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Incidence of Carcinoma of Gall Bladder Among Patients of Cholelithiasis

Urooj Mehtab Raina[1], Gulzar Ahmed[2], Aemun Javed[1], Tehwarsham Bin Fayyaz[1]

[1]Department of Surgery, Shahida Islam Medical & Dental College/Teaching Hospital, Lodhran, Punjab, Pakistan.
[2]Professor of Surgery, Shahida Islam Medical & Dental College/Teaching Hospital, Lodhran, Punjab, Pakistan.

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Corresponding Author: Urooj Mehtab Raina,
Department of Surgery, Shahida Islam Medical & Dental College/Teaching Hospital, Lodhran, Punjab, Pakistan.
Email: gulrana007@gmail.com

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ABSTRACT

Introduction: Cholelithiasis, gallbladder adenomatous polyps, gallbladder wall calcification, choledochal cysts, and chemical carcinogens are risk factors for gallbladder cancer. Usually discovered by chance, gallbladder cancer is identified by histological analysis after cholecystectomy for cholelithiasis. I have chosen to carry out this investigation in order to ascertain the prevalence of gallbladder cancer in cholelithiasis patients. **Study design:** Descriptive, cross sectional study. **Settings:** Department of Surgery, Shahida Islam Teaching Hospital, Lodhran. **Study Duration:** 23rd July 2024 to 22nd January 2025. **Materials & Methods:** A total of 370 patients aged 40-80 with cholelithiasis for over four weeks undergoing cholecystectomy were included. Exclusions: gallbladder cancer, chronic liver/renal disease, and pregnancy. After informed consent and pre-anesthesia evaluation, specimens were analyzed for gallbladder cancer, identifying glands lined by cuboidal or columnar cells, potentially containing mucus. **Results:** Age range in this study was from 40 to 80 years with mean age of 57.95 ± 9.20 years. Majority of the patients 218 (58.92%) were between 40 to 60 years of age. Out of 370 patients, 66 (17.84%) were male and 304 (82.16%) were females with male to female ratio 1:4.6. Mean duration of disease in our study was 5.85 ± 2.36 months. Mean BMI was 27.36 ± 2.94 kg/m2. In our study, incidence of carcinoma of gall bladder among patients of cholelithiasis was found in 28 (7.57%) patients. **Conclusion:** The research population had a 7.57% incidence of gall bladder cancer, which was mostly associated with porcelain gall bladder and chronic cholecystitis.

INTRODUCTION

Cholecystectomy is the most common major abdominal surgical treatment performed globally, and gallbladder stones illness is prevalent, with a prevalence of 10-15% in the USA and over 16% in Pakistan[1]. Chronic cholecystitis and a lengthy history of cholelithiasis are known risk factors for gallbladder cancer[2]. During or after surgery for symptomatic gallstone disease, cancer of the gall bladder is typically discovered by chance.

Gallbladder cancer is the most frequent primary tumor of the billiary tract and a common digestive system cancer[3]. The most common age group for this malignancy is middle-aged to older women. Recent clinical and epidemiological research has shown a connection between prior Helicobacter species infection and gallstone disease, gall bladder cancer, and other hepatobiliary disorders[4].

One of the most affected areas has been found to be Pakistan (13.8/100000)[5]. Risk factors include gall bladder diseases or abnormalities, infection, exposure, cholelithiasis, and inflammatory causes. 70 to 90% of GBC patients have cholelithiasis, and dysplasia is believed to be caused by calculi's persistent irritation of the mucosa[6]. According to the present theory, persistent inflammation of the bile duct tissue accumulates successive genetic changes that result in malignant transformation. The most often reported mutations are in the tumor suppressor beta-catenin and the oncogene K-ras (CTNNB1)[7]. No indication of a hereditary familial risk has been found.

Among patients with cholelithiasis, the incidence of gallbladder cancer was 4%.[8] Similar results were also obtained by Naqvi SQH et al[9]. because 5.9% of cholelithiasis patients had GB cancer. Junejo A et al. consistently reported that 10.86% of 138 individuals had GB cancer[10].

