

FREQUENCY OF INCIDENTAL CARCINOMA GALL BLADDER IN CHOLECYSTECTOMY

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ABSTRACT

Objective: To determine the frequency of incidental gall bladder carcinoma in patients of a tertiary care hospital undergoing cholecystectomy.

Methodology: This descriptive case series was carried out at Department of General Surgery, Pakistan Institute of Medical Sciences (PIMS), Islamabad from 1st January, 2012 to 30th June, 2014. The histopathology reports of 1003 patients undergoing cholecystectomy (either by laparoscopic or open) were reviewed retrospectively and 940 patients fulfilling our criteria were included.

Results: Gall bladder adenocarcinoma was detected in only two patients (0.21%) undergoing cholecystectomy. Male to Female ratio was 1:1 and the mean age was 68.5 years for incidental carcinoma patients. One patient had a pre-malignant porcelain gall bladder while the rest of 937 histopathology results were benign.

Conclusion: In this single institute study, the frequency of incidental gall bladder carcinoma was found to be 0.21 % and that too in elderly patients.

Key Words: Incidental carcinoma gall bladder, Cholecystectomy, Cholelithiasis, Histopathology

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INTRODUCTION

Cholelithiasis is a significant health problem affecting 10-15% population of the developed world¹⁻³. Cholelithiasis and its complications are the most frequent indication for performing cholecystectomy^{4,5}. 85% of the cases of carcinoma gall bladder are associated with cholelithiasis^{1,2} and is thought to arise due to chronic irritation caused by the presence of gallstones². Other risk factors for developing carcinoma gall bladder include genetic susceptibility, advancing age, female gender, chronic biliary infections, some dietary factors and anatomical anomalies³. Women have two to six times more incidence of carcinoma gall bladder as compared to men^{1,3}.

Carcinoma gall bladder, though rare, is the most common malignancy of the biliary tract, accounting for 80%–95% of biliary tract carcinomas². It is the fifth most common gastrointestinal malignancy^{2,3}. An early diagnosis is essential as this malignancy progresses silently over 5 to 15 years but mostly presents late at an incurable stage¹⁻³. Delay in diagnosis and aggressive nature leads to a median survival of less than six months while 5 years survival is less than 5%². The stage of disease at the time of presentation determines the complete resection and thus outcome of the surgery⁴.

The frequency of carcinoma gall bladder is varied

across the regions and between ethnicities^{1,2}. Asians have a high risk of gall bladder carcinoma especially in northern Indian females, Pakistani females and Korean males². According to an estimate the frequency of gall bladder cancer is 11/100,000 in Pakistan, 22/100,000 in North of India, 16-27/100,000 in Native American Indian females and 8-12/100,000 in Native American Indian males. The regions with low Frequency include Canada (1.6/100,000), USA (1.5/100,000) and New Zealand Marios (1.59/100,000 in females and 1.49 in males)².

The frequency of finding intra or post-operative incidental gall bladder carcinoma diagnosis is reported around 0.2 and 2.8%⁵. Our country is reported to have a high frequency of carcinoma gall bladder² and our local studies have reported a high frequency of incidental carcinoma in cholecystectomy specimens. Introduction of ultrasonography has contributed to early diagnosis of gallstones^{3,6} and accessibility to laparoscopic surgery had particularly increased the rate of operative management^{2,3,7}. Owing to availability of large number of gall bladder specimens and their histopathology reports, we undertook this study to determine the true frequency of incidental carcinoma gall bladder in our setup.

METHODOLOGY

This descriptive case series was carried out at the Department of General Surgery of Pakistan Institute of Medical Sciences (PIMS) Islamabad, Pakistan from 1st January 2012 to 30th June 2014 after taking approval from the hospital ethical committee. The histopathology of all the patients was carried out at the Department of Pathology PIMS. The data for the study was retrieved retrospectively from computerized histopathological records. Histopathology reports of patients of all ages and genders, who underwent cholecystectomy (by open or laparoscopic technique), were reviewed. Patients with suspicion of malignancy, diagnosis of malignancy, metastatic gall bladder disease, hepatic hilar lymphadenopathy, and gross mass formation or autolysed specimens were excluded from study.

