Research Article

Clinical Study of Incidental Carcinoma Gall Bladder in Cholecystomies at Palnadu Region

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ABSTRACT

Katuri Medical College & Hospital is a tertiary referral rural Medical Institution catering to the Health needs of surrounding villages of Palnadu region

The objective of this research study is to correlate between various etiological factors, age and sex prevalence with special emphasis on its early detection and management since gall bladder carcinoma is a lethal disease and associated with decimal prognosis

Cholelithiasis is common surgical condition encountered in our surgical outpatient department. Moreover, the wide spread usage of laparoscopic cholecystectomy now – a – days, had enabled early diagnosis of incidental gall bladder carcinoma. Therefore a prospective study of 1123 cases of cholecystectomies for benign gall bladder disease was undertaken from January 2010 to January 2016. For each and every patient, detailed clinical history was recorded and subjected to specific hematological and biochemical tests. Radiological imaging studies like ultra sonography of abdomen were performed in all cases and Contrast Enhanced Computer Tomography for few selected cases. In present study comprising of 1123 cases, 1105 underwent laparoscopic cholecystectomy, 07 cases had open cholecystectomy and 11 cases were converted to open cholecystectomy with good results. Only 07 cases of Incidental gall bladder carcinoma were detected from among 1123 cases out of which 03 are Males and 04 are Females accounting for 0.62% in this study.

Gall bladder carcinoma as an incidental finding has been reported in 0.25-3% patients and almost 50% of these are discovered during laparoscopic cholecystectomy for benign conditions. This incidental finding has altered the management and outcome of this dreadful disease.

Keywords: CECT-Contrast enhanced computer tomography, EUS- Endoscopic Ultrasound, GBC-Gallbladder Carcinoma, HPE-Histopathological examination, MRCP-Magnetic Resonance Cholangio Pancreaticography, USG-Ultrasonography

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INTRODUCTION

The gall bladder is a pear shaped organ of about 7.5 – 12 cm in length with a normal capacity of about 5ml,but capable of considerable distention in pathological conditions. It is anatomically divided into a fundus, body and neck that terminate into a narrow infundibulam. The cystic duct is about 3cm in length but variable in its lumen and is usually 1-3mm in diameter. The common hepatic duct is usually less than 2.5 cm long and is formed by the union of right and left hepatic ducts. The common bile duct is about 7.5 cm long and is divided into supra duodenal portion, retro duodenal portion, infra duodenal portion and intra duodenal portion. In depth anatomical knowledge is crucial and essential for management of gall bladder carcinoma. The location of the tumor within gall bladder with respect to proximity to portal vein, hepatic artery, common hepatic and bile duct are important anatomical considerations in surgical management. Gall bladder is attached to the under surface of segments IVb and V of liver and hence these segments are involved early in carcinoma arising from body and fundus of gall bladder. Similarly the lesions arising from the infundibulum and cystic duct tend to involve common bile duct and portal vein in

the early course of the disease Shiral et all reported most frequent involvement of cystic nodes (38%), pericholedochal nodes (54%) followed by posterior pancreatic, portal vein and hepatic artery nodes (29-19%) and rare involvement of more distant nodes (less than 5%) in gall bladder carcinoma. [1]

Gall bladder carcinoma is the most common biliary tract malignancy accounting for 3% of all tumors. [2] Women are 2-6 times more commonly affected and the incidence steadily increases with age. [3] There are also marked geographical and racial differences in the frequency of the disease with high incidence rate have been reported from Japan, South American countries, Central and Eastern European nations and it is rare in the western world including the USA, UK, CANADA, AUSTRALIA and NEWZEALAND. [4,5] Incidence of gall bladder carcinoma varies greatly within India, with highest rates from Northern and Central parts of India i.e as high as 6.6-5.2 per 100000 population and lowest in Chennai and Bangalore in Southern India i.e between 0.6-0.8 per 100000 populations.

