Original Article

Histopathological Diagnosis of Incidental Gall Bladder Carcinoma in Patients Undergoing Routine Laparoscopic Cholecystectomy

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ABSTRACT

Objective: To determine the frequency of gall bladder carcinoma incidentally diagnosed in patients undergoing routine laparoscopic cholecystectomy.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Pathology Department of Nishtar hospital, Multan from January 2022 to January 2023.

Materials and Methods: A total of 240 simple laparoscopic cholecystectomy specimens from 240 patients were taken and sent for histopathological examination. A detailed gross and microscopic examination was performed. All histological findings like Chronic Cholecystitis with Cholelithiasis, Chronic Cholecystitis, and acute on chronic Cholecystitis with Cholelithiasis were included. SPSS version 23 was used for data analysis.

Results: The most common histological diagnosis was chronic cholecystitis with cholelithiasis and chronic cholecystitis as 62.5% and 15.8%, respectively. There was no association between histological diagnosis and sex, (p=0.812). There were 6 (2.5%) patients who were diagnosed incidental gall bladder carcinoma.

Conclusion: Histopathological analysis of gall bladder specimens is highly essential in diagnosing and managing various gallbladder diseases. It helps in identifying the type and severity of the disease, which is essential for determining the appropriate treatment plan. A comprehensive clinical history and strong radiological correlation, coupled with detailed histopathological evaluation, can provide a more accurate diagnosis and ensure early detection, resulting in better prognosis for the patient.

Key Words: Cholelithiasis, Incidental carcinoma, Gall bladder, Cholecystectomy.

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INTRODUCTION

Unexpected gallbladder carcinoma refers to the discovery of malignant cells in the gallbladder, which were not previously suspected or detected[1]. It is usually discovered during surgery to remove the gallbladder for other reasons, such as gallstones or inflammation.

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Gallbladder carcinoma is a rare but aggressive cancer that can be difficult to diagnose early[2]. It often presents with nonspecific symptoms, such as abdominal pain, nausea, and vomiting, which can be mistaken for other conditions. In routine different types of sonographically test are used for the diagnosis of cancer in the gallbladder i.e. ultrasound, CT and MRI[3].

The incidence of gallbladder cancer (GBC) varies widely between different regions. In the United States, an incidence of 1.2/100,000 is reported, while in some countries, GBC is more prevalent[4]. Preoperatively, only about 30% of GBC cases are suspected, while the majority (almost 70%) are incidentally diagnosed either during surgery or routine histopathological examination (HPE). This is because GBC often does not show any symptoms until it has reached an advanced stage[5].

Incidence of IGBC, or incidental gallbladder carcinoma, is reported to be between 0.2-2.8% and can vary in different geographic regions of the world[6]. To ensure that any potential pathologies are not overlooked, it is recommended to submit all routine cholecystectomy specimens for histopathological examination. This will help in the early detection and

management of any underlying conditions, such as gallbladder cancer, and can ultimately improve patient outcomes[7].

Histopathological diagnosis of gallbladder carcinoma involves the examination of tissue samples obtained during a biopsy or surgical resection[8]. The following are the key features that are evaluated during the diagnosis: Tumor size: The size of the tumor is measured and recorded. Tumor grade: The grade of the tumor is determined by evaluating the degree of differentiation of the cancer cells under a microscope[9]. The grading system ranges from 1 to 3, with grade 1 being well-differentiated and grade 3 being poorly differentiated. Tumor stage: The stage of the tumor is determined based on the extent of its spread. The TNM (Tumor, Node, Metastasis) system is commonly used to stage gallbladder carcinoma[10].

MATERIALS AND METHODS

Study was conducted at pathology department of Nishtar hospital, Multan from January 2022 to January 2023 in duration of one year. Study was started after ethical approval from hospital board of ethics. Non probability consecutive sampling technique was used. Sample size was calculated by using online sample size calculator openepi.com with 95% confidence interval, 80% power of study and 1.4% incidental gallbladder carcinoma. The study included patients who had simple open or laparoscopic cholecystectomy specimens, as well as those who had previously incised and fragmented specimens, both gender and all ages. Patients with radical cholecystectomy through resection and lymphodenectomy and metastatic cases were excluded from the study.

During surgery tissue specimens received fixed in 10% neutral buffered formalin. The specimens were grossly examined for any abnormal wall thickening or growth. In cases where carcinomas were suspected, the specimens were meticulously sectioned as per the protocol of the American College of Pathologists. This indicates that the examination was carried out with great care and attention to detail, in order to accurately diagnose any potential abnormalities or cancerous growths. The cystic duct resection margin and liver parenchymal resection margin were marked with ink and examined for any signs of tumor involvement. The resection margins were then cut and examined in detail to determine the type and pTNM staging of the carcinoma.

The tissue processing mentioned here is a common method used in histopathology to prepare tissue samples for microscopic examination. The process involves dehydrating the tissue with increasing concentrations of alcohol, clearing it with xylene, and then impregnating it with paraffin wax, which allows for thin slicing of the tissue. These thin slices are then mounted on slides and stained with hematoxylin and eosin (H&E) to highlight the cellular and tissue structures.

