Original Research Article

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Gall bladder specimen following cholecystectomy: a resource

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ABSTRACT

Background: Gallbladder stones are very common and cholecystectomy is the most commonly performed surgery globally. Gallbladder stones have been reported to be the leading cause of cholecystectomies worldwide. Other mechanisms have also been known to constitute for cholecystectomy, but the evidence is still weak with the exact mechanism unknown. The present study thus aims to assess the importance of routine histopathology of the gall blabber following cholecystectomy.

Methods: The study is a retrospective one that employs the use of patient records to achieve the objective.

Results: The findings of the study depict a significant association between the findings of the histopathology, ultrasound and clinical features.

Conclusions: The researcher presents the relevance of histopathology with respect to ultrasound and clinical presentation of the patient, thereby stating the need for a routine gall bladder specimen following cholecystectomy.

Keywords: Cholecystectomy, Gall bladder disease, Histopathology

INTRODUCTION

Cholecystectomy is one of the most commonly performed procedures globally, for both neoplastic as well as benign conditions. However, cholecystectomy of benign conditions is performed based on the ultrasound, clinical signs and symptoms and computed tomography. This leads to a fair chance of missing early malignant lesions such as carcinoma in-situ and other early carcinomas. Routine histopathology of the gallbladder post cholecystectomy has been most often regarded to be discarded. This again can be deemed a selective approach which can result in excluding valuable diagnosis of malignancies and other discrete pathologies such as porcelain gall-bladder.

Gallstones as a clinical finding are most common in the Western population such as those belonging to the US and Europe regions. The mean prevalence has been reported to be 10-15% in the European population and 3-5% in both the Asian as well as African populations.³ In

the US the prevalence rates have been pegged between 5 and 27% with variances reported among different ethnicities. Most of the cases of gallbladder stones are mostly unaware that they are carriers of gallstones as the stones are asymptomatic.^{4,5} However, they tend to develop complications later on which warrant the need for surgical intervention.⁶

For the case of India, the prevalence of gallbladder stones have been documented adequately however, not much importance has been regarded to it in the Western countries. This may be attributed to the fact that Indians in general has a low incidence of gallstone disease. Within the context of India itself, it has been depicted that North India shows a larger prevalence of gallstone disease as compared to the population in South India. 6-10 The prevalence however has been reported to be significantly higher in multiparous women. While the prevalence of gallbladder stones has been unrelated to the prevalence rates of laparoscopic cholecystectomy, gallbladder stones and the prevalence for gallbladder

carcinoma does depict an association. ¹⁰ The pathogenesis of the transformation of gallbladder stones to cancer has not been very well understood. It has been estimated that the concentration of glucoursodeoxycholate as well as the duration of the stones are contributory to the transformation to carcinoma. Even so, the prevalence of conversion is a relatively rare event. ¹¹ For the case of Indians who migrate to countries such as the UK, Australia, Kuwait and Singapore, a higher probability of mortality as a result of gallbladder carcinoma is seen. ¹²

Pathogenesis of gallstone formation

Three types of gallstones have been reported thus far such as cholesterol, black and brown pigmented stones. This has been typified based on their composition and pathogenesis. Gallstones have been noted to form as a result of change in the composition of bile. The increase in bilirubin or cholesterol in bile leads to the decrease in solubility as well as the solubilizing components. As result a 'nidus' forms which is then supersaturated with insoluble particles which then sequesters to form a calculus or a stone. The prevalence of cholesterol stones are the highest with 80% of the cases presenting with cholesterol type of stones. Stones that are pigmented black are seen to be more common with patients who have haemolytic diseases such as sickle cell anaemia and thalassemia and also among those with liver cirrhosis. 13-17 Stones that are brown on the other hand are caused by stasis or infection in the biliary system. The size of the gallbladder stones have been seen to be varied less than a millimetre to several centimetres in diameter. Most of the stones are in the gallbladder but about 10-15% migrates on to the common bile duct.³

In view of this, gallbladder stones remain the main cause of cholecystectomies worldwide. 18-24 While it has been documented that other mechanisms also constitute towards the need for cholecystectomies, and also the techniques and indications for cholecystectomy, there are very few studies that have discussed the importance of histology of the gallbladder post cholecystectomy. This is especially important in detecting incidental cancers as well as to better understand the typology of the disease. The study thus aims to assess whether routine histopathology of the gallbladder post laparoscopic cholecystectomy is necessitated or not.

