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A Study On Predictors Of Incidental Gall Bladder Cancer Operated For Benign Gall Bladder Disease

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ABSTRACT-
Introduction*-Gallbladder cancer is sometimes/occasionally discovered incidentally after cholecystectomy performed for presumed benign disease. Unfortunately, cholecystectomy is an incomplete operation except for the earliest stage of malignant disease.*
Aim*-1).To determine the predictors of incidental gall bladder cancer detected in patients operated for benign gall bladder disease.2). To determine the mortality and morbidity based on these predictors.3). To determine the incidence of incidental gall bladder cancer detected after gall bladder surgery in study population.*
Material and methods*- A Prospective observational study was conducted involving 210 patients of benign gall bladder disease at Department of surgery ,Silchar Medical college and hospital,Assam,India from july 2021 to July 2022.Patients having history of right hypochondrial pain, pain with/without fever, jaundice and diagnosed with cholelithiasis,empyema of gall bladder, mucocele of gall bladder, emphysematous cholecystitis, gall bladder polyp,cholesterosis ,Chronic cholecystitis on imaging were selected for laparotomy/open cholecystectomy.*
Results*- This study includes 60 (28.5%) males and 150 (71.5%) females. The mean age was 46.67 years for incidental gall bladder carcinoma and 83.33% of incidental GB cancer cases were female. Incidental gall bladder cancer was predominantly a disease of elderly female patients.*
Conclusion*-Incidence of Incidental gall bladder cancer were detected among elderly female patients. Patients with benign gall bladder disease should be screened by imaging studies like USG, CT Scan to rule out carcinoma of gall bladder.*
Key words*-Gall bladder cancer, Chronic Cholecystitis, Benign gall bladder disease, Ultrasonography, CT scan.*

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I. INTRODUCTION

Gallbladder cancer, although rare, is the most common of biliary tract malignancy[1]. It traditionally has been considered an incurable disease with an extremely poor prognosis. Gallbladder cancer is sometimes/occasionally discovered incidentally after cholecystectomy performed for presumed benign disease. Unfortunately, cholecystectomy is an incomplete operation except for the earliest stage of malignant disease. All surgeons who treat gallbladder disease must understand the natural history, biology, imaging, staging, and proper surgical treatment of gallbladder tumours. It is crucial to make proper treatment decisions early rather than after an incomplete, noncurative cholecystectomy.

For surgeons whose specialty includes gallbladder cancer, it is important to understand the outcome and limitations of surgical resection so that a complete understanding of the risks and benefits can be analysed, presented to patients, and result in a rational treatment strategy. The nihilism historically associated with gallbladder cancer stems from its late presentation, often with disseminated disease, overall dismal prognosis, and lack of effective systemic therapy. Gallbladder cancer has a tendency to spread early via lymphatic, hematogenous, and peritoneal metastases and also has the unique ability to implant along biopsy tracts and wounds.

Pessimistic attitudes about gallbladder cancer have persisted from the original description of gallbladder cancer in 1778 (Kato et al, 1994)[2] to more recent times and are supported by reports of overall 5-year survival of 20% with median survival of just 16 months (Mayo et al, 2010)[3] for patients with resectable disease. For advanced, untreated gallbladder cancer, the median survival is generally 2 to 5 months, and long-

term survival is exceedingly rare (Perpetuo et al, 1978; Piehler & Crichlow, 1978)[4,5]. Systemic chemotherapy remains limited in its effectiveness, but with improvements in systemic chemotherapy in other diseases, it is possible that these benefits will begin to extend to patients with gallbladder cancer.

The role of definitive resection, however, has now been shown to be effective in properly selected patients. Complete surgical removal of gallbladder cancer is the only potentially curative therapy. With improvements in imaging, staging, and hepatic and biliary resection, there is hope for patients with non metastatic gallbladder cancer. Effective and proven adjuvant therapy is still lacking, however, and represents a significant limitation of current treatment options.

Cancer of the gallbladder is a rare malignancy that occurs predominantly in the elderly. It is an aggressive tumour, with a poor prognosis that is usually not diagnosed until it has become advanced and is causing symptoms. The median survival for gallbladder cancer is around 6 months with a reported 5-year survival rate of 5%.

Carcinoma of the gallbladder is a rare disease, but extremely variable by geographical region and racial–ethnic groups. The highest incidence is among Chileans, American Indians and residents in parts of northern India, where it accounts for as much as 9% of all biliary tract disease. Women appear to have a higher incidence across all geographical areas. In Western practice, gallbladder cancer accounts for less than 1% of new cancer diagnoses. The disease usually presents in the 7th or 8th decade. The etiology is unclear but there appears to be an association with pre-existing gallstone disease, suggesting that chronic inflammation may play a role in a manner similar to tumors of the common bile duct.