Preoperative record, laboratory and radiological investigations and operation notes of the patients with malignancy were traced. The American Joint Committee on Cancer (AJCC) Tumor Node Metastasis (TNM) system was used as reference for staging carcinoma gall bladder⁸. The data were analyzed using IBM SPSS Statistics Version 20.0 with descriptive statistics to calculate percentages, frequencies, means and standard deviations. The numerical data such as age were expressed as mean and standard deviation while the categorical data such as the gender and histopathology reports were expressed as frequency and percentages.

RESULTS

In our study a total of 1003 histology reports of cholecystectomy specimens were retrieved. There were 940 cases fulfilling our inclusion criteria. Gender distribu-

tion is shown in figure 1. 98.5 % (n=926) patients had cholelithiasis. The age of the patients ranged from 21 to 81 years. Overall mean age was 46.22 ± 10.15 years. Mean age for the female patients was 46.70 ± 10.38 years and mean age for male patients was 44.87 ± 9.35 years.

Table 1 gives the summary of histopathology findings of all 940 specimens. Chronic cholecystitis is the predominant pathology in 89.15 % followed by acute on chronic cholecystitis in 4.25 % cases.

The hospital based frequency of adenocarcinoma gall bladder after cholecystectomy was 0.21% (n=2). Male to Female ratio was 1:1 and the mean age was 68.5 years for incidental carcinoma patients. A 61 years old male patient had his tumor staged as pT3 with a high grade papillary adenocarcinoma at the fundus of gall bladder. His pre-operative records showed that there were polyps greater than 1 cm along with multiple gallstones on ultrasonography while operation notes indicated difficulty in resection per-operatively due to hardening and thickened gall bladder. The other patient, 76 years old female had her gall bladder filled with multiple polyps and was staged pT1 on histopathology. She had multiple polyps visualized on pre-operative ultrasonography but without any gallstones. Only one case of pre-malignant lesion, porcelain gall bladder was reported. There were no cases of carcinoma in situ.

DISCUSSION

Incidental gall bladder carcinoma is defined as the gall bladder carcinoma diagnosed during or after the cholecystectomy done for benign gall bladder disease. The relative risk of developing carcinoma is 2–24 times

