

## ORIGINAL ARTICLE

# IS ROUTINE HISTOPATHOLOGY OF GALL BLADDER AFTER LAPAROSCOPIC CHOLECYSTECTOMY NEEDED? : A LOCAL PERSPECTIVE

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## ABSTRACT

**Background:** Laparoscopic Cholecystectomy is one of the most commonly performed routine operation in modern general surgery. All surgical specimens are routinely sent for histopathology. A wide spectrum of variations is seen under the microscope. Rarely, carcinoma is discovered on histopathological examination. The purpose of the article was to identify and elaborate the major histopathological findings of gallbladder after laparoscopic cholecystectomy in a tertiary health care hospital in Pakistan.

**Methods:** This was a retrospective study and included histopathological specimens of gall bladder after cholecystectomy from February 2004 to April 2013. Data was analysed using MS Excel and SPSS 19.0.

**Results:** Total number of cases: 8376, Chronic Cholecystitis: 7705, Acute or chronic cholecystitis with empyema, mucocele or gangrene: 554, Adenocarcinoma: 91, Adenomatous polyp: 3, Squamous cell carcinoma: 5, Papillary carcinoma: 3, Clear cell carcinoma: 4, Adenosquamous carcinoma: 2, Xanthogranulomatous changes: 54, Dysplasia: 13 and Cholesterosis: 1050.

**Conclusion:** Considering the evidence from our study and the evidence from the literature reviewed, it can be concluded that prevalence of all kinds of gall bladder disease, benign or malignant including carcinoma is no different from the rest of the world. Routine histopathology of gall bladder can be omitted without compromising patient safety as proven and practiced by many centers across the globe.

**KEY WORDS:** Histopathology, Gallbladder, Laparoscopic Cholecystectomy

## INTRODUCTION

Gallbladder is one of the most commonly encountered specimens in the Surgical Pathology laboratory. While a majority of such specimens reveal changes associated with chronic cholecystitis, a minority harbour a highly lethal carcinoma. Most of the cases of gall bladder carcinomas are found incidentally in patients who underwent cholecystectomy for cholelithiasis. Research shows that a tumor will be found in 1 to 2 percent of such cases.<sup>1</sup> Cholelithiasis, which is a common disease of the digestive tract affecting 10-15% of the global population, is an important risk factor in long-standing cases for the development of carcinoma of the gallbladder.<sup>2, 3</sup> Pakistan has one of the highest gallbladder cancer incidence rates worldwide (13.8/100,000), making diagnosis of gallstones and

subsequent cholecystectomy a keystone for early diagnosis and secondary prevention of gall bladder carcinoma.<sup>4</sup>

The histopathological spectrum of gallbladder is extremely variable ranging from acute and chronic inflammatory changes to degenerative and proliferative changes like cholesterosis, to pre-malignant lesions like adenomas and dysplasias to a variety of malignancies.

Simple cholecystectomy is curative for all benign and pre-malignant pathologies of the gallbladder. It is also the treatment of choice if cancer is limited to the mucosa.<sup>5</sup>

This study identifies the different histopathological variations of gall bladder after cholecystectomy to

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contribute to the prevalence of different gallbladder diseases in our population. Life expectancy of gall bladder cancer varies greatly with clinical stage at the time of detection and since incidental diagnosis is not rare, routine histopathology of gallbladder specimens provides a tool for subclinical malignancies to be identified early preventing progression to lethal malignancies and increasing the five year survival rate for already developed malignancies.

## METHODS

This was a retrospective study design which was conducted at Ziauddin University Hospital, a tertiary health hospital of Karachi. The university has three affiliated hospitals across the city in different locations which include Nazimabad, Clifton and Keamari. The electronic records of the all the Ziauddin hospitals were searched in order to identify those patients who had undergone cholecystectomy from February 2004 to April 2013. Specimens were examined under the light microscope by trained, qualified and certified pathologists employed at Ziauddin University Hospitals. The histopathology was reported based on a combination of gross and microscopic description of the specimens at different magnifications and the observations were recorded individually. The recorded basic demographic and histopathological data of 8376 cholecystectomy specimens was obtained

which were performed during the specified time frame. The cases were divided into 11 categories namely chronic cholecystitis, acute or chronic cholecystitis with empyema, mucocele or gangrene, adenocarcinoma, adenomatous polyp, squamous cell carcinoma, papillary carcinoma, clear cell carcinoma, adenosquamous carcinoma, xanthogranulomatous cholecystitis, dysplasia and cholesterosis.

The data was analysed using Microsoft Excel and SPSS version 19.0.

