



PREVALENCE OF CARCINOMA GALLBLADDER IN PATIENTS OF CHOLELITHIASIS

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ABSTRACT

Gall stone is the most common risk factor for carcinoma gall bladder. The aim of this study finds out the prevalence of malignancy in patients with Cholelithiasis. All the radiologically diagnosed cases of cholelithiasis underwent surgery were taken into consideration. All the cases of cholelithiasis operated of in General Surgery Department of VSSIMSAR, Burla were considered for study. The diagnosis confirmed by Ultrasonography /MRCP in Department of Radio diagnosis. Total numbers of patients operated are 347, out of which 279 undergone laparoscopic surgery, 58 cases undergone open surgery and 10 cases converted from laparoscopic to open surgery. Most number of patients belongs to age group 31-40, consisting of 32.85% of total number, followed by age group 41-50, and consisting of 25.07%. A female patient constitutes about 77.81 % of total number. Male: female ratio is 1: 3.5. The mean age of the patients of study group is 41.71. Mean age of female patients is 41.09 and male is 43.88, p value 0.072 (no significant difference between mean of female and male). The excised specimens sent for histopathological examination in Department of Pathology, VSSIMSAR, Burla. Out of 347 cases nine cases found to have carcinoma specifically adenocarcinoma of gallbladder.

KEYWORDS : Cholelithiasis, carcinoma gallbladder

INTRODUCTION

Cancer of the gallbladder is the most common biliary malignancy, accounting for 80%–95% of biliary tract cancers, and it is the fifth most common gastrointestinal cancer. Because of its aggressive nature and vague symptoms it is usually diagnosed at an advanced stage.

Cholelithiasis is the most important risk factor for gallbladder carcinoma, and up to 95% of patients with carcinoma of the gallbladder have gallstones.¹ The pathogenesis has not been defined but is probably related to chronic inflammation. Larger stones (>3 cm) are associated with a 10-fold increased risk of cancer.² The risk of developing cancer of the gallbladder is higher in patients with symptomatic than asymptomatic gallstones. Polypoid lesions of the gallbladder are associated with increased risk of cancer, particularly in polyps >10 mm.³ Calcified "porcelain" gallbladder is associated with >20% incidence of gallbladder carcinoma. These gallbladders should be removed, even if the patients are asymptomatic. Patients with choledochal cysts have an increased risk of developing cancer anywhere in the biliary tree, but the incidence is highest in the gallbladder. Sclerosing cholangitis, anomalous pancreaticobiliary duct junction, and exposure to carcinogens (azotoluene, nitrosamines) also are associated with cancer of the gallbladder.

The prevalence of gallbladder cancer appears to be highest in South America, intermediate in Europe, and lower in the United States and United Kingdom. In the United States the incidence is 1 to 2 per 100,000, but incidence rates are as high as 22 per 100,000 in women in Delhi, India.⁴ India is a high incidence area for gallbladder cancer and contributes to about 10% of the global burden. Within India, the incidence is high in North, North-East, Central and Eastern India, and less common in South and West India.⁵ Gallbladder cancer in India usually affects younger patients in the 5th and 6th decade in comparison to the western countries. The age standardized incidence rate of gallbladder cancer showed that the incidence rate was high in northern and eastern India i.e. 7–14/100,000 population as compared to south and western India i.e. <1/100,000 population. Amongst patients living in north, eastern and central India the risk for developing gallbladder carcinoma is higher than that among patients living in southern India. The ICMR population-based

registry (2009–2011) clearly divides India into high risk area and low risk area for gallbladder cancer.⁶

Large multicentre comprehensive studies are required in India to assess the attributable risk of each of the identified risk factors. This will help in formulating cost effective national strategies in preventing gallbladder cancer related mortality in the country. Meanwhile a high index of suspicion to pick up incidental gallbladder cancer and improved access to healthcare facilities to manage gallstone diseases appropriately will help in reducing gallbladder cancer related mortality.

The Primary Objective was to study the prevalence of gall bladder carcinoma in patients with cholelithiasis with Secondary objectives like the mean age of patients of cholelithiasis, whether any significant difference in mean age between male and female patients, to study the relationship if any between size and number of stones in patients of gallbladder cancer with gall stones.

MATERIALS AND METHODS:

A cross-sectional study was conducted involving 347 number of patients those underwent cholecystectomy in Department of General Surgery, VSSIMSAR, Burla and excised specimens were sent for Histopathological examination in Department of Pathology, VSSIMSAR, Burla. The study period is November 2018 to October 2020. All the radiologically diagnosed cases of cholelithiasis attending Surgery OPD and admitted to Department of General Surgery, VSSIMSAR, Burla and those were fit to undergo cholecystectomy were included under study. Patients unfit for surgery, patients with evidence of carcinoma gallbladder, on clinical grounds and confirmed on ultrasonography and/or CT scan were excluded. With the prior consent a Comprehensive History, General examination and Systemic examination carried out initially. After making clinical diagnosis, the diagnosis confirmed radiologically.