SPSS version 23 was used for data entry and analysis. Mean and SD was calculated and mentioned for numerical variables like age and frequency percentages were calculated and mentioned for categorical data like gender and incidental gallbladder carcinoma. T test and chi square test were applied to see association among variables. P value less than or equal to 0.05 was taken as significant.

RESULTS

Overall, 240 patients were included in our study, in which 46 (19.2%) were males and 194 (80.8%) were females. The mean age of all the patients was 48.41±7.94 years. The most common histological diagnosis were chronic cholecystitis with cholelithiasis and chronic cholecystitis as 150 (62.5%) and 38 (15.8%), respectively. The distribution of histological diagnosis was presented according to gender in table. I. There was no association between histological diagnosis and sex, (p=0.812). (Table. I).

Table No. 1: Distribution of histological diagnosis according to gender

Histological Diagnosis	Sex		Total
	Male	Female	
Chronic Cholecystitis with Cholelithiasis	25 (54.3)	125 (64.4)	150 (62.5)
Chronic Cholecystitis	8 (17.4)	30 (15.5)	38 (15.8)
Acute on Chronic Cholecystitis with Cholelithiasis	5 (10.9)	16 (8.2)	21 (8.8)
Chronic Cholecystitis with Cholelithiasis and cholesterolosis	2 (4.3)	8 (4.1)	10 (4.2)
Xanthogranulomatous Cholecystitis	3 (6.5)	4 (2.1)	7 (2.9)
Incidental Malignancy	1 (2.2)	4 (2.1)	5 (2.1)
Follicular Cholecystitis with Cholelithiasis	1 (2.2)	2 (1.0)	3 (1.3)
Empyema Gall Bladder	1 (2.2)	3 (1.5)	4 (1.7)
Adenomyomatous Hyperplasia associated with Chronic Cholecystitis with Cholelithiasis	0 (0.0)	2 (1.0)	2 (0.8)
Total	46 (100.0)	194 (100.0)	240 (100.0)

There were 6 (2.5%) patients who were diagnosed as incidental gall bladder carcinoma. Further, incidental gall bladder carcinoma distribution according to gender presented in table. 2. There was no association between incidental gall bladder carcinoma and sex, (p=0.875). (Table. I).

Table No.2: Incidental gall bladder carcinoma distribution according to gender

Incidental gall bladder carcinoma	Sex		Total	p-value
	Male	Female		
Yes	1 (2.2)	5 (2.6)	6 (2.5)	0.875
No	45 (97.8)	189 (97.4)	234 (97.5)	
Total	46 (100.0)	194 (100.0)	240 (100.0)	

DISCUSSION

Based on the studies conducted by the Royal College of Pathologists, it has been recommended that all routine cholecystectomy specimens should be submitted for histopathological examination (HPE) [11]. This is because much significant pathology, including malignancy, can present with non-alarming clinico-radiological findings. Traditionally, a gallbladder removed for presumed benign disease has been sent for HPE, but this practice has been questioned as it may not always be sufficient to detect occult pathologies[12].

In this study 19.2% were males and 80.8% were females, mean age of all the patients was 48.41±7.94 years. Incidental carcinoma was diagnosed in 2.5% patients. A study was conducted by Khalid et al[13] and reported 6.1% carcinoma gallbladder, among them 4 were male and 12 were female. In another study by Dattal et al[14] reported mean age of patients was 44 years and concluded that lesions can range from chronic cholecystitis to more serious conditions like carcinoma, which is cancer of the gallbladder. It's important to note that most patients who undergo routine cholecystectomy do not have cancer, but the procedure allows for the detection and treatment of any potentially serious conditions.

The study conducted by Turkish author Kanlioz et al[15] found that the mean age of patients diagnosed with GBC was 60.85 years. Out of the total 6314 patients, only nine were diagnosed with GBC through postoperative histopathological examination, which accounted for 0.14% of the total patient population. The incidence of incidental carcinoma in Islamabad has been reported to be 0.21% and 1.55% by Manzoor et al[16] and Tanveer et al[17], respectively. This suggests that a small but significant proportion of cases may involve incidental carcinoma. It is important for healthcare professionals to be aware of this possibility and to take appropriate measures to screen for and treat any potential cases of carcinoma.

In this study out of six patients diagnosed with incidental carcinoma by histopathology 5 patients were female and 1 male, female gender is more suspicious and prone to disease. Two previous studies reported a higher incidence of incidental carcinoma in females. Specifically, Pitt et al[18] found that incidental carcinoma was diagnosed in 1.13% of females, while Abbasi et al[19] reported a slightly higher incidence of 2%. These findings suggest that incidental carcinoma may be more prevalent in females compared to males. It is important to note, however, that further research is needed to confirm these findings and to better understand the factors contributing to the gender disparity in incidental carcinoma incidence.

According to a study conducted by Faisal G Siddiqui et al[20], the incidence of adenocarcinoma gallbladder cancers was 2.8%. However, it is important to note that the incidence rates can vary depending on various factors such as age, gender, and geographical location, but in his study male to female ratio is found equal.

