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Histopathological Changes in The Gall Bladder Mucosa Associated with Helicobacter Pylori Gastritis

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Author`s Contribution

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ABSTRACT

Objective: To identify Helicobacter Pylori (HP) gastritis-associated histopathological changes in Gall Bladder (GB) mucosa in patients undergoing cholecystectomy.

Methodology: This prospective comparative cross-sectional study was conducted in the Gastroenterology department of Liaquat National Hospital, Karachi, Pakistan, from December 2021 to December 2022. The study included all patients admitted with a diagnosis of any Gall Bladder pathology and those who were electively scheduled for cholecystectomy. Participants were categorized into two groups based on the presence of HP: group A (HP positive) and group B (HP negative) in gastric mucosa before cholecystectomy. HP detection was performed using various methods, including HP stool antigen (HPSA), Urea breath test (UBT), HP antibodies, and biopsy confirmation through gastroscopy.

Results: The mean age of patients in group A was 42.88 ± 8.28 years, and in group B, it was 43.35 ± 8.74 years (p=0.458). According to the GB histological findings, Chronic cholecystitis with focal Cholesterolosis was significantly more common in group A (75.4%), while Chronic cholecystitis alone was significantly higher in group B (66.2%) (p=0.001). Dysplasia was observed more frequently in group B compared to group A. Erosion was more prevalent in group A, patients than in group B (p=0.001). Although symptom improvement in the HP positive group with persistent symptoms post-eradication was not statistically significant, it did show some improvement (p=0.527).

Conclusion: The histological findings of chronic cholecystitis with focal Cholesterolosis were significantly higher in the HP positive group compared to the HP negative group, while chronic cholecystitis alone was significantly more common in the HP gastritis negative group. Some HP gastritis group patients experienced symptom improvement after HP eradication.

Keywords: Helicobacter Pylori, Gastritis, Cholecystitis, Gall bladder.

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Introduction

Approximately 50% of people worldwide are infected with the gram-negative spiral-shaped bacterium Helicobacter pylori (H. pylori), with a higher prevalence in developing nations.[1] If left untreated, H. pylori can persist for the rest of one's life. The prevalence of this bacterium varies by region and sanitary standards.[2]

Chronic gastritis caused by Helicobacter pylori infection can lead to serious gastroduodenal diseases such as peptic ulcers, gastric cancer, and gastric mucosa-associated lymphoid tissue lymphoma, among others.[3] Research and reports have also explored the connection between H. pylori and illnesses affecting organs other than the stomach and duodenum.[4,5] In 1996, Chang et al.[6] unintentionally identified H. pylori in the gallbladder mucosa of a patient with cholecystitis, suggesting a potential link between gallstone development and H. pylori infection.

Gallstones are a common condition globally, with the highest prevalence rates in Western nations.[7] The pathophysiology of gallstones involves multiple factors that vary depending on the type of gallstones. Gallstones can be primarily categorized into two types: pure

gallstones, constituting 10% of all gallstones, and mixed or combination gallstones, making up the remaining 90%. Mixed gallstones are commonly associated with cholecystitis.[8]

Approximately 76.66% of patients with symptomatic cholelithiasis also have concurrent H. pylori gastritis infection, indicating an increasing occurrence of cholelithiasis among adults.[9] Symptoms in cholelithiasis patients commonly include heartburn, dyspepsia, bloating, and abdominal discomfort, which can be felt in the right hypochondrium or epigastrium.[10,11] Most cholelithiasis patients exhibit moderate to severe gastritis based on endoscopic results, and a significant three-fourths of them also have gastroduodenal issues.[9]

H. pylori can enter the gallbladder through the portal blood circulation or directly from the stomach.[12] This raises the possibility that the pathophysiology underlying cholecystitis and gastritis may be linked to another H. pylori infection of the gallbladder.[13] However, data regarding the concomitant prevalence of H. pylori in the stomach among patients with gallstones and its association with gallstone pathologies are limited. Since some patients continue to experience upper abdominal discomfort after cholecystectomy, it can be concerning for surgeons and may increase the likelihood of an undiagnosed concurrent upper gastrointestinal problem.[14] Therefore, it is crucial to investigate any potential correlation between the presence of Helicobacter pylori gastritis and its contribution to histopathological changes in the gallbladder mucosa in this context.