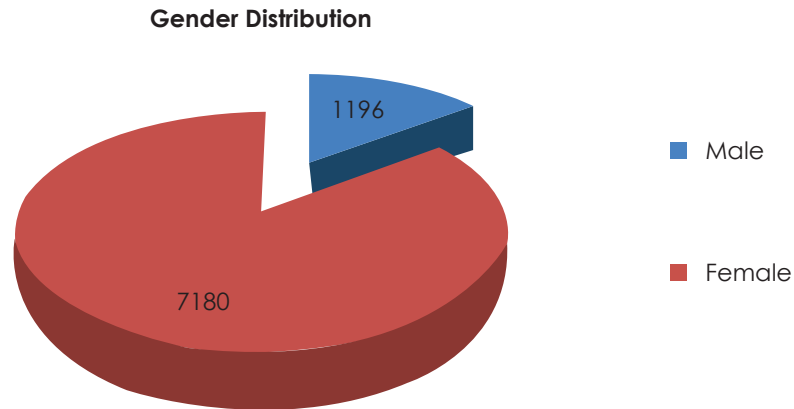
## RESULTS

The age distribution of the patients included in our study ranged from 12 to 80 years with a mean of 35 years and standard deviation of +/- 9.8.1356 (14.3%) of the patients were male while 8127 (85.7%) were female with a gender distribution ratio of 1:6. The gender distribution chart is shown in Figure 1.

Chronic cholecystitis was by far the most common histopathological diagnosis with as many as 7705 (81.2%) cases. It was followed by Cholesterosis 1050 cases (11.1%) and acute on chronic cholecystitis 554 (5.84%) cases. 9366 (98.8%) of the cases had benign findings. The rest 118 (1.24%) were malignant or pre-malignant. Adenocarcinoma was the most common malignancy with 54 (0.57%) cases.

**Table 1: Frequency of different histopathological diagnosis**

Histopathological finding	No. of cases
<b>Chronic Cholecystitis</b>	7705
<b>Acute or chronic cholecystitis with Empyema , mucocele or gangrene</b>	554
<b>Adenocarcinoma:</b>	91
<b>Adenomatous polyp</b>	3
<b>Squamous cell carcinoma</b>	5
<b>Papillary carcinoma</b>	3
<b>Clear cell carcinoma</b>	4
<b>Adenosquamous carcinoma</b>	2
<b>Xanthogranulomatous changes</b>	54
<b>Dysplasia</b>	13
<b>Cholesterosis</b>	1050
<b>Total</b>	8376



**Figure 1: Gender distribution of patients undergoing Laparoscopic Cholecystectomy**

### DISCUSSION

Gallbladder cancer (GBC) is a rare malignancy. It is the fifth most common cancer involving the gastrointestinal tract, but it is the most common malignant tumour of the biliary tract worldwide. Our study indicates the prevalence of gall bladder cancer after cholecystectomy to be 1.26% which is comparable to globally reported figures of 0.5-1.5%.<sup>5</sup>

The demographics of patients undergoing cholecystectomy are also comparable to the rest of the world. Our sample indicates a female to male preponderance of 6:1, comparable to the ratio elsewhere in Pakistan and the rest of the world.<sup>6,7</sup> Age distribution of the patients as described in the results is also comparable to other reported results.<sup>6,7</sup> Percentage of benign findings such as chronic cholecystitis, acute or chronic cholecystitis with empyema or gangrene, cholesterosis are also comparable to the numbers reported elsewhere.<sup>6,7</sup> Although we have encountered only 54 (0.64%) of xanthogranulomatous cholecystitis which is different from other reported figures.<sup>7</sup>

Our study showed that all the patients who had Gall bladder cancer (GBC) stage T1b or greater reported on microscopy of the specimen had age greater than 40 years. Also, gross features suggestive of malignancy such as a growth, a polyp or a thick gall bladder wall were seen pre or intra-operatively. Our study supports the recommendation that selective histopathological analysis should be carried out only in cases where gross features of the gall bladder arouse suspicion of malignancy. This will save valuable time and resources, improve efficiency and boost productivity of the department without compromising safety of the patients.

Similar findings were observed in Mexico.<sup>6</sup> All cases

of GBC which were undetected on gross examination were reported to be stage T1a or limited to mucosa, for which a simple cholecystectomy is curative. Hence a selective policy rather than routine histological examination of non-fibrotic or thickened-wall gallbladder has to be considered. This will reduce the burden on pathology department, with significant cost savings.<sup>7</sup>

Research conducted in a medical centre in England using a total number of 1452 specimens showed four (0.27%) cases of primary gall bladder carcinoma, one case of primary B-cell lymphoma and one secondary carcinoma as well as one case of intra-epithelial neoplasia. Operative notes revealed that there was a high index of suspicion of malignancy in all cases. Of the 4 primary gall bladder carcinomas, 3 were stage T2 and one T4. Pre-operative ultrasound suspected carcinoma was helpful in only one case but a thickened gall bladder wall was noted in all cases. All cases of gall bladder carcinoma were suspected pre-operatively or intra-operatively. Histological examination did not alter the management or outcome in any of the cases. It is suggested that selectively sending specimens for histopathological examination would result in reduced demands on the histopathology department without compromising patient safety.<sup>9</sup>