Cholelithiasis, gallbladder adenomatous polyps, gallbladder wall calcification, choledochal cysts, and chemical carcinogens are risk factors for gallbladder cancer. Usually discovered by chance, gallbladder cancer is identified by histological analysis after

cholecystectomy for cholelithiasis[11,12]. Adenocarcinomas make up the majority of gallbladder carcinomas; papillary carcinomas, well- to poorly-differentiated infiltrating carcinomas, and squamous cell carcinomas are less frequent[13].

I have chosen to carry out this investigation in order to ascertain the prevalence of gallbladder cancer in cholelithiasis patients. The significance of considering the risk of gallbladder cancer in patients having cholecystectomy for cholelithiasis will be emphasized by this study. It is feasible to enhance patient outcomes and lower the mortality rate linked to gallbladder carcinoma by identifying incidental carcinomas and putting suitable treatment plans into place.

MATERIALS AND METHODS

This descriptive cross-sectional study was done from 23rd July 2024 to 22nd November 2024 at Department of Surgery, Shahida Islam Teaching Hospital, Lodhran. A total of 370 patients who met the inclusion criteria were chosen through non-probability consecutive sampling following approval by the institutional ethical review committee. Every patient will be asked for their informed permission. With a 95% confidence level, a 2% margin of error, and a 4.0% frequency of gallbladder cancer among cholelithiasis patients, a sample size of 370 cases has been determined.[8] All patients between the ages of 40 and 80 who had cholelithiasis lasting more than four weeks and were having a cholecystectomy were included, regardless of gender. Patients with pre-existing gallbladder cancer, those with chronic liver disease (defined as defined by history and s/bilirubin >1.0 mg/dl), those with chronic renal failure (defined as defined by history and s/creatinine >1.5 mg/dl), and pregnant women (defined as defined by USG) were not included.

A thorough medical history, physical examination, and standard laboratory tests were conducted. Patients were transported for cholecystectomies following informed permission and a pre-anesthesia examination. At least three years after the fellowship experience, a consultant surgeon performed a cholecystectomy. Specimens were submitted right away to the hospital diagnostic laboratory to assess for gall bladder cancer (the presence of glands lined by cuboidal or columnar cells, which may contain mucus). A freshly created proforma was used to record all of the data.

Software called SPSS 25.0 was used to evaluate the data that was gathered. The data's normality was examined using the Shapiro-Wilk test. The mean and standard deviation or median (IQR) of age, height, weight, BMI, and length of illness were displayed. Frequencies and percentages for gender, smoking, diabetes mellitus, hypertension, place of residence, and gallbladder cancer (present or absent) were displayed. Stratification was used to account for effect modifiers such as age, gender, smoking, place of residence, BMI, diabetes mellitus, hypertension, and length of disease. The chi square test for post-stratification will be used, and a p-value of less than 0.05 was considered significant.

RESULTS

Age range in this study was from 40 to 80 years with mean age of 57.95 ± 9.20 years. Majority of the patients 218 (58.92%) were between 40 to 60 years of age. Out of 370 patients, 66 (17.84%) were male and 304 (82.16%) were females with male to female ratio 1:4.6. Mean duration of disease in our study was 5.85 ± 2.36 months. Mean BMI was 27.36 ± 2.94 kg/m^2. Distribution of patients with other confounding variables is shown in Table I.

In our study, incidence of carcinoma of gall bladder among patients of cholelithiasis was found in 28 (7.57%) patients (Figure I). Stratification was used to account for effect modifiers such as age, gender, smoking, place of residence, BMI, diabetes mellitus, hypertension, and length of disease is shown in Table II.