Carcinoma gallbladder is an aggressive malignancy that occurs predominantly in the elderly and apart from incidentally diagnosed cancer, the prognosis is poor with 5 years survival rate ranging from 05-40%. The poor prognosis relates to difficulty in early diagnosis of the disease due to absence of specific signs and symptoms. Most of the patients have systemic disease at the time of presentation. The association of gall bladder cancer and gall stone disease has been known since the advent of surgical treatment of cholelithiasis. This association has been proven in various observational studies conducted by researchers including Kazama et all in 1924, Kowalewski et all in 1971 [6]. About 80% of patients with gall bladder carcinoma have cholelithiasis and is found incidentally in 0.2-3% of all cholecystectomies for benign gall bladder pathology. Increased usage of imaging modalities for evaluation of abdominal symptoms has led to dramatic increase in the diagnosis of gall bladder stones Incidentally detected gall bladder carcinoma has an excellent over all prognosis due to detection at very early stage. Most of the lesions being Tis and T1a, a simple cholecystectomy is considered as optimum treatment for these early cases. The interest in the incidental finding of gall bladder carcinoma arises from an excellent outcome associated with it when compared in terms of survival and out come with that of Gall bladder carcinoma. Cancer detected on HPE of the cholecystectomy specimens performed for benign gall bladder disease is termed as incidental gall bladder cancer. Literature is replete with studies and reports on incidental gall bladder carcinoma to be 0.2-3% in various studies.

MATERIALS AND METHODS

This is a prospective study enrolling 1123 no. of subjects admitted to surgery department for benign gall bladder disease at Katuri Medical College and Hospital from January 2010 to January 2016. Out of 1123 no. of cases, 358 were Males (31.88%) and 765 were Females (68.12%) with M:F ratio, 1:2.13. Due clearance from the Institutional (Human) Ethics Committee was obtained for this research study

Inclusion criteria

All patients undergoing cholecystectomy for benign gall bladder disease

Exclusion criteria

Patients with pre-operative suspicion or proven carcinoma of the gall bladder.

All patients undergoing cholecystectomy during the present study were evaluated with a thorough history, clinical examination and detailed hematological and biochemical tests like liver function tests including serum alkaline phosphatase levels etc. Further the nature of surgery, intra operative findings, post operative events and histopathological diagnosis were recorded and analysed. Ultra sound scan of the abdomen was first line imaging modality for patients with gall stone disease which revealed.

I. Multiple or single calculus
II. Presence of polyp
III. Wall thickness >4 mm
IV. Pericholecystic fluid collection.

CECT Abdomen was done in selected cases that had abnormal gall bladder wall thickness or had a suspicion of malignancy on **USG** of the abdomen. MRI with cholangio pancreaticography was done for the cases

that had obstructive jaundice or associated choledocholithiasis and were expected to undergo **Endoscopic** retrograde cholangio pancreaticography prior to cholecystectomy.

The nature of surgery such as **(Laparoscopic/Open/Lap. converted to open)** and intra operative findings were recorded, including any macroscopic abnormality of gall bladder wall on cut opening the specimen. All the gall bladder specimens were sent for histo-pathological examination and the diagnosis was recorded. Later AJCC (American joint committee on cancer) staging was adopted for 07 cases of incidental carcinoma of gall bladder detected in this study group.

RESULTS AND DISCUSSION

In this study group, 1123 patients underwent cholecystectomy for benign gall bladder disease. There were 358 Males (31.88%) and 765 Females (68.12%).

The mean age of Male patients were 46.03 years and Female patients were 46.26 years and not significantly different. 46% of the patients were in the age group of 31-50 years.

Table 1: Age distribution

Age	Number
0-10	06
11-20	28
21-30	216
31-40	261
41-50	255
51-60	189
61-70	124
71-80	36
81-90	08

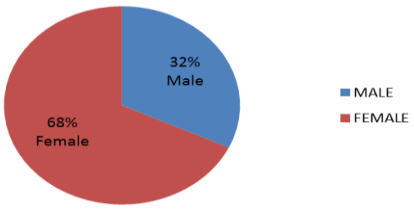

Figure 1: Sex distribution

The **Male/Female** ratio was 1:2.13 in the present study.