Calcification of the gallbladder wall, presumably due to chronic inflammation (porcelain gallbladder), is also associated with a small increased risk of cancer. Chronic infection may also promote development of gallbladder cancer and the risk in typhoid carriers is significantly increased over the general population. Gallbladder polyps may be found in approximately 5% of patients who undergo ultrasonography. The majority are either adenomyomatosis or cholesterol polyps and have no malignant potential. True adenomatous polyps occur in 0.3–0.5% of the population. The risk of malignant transformation increases with increasing size of the polyp.

Objectives-

1).To determine the predictors of incidental gall bladder cancer detected in patients operated for benign gall bladder disease.

2). To determine the mortality and morbidity based on these predictors.

3). To determine the incidence of incidental gall bladder cancer detected after gall bladder surgery in study population.

II. MATERIALS AND METHODS

A Prospective observational study was conducted involving 210 patients of benign gall bladder disease at Department of surgery ,Silchar Medical college and hospital ,Silchar, Assam,India from july 2021 to july 2022.Ethical approval was obtained from Institutional Ehtics Committee and Consent were taken from each patients. Patients of any age group and either sex having history of right hypochondrial pain,with/without fever,jaundice were included in the study. All selected patients who were diagnosed with cholelithiasis, empyema of gall bladder, mucocele of gall bladder, emphysematous cholecystitis, gall bladder polyp, cholesterosis on imaging were selected for laparotomy/open cholecystectomy**.** After laparotomy/open cholecystectomy all sample were sent for histopathological examination.

Exclusion criteria: Patients not willing to participate/ giving consent for study . Preoperative suspicion of Gall Bladder cancer and Diagnosed case of carcinoma gall bladder by USG or CECT were also excluded.

III. RESULTS

Out of 210, 60 cases were male (28.5%) and 150 cases were female(71.4%). On histopathological examination 1 out of 60 male cases came out to be IGBC and 5 out of 150 female cases came out to be IGBC. Out of 6 cases that came out to be IGBC, 2 cases fall under the age group of 21- 40 years and rest 4 came under 41-60 years of age. The cases that fell under the age group of 21-40 years were above 30 years of age. It can be concluded that 30-60 years of age group had maximum IGBC cases preponderance.

Table 1: Symptomwise distribution of study subjects.

Symptoms		Chronic Cholecystitis	IGBC
Pain	Present	179	5
	Absent	25	1
Nausea and Vomiting	Present	32	0
	Absent	172	6
Anorexia	Present	97	2
	Absent	107	4
Jaundice	Present	42	1
	Absent	162	5
Weight Loss	Present	9	1
	Absent	195	5
Lump in abdomen	Present	51	4
	Absent	153	2

Table 2: Distribution of study subjects as per personal and family history of study subjects.

Personal and family history		Chronic Cholecystitis	IGBC
Diet	Vegetarian	9	0
	Non-vegetarian	195	6
Addiction	Present	56	1
	Absent	148	5
Family History of GB Cancer	Present	6	1
	Absent	198	5

TABLE 3: BIOPSY REPORT

BIOPSY REPORT	**CHRONIC CHOLECYSTITIS**	**CARCINOMA OF GALL BLADDER**
MALE	59	1
FEMALE	145	5
TOTAL	204	6

Table: 4: Distribution of symptoms as found in different studies.

Series	Pain	Anorexia	Jaundice	Weight loss	Nausea/Vomiting
Piehler and Crichlow[5]	76%	34%	38%	39%	32%
Shieh et al[14]	60.4%	43.7%	35.4%	33.3%	35.4%
Al-Hadeedi et al[15]	47.3%	39.4%	36.4%	39.4%[a]	10.5%
Shukla et al[6]	85%	40%	60.3%	14.9%	24.7%
Klamer and Max[16]	70%	-	40%	40%	30%
Silk et al[17]	78.5%	35.6%	28.5%	45.7%[b]	35.6
Perpetuo et al[18]	97%	-	44%	77%	64%
Kelly and Chamberlain[19]	74%	-	32%	48%	51%[c]
White et al[20]	83%	-	47%	70%	-
Chao and Greagor[7]	54.1%	18.9%	45%	28.4%	18.9%

IV. DISCUSSION

This was a prospective observational study. 210 patients were included in study population. The minimum age was 6 years and the maximum age was 78 years with the mean age of 42 years. The mean age of study population was 44.46 years. This finding is going parallel with previous studies. Shukla et al (1985)[6] reported mean age of the Carcinoma gall bladder patients to be 50 years , the mean age of 1,728 patients from 29 series, reported upon since 1960 was 65.2 years with incidence of carcinoma of the gallbladder of 0.1; 1.5; 8.9; 19.6; 37.0 and 32.0 % in third, fourth fifth, sixth, seventh and eighth decades respectively.