CONCLUSION

Histopathological analysis of gall bladder specimens is highly essential in diagnosing and managing various gallbladder diseases. It helps in identifying the type and severity of the disease, which is essential for determining the appropriate treatment plan. A comprehensive clinical history and strong radiological correlation, coupled with detailed histopathological evaluation, can provide a more accurate diagnosis and ensure early detection, resulting in better prognosis for the patient.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Di Mauro D, Orabi A, Myintmo A, Reece-Smith A, Wajed S, Manzelli A. Routine examination of gallbladder specimens after cholecystectomy: a single-centre analysis of the incidence, clinical and histopathological aspects of incidental gallbladder carcinoma. Discover Oncol 2021;12:1-7.
2. Bastiaenen VP, Tuijp JE, Dieren S, Besselink MG, Gulik TM, Koens L, et al. Safe, selective histopathological examination of gallbladder

specimens: a systematic review. J British Surg. 2020;107(11):1414-28.
3. Iqbal S, Sahrish F, Sameen S, Iqbal F, Aitzaz S, Cheema SM. Unexpected gall bladder carcinoma- a surprising histopathological diagnosis. Pak J Pathol 2022;33(3):83-87.
4. Khan S, Rashikh MA, Rehman KU, Berjis H. Selective or Routine Histology of Cholecystectomy Specimens for Diagnosing Incidental Carcinoma of Gallbladder and Correlation with Careful Intraoperative Macroscopic Examination? A Systematic Review. Asian Pacific J Cancer Prevention: APJCP 2021;22(3):651.
5. Di Mauro D, Saunders S, Orabi A, Myintmo A, Reece-Smith A, Wajed S, et al. Incidental Gallbladder Cancer: The Role of Routine Versus Selective Histopathological Examination of Gallbladder Specimens After Cholecystectomy. Gallbladder Cancer: Current Treatment Options 2023:89-92.
6. Altiok M, Özdemir HG, Kurt F, Gul MO, Gumus S. Incidental gallbladder cancer: a retrospective clinical study of 40 cases. Annals Surgical Treatment and Research 2022;102(4):185-92.
7. Jeelani T, Amin J, Reshi R, Rasheed R. Incidental gall bladder carcinoma in routine cholecystectomy cases: Need for Histopathology. Int J Res Rev 2019;6:12-5.
8. Nagarajan G, Kundalia K. Should every cholecystectomy specimen be sent for histopathology to identify incidental gall bladder cancer? Ind J Cancer 2020;57(1):2-3.
9. Poudel R, Shah A. Incidence of Incidental Gall Bladder Cancer and Role of Routine Histopathological Examination in Cholecystectomies Specimens for Benign Disease. J Nepal Health Res Council 2020;18(3):547-50.
10. Alabi A, Arvind AD, Pawa N, Karim S, Smith J. Incidental gallbladder cancer: routine versus selective histological examination after cholecystectomy. The Surg J 2021;7(01):e22-5.
11. Dincel O, Goksu M, Hatipoglu HS. Importance of routine histopathological examination of a gallbladder surgical specimen: unexpected gallbladder cancer. J Cancer Res Ther 2018; 14(6):1325–9.
12. Swank HA, Mulder IM, Hop WC, van de Vijver MJ, Lange JF, Bemelman WA. Routine histopathology for carcinoma in cholecystectomy specimens not evidence based: a systematic review. Surg Endosc 2013;27(12):4439–48.
13. Khalid MA, Masood J. Incidental gallbladder carcinoma in patients undergoing cholecystectomy for cholelithiasis. Pak J Surg 2009;25(4):262–65.
14. Dattal SD, Kaushik R, Gulati A, Sharma VK. Morphological spectrum of gall bladder lesions and their correlation with cholelithiasis. Int J Res Med Sci 2017;5(3):840-46.
15. Kanlioz M, Ekici U, Ayva Y. Analysis of Incidental Gallbladder Cancer in Cholecystectomies. Cureus 2019;11(9):1–5.
16. Manzoor A, Khan F. Frequency of incidental carcinoma gall bladder in cholecystectomy. J Postgrad Med Inst 2016;30(1):141–46.
17. Tanveer SM, Mukarram HS, Nayyar HS, Qurat Ul Ain M, Nelofar S. Incidental gallbladder cancer: Missing links in Pakistani population. Int J Hepatobiliary Pancreat Dis 2017;7(2):1-10.
18. Pitt SC, Jin LX, Hall BL, Strasberg SM, Pitt HA. Incidental gallbladder cancer at cholecystectomy: When should the surgeon be suspicious? Ann Surg 2014;260(1):128–33.
19. Abassi A, Qasmi SA, Ghafoor A, Kiani F, Abassi H. Frequency of carcinoma gallbladder in cases of cholelithiasis undergoing cholecystectomy at tertiary care hospital. Rawal Med J 2012;37(4): 406-8.
20. Siddiqui FG, Memon AA, Abro AH, Sasoli NA, Ahmad L.Routine histopathology of gallbladder after elective cholecystectomy for gallstones: waste of resources or a justified act? BMC Surg 2013; 13: 26.