rate was significantly greater in Group P and Group SP (P=0.012) (Table 4).

Table 4: HP relationships across groups

	Group P 58 (23.8%)	Group SP 22 (9%)	Group S 90 (36.9%)	Group No 74 (30.3%)	P Value
H.P					
No	19 (32.8%)	5 (22.7%)	41 (45.6%)	38 (51.4%)	**0.012**
Yes	39 (97.2%)	17 (77.3%)	49 (54.4%)	36 (48.6%)	

Discussion

H. pylori is the main pathogen responsible for the development of various diseases, especially gastric cancer (10). In some studies, H. pylori was detected in the skin, nose, gallbladder, and stomach (11). However, few studies have explored the relationships between H. pylori and the formation of gallstones and cholecystitis. However, in a study in which Pandey M and Shukla M. (12) investigated the relationship between biliary tract diseases and H. pylori, they reported that the incidence of H. pylori was 42.9%.

In some studies, the frequency of H. pylori infection varies between 30% and 70% (13-14). Bulajic et al. (14) reported that H. pylori detected in the gastric mucosa via the 13C urease breath test was also detected in the biliary tract in 81% of patients. Similarly, in our study, 57.8% of all patients were positive for H. pylori.

In another meta-analysis, Zhou et al. (15-16) reported the relationship between the presence of H. pylori in the gallbladder and cholelithiasis and reported that premalignant lesions were observed more frequently in H. pylori positive patients. Hassan et al. (17) reported that H. pylori infection may increase the number of mucosal precancerous lesions.

Several mechanisms have been used to explain this relationship in the literature. First, the inflammatory response, which is due to oxidative reactions and free radicals, is blamed (15, 18). Additionally, H. pylori acts as a foreign body and increases the risk of stone formation (19). Another publication reported that the ability of urease-positive H. pylori bacteria to precipitate calcium and substances involved in the formation of gallstones may be effective (20). Finally, it has been suggested that it may play a role in brown bile pigment stone formation by inducing beta-glucuronidase, bacterial hydrolase, and phospholipase enzymes (21).

We believe that these mechanisms might be effective and we found that there are publications in support of our article in our literature review.

Fatemi et al. (22) examined the relationship between H. pylori strains and acute and chronic cholecystitis with/without stones and reported a high incidence of H. pylori in cases of calculous cholecystitis, whereas they did not find a statistical relationship between gallstones and H. pylori. A meta-analysis including 18 studies by Cen et al. (23) reported that cholecystitis and H. pylori were related. In the same study, the H. pylori density was reported to be significantly greater in patients who underwent cholecystectomy for chronic cholecystitis and had stones in the gallbladder than in the control group. Although the rate of H. Pylori infection in patients with acute calculous cholecystitis was not evaluated in our study, no significant difference was found between H. Pylori infection in the group with only gallstones in the gallbladder and the control group. We believe that this difference may be because the pathology results of the groups did not differ between acute and chronic cholecystitis patients.

In two separate studies by Zhou et al. (15) and Helaly et al. (24), a statistically significant correlation was found between Helicobacter positivity in the stomach and gallbladder. Similarities between gallbladder diseases and H. pylori symptoms are frequently encountered in the clinic. In a study conducted by Takahashi et al. (25) in 2013 in which 15551 patients were examined with a 13C urease breath test, H. pylori was found to be positive in 4493 (28.8%) patients with stones in the gallbladder, and this was also shown to be significant in their multivariate analysis.

In some studies, no significant relationship was found between H. pylori positivity in patients with gallstones and preoperative upper gastrointestinal tract endoscopy (11, 26). In a retrospective study including a large population conducted by Xu et al. (3), no relationship was found between patients with positive Helicobacter antibodies in

the blood and gallstones. However, in the same study, a statistically significant relationship was found between gallbladder polyps and H. pylori positivity. In our study, similar to these results, we found significantly greater H. pylori positivity in 39 (97.2%) polyp and 17 (77.3%) polyp-stone coexistence groups than in the control group. Pylori positivity, which suggests that H. pylori may increase polyp formation in the gallbladder. Since our results did not cover a long follow-up period, the mechanisms of gallstone and gallbladder polyp formation were not evaluated in detail. For this reason, our study does not include the effect of the presence of H. pylori on the formation of gallstones and gallbladder polyps, but only the data related to their association. For definitive results on this subject, studies involving larger samples and pathophysiologic investigations are needed.

In studies on the incidence of H. pylori, the prevalence of H. pylori increases with age in Eastern countries, but the sex difference is not significant. Colonization has been reported to increase, especially in people over 70 years of age (14, 27). Gallstones are more common in women than in men. Some sources have reported that approximately 6% of men and 9% of women in the United States have gallstones (28). When sex differences were evaluated, the proportion of women was greater in the group with only gallstones in our study (p=0.009). No significant sex-related differences were found in the other groups, and our findings are consistent with the literature.

There are publications mentioning the relationship between obesity and biliary tract diseases (29). Zhang et al. (30) reported that BMI was greater in patients with H. Pylori infection (p=0.048), whereas no significant difference was found between the groups in terms of BMI in our study (p=0.043).

We believe that our study will make an important contribution to the literature in terms of evaluating the relationships among gallstones, polyps and their associations with the incidence of H. pylori. Indeed, our results show this association.

Our study has important limitations. First, because this was a retrospective study without a good preparation, selection bias was possible. Second, the presence of H. pylori in gallbladder slides was not analyzed. Our findings imply that the development of gallbladder polyps or gallstones is influenced by H. pylori infection.

Declarations

Conflict of interest

The authors do not declare any

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Ethics approval number

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Author Contributions

Cenk Ozkan, Serhan Yilmaz, Emre Bozdag, Osman Sibic and Erkan Somuncu are responsible for the design of the manuscript. Cenk Ozkan, Emre Bozdag and Erkan Somuncu collected the data, and Serhan Yilmaz, Cenk Ozkan and Osman Sibic analyzed the data. All the authors discussed the results and wrote, reviewed, and edited the manuscript and title page. Approval of final manuscript: Cenk Ozkan, Serhan Yilmaz, Emre Bozdag, Erkan Somuncu and Osman Sibic

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