With the increasing popularity of laparoscopic procedures, there were concerns regarding performing laparoscopic cholecystectomies on patients with possible malignancies. These fears were alleviated by a clinico-pathologic study performed on 41 patients with postoperatively diagnosed gallbladder cancer from among 5,027 patients undergoing Laparoscopic Cholecystectomy (LC) at 24 institutions. The cumulative survival rate was compared with that reported for gallbladder cancer diagnosed after open cholecystectomy

(OC). The 5-year survival rate was 92% for early cancer and 59% for advanced cancer. These results were comparable with 5-year survival rates for gallbladder cancer diagnosed after OC. Although port-site recurrence occurred in four patients with advanced gallbladder cancer, the long-term prognosis of patients with undiagnosed gallbladder cancer who underwent LC was not worsened by the laparoscopic procedure. It was concluded that surgeons can perform LC with reasonable confidence, even if the lesion is possibly malignant.<sup>10</sup> The same was proposed in Japan; the LC procedure does not adversely affect the prognosis of unsuspected GBC, regardless of whether it is detected during or after LC.<sup>11</sup>

In another study all specimens from routine appendectomies, cholecystectomies, haemorrhoidectomies and inguinal hernia repairs performed between 1993 and 2002 were included. The analysis included a comparison of histological and macroscopic diagnoses, review of preoperative and per-operative findings, and an evaluation of the consequences of routine histopathological assessment on patient management and costs. Among 1523 cholecystectomy specimens, all adenomas (0.6 per cent) and carcinomas (0.4 per cent) were suspected macroscopically or developed in association with a known disease. Keeping in mind the rarity of incidental histological findings relevant to patient management, especially in the absence of macroscopic abnormalities, it was suggested that routine histological examination of certain specimens may be omitted. A more elementary role for macroscopic examination of the specimen by the surgeon and the pathologist was also proposed.<sup>12</sup>

A comparative prospective trial conducted in Mexico, using macroscopic gall bladder analysis performed by the surgeon intra-operatively and selective gall bladder analysis performed by pathologist in the laboratory concluded that it would be safe to omit routine histopathology in as much as 46% of the patients.<sup>6</sup>

From 1995 to 1999, 1308 patients had undergone cholecystectomy (mean 262/year) at the Blackpool Victoria Hospital in the U.K. All specimens had been sent for histology. 1249 of the specimens showed chronic cholecystitis, 38 acute cholecystitis or empyema and 16 were removed as part of another procedure. In five gallbladders there was evidence of primary carcinoma. In all cases the gallbladder was opened at the time of surgery (as commented upon in the operation notes) and all showed macroscopic evidence suggestive of carcinoma.

Pre-operative ultrasound scanning identified probable carcinoma in three of the five cases. The study concluded that all cases of gallbladder carcinoma were diagnosed pre-operatively or intra-operatively and a histological diagnosis did not alter the management or outcome of any of these patients. Thus selective histopathology of the gallbladder is safe and may be a more measured approach saving histopathology departments time and money.<sup>13</sup>

In a similar study in India, a total of 1312 patients underwent cholecystectomy for gallstone disease. Gallbladder carcinoma was detected in 13 patients. Macroscopic abnormalities of the gallbladder, such as thick wall or a polyp or a growth were found in all the 13 patients. In patients with a macroscopically normal gallbladder, there were no cases of gallbladder carcinoma.<sup>14</sup> Nusret Akyurek and colleagues also recommend that a simple procedure; that is, incision and inspection, and palpation of the gallbladder by the surgeon in the operating room can be useful for the diagnosis of incidental gallbladder pathologies.<sup>15</sup>

Another study comparing the composition of gall stones and the histopathology of gall bladder reported that twenty-eight patients had mixed stones, 8 had pigment stones and 4 had cholesterol stones. Out of 28 patients with mixed stones 14 had histological picture of chronic cholecystitis, 8 had granulomatous cholecystitis, 4 had adenomatous hyperplasia, 1 had dysplasia and 1 had carcinoma. All 8 patients having pigment gallstones had chronic cholecystitis. Out of 4 patients with cholesterol gallstones, 2 had chronic cholecystitis, 1 had adenomatous hyperplasia and 1 had cholesterosis.<sup>16</sup> Thus the composition of gall stones may need to be explored as a possible risk factor for gall bladder cancer.

## CONCLUSION

Considering the evidence from our study and the evidence from the literature reviewed, it can be concluded that prevalence of all kinds of gall bladder disease, benign or malignant including GBC is no different from the rest of the world. Routine histopathology of gall bladder can be omitted without compromising patient safety as proven and practiced by many centers across the globe. However our study does not explore the risk factors of gall bladder cancer and a larger multi-center study should be designed to analyze the factors associated with gall bladder cancer and the factors which should prompt a surgeon to obtain histopathology

of the gall bladder specimen.

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