Among 204 chronic cholecystitis patients 28.92 % are males and 72.05 % are females. The seemingly greater number of females could be explained by the fact that cholecystitis is most common in female. Thus, in a hospital-based study, women patients form a majority of the study population. Piehler JM and Crichlow RW showed that "Carcinoma of the gallbladder is predominantly a disease of elderly females of 2,998 patients from 51 series reported over last 20 years, there were 2,292 females (75%) and 706 males (25%), a female to male ratio of 3.2:142. In the study by IARC under SEARCH program gallbladder cancer was found to be commonest among women (56%) with cancer of the ampulla of the Vater coming second with 30 percent". According to our

study IGBC is common in female population because of chronic cholecystitis being more prevalent in the female population. Also, in our study the female to male ratio came out to be 2.5:1 (150 females and 60 males). Among 210 patients 68.5% are from rural area & 31.5% are from urban area. This only indicates Geographical distribution of population. Shukla et al (1985)[6] reported an incidence of 4.4% of all malignancies and 0.03 % of total hospital admissions from Varanasi, India. Chao and Greager (1991)[7] reported an incidence of 2.5/100,000 population and found carcinoma of the gallbladder in 1-3 percent of cholecystectomy specimens. In our study the incidence of incidental Carcinoma gall bladder is 2.85% which was 0.3%, 0.6%,0.9%,1.1%,1.9% and 4.7% in Daphna et, Tantia et al, Mittal et al, Morera et al, Amanullah et al and Shigeki et al respectively.

Among 210 patients 88.09% of the total study population had upper abdominal pain. 90% of male population and 87.33%of female population had pain at the time of presentation. In this population 21.42% had jaundice and 10.95% patient had vomiting. Fever was not present in any of the patients. 27.14% patient c/o palpable lump, 46.66% had anorexia. No patients had hepatomegaly. In comparison, data regarding presentation of Carcinoma Gall bladder is shown in table 4. Pain was present in 47-97% of patients in the above studies. This is comparable to the data (88.09%) in our study. Similarly, anorexia, jaundice and vomiting were comparable in this study and jaundice is a feature of advanced Carcinoma Gall Bladder. This shows that there are no clinical features that would be suggestive of gall bladder cancer in a patient who presents with symptoms of chronic cholecystitis. However, in the IGBC group in our study shows a consistent feature of thickness of the gall bladder wall in the fundal region in CECT that might help in arising a strong suspicion towards the potential of Gall Bladder Carcinoma. No suggestive single clinical parameter of incidental gall blabber cancer could be obtained from this comparison. Other parameters were also compared but no result obtained. Taking into consideration 2 clinical parameters together might help in assessing IGBC. In our IGBC study population pain and lump were promising factors. But based on clinical parameters alone one should never suspect any case to be a malignancy. These clinical parameters along with the imaging modalities might help in raising a strong suspicion towards malignancy. Only intraoperative findings are suggestive of IGBC in a few cases. These findings include adhesions, thickening, irregularity of gall bladder wall and abnormal mucosa of the gall bladder. Open cholecystectomy was performed in 5 cases (in which 2 cases had to undergo extended cholecystectomy) and 1 case was operated via the laparoscopic technique. The following parameters of incidental gall bladder carcinoma were compared with chronic cholecystitis patients: Among IGBC patients mean age was 46.67 years. Minimum age was 34 years and maximum age was 60 years. Among incidental GB cancer cases (n=6), male patients were 16.67% & female patients were 83.33%. Among incidental GB cancer patients 33.33% were living in urban area 66.67% were living in rural area. Among incidental Carcinoma GB patients 83.33% had pain abdomen and 16.67% had no pain; 0% patient had vomiting; 83.33% had lump; 16.67% had jaundice and anorexia. USG was suggestive of chronic cholecystitis in 204 cases and all the 6 IGBC patients had size of a largest calculous >2cm and thickened gall bladder wall. CECT Abdomen was suggestive of thickened gall bladder wall(>3mm) and chronic calculous cholecystitis in all the IGBC patients. From the current study an inference can be made that the size of a calculous >2cm and thickened gall bladder wall(>3mm) can be the predictors of gall bladder cancer. There are no characteristic clinical features of EGBC (Early Gall Bladder Carcinoma). Unfortunately, it becomes clinically apparent only when it is locally advanced, the symptoms being due to invasion of neighboring organs. In two series, both from areas with a high incidence of GB Carcinoma, where the index of suspicion was high, none of the EGBC was diagnosed clinically and almost half of these were first diagnosed on histopathological examination of resected specimen, thereby highlighting the elusive nature of EGBC. All patients diagnosed with IGBC were subsequently taken for staging work up with CECT abdomen, tumour markers like Ca 19-9 and CEA. They were then referred to higher centre for better management. During the study period no death was reported among the study population. One patient among the 6 IGBC cases had the morbidity of weight loss and generalised weakness i.e.,16.66%.

V.CONCLUSION

In the current study, 210 patients of apparently benign gall bladder cases were histopathologically analysed. In the process 6 patients were diagnosed with incidental GB cancer after cholecystectomy for chronic cholecystitis. In our study the incidence of incidental Ca GB was 2.8%.Unfortunately, no clinical or biochemical parameter was suggestive or predictive of GB cancer in patients who underwent cholecystectomy for apparently benign disease. The size of a largest calculous (>2cm) and thickened GB wall (>3mm) were the consistent features in all the IGBC patients. In view of the findings from this study it may be concluded that chronic cholecystitis remains a significant surgical entity in our population.

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