

Frequency of Gallbladder Carcinoma and Its Precursors in Routine Cholecystectomy Specimen: An Experience at Tertiary Care Hospital

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ABSTRACT

Introduction: Gallbladder diseases are a common problem with cholelithiasis being the common disease of gallbladder. Gallbladder carcinoma is associated with cholelithiasis. Carcinoma of gallbladder is thought to occur as multistep process starting from intestinal metaplasia to dysplasia to invasive carcinoma. The object of our study is to determine the frequency of precursor lesions and incidental carcinoma on routinely performed cholecystectomies.

Methods: Gallbladders from patients undergoing routine cholecystectomy between January 2017 and January 2019 were examined histopathologically for presence of intestinal metaplasia, dysplasia and carcinoma. The study was conducted at Department of Histopathology, Liaquat National Hospital, Karachi.

Results: A total of 754 specimens were examined during the two year period. Intestinal metaplasia was identified in 119 cases, dysplasia was observed in 12 cases and 7 incidental carcinomas were seen. There was significant association between intestinal metaplasia and dysplasia ($P < 0.001$).

Conclusion: Gallbladder carcinoma is rare disease and may be incidentally seen in routine cholecystectomy specimens. It is our opinion that all gallbladder specimens should undergo histopathological examination as gallbladder carcinoma are aggressive diseases and even small invasive tumors may show recurrence.

Keywords: Cholecystectomy, Gallbladder, Carcinoma, Intestinal metaplasia, Dysplasia.

INTRODUCTION

Diseases of the gallbladder are the universal health problem [1]. More than 95% of gallbladder diseases are due to cholelithiasis. Surgery is the mainstay of management of gallbladder stones. In recent time there has been an increase in the disease of gallbladder disease in the Asian population [2]. Non modifiable risk factors for gall stone diseases include age, female sex, family history and ethnicity. Modifiable risk factors include high calorie/high carbohydrate diets, low dietary fiber, pregnancy, obesity, diabetes mellitus, certain drugs, hemolytic anemia's and biliary infections [1, 3].

Gallbladder carcinomas are rare tumors overall. However, they are aggressive with overall 5 years survival being around 5% [2, 4]. Pathologic tumor stage is considered the most powerful predictor of outcome [5]. Incidental carcinoma in cholecystectomy specimens carries a better prognosis possibly due to early stage disease.

Gallbladder carcinoma are thought to arise in a background of prolonged chronic inflammation giving rise to the theory that most arises as step wise progression of metaplasia to dysplasia to carcinoma sequence [6].

Intestinal metaplasia and dysplasia of the gallbladder is considered to be a risk factor for subsequent development of carcinoma of the gallbladder. Incidence of intestinal metaplasia, dysplasia and carcinoma exhibits a wide range with intestinal metaplasia being reported as 15.6% to 39% in routine cholecystectomy patients [7, 8], dysplasia ranging between 0.2% to 4.9% and gallbladder carcinoma incidence ranging between as high as 21.5/100,00 to as low as 1.5/100,00 [9].

At our hospital, all routinely performed cholecystectomy specimens are submitted for gross and histopathological examination. The objective of this study is to determine the frequency of precursor lesions and incidental carcinoma on routinely performed cholecystectomies at our institute.

MATERIAL AND METHOD

A retrospective analysis of all patients undergoing routine cholecystectomy between January 2017 and January 2019 was performed. Patient's hospital records were reviewed and demographics (age and gender) and histopathological reports were retrieved. Cases, in which a preoperative diagnosis of malignancy was present, were excluded.

Dysplastic epithelium was defined as epithelial cell showing cytologically atypical nuclei with mitotic activity, the extent of nuclear atypia being discordant with the

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degree of any regional inflammation [10]. The sharp circumscription of dysplasia was a helpful diagnostic feature.

Intestinal metaplasia was defined as presence of scattered intestinal type goblet cells, basal pseudostratification of nuclei was acceptable [11].

The data was entered and analyzed using SPSS version 21 (IBM, Chicago, IL). Frequency was computed for categorical variable and mean \pm standard deviation was calculated for quantitative variable. Chi-square test was applied to determine the association of metaplasia with dysplasia. P-value < 0.05 was taken statistically significant.