Table 2: Incidental carcinoma gall bladder in various studies

S.no	Study period & author	Number of cases	Incidence of incidental Ca Gallbladder
1	Daphna et all (2002)	1697	0.35
2	Naqvi et all (2005)	1109	5.9
3	Frena A et all (2007)	3012	0.66
4	Mittal et all (2010)	1312	0.99
5	Ferrarese et all (2013)	508	1.37
6	Waghmare et all (2014)	270	2.59
7	Present studies (2016)	1123	0.62

The Present study revealed 0.62% incidence of incidental carcinoma gall bladder which is compared with the published studies. [7-12].

Table 3: Symptomatology

Symptom	Frequency	Percentage
Rt. Upper Abdominal Pain	1104	98.3
Dyspepsia	571	50.8
Jaundice	01	0.1

Right sided upper abdominal pain was the chief complaint in majority of patients (98.3%) followed by dyspepsia (50.8%). In this study only 01 patient had choledocholithiasis and presented with jaundice and none of the patients had a palpable lump or ascites.

110 (9.8%) patients had associated co morbid conditions in the form of hypertension, diabetes, ischemic heart disease or chronic obstructive pulmonary disease.

USG studies reveal multiple calculi in 55.8% of cases, single calculus in 43.2% of cases and gall bladder polyp in only 1% of cases. Gall bladder wall thickness was more than 4mm in 05 cases and 04 cases showed diffusely thickened wall. Only one case had

focal gall bladder wall thickening involving the fundas.

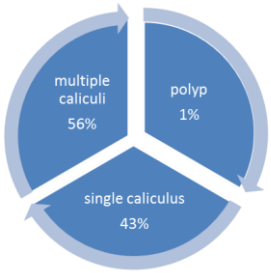

Figure 2: Ultra sonograph scan of abdomen

Histopathological examination of gall bladder specimen revealed chronic cholecystitis in majority of cases and only 07 cases had proven adenocarcinoma which constitutes 0.62% in this study.

Present study revealed that chronic gall bladder disease in the age group of 50 years and above are more vulnerable for incidental carcinoma of gall bladder.

The incidence of incidental gallbladder carcinoma in present study constitutes 0.62% which tallys with national cancer registry programme of I.C.M.R for south zone. [13]

Table 4: Histopathological diagnosis

Histo pathological diagnosis	Number	Percentage
Chronic Cholecystitis	1105	98.39%
Adenocarcinoma	07	0.62%
Xantho granulomatus Cholecystitis	04	0.36%
Chronic Cholecystitis+Benign papillary hyperplasia	02	0.18%
Chronic Cholecystitis+Intestinal Metaplasia	02	0.18%
High grade dysplasia	01	0.09%
Low grade dysplasia	01	0.09%
Chronic cholecystitis+Adenomatus hyperplasia	01	0.09%

Table 5: Age category HPE crosstabulation

		HPE		Total
		Benign	Malignant	
Age category	<50yrs	765	1	766
	>50yrs	351	6	357
Total		1116	7	1123

Table 6: Age adjusted incidence of gall bladder cancer in India, 1988-89 (per 100000 populations per year)

City	Zone	Men	Women
Delhi	North	1.9	6.6
Bhopal	Central	2.6	5.2
Mumbai	West	1.6	2.3
Bangalore	South	0.5	0.8
Chennai	South	0.3	0.6

Table 7: AJCC cancer staging TNM classification

PRIMARY TUMOR (T)
Tx:Primar tumor could not be assessed
T0: No evidence of primary tumor
Tis: Carcinoma in – situ
T1:Tumor invades lamina propria or muscle layer
T1a: Tumor invades lamina propria
T1b: Tumor invades muscle layer
T2:Tumor invades peri muscular connective tissue, no extension beyond serosa or into liver
T3:Tumor perforates the serosa and/or directly invades the liver/or one other adjacent or

structure such as stomach, dudenam, colon, pancreas, omentum, extra hepatic bile ducts
T4:Tumor invades main portal vein or hepatic artery or invades two or more extra hepatic organs or structures

