

# A Prospective Study of Incidental Gall Bladder Carcinoma in Patients Undergoing Cholecystectomy

Chitta Ranjan Sarangi<sup>1</sup>, Arun Kumar Mohanty<sup>2</sup>

<sup>1</sup>Associate Professor, Department of Endocrine Surgery, SCB Medical College, Cuttack, Odisha, India.

<sup>2</sup>Assistant Professor, Department of Endocrine Surgery, SCB Medical College, Cuttack, Odisha, India.

Received: November 2019

Accepted: November 2019

**Copyright:** © the author(s), publisher. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

## ABSTRACT

**Background:** Carcinoma of gall bladder is the sixth most common malignancy of the gastrointestinal tract worldwide. Incidental gall bladder carcinoma (IGBC) is an incidental finding of carcinoma diagnosed during cholecystectomy. The incidence of IGBC is around 0.19 - 3.3% in the literature. **Aim:** The aim of our study was to report incidence of gall bladder cancers which were incidentally diagnosed during histopathological examination of cholecystectomy specimens done for benign gall bladder disease. **Methods:** This study includes 200 cholecystectomy specimens which were done, during June 2016 to July 2018 in a tertiary care hospital. The clinicopathological findings of cases with incidentally detected gall bladder cancers were recorded; age, sex, presenting symptoms, presence of gall stones and histologic grade and staging of tumours were recorded. **Results:** In our study laparoscopy or open cholecystectomy was attempted in 200 cases during the two year period. Incidental gall bladder carcinomas were diagnosed in 5 cases (2.5%), with mean age of 63 years. Pain, vomiting, and dysphagia were the presenting complaints. USG revealed thickened gall bladder in 115 cases, and polyp in 19 cases. Gall stones were seen in 54 cases. Histopathology showed moderately differentiated adenocarcinoma in 5 cases. **Conclusion:** Incidental gall bladder carcinomas were diagnosed in 5 cases (2.5%). Prognosis of incidental gall bladder carcinoma is better, if diagnosed in early stages.

**Keywords:** Cholecystectomy, gall bladder carcinoma .

## INTRODUCTION

Gall bladder carcinoma (GBC) is the sixth most common cancer involving the gastrointestinal tract but it is the most common malignant tumour of the biliary tract worldwide. GBC is a rare entity, and diagnosed in 0.3-1.5% of all cholecystectomies.<sup>[1]</sup> Life expectancy of GBC varies greatly with clinical stage at the time of detection. Incidental gall bladder carcinoma (IGBC) is defined as carcinoma of gall bladder suspected for the first time during cholecystectomy or accidentally found on histological examination of gall bladder. Carcinoma gall bladder, the most common biliary malignancy and the 5th most common GI malignancy in the west is seen predominantly in the 7<sup>th</sup> and 8<sup>th</sup> decades of life. It's an aggressive tumour with poor prognosis except when incidentally diagnosed at an early stage after cholecystectomy for cholelithiasis. Review of literature suggests only 10% cases are confined to the gall bladder wall, 5% have direct invasion into hepatic parenchyma, 45% have lymph node

metastases and 20% have distant extrahepatic metastases at the time of diagnosis.<sup>[1]</sup> Clinical manifestations of gall bladder carcinomas are generally indistinguishable from those of benign gall bladder diseases such as cholecystitis or cholelithiasis. Therefore, gall bladder carcinomas are diagnosed during or after surgery performed for gall bladder stones or benign gall bladder diseases. It's occurrence in random autopsy series is around 0.4% but approximately 1% of the patients undergoing cholecystectomy for gall stone diseases are found incidentally to have gall bladder cancer.<sup>[2]</sup> This study is done to find the incidence of incidental gall bladder cancer in routine open/laparoscopic cholecystectomy done for benign indications at a tertiary care hospital. Routine cholecystectomy is usually undertaken for cholelithiasis, trauma, torsion of the gall bladder, empyema gall bladder, diverticulosis, typhoid gall bladder and biliary dyskinesia. Cholelithiasis, the most important risk factor for gall bladder carcinoma is 7 times more common in patients with gall stone disease than in those without it.<sup>[3]</sup> 69% to 86% of the patients with gall bladder cancer have a personal history of gall stone disease. Larger stones (>3cm) are associated with 10-fold increase risk of developing cancer of the gall bladder with chances being higher in symptomatic cases than in asymptomatic ones.<sup>[4]</sup>