RESULTS

The study included 754 cases of patients, between January 2017 to January 2019 who underwent routine cholecystectomy, and histopathological examination was done of the resected gallbladders. The patients' age range was 2 to 90 years with mean age of 46.29 \pm 12.25 years. Out of the total 754 patients, 575 were females (76.3%) (Fig. 1). Intestinal metaplasia was identified in 119 cases (15.8%), dysplasia was observed in 12 cases (1.6%) and 7 incidental carcinoma (0.9%) were seen. There was significant association between intestinal metaplasia and dysplasia (P < 0.001) (Table. 1).

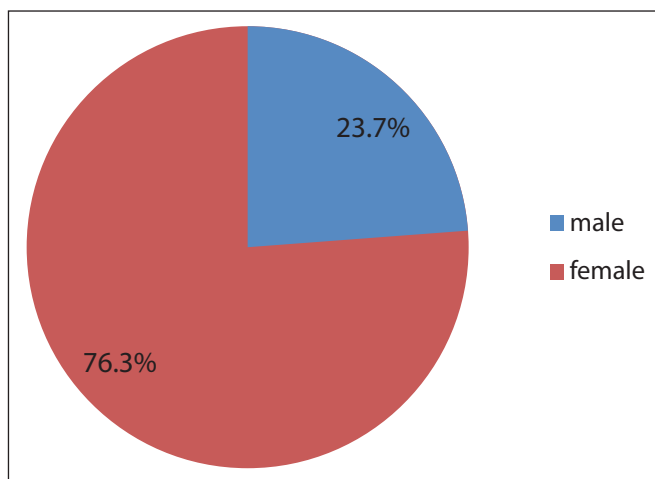


Fig. (1): Distribution of gender.

Table 1: Association of intestinal metaplasia with dysplasia.

Metaplasia	Dysplasia		Total	P-value
	Absent Frequency (%)	Present Frequency (%)		
Absent	631 (99.37)	4 (0.63)	635	** < 0.001
Present	111 (93.28)	8 (6.72)	119	
Total	742	12	754	-

**Statistically significant at P < 0.01

DISCUSSION

In our study among seven hundred and fifty four cholecystectomy specimens a total of 7 patients had incidental adenocarcinoma. Intestinal metaplasia was observed in 15.6% and dysplasia in 1.6% patients respectively.

Our study showed lower incidence of intestinal metaplasia as compared to a study by Khan *et al.* [7] conducted in Karachi who reported a high percentage i.e. around 39%. A Turkish study by Esendağlı [8] reported around 16% incidence and in India finding ranged between 3.4 to 15.5% [12, 13].

In our study dysplasia was observed at a much higher rate than reported by Chin *et al.* [2] and Segovia *et al.* [6] who reported a figure of 0.2% cases of dysplasia. Studies from Mexico by Albores-Saavedra *et al.* [13] reported dysplasia in 13.5% of 200 consecutive cases of cholecystectomy while Sanjay *et al.* [14] reported a rate of 5% in a series of 400 gallbladder specimens.

The rate of incidental carcinoma in our study was 0.9%, close to 0.6% reported by Segovia *et al.* [6]. No cases of invasive carcinoma were reported by Rahul *et al.* [12] in their series of 140 cases and only one case (0.25%) was reported by Sanjay *et al.* [14].

The variance in the rate of dysplasia and intestinal metaplasia may be due to a combination of multiple reasons, namely how thoroughly gallbladders are examined and sampled grossly, interobserver variability in assessment of dysplasia and reactive atypia. The role of genetic, environmental and ethnic factors may also play a part in the variable rates of epithelial changes across the world.

The rate of incidental carcinoma was low overall; this could be due to slow progression from precursor lesion to invasive carcinoma.

Our study is limited firstly being a retrospective design. Secondly it is a single centre study with a limited sample size. Thirdly we used only morphological features and no ancillary studies were carried out.

CONCLUSION

Gallbladder carcinoma is a rare disease and may be incidentally seen in routine cholecystectomy specimens. Gallbladder carcinoma is an aggressive disease and even small early stage tumors may show recurrence and require adjuvant treatments. Therefore all gallbladders specimens should undergo gross and microscopic examination.

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None.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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