REGIONAL LYMPH NODES (N)

Nx:Regional lymph nodes canot be assessed
N0:No regional lymph node metastasis
N1:Metastasis to nodes along the cystic duct, common bile duct and /or hepatic artery
N2:Metastasis to periaortic, peri caval,superior mesenteric artery and/or celiac artery nodes

DISTANT METASTASIS (M)

M0:No distant metastasis
M1:Distant metastasis

The most commonly used staging system worldwide is the American Joint Committee on Cancer Tumor Node Metastasis staging system. However the other staging systems like modified Nevin and the Japanese Biliary Surgery Society staging systems are also in usage.

Figure 3: Gall bladder specimen with cholesterosis

Figure 4: Gallbladder specimen with pigment stones

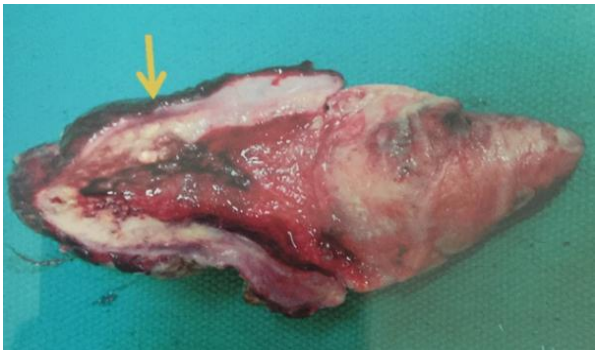

Figure 5: Thick wall gallbladder (As depicted by the arrow)

Figure 6: Incidental gallbladder cancer with port site Metastasis (depicted by markings), post Laparoscopic cholecystectomy

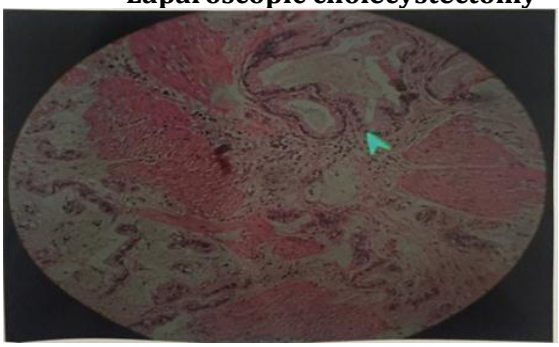

Figure 7: Abnormal glandular elements lying in the muscle layer: T1b gallbladder cancer

DISCUSSION

Gall bladder carcinoma is a relatively rare and aggressive malignancy. Despite improvement in the diagnostic and treatment modalities, the overall survival of patients is low. Diagnosis at an early stage offers the best chance of cure and better survival. However, due to non specific symptoms the presentation is often late leading to poor outcome regardless of the modality of treatment. The importance of detection of incidental gall bladder carcinoma lies in the improved survival and disease free status for a longer period. Carcinoma detected on histopathological examination of the cholecystectomy specimens of benign gall bladder disease is termed as incidental gall bladder carcinoma. Increase in the number of cholecystectomies performed now a days had led to rise in the detection of early gall bladder carcinoma. The incidence of incidental gall bladder carcinoma in present study stands at 0.62% which is consistent with the reported studies as 0.2-3%. [14]

In the present study 07 cases of incidental carcinoma of gall bladder were detected from among 1123 cases of cholecystectomies. Most of the patients in this study had cholelithiasis and the number of **Female** patients exceeded that of Males by more than twice. It is also well documented that women are more commonly affected by gall stone disease and more so in the reproductive age group. [15] The incidence of gall stones is known to increase with advancing age and adults over 40 years of age and those over 70 years of age are more prone to have gall stone disease. [16] The association of gall bladder cancer with gall stone disease, porcelain gall bladder, gall bladder polyp, chronic infection with Salmonella and Helicobacter, congenital biliary cysts, abnormal pancreatico - biliary junction, carcinogen exposer and obesity have been well documented by various observational studies.