### Name & Address of Corresponding Author

Dr. Arun Kumar Mohanty,  
Assistant Professor,  
Department of Endocrine Surgery,  
SCB Medical College, Cuttack,  
Odisha, India.

Gall bladder polyps are found in 5% of patients who undergo USG. True adenomatous polyps are found in 0.3% to 0.5% of the population.<sup>[5]</sup> In a series of patients with gall bladder polyps, none were malignant if < 1cm diameter, but 23% of polyps > 1cm diameter were malignant. Polyps > 1.8cm diameter were more likely to contain an advanced stage of cancer.<sup>[6]</sup> Cholecystectomy should be performed in these cases through an open approach because laparoscopic perforation in these setting may convert a potentially curable disease into an incurable one. The incidence of gall bladder cancer is between 7% and 25% in calcified “porcelain” gall bladder.<sup>[7]</sup> Hence cholecystectomy should be performed in such cases even if the patient is asymptomatic. Cholecystectomy is also indicated when USG is done for other abdominal conditions and accidentally discovers gall stones. The presence of abnormal pancreatiko-biliary duct junction with chronic biliary inflammation has been associated with both choledochal cyst and gall bladder cancer. Patients with choledochal cysts have an increased risk of developing cancer anywhere in the biliary tract, but the incidence is highest in the gall bladder. Carcinoma of the gall bladder involves the fundus in 60%, body in 30% and neck in 10% of the cases. Because 90% of the cancers originate in the fundus and body of the gall bladder most do not produce symptoms until the disease is advanced. Those that involve the neck of the gall bladder portends a better prognosis because of earlier presentation.<sup>[8]</sup> A review of Memorial Sloan Kettering cancer center experience highlighted the observation that 95% patients suspected of carcinoma gall bladder presenting with jaundice were ultimately noted to harbour unresectable disease.<sup>[9]</sup> Macroscopically, they have been divided into infiltrative (most common), nodular, nodulo-infiltrative, papillary (best prognosis), and papillary-infiltrative. Microscopically adenocarcinoma (98%),<sup>[10]</sup> are the most common histologic subtypes . Others include adenosquamous, oat cell carcinoma, sarcoma, carcinoid, lymphoma and melanoma. In cases of incidental gall bladder carcinomas, cholecystectomy is performed. For benign diseases, surgeons most commonly come across a Stage 1 carcinoma (cancer within the muscular layer of the gall bladder). In T1a tumors with less likelihood of N1 disease, simple cholecystectomy is curative. In cases of cystic duct margin positivity re-resection to negative margins is imperative. If necessary common bile duct resection with establishment of biliary enteric continuity should be done. 66% of those presenting after incidental discovery of gall bladder cancer were eligible for re-exploration and of those 17% had no evidence of residual disease.<sup>[11-12]</sup>

## MATERIALS AND METHODS

A prospective observational study conducted with 200 cases was done at a tertiary care hospital from June 2016 to July 2018 with an aim to evaluate the incidence of incidental gall bladder carcinoma in cases of routine cholecystectomy. All patients undergoing routine cholecystectomy for cholelithiasis and benign gall bladder diseases were included in this study. All patients with pre diagnosed gall bladder carcinomas, gall bladder mass, empyema gall bladder and gall stone associated with obstructive jaundice were excluded from this study. Patients presenting with right upper quadrant pain, jaundice and dyspepsia were subjected to thorough history taking, clinical examination and relevant haematological, radiological and biochemical tests. Patients diagnosed with gall stone disease and other benign biliary diseases that required simple cholecystectomy were subjected to open or laparoscopic cholecystectomy and the excised gall bladder specimen was sent for histopathological study. Patients with positive histology were called up and managed depending upon the stage of the disease and followed up for a period of one year. The data was collected and analysed through Statistical data analysis (SPSS 16).