All radiologically diagnosed and surgically fit cases undergone cholecystectomy either open or laparoscopic. The removed gall bladders was inspected for the outer surface, incised to remove gall stones, the gallbladder mucosa inspected, the number, size and type of gall stones noted.

Resected specimens sent to Pathology Department for Histopathological examination. Reports collected for analysis. The study variables are demographic and clinical profile of patients presenting with gallstone diseases.

Data analysis done using SPSS software. Research initiated only after due approval of institutional ethics committee of VSSIMSAR. The procedures followed in accordance to ethical norms. The research is done after taking written consent with the patient or her/his parents or her/his legal guardian whichever is applicable. The benefits outweigh the risk involved to the study participants as there was apparently no risk for patients in this study. Secrecy of the personal information of the patients maintained.

OBSERVATION

Total numbers of patients are 347 considered for study. 32.85% of patients belong to age group 31-40 years, followed by 25.07% of patient in age group 41-50 years, very less number of patients represented from extreme age groups.

Table No – 1: Age Distribution of Patients

| Age | Number | Percentage |
|-------|--------|------------|
| <20 | 7 | 2.02 |
| 21-30 | 62 | 17.87 |
| 31-40 | 114 | 32.85 |
| 41-50 | 87 | 25.07 |
| 51-60 | 50 | 14.41 |
| 61-70 | 26 | 7.49 |
| >70 | 1 | 0.29 |
| Total | 347 | 100 |

Table No – 2: Mean age of patients with cholelithiasis

| Minimum age | Maximum age | Total number of patients | Mean | Standard deviation |
|-------------|-------------|--------------------------|-------|--------------------|
| 14 | 75 | 347 | 41.71 | 12.016 |

The mean of the patients of our study group is 41.71

Table No – 3: Mean age comparison among male and female patients of cholelithiasis.

| Sex | Total number | Mean age | Standard deviation | Standard error mean |
|--------|--------------|----------|--------------------|---------------------|
| Male | 77 | 43.88 | 12.710 | 1.488 |
| Female | 270 | 41.09 | 11.761 | 0.716 |

No significant difference between mean age of male and female patients in our study with p value 0.072.

Table No – 4: Gender distribution of patients

| Gender | Frequency | Percent |
|--------|-----------|---------|
| Male | 77 | 22.19 |
| Female | 270 | 77.81 |
| Total | 347 | 100 |

Gallstone disease is predominately a disease of female

Table No – 5: Types of surgery performed.

| Types of surgery | Frequency | Percentage |
|-----------------------|-----------|------------|
| Laparoscopic surgery | 279 | 80.4 |
| Open surgery | 58 | 16.7 |
| Lap converted to open | 10 | 2.9 |

Laparoscopic cholecystectomy is considered Gold standard for treatment of cholelithiasis worldwide, similarly in our institution also.

All 347 gallbladders were palpated and were opened intraoperatively for any focal or diffuse thickening of the gallbladder wall, a raised mucosal plaque, polypoid growth or an infiltrating grey white mass. Intraoperative, gallbladder wall appeared normal in all the patients.

Table no 6 Histopathological report

| Histopathology | Male | Female | Total | Percentage |
|-----------------------|------|--------|-------|------------|
| Chronic cholecystitis | 72 | 264 | 336 | 96.82 % |
| Adenocarcinoma | 3 | 6 | 09 | 2.6% |
| Polyp | 2 | 0 | 02 | 0.58 % |
| Total | 77 | 270 | 347 | 100 % |

Histopathological study of specimen revealed 336 of the specimens showed evidence chronic cholecystitis, 2 specimen had gallbladder polyp. Nine gallbladders (2.6 %) showed evidence of adenocarcinoma of varying differentiation along with cholelithiasis. Subsequent staging revealed 3 specimens in stage T1a, 4 in stages T1b and 2 in T2 stage. Out of the 9 patients 6 are female patients and rest 3 are male. All 9 patients had multiple stone, out of which 3 patients had the largest stone size of >3 cm and rest 6 patients had stone size less than 3 cm.