USG was the imaging modality of choice in present study group and was done for all the cases. **CECT** abdomen was done for 05 patients who had gall bladder wall thickness on **USG**. **MRCP** was done for one patient who had associated choledocholethiasis. **USG** is considered to be accurate in the gall stone disease up to 96% of cases. The role of prophylactic cholecystectomy for asymptomatic gall stones is not well documented. However, in the regions with high incidence of Gall Bladder cancer and in cases associated with abnormal biliary pancreatic junction, prophylactic or preventive cholecystectomy may be considered in view of development of malignancy in future. The role of adjuvant radiotherapy or chemo radiotherapy is not clear despite reports and studies from various parts of the world. However it is reserved for the advanced stages of gall bladder malignancy. The present study demonstrated no association between the symptomatology, co-morbidities, ultra-sound findings and incidentally detected gall bladder carcinoma. These results are consistent with the published study of **Penebianco** et all which stated that advanced age has significant association with incidental gall bladder carcinoma. [17]

Diagnosis at an early stage is the hall mark of incidentally detected gall bladder carcinoma. In this study all cases of incidental gallbladder carcinoma were early malignancies and none of the patients had stage III or IV disease which correlates with the reported studies of **Kalita et all.** [18] It is not the laparoscopy or open technique that influences the outcome of cholecystectomy. The intra operative events such as inadvertent perforation of the gall bladder with spillage of bile, improper specimen retrieval and the stage of disease are the determinants. Although removal of the gall bladder in the retrieval provides protection but it does not fully exclude intra peritoneal spillage. **Port site** metastasis is the most common form of parietal recurrence and has been reported in all stages of GBC. Recurrence at port site occurs ranging from few months to 3-4 years following laparoscopic procedure. Several factors such as gall bladder perforation, spillage of bile during cholecystectomy, increased intra peritoneal pressure and immunosuppressive action of carbon dioxide may contribute to port site recurrence.

In present study only 07 cases of incidental carcinoma of gallbladder was detected. **Lap**

cholecystectomy was done in 06 cases and one case had open cholecystectomy due to previous abdominal scar. Focal wall thickening was observed only in 01 case intra operatively (14.3%). Pathologically 02 cases were reported to be well differentiated adenocarcinoma (28.6%), 02 case to be moderately differentiated (28.6%) and 03 cases were poorly differentiated (42.8%). As per the **AJCC** classification 01 case was in stage T1a N0 M0 (14.4%) 03 were in T1b N0 M0 (42.8%) and 03 case were in category of T2 N0 M0 (42.8%). In the preset study all the cases had simple cholecystectomy since they were in early stage of malignancy. Only 01 case had presented with evidence of port site metastasis following laparoscopic cholecystectomy during follow up at 3 months period and had revised surgery.

CONCLUSION

The present study concluded that

1. The incidence of incidental gall bladder carcinoma is 0.62% in this study which is very well consistent with the published reports.
2. Females are predominantly affected which accounts for 68.12% of cases with F: M ratio of 2.13:1
3. The association between chronic gall stone disease and gallbladder carcinoma has also been well established in the present study. It was also confirmed by various observational studies and animal experiments in this regard.
4. The mean age of the patients in this study was significantly higher than the study population.
5. Ultrasonography of abdomen is the most invaluable diagnostic test available. It was done in all cases with an accuracy rate of 96% approximately and **CECT** abdomen was reserved for selected cases with gallbladder wall thickening.
6. In the present study, all the 07 cases of incidental gallbladder carcinoma presented in early stage of malignancy with no T3 or T4 disease. Simple cholecystectomy had given good results. Only 01 case with port site metastasis needed revised surgery.
7. Routine histopathological examination of all gall bladder specimens following cholecystectomy is recommended and mandatory for diagnosis of this aggressive disease at an early stage.

The main stay in the management of incidental gall bladder carcinoma is only early detection which improves survival and it is now accepted worldwide. It is also concluded from the present study that cholecystectomy for gall stone disease still holds the key for early detection and management of this dreadful disease.

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