METHODS

This study was conducted in the Department of General Surgery, in Mel Maruvathur Medical Institute in India. The study was designed within the purview of the Helsinki Declaration with approval obtained from the Institutional Ethics Committee (IEC). This retrospective study consists of 69 patients records presenting with acute or chronic cholecystitis admitted through the outpatient department. The data was retrieved on the basis of clinical signs and symptoms, ultrasound diagnosis, clinical diagnosis and histopathology.

Complete history as well as thorough examination of the records was carried out. Co-morbidity was also assessed. Baseline and other specific tests were to be done including the ultrasonography of the abdomen for all the patients. Records showing laparoscopic cholecystectomy were considered for the study.

The study employs SPSS v.20.0 software for the statistical analysis. Percentage analysis as well as Chi-Square test was carried out to achieve the objective.

RESULTS

Table 1 reveals the age distribution of patients. Male contributed 11 cases (15.9%) and females 58 cases (84.1%), with a male to female ratio of 1:5. The age of the patients ranged from 13-68 years (mean 44 years). Majority 34 (49.3%) of patients belongs to 41-60 years.

Table 1: Distribution of age of patients.

Age	No. of patients	Percentage	Male	Female
11-20	4	5.8	4	-
21-40	25	36.2	1	24
41-60	34	49.3	6	28
>61	6	8.7	-	6
Total	69	100.0	11	58

Table 2 presents the number of patients with Thin-layer chromatography. Majority 59 percent of the patients are normal followed by 38 percent are raised and least 3 percent are non-specific.

Table 2: Frequency for thin-layer chromatography.

Thin-layer chromatography (TLC)	No. of Patients	Percentage
Normal	41	59.4
Raised	26	37.7
Non specific	2	2.9
Total	69	100.0

Table 3: Frequency for liver function tests.

Liver function tests (LFT)	No. of Patients	Percentage
Normal	67	97.1
Non specific	2	2.9
Total	69	100.0

Table 3 reveals the number of patients with Liver function tests. Majority 97 percent of the patients are normal in Liver function tests and 3 percent are non-specific.

Table 4 presents the number of patients with histopathological examination. Majority 51 percent of the patients has acute cholecystitis followed by 46 percent

has chronic cholecystitis and least 3 percent has adenocarcinoma.

Table 4: Frequency for histopathological examination.

Histopathological examination	No. of patients	Percentage
Acute cholecystitis	35	50.7
Chronic cholecystitis	32	46.4
Adenocarcinoma	2	2.9
Total	69	100.0

Table 5 reveals the clinical presentation of gallbladder disease. Of total 12 cases, 8 (11.6%) cases with dyspepsia, 4 (5.8%) cases with fever and 48 (69.6%) cases with multi parity. When considering the obesity, of total 24 cases 9 cases with severe, 8 cases with mild and 7 cases with moderate.

Table 5: Common clinical presentation of gallbladder disease.

Clinical Presentation	No. of cases (%)
Fever	4 (33.0)
Jaundice	-
Dyspepsia	8 (67.0)
Total	12
Multi parity	48 (69.6)
Obesity	
Mild	8 (11.6)
Moderate	7 (10.1)
Severe	9 (13.0)
Total	24

Table 6: Association between clinical presentation and histopathological examination.

	Histo pathological examination						
Clinical Presentation		Acute cholecy		Chronic cholecystitis		Adeno carcinoma	
		n	%	%	%	n	%
Fever	Absent	33	94.3	30	93.8	2	100.0
revei	Present	2	5.7	2	6.2	0	0.0
Jaundice	Absent	35	100.0	32	100.0	2	100.0
Jaundice	Present	0	0.0	0	0.0	0	0.0
Description	Absent	32	91.4	27	84.4	2	100.0
Dyspepsia	Present	3	8.6	5	15.6	0	0.0

Table 7: Association between ultra sound and histopathological examination.