Methodology

This comparative cross-sectional prospective study was conducted at the Gastroenterology department of Liaquat National Hospital, Karachi, Pakistan, from December 2021 to December 2022. In the preliminary phase, a pilot study was undertaken, with 30 patients in each arm. Within the groups of HP gastritis positive and negative patients, the frequency of chronic cholecystitis was 16.4% and 61.8%, respectively. Based on a 95% confidence level and 80% statistical power, a sample size of 65 patients per group was determined through sample size calculation using the two-proportion option in the WHO calculator, resulting in a total sample of 130 patients.

All patients admitted under the General Surgery services, diagnosed with gallbladder (GB) pathology, primarily cholecystitis secondary to any cause and cholelithiasis, and scheduled for elective cholecystectomy, were eligible for enrollment in this study. The study encompassed individuals of both genders, aged between 25 and 65 years, who provided informed consent to participate and agreed to undergo all necessary investigations as part of the study. Exclusions from the study criteria consisted of patients with GB empyema, carcinoma, or perforations, as well as those who declined to participate.

Prior to cholecystectomy, patients were categorized into two groups based on the presence of Helicobacter pylori (HP) infection, with Group A representing those with HP infection and Group B comprising those without. The detection of HP infection in the gastric mucosa was accomplished using various methods, including HP stool antigen (HPSA), the Urea breath test (UBT), HP antibodies, or biopsy confirmation through gastroscopy. After cholecystectomy, gallbladder specimens were sent to a single histopathology laboratory and reviewed by a single histopathologist to minimize the potential for operator error when identifying histopathologic changes in the mucosa of both groups.

Results

A total of 130 patients were enrolled to assess HP infection-related histopathological changes in the gall bladder mucosa of patients undergoing cholecystectomy. The mean age of patients in group A was 42.88 ± 8.28 years, while in group B, it was 43.35 ± 8.74 years (p=0.458). Females were the majority in both groups, with 41 (63.1%) in group A and 45 (69.2%) in group B. Comorbidities, symptoms, ultrasound findings, and duration of symptoms were statistically insignificant in both groups, as shown in Table I.

The most common detection methods were gastroscopy and HPSA in both groups, with no significant difference (p=0.241), as indicated in Table II.

Regarding the gastroscopy findings, mild to moderate gastritis was the most common in both groups, and the differences were statistically insignificant (p=0.521).

In terms of gallbladder histological findings, chronic cholecystitis and focal cholesterolosis were present in 75.4% of group A specimen, whereas in group B, 66.2% of specimens had chronic cholecystitis only (p=0.001). Additionally, dysplasia was observed in one case in group A and in three cases in group B, while erosion was found in three cases in group A and in two cases in group B (p=0.001).

Table I: Demographic and clinical characteristics of the patients in both groups. (n=130)

Variables		Study groups: H.P Gastritis positive	Study groups: H.P negative gastritis	p-values
Age (years)		42.88±8.28 years	43.35±8.74 years	
Gender	**Male**	24	20	0.458
		36.9%	30.8%	
	Female	41	45	
		63.1%	69.2%	
Comorbidities	None	26	26	0.438
		40.0%	40.0%	
	HTN	10	16	
		15.4%	24.6%	
	DM	8	4	
		12.3%	6.2%	
	Dyslipidemia	7	8	
		10.8%	12.3%	
	Thyroid issues	0	1	
		0.0%	1.5%	
	HTN+DM	14	9	
		21.5%	13.8%	
	HTN+DM+IHD	0	1	
		0.0%	1.5%	
Symptoms	Upper abdominal pain	36	28	0.445
		55.4%	43.1%	
	vomiting	0	1	
		0.0%	1.5%	
	fever	0	1	
		0.0%	1.5%	
	upper abdominal pain and fever	22	28	
		33.8%	43.1%	
	upper abdominal pain and vomiting	7	7	
		10.8%	10.8%	
Ultrasound findings	Cholecystitis	9	15	0.356
		13.8%	23.1%	
	Cholelithiasis	28	27	
		43.1%	41.5%	
	Cholecystitis + cholelithiasis	28	22	
		43.1%	33.8%	
	GB polyps	0	1	
		0.0%	1.5%	
Duration of symptoms		4.95+172 months	4.52+180 months	0.167

Table II: Frequency of detection methods in the patients of both groups .(n=130)

Variables		Study groups: H.P Gastritis positive	Study groups: H.P negative gastritis	p-values
Detection methods	EGD	1	0	
		1.5%	0.0%	
	EDG	1	0	0.241
		1.5%	0.0%	
	EGD	39	28	
		60.0%	43.1%	
	H.P ABX	1	2	
		1.5%	3.1%	
	HB ABX	0	1	
		0.0%	1.5%	
	HP ABX	4	2	
		6.2%	3.1%	
	HPSA	17	28	
		26.2%	43.1%	
	UBT	2	4	
		3.1%	6.2%	