## RESULTS

The study shows a female preponderance with 130 females undergoing cholecystectomy in a sample of 200 patients. The minimum age is 16 years and maximum age of presentation is 83 years. [Figure 1]

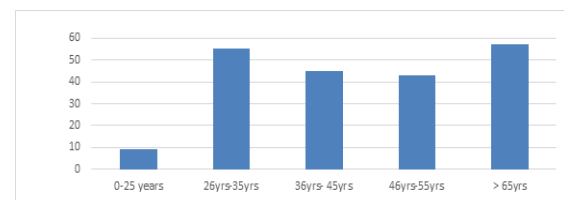


Figure 1: Age Range Distribution

The age group most commonly affected with gall bladder diseases range more than 65yrs.

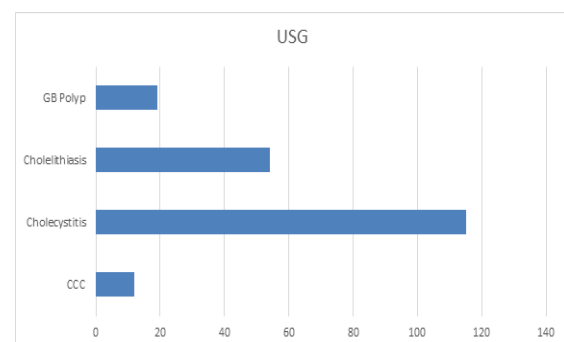


Figure 2: USG Findings

The most common radiological diagnosis is that of cholecystitis among all patients presenting with

clinical symptoms of gall bladder diseases. [Figure 2]

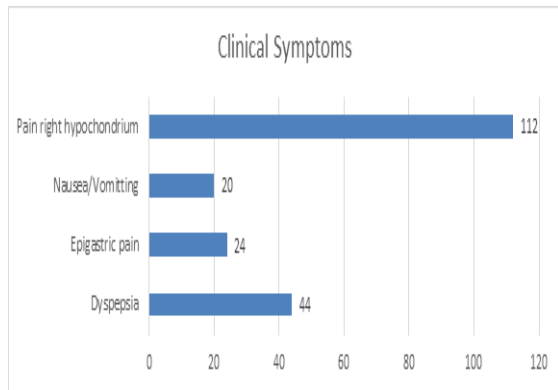


Figure 3: Clinical Symptoms

Right hypochondrium pain is the most common presenting symptom among all other symptoms of Gall stone disease. [Figure 3]

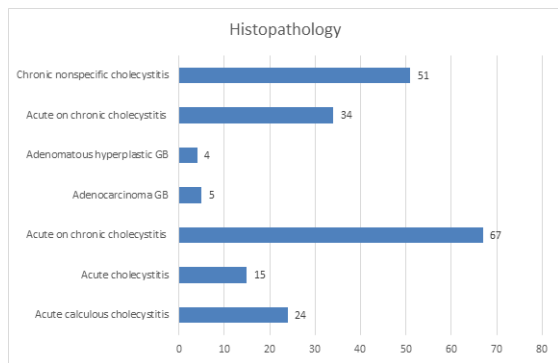


Figure 4: Histopathology

In this series 200 patients who underwent routine cholecystectomies, 5 patients were found to have adenocarcinomas in the specimens sent for histopathology. [Figure 4]