Table I

Distribution of patients with other confounding variables (n=370)

Confounding variables		Frequency	%age
Age (years)	40-60	218	58.92
	61-80	152	41.08
Gender	Male	66	17.84
	Female	304	82.16
Duration of disease (months)	≤6	255	68.92
	>6	115	31.08
BMI (kg/m^2)	≤25	103	27.84
	>25	267	72.16
DM	Yes	92	24.84
	No	278	75.16
HTN	Yes	82	22.16
	No	288	77.84
Smoking	Yes	49	13.24
	No	321	86.76
Place of residence	Rural	132	35.68
	Urban	238	64.32

Figure I

Incidence of carcinoma of gall bladder among patients of cholelithiasis (n=370).

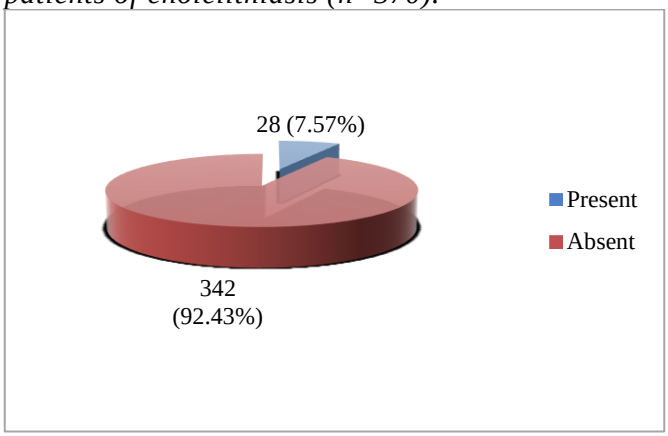
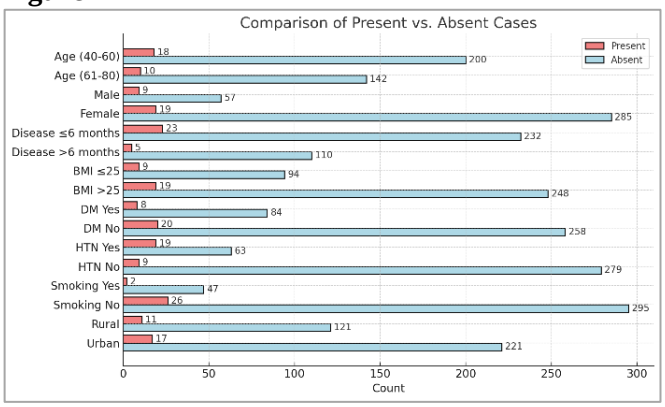


Table II

Stratification of gallbladder carcinoma with respect to age, gender, smoking, place of residence, BMI, diabetes mellitus, hypertension, and length of disease.

		Present (n=28)	Absent (n=342)	P-value
Age (years)	40-60	18	200	0.548
	61-80	10	142	
Gender	Male	09	57	0.039
	Female	19	285	
Duration of disease (months)	≤6	23	232	0.116
	>6	05	110	
BMI (kg/m^2)	≤25	09	94	0.597
	>25	19	248	
DM	Yes	08	84	0.636
	No	20	258	
HTN	Yes	19	63	0.0001
	No	09	279	
Smoking	Yes	02	47	0.322
	No	26	295	
Residence	Rural	11	121	0.678
	Urban	17	221	

Figure 2



DISCUSSION

A terrible condition with a high death rate is gall bladder cancer. The fact that gall bladder cancer is discovered at an advanced stage is one of the factors contributing to its poor prognosis. The frequently carried out histological assessment is a laborious process with little predictive value[14,15].

According to our study's findings, the patients' average age was 57.95 ± 9.20. According to tertiary hospitals in Pernambuco, Brazil, the incidence of gallbladder cancer in all cholecystectomy specimens is 0.4%[16]. According to Meng et al[17], the average patient age was 58 years old. In contrast, Kazmi et al[18] found that the average age of the patients in their study was just 43.87 years. On the other hand, gall bladder cancer is very uncommon in younger people. According to epidemiological research conducted in bigger settings, the median patient age is over 60[14].