DISCUSSION

The cross sectional Observational study conducted over a period of two years starting from November 2018 to October 2020, on 347 number of patients with radiological diagnosis of Cholelithiasis those underwent cholecystectomy in General Surgery Department, VSSIMSAR, Burla. Most number of patients belongs to age group 31-40, consisting of 32.85% of total number, followed by age group 41-50, and consisting of 25.07%. Very less number of patients from extreme age groups. The mean age of the patients of our study group is 41.71. According similar study conducted by Dr Alok Chandra Prakash, Dr Samir Toppo, Dr Vinay Pratap, Prevalence and Management of Cholelithiasis in East India, the mean age was found to be 38 years⁷. Similar study conducted by V Jayanthi et al, EPIDEMIOLOGY OF GALLSTONE DISEASE - TOPLINE FINDINGS, the mean was found to be 51.1. The age range for the cases was between 15 and 85 years and the mean age was 51.1 years (+ 14.1 years)⁸. The mean of patients with gallstone disease is higher in South India in comparison to north and east India. According to our study the mean age group of male and female patients are 43.88 and 41.09 respectively with p value 0.072. There is no significant difference. Many similar studies suggest same findings. According to our study female patients constitute about 77.81 % of total patients. Male: female ratio is 1: 3.5. Its similar in study conducted by Dr Alok Chandra Prakash, Dr Samir Toppo, Dr Vinay Pratap, the mean age of the patients was 38 years with a male-female ratio of 1:3 in east india⁷. Similar study conducted by Sultan Alshoabi shows the prevalence of gallstones in this study is 18-23.5% and exactly 69.57% of gallstones were in females and 30.43% in males⁶.

The most common histopathological finding in our study was chronic cholecystitis 336 (96.82%) specimens were reported as chronic inflammation with mucosal ulceration, denudation, metaplasia to dysplasia and wall infiltration by chronic inflammatory cells like neutrophils, macrophages, plasma cells and varying degrees of fibrosis. A similar study by Memon⁹ also reports chronic cholecystitis as major histopathological finding, identified in 64.8% cases.

Gallbladder polyps have an incidence ranging from 4.6 to 6.9 per cent¹⁰. In our study two cases of gallbladder polyp were identified. This low incidence can be attributed to small number of cases in our series. The polyp discovered in our study was one in a female and other in male. However, the prevalence of this pathology is much higher amongst males¹¹. In our series, incidental carcinoma of gallbladder was found in 9 cases (2.6%). So, the prevalence of gallbladder cancer is 2.6 % in patients of cholelithiasis without previous radiological evidence of malignancy. Its incidence in women of North and Central India is as high as 6.6 and 5.2 respectively, while that in Chennai and Bangalore in southern India are 0.6 and 0.8 respectively. The incidence of

gallbladder malignancy in this series was considerably low compared to other studies, which show an incidence varying from 6.9 to 12 per cent^{12,13}. The low incidence of malignancy in our series can be attributed to high sensitivity to exclusion criteria, where all patients with any preoperative evidence of malignancy, no matter how trivial, were excluded from the study. Low incidence of malignancy in our patients can also be attributed to increased acceptance and early reporting for laparoscopic cholecystectomy due to resort to day-care surgery at our institution. Samad¹⁴ reports an incidence of 1.1% of malignancy in patients who underwent cholecystectomy for presumed chronic cholecystitis with cholelithiasis.

All patients in our series presented with longstanding history of chronic cholecystitis. There were no symptoms or signs suggestive of underlying malignancy in any patient; gallbladder malignancy usually does not have any characteristic clinical features with over 90 per cent of patients presenting with symptoms of acute or chronic cholecystitis¹⁵. Although ultrasound has a high diagnostic accuracy for both advanced and early gallbladder cancer¹⁶, none of the nine carcinomas in this series were picked on preoperative ultrasound. In addition, all nine gallbladder specimens showed no macroscopic evidence of malignancy when they were opened during surgery. This is in contrast to the study by De Zoyasa et al. in whom all four cancers were suspected either on preoperative ultrasound or grossly during surgery; they suggest a more selective approach to gallbladder histology which may have saved both time and cost without having any unfavourable effects on patients well-being¹⁷. Similar observations and recommendations are made by other studies^{18,19}.

Although there are myriad of premalignant conditions, carcinoma gallbladder has a strong association with gallstones¹². The strong association between the two warrants attention paid to histopathology of specimen in all cases undergoing cholecystectomy for cholelithiasis, irrespective of presence or otherwise of any gross abnormalities. It is widely reported that long standing mucosal irritation by the stones cause atypical cellular changes and increased cellular proliferation. It has been hypothesized that in long standing cases, these areas of hyperplasia progress to metaplasia and carcinoma-in-situ²⁰. Studies confirm presence of such changes in the vicinity of gallbladder carcinoma²¹. The incidence of malignancy in our study was 2.6%, which is similar to that reported by Khan AH²².

CONCLUSION

In conclusion, GB carcinoma is not an uncommon clinical entity in our Indian scenario, unlike western countries. It is predominantly a disease of females. Therefore, a female especially in forties and fifties with a history of recent onset of constant pain in the right hypochondrium or change in the character of pain should be thoroughly evaluated. Though the association between gallstones and GBC is strong, the causal relationship between them is not clear. In spite of the advances made in the field of gallbladder imaging, the detection of carcinoma of the gallbladder in early stages remains low. Therefore, every gallbladder should be subjected to routine histopathological examination because with identification of an early gallbladder carcinoma a curative resection may be possible and these patients have a good long term survival.

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