Figure 1: Gender distribution of cholecystectomy patients

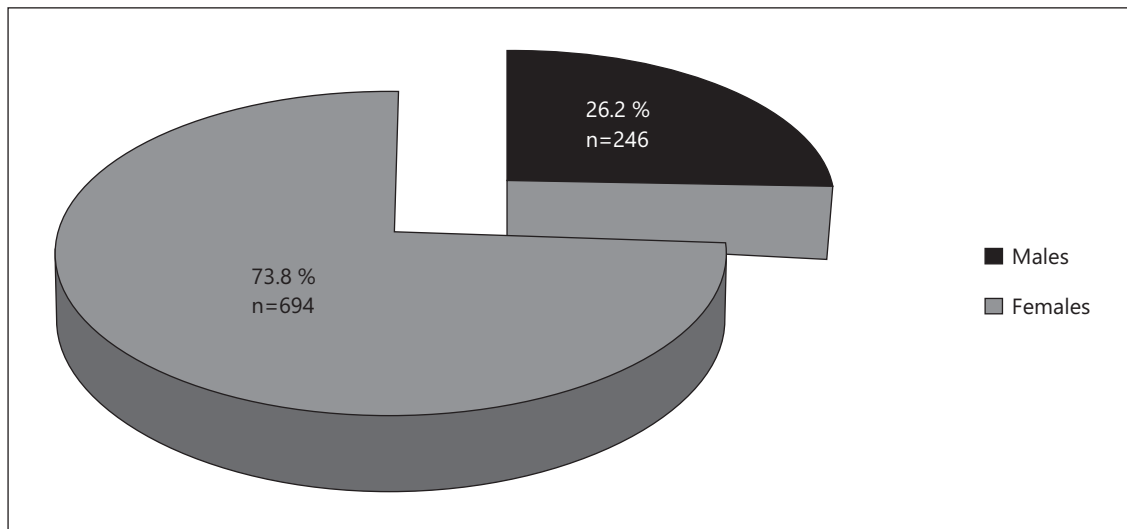


Table 1: Histopathological report (n=940)

Histopathology	Female	Male	Total (n)	%
Chronic cholecystitis	624	214	838	89.15
Acute on chronic cholecystitis	29	1	40	4.25
Chronic cholecystitis with cholesterolosis	23	6	29	3.08
Empyema gall bladder	6	6	12	1.27
Eosinophilic cholecystitis	3	4	7	0.74
Acute cholecystitis	1	1	2	0.21
Papillary adenocarcinoma	1	1	2	0.21
Acute cholecystitis with cholesterolosis	1	0	1	0.10
Chronic cholecystitis with pyloric metaplasia	1	0	1	0.10
Chronic granulomatous cholecystitis	1	0	1	0.10
Adenomyomatous hyperplasia	1	0	1	0.10
Follicular cholecystitis	0	1	1	0.10
Giant cell reaction against foreign body	0	1	1	0.10
Mucocele	1	0	1	0.10
Xanthogranulomatous cholecystitis	0	1	1	0.10
Porcelain gall bladder	1	0	1	0.10
Subacute cholecystitis	1	0	1	0.10
Total	694	246	940	100

Table 2: List of some local studies showing frequency of incidental carcinoma gall bladder

Studies	Duration	Place of study	Sample size	Mean age (yrs)	M:F	Frequency (%)
Our study	2012-2014	Islamabad	940	68.5	1:1	0.21
Khan et al ³	2008-2012	Rawalpindi	500	45	0:1	0.20
Siddiqi et al ⁹	2010-2012	Hyderabad/ Jamshoro	220	32.3	1:7	2.8
Qazi et al ¹⁰	2009-2011	Kohat	200	52.57	1:7	4.0
Shah et al ¹¹	2008-2011	Peshawar	260	55.25	1:10	4.23
Junejo et al ¹²	2011	Jamshoro	138	49.3	1:2.36	10.86
Shaikh et al ¹³	1997-1998	Larkana	100	-	-	10.0
Abassi et al ¹⁴	2008	Rawalpindi	100	62.5	0:2	2.0
Soomro et al ¹⁵	2007-2008	Jamshoro	521	-	1:3.75	3.64
Lohana et al ¹⁶	2006-2008	Hyderabad	200	-	1:3	4.0
Iftikhar et al ¹⁷	2006-2008	Peshawar	107	58.5	-	4.67
Naqvi et al ¹⁸	1985-2004	Nawabshah	1,109	-	1:1.4	5.90
Malik KA ¹⁹	1998-2001	Nawabshah	260	-	1:3	6.15
Ahmed G ²⁰	1995-1997	Bahawalpur	50	-	-	28.0
Ahmed I ²¹	1992-1993	Faisalabad	100	-	-	20.0

Table 3: List of some international studies showing frequency of incidental carcinoma gall bladder