	Histopathological examination				
Ultrasound	Acute cholecystitis	Chronic cholecystitis	Adeno carcinoma	Total	
	n (%)	n (%)	n (%)		
Chronic cholecystitis with calculus	2 (7.7)	18 (75.0)	2 (100.0)	22 (42.3)	
Chronic cholecystitis with acalculus	1 (3.8)	4 (16.7)	0 (0.0)	5 (9.6)	
Acute cholecystitis with calculus	16 (61.5)	1 (4.2)	0 (0.0)	17 (32.7)	
Acute cholecystitis with acalculus	7 (26.9)	1 (4.2)	0 (0.0)	8 (15.4)	
Total	26 (100.0)	24 (100.0)	2 (100.0)	52 (100.0)	

Chi-square value: 35.099, p<0.01

Table 8: Association between histopathological examination and sex.

	Sex	Sex		Chi aguana valua
Histopathological examination	Male	Female	Total	Chi-square value (p-value)
	n (%)	n (%)		(p-varue)
Acute cholecystitis	6 (54.5)	29 (50.0)	35 (50.7)	
Chronic cholecystitis	5 (45.5)	27 (46.6)	32 (46.4)	0.410 (0.911)
Adenocarcinoma	0 (0.0)	2 (3.4)	2 (2.9)	0.419 (0.811)
Total	11 (100.0)	58 (100.0)	69 (100.0)	

Table 6 presents the association between clinical presentation and histopathological examination. Majority 8.6% of the acute cholecystitis and 15.6% of chronic

cholecystitis patients have dyspepsia, while none of the adeno carcinoma patients have clinical presentation. Table 7 compares the ultra sound and histopathological examination. It is observed that 42% of the patients were identified the chronic cholecystitis with calculus through ultra sound. Further 61.5% of acute cholecystitis patients were identified acute cholecystitis with calculus, while 75% with chronic cholecystitis patients and 100% with adeno carcinoma patients were identified chronic cholecystitis with calculus. From the observed chi square value of 35.099 and p value of 0.000 which is less than 0.01 so it is declared that there is an association between

the ultra sound and histopathological examination. Table 8 compares the histopathological examination and sex. It is observed that 51% of the patients have acute cholecystitis. Further male (54.5%) and female (50.0%) patients have acute cholecystitis. From the observed chi square value of 0.419 and p value of 0.811 which is greater than 0.05 so it is declared that there is no association between the histopathological examination and sex.

Table 9: Association between gallbladder and sex.

Gallbladder	Sex		Total	Chi-square value
	Male	Female	Total	(p-value)
Acalculus	3 (27.3)	17 (29.3)	20 (29.0)	
Calculus	8 (72.7)	41 (70.7)	49 (71.0)	0.019 (0.891)
Total	11 (100.0)	58 (100.0)	69 (100.0)	

Table 10: Association between gallbladder and histopathological examination.

	Histo pathological ex		Chi-square		
Gall bladder	Acute cholecystitis	Chronic cholecystitis	Adeno carcinoma	Total	value
	n (%)	n (%)	n (%)		(p-value)
Acalculus	11 (31.4)	9 (28.1)	0 (0.0)	20 (29.0)	
Calculus	24 (68.6)	23 (71.9)	2 (100.0)	49 (71.0)	0.929 (0.628)
Total	35 (100.0)	32 (100.0)	2 (100.0)	69 100.0)	

Table 9 compares the gallbladder and sex. It is observed that 71% of the patients have calculus. Further male (72.7%) and female (70.7%) patients have calculus. From the observed chi square value of 0.019 and p value of 0.891 which is greater than 0.05 so it is declared that there is no association between the gallbladder and sex.

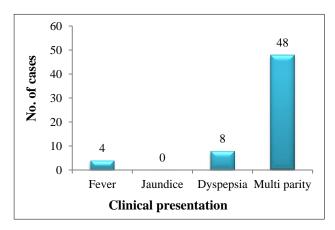


Figure 1: No. of cases with common clinical presentation of gallbladder disease.