Table III: Comparison of GB pathologies and improved symptoms in both groups. (n=130)

Variables		Study groups: H.P Gastritis positive	Study groups: H.P negative gastritis	p-values
EGD findings	Mild gastritis	42	40	
		64.6%	61.5%	
	Moderate gastritis	20	23	0.521
		30.8%	35.4%	
	Severe gastritis	3	1	
		4.6%	1.5%	
	Duodenal ulcers	0	1	
		0.0%	1.5%	
GB histological findings	Chronic cholecystitis + focal Cholesterolosis	49	17	
		75.4%	26.2%	0.0001
	Chronic cholecystitis	12	43	
		18.5%	66.2%	
	Dysplasia	1	3	
		1.5%	4.6%	
	Erosions	3	2	
		4.6%	3.1%	
Improved symptoms	Yes	52	49	
		80.0%	75.4%	0.527
	No	13	16	
		20.0%	24.6	

Discussion

Helicobacter pylori (HP) is a bacterium known to colonize the human stomach, potentially causing gastritis, peptic ulcers, and gastric cancer. Recent studies have indicated that HP infection might also impact the gallbladder (GB), as an increased prevalence of HP infection has been reported in patients with GB diseases, such as chronic cholecystitis, cholelithiasis, and GB cancer.

In our current study, we compared 130 patients who underwent cholecystectomy to evaluate the histopathological changes in the GB mucosa related to HP infection. Group A had a mean age of 42.88±8.28 years, and group B had a mean age of 43.35±8.74 years (p=0.458), with a majority of female patients in both groups. When comparing our study to others, Nahon S et al[15] reported a majority of female subjects (76) and 29

male subjects, with an overall mean age of 57.4 ± 21.4 years. In a study by Arisawa T et al[16] the average age of the patients was approximately 62.03 years, and they reported a male-to-female ratio of 102:57. It is essential to note that the higher prevalence of HP infection in females is not universal and may vary depending on the studied population and the methods used to detect the infection.

In our study, according to the GB histological findings, chronic cholecystitis and focal cholesterolosis were significantly higher in the HP-infected positive group (75.4%), while chronic cholecystitis was significantly higher in the HP non-infected negative group (66.2%) (p=0.001). Dysplasia was observed in one case of group A and in three cases of group B, while erosion was found in three cases of group A and in two cases of group B (p=0.001). Yakoob J et al[17] observed the presence of HP DNA in patients with chronic cholecystitis and GB carcinoma in association with cholelithiasis, although this relationship requires further investigation. In another study by Helaly GF et al [18], it was noted that HP infection might contribute to cholecystitis, and the colonization of HP in the stomach could potentially lead to GB infection and the formation of pigmented gallstones, particularly in cases of pure pigmented gallstones. However, Raza M et al[19] found no significant correlation between HP infection and calculous cholecystitis, even though HP infection was associated with a high degree of hyperplasia, fibrosis, and mononuclear infiltrate inflammation in the GB. Abd-Almahdi AH et al[20] revealed a significant correlation between chronic cholecystitis with calculi and HP infection, but no significant correlation was observed between HP infection and acalculous cholecystitis or other GB pathologies. On the other hand, Mishra RR et al.[21] reported that HP was present in a large population of patients with both GB carcinoma (GBC) and GB diseases, suggesting that the bacterium is endemic in the Varanasi region. Therefore, it appears that HP may not play a significant role in the development of GBC in this region. Although there are still controversies in the association between HP infection and GB disorders, most studies recommend further research.

Our study also observed that symptom improvement following post H. pylori eradication in the gastritis-positive group was not significantly different from symptom improvement among those without HP infection. However, many studies did not compare symptom improvement between patients with and without HP infection.

Several limitations of our study should be acknowledged. The sample size is relatively small, which may limit the generalizability of our findings to a larger population. Additionally, the study was conducted in a single center, which may impact the diversity of the patient population and limit the applicability of the findings to other regions or settings.

Conclusion

The histological findings of chronic cholecystitis and focal cholesterolosis were significantly more prevalent in group A, which was infected with Helicobacter pylori (HP), compared to group B, which was not infected with HP. These results suggest that there may be distinct underlying factors contributing to the development of gallbladder (GB) disease in these two groups. Further research is required to elucidate the clinical implications of these findings and to identify potential risk factors for GB disease.

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