Studies	Years of study	Country	Sample size	Mean age (yrs)	M:F	Frequency (%)
Yi et al ²²	2006-2013	China	14073		-	0.18
Kalita et al ²⁴	2009-2012	India	4,115	54	0.87:1	0.44
Jetley et al ²⁵	2007-2012	India	622	53	0:6	0.96
Ghnnam et al ²⁷	2007-2012	Egypt	1,892	73.6	2:8	0.5
Genc et al ²³	1999-2010	Turkey	5,164	66.2	1:4	0.09
Almuslamani et al ²⁸	2008-2010	Jordan	1,984	64.4	1:1.2	0.55
Ghimire et al ²⁹	1998-2008	Nepal	783	63.8	1:2.3	1.28
Mittal et al ²⁶	1998-2007	India	1,305	45.3	1:4.5	0.99

for patients with cholelithiasis compared to those without gallstones⁷. It is asymptomatic in 15-30 % of cases or presents with atypical symptoms⁵. It is reported in 0.2–2.8 % of histopathological examinations in patients undergoing open or laparoscopic cholecystectomy^{5,7}.

Literature search has demonstrated that our study had a very low frequency of incidental carcinoma as compared to other local studies. Frequency reported by our study (0.21 %) is comparable to only one local study by Khan et al³ who reported a frequency of 0.20 % for incidental carcinoma gall bladder. All the other studies from different regions of Pakistan have reported a higher frequency between 2.0 % to 28.0 %⁹⁻²¹. Table 2 gives a comparison of studies conducted in Pakistan along with the results of our study.

We reviewed international literature on the subject and found out that they have reported a lower frequency of incidental carcinoma gall bladder as compared to local literature. Study by Yi et al²² and Genc et al²³ have reported a frequency of 0.18 and 0.09 % which is comparable to our study. India has also high frequency of gall bladder carcinoma like our country (2) but the Indian studies by Kalita et al²⁴, Jetley et al²⁵, and Mittal et al²⁶, have also reported a lower frequency of 0.44, 0.96 and 0.99 % respectively as compared to the frequencies reported in our local studies between 2.0 to 28 %⁹⁻²¹. Table 3 has listed some international studies on the subject.

Curative management of gall bladder carcinoma by surgical resection is dependent on the stage at diagnosis i.e. the depth of invasion^{4,5,7}. Incidental carcinomas are usually at an early stage, with rare vascular or venous invasion, which can be treated by a simple cholecystectomy^{5,7}. Stage T1 is treated by cholecystectomy alone whereas higher stages need multimodality management or at times only palliative care.

Mean age of our carcinoma patients was 68.5 years. Male to female ratio was 1:1. Studies that we have com-

pared with have indicated a female predominance and increasing age to be demographic risk factor^{1-3, 23-29}. Our study had an equal gender distribution but advanced presenting age for incidental carcinoma so we should keep the suspicion of gall bladder carcinoma high on the list in aging population, especially in females in light of demographic evidence we have from other larger studies.

The significantly higher ratio of gall bladder carcinoma reported in our local literature as an incidental carcinoma is probably due to inadequate pre-operative evaluation. In our institute, a routine pre-operative work up includes laboratory and radiological investigations, especially ultrasonography, making pre-operative diagnosis of malignancy more likely. Ultrasonography has changed the management of cholelithiasis by early detection¹ but malignancy is rarely picked before a solid intramural mass is present²⁴. Low frequency of malignancy in our patients can also be attributed to increased and early acceptance of patients for laparoscopic cholecystectomy at our institution before development of carcinoma in diseased gall bladders. These strategies can account for the low frequency of incidental carcinoma in our operated cases compared to other local studies. However we still believe that our study has certain limitations so we propose to carry out larger, longer, multi-centric and if possible prospective studies to establish with accuracy the true frequency of incidental carcinoma gall bladder in our country.

CONCLUSION

The frequency of incidental gall bladder carcinoma was found to be very low (0.21 %) and that too in elderly patients. Our findings are in contrast to the earlier published local literature on the frequency of incidental carcinoma gall bladder and calls for large scale and multi-centric studies to further authenticate our study.

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CONTRIBUTORS

AM conceived the idea, planned the study, and drafted the manuscript. FK helped acquisition of data and did statistical analysis. All authors contributed significantly to the submitted manuscript.