Table 10 compares the gallbladder and histopathological examination. It is observed that 71% of the patients have calculus. Further patients with acute cholecystitis (68.6%), chronic cholecystitis (71.9%) and adenocarcinoma have calculus. From the observed chi square value of 0.929 and p value of 0.628 which is

greater than 0.05 so it is declared that there is no association between the gallbladder and histopathological examination.

DISCUSSION

In this study, the average rate of males to females that have been diagnosed with gallbladder disease shows a significant difference between the genders (female predominance to males) for the aspect of predominance of gall bladder. This however constitutes for an interesting finding as previous studies have reported that females show a higher predominance than males for gallbladder disease. Majority of the patients were found to have presented with pain in the abdomen which is consistent with the findings of Siddiqui et al. and slightly different from the reports of Fletcher et al. who reported that all patients presented with pain. 27,28

With respect to the histopathological findings, the most common finding that was seen was acute cholecystitis (51%) followed by chronic cholecystitis(46%) with 3% depicting adenocarcinoma. Specimens reportedly had inflammation presenting with mucosal denudation, ulceration with some reports of metaplasia to dysplasia. Other studies have however reported that chronic cholecystitis is more commonly found.²⁹

For this particular study, incidental gallbladder carcinoma was only found in 2 cases of the 69 (3%). These gallbladders also showed no gross abnormality before the

gallbladder was removed. The incidence can however be stated as being comparatively low. Only one study by Siddiqui et al. matches the incidence as found by this study.27 Some studies have however depicted an incidence of 0.3-1.5% which is lower than the rate of this study.30,31 Conversely, other studies have depicted a higher prevalence rate such as 6.9 - 12.3 %. 34-36 The rate of incidence that has been found in this study can be attributed to the high sensitivity of the criteria that were set for exclusion. Apart from this, a regional and ethnic variation has also been noted in the global incidence of gallbladder carcinomas. This has been evidenced in the high rates of incidence found in the regions of North India, Eastern Europe, South America, Pakistan and East Asia.³⁷⁻³⁹ It has also been reported that gall bladder cancer is rare in the regions of northern Europe and also North America.³⁸ As reported above, the highest incidence of gall bladder cancer as per WHO is Japan.³⁹ Furthermore, this study also evidences that there is a significant association between the histopathological findings, ultrasound and clinical presentation constituting for a better clinical acuity.

With respect to studies that recommend the use of selective histology state that incidental gallbladder carcinoma is unlikely to occur in specimens that do not have gross morphological issues. Therefore, these researchers offer the view that only specimens with macroscopic abnormalities need to be evaluated histopathologically. This also brings to fore, interestingly, the diagnostic acuity of the ultrasonography. The preoperative ultrasound in the present study did not show malignancy of both the cases of carcinomas. Other studies such as the one by De Zoysaet al. however depicted that the carcinomas were visible in the ultrasound.40 Due to this, some researchers have suggested that while histology of the gallbladder is invasive, the untrasonography can be used with the histology being a more selective method. It can therefore be stated that much ambiguity exists between the uses of histology as a routine or selective procedure.

The present study in this regard however advocates for the histology to be a routine procedure. This is mainly because both the gallbladder specimens did not display macroscopic formations nor was the carcinoma detected through the ultrasonography. While there are a number of premalignant conditions, gallbladder carcinoma is more or less associated with gall stones.³⁵ This association warrants necessary attention to be given to histology of the gallbladder as more of a routine procedure rather than selective.

The histopathology of the gallbladder in this study revealed that both the specimens displayed adenocarcinoma which incidentally was also associated with gall stones which support the notion that irritation by gallstones can lead to gall bladder malignancies.

CONCLUSION

The current regulations suggest that the histology of the gallbladder is meant to be routine. In light of this, it would be rather crude to make the change to selective histology especially for the cases of symptomatic cholethiasis. This is also because while this study finds for the use of routine histology, other findings recommend selective histology, thereby making the issue of histology inconclusive. Also, the researcher offers the view that valuable information on incidental carcinoma will be lost if the histology were to become selective. Lastly, the researcher presents the relevance of histopathology with respect to ultrasound and clinical presentation of the patient, thereby stating the need for a gall bladder specimen following cholecystectomy.

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institutional ethics committee

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