The majority of the study sample (82.16%) was female. Regarding gall bladder cancer and cholelithiasis, there were no gender-based differences. Worldwide, there have been numerous reports of sex disparities that indicate a greater proportion of women than men[19, 20]. According to epidemiological research conducted in India, women are more likely than men to have gallstone disease and gall bladder cancer[21]. The current study's results support this.

In our investigation, we discovered that 28 (7.57%) of the patients with cholelithiasis had gallbladder cancer. Khoo et al. in Johor, Malaysia, found 9 (0.8%) cases of gallbladder cancer in a study of 1122 cholecystectomy specimens, with 77.77% of incidental carcinoma and 22.22% of clinically suspected carcinoma. There was one incidence of clinically likely gallbladder cancer in each of the seven incidental carcinoma patients, three of whom were male and four of whom were female[22].

According to Sutradhar PK et al., the prevalence of gall bladder cancer was 5.3%, with eight (eight) out of 150 patients who had surgery for gall bladder stone disease later developing gall bladder cancer. Gall bladder cancer was preoperatively suspected in just three (37.5%) of the patients based on ultrasonography. Women are more likely than men to be affected by this illness[23].

Gallbladder cancer is incidental in 1.67% of cases, according to Poudel R et al. For early diagnosis and to improve the patient's chances of surviving gall bladder cancer, routine histopathology of cholecystectomy specimens is recommended[24].

To determine the prevalence of gallbladder cancer in patients undergoing cholecystectomies due to gallbladder disease, Faik Tatli, Abdullah Ozgönül, and colleagues conducted a study. They presented the pathological results of their analysis of the medical records of 341 patients who had routine cholecystectomy procedures performed between January 2013 and March 2016. With an average age of 67.71 years, seven patients (2.05%), six of whom were female and one of whom was male, had gallbladder tumors[25].

Thirteen participants out of 610 macroscopically aberrant gallbladder specimens in the research by Mittal et al. of 1305 patients had incidental GBC.[26] The existence of early GBC in a gallbladder specimen that seems normal has raised concerns. But for these patients, a straightforward cholecystectomy is thought to be sufficient, and no additional treatment is needed.[27] Prior to doing a macroscopic examination of the gallbladder specimen immediately following surgery, the surgeon in their study first determined the risk variables for GBC. After macroscopic investigation, the surgeon suspected all three of the histopathologically proven GBCs in their study. Additionally, Wrenn et al. have determined that selective screening may be a practical and more economical option than universal screening, depending on risk factors (such as older

patients), intraoperative observations, and on-table specimen inspection[28].

Gall bladder cancer was found in 6.15% of cholelithiasis patients in the Malik KA research[29]. Six patients (0.96%) out of all research participants had incidental gallbladder carcinomas, according to SuJata J et al.[30] Five individuals out of 310 specimens had gall bladder cancer in another investigation by Jan Y et al.[31] Lohana D et al[32] consistently found 45 gall bladder cancers in cholelithiasis patients. Similar results were also obtained by Naqvi SQH et al[9], who found that 5.9% of patients with cholelithiasis had GB cancer.

The study's single-center design, small sample size, possible selection bias, disregard for confounding variables, and lack of standardized procedures are among its drawbacks. These restrictions limit the findings' generalizability and could have an impact on the study's statistical power and dependability. Furthermore, the study did not offer thorough insights into the mechanisms driving the development of gallbladder cancer or patient outcomes. To get a more thorough understanding of gallbladder cancer and incidental carcinoma, more research addressing these shortcomings is required.

CONCLUSION

The research population had a 7.57% incidence of gall bladder cancer, which was mostly associated with porcelain gall bladder and chronic cholecystitis. This study emphasizes how crucial it is to take gallbladder cancer risk into account when treating patients with cholecystectomy for cholelithiasis. It is feasible to enhance patient outcomes and lower the mortality rate linked to gallbladder carcinoma by identifying incidental carcinomas and putting suitable treatment plans into place.

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