## DISCUSSION

Gall bladder carcinoma is a very aggressive malignant disease with late symptoms. Hence patients often present in late stage and the disease is associated with poor prognosis with 5-year survival rates reported to be less than 5%.<sup>[13]</sup> A pseudo tumoral condition of the gall bladder called as xanthogranulomatous cholecystitis is also known radiologically to simulate malignancy. A difficult gall bladder at surgery usually raises the suspicion of cancer. Unusual findings at surgery like a gall bladder mass, dense adhesions of the organs adjacent to the gall bladder and a difficult dissection of the gall bladder from the liver bed are all pointers to the presence of possible malignancy. After cholecystectomy the entire gall bladder should be submitted for microscopic examination and at least 3 levels are to be obtained from each paraffin block

which demonstrated a carcinoma, so as to be certain that the muscularis propria was not involved. Amanullah et al (1.8%),<sup>[14]</sup> and Shrestha R et al (1.4%),<sup>[5]</sup> have found the incidence similar to ours whereas Zhang WJ et al,<sup>[3]</sup> have shown its occurrence to be as low as 0.19%. The variation in the incidence may be due to inadequate preoperative evaluation or less number of cholecystectomy used for the study purpose. This is because the incidence of primary carcinoma of the gall bladder is itself low. A study done by A. Panebianco, et al,<sup>[15]</sup> stated that patients with GBC are around 15–20 years older than patients with gallstones, suggesting that the intraepithelial evolution takes over 10 years. Various studies including the working report of Royal College of Pathologists have recommended for this routine standard practice.<sup>[16]</sup> Recently few other investigators have challenged this practice. They have suggested that all cases of GB carcinoma have some macroscopic features like thickened fibrotic wall, mucosal ulceration, nodular mucosa or polypoid projections which can be used as a guide for sending for histopathology. In our study we have found that two cases had thickened wall whereas rest 26 (92.8%) of the cases of incidental carcinoma GB had no macroscopic intraoperative findings suggesting the need of routine histopathology of all cholecystectomy sample. Adenocarcinoma is the most common histologic type, accounting for 98% of all gallbladder tumours, two-thirds of which are moderately/poorly differentiated. The remaining common histopathological variants include papillary, mucinous, squamous, and adenosquamous subtypes were noted by R. Hundal and E. A. Shaffer, in their study on —Gallbladder cancer: epidemiology and outcome.<sup>[17]</sup> It is a standard practice to perform routine histopathological examinations for all cholecystectomy specimens. In the era of laparoscopic cholecystectomy for treatment of benign diseases, incidental gallbladder carcinoma has dramatically increased and allows to detect cancer at early stages with a better prognosis. In our study majority of the cholelithiasis patients were less than 50 years and IGBC patients were more than 50 years. By using Mann-Whitney U test the mean age in malignant patients was 51.96 with SD  $\pm 2.09$  and the mean age in benign patients was 42.48 with SD  $\pm 2.28$ . The p value was 0.0041. The result was significant as p value was Ultrasonography is most frequently the initial diagnostic study obtained when gallbladder disease is suspected. G. Miller and W. R. Jarnagin,<sup>[18]</sup> stated that in advanced gall bladder malignancy disease, sensitivity and specificity of ultrasound imaging is 85% and 80%, respectively; however, in early disease, ultrasound examination often fails to detect any abnormality, particularly when the tumour is flat or sessile and is associated with cholelithiasis. In our study all patients underwent abdominal ultrasonography as the first-line imaging modality. Shrikhande SV et al in their

study on —cholelithiasis in gallbladder cancer: coincidence, cofactor, or cause.<sup>[19]</sup> Stated that gallstones appear to have a causative role for cancer, the risk increases with increasing size, volume and weight, and number of the stones. In our study only number of stones was taken for study as riskfactor. In IGBC cases, multiple gall bladder calculi were present in 20 patients and single calculi were present in 08 patients. Results observed in our study are similar to what observed in above study. The gallbladder wall thickness was reported to be more than 4 mm in two patients out of 28 IGBC patients. They had focal wall thickening involving the fundus. These two patients were further evaluated with a CECT scan which did not reveal any features suggestive of gallbladder malignancy. MRCP was done for two patients who had choledocholithiasis and they subsequently underwent ERCP for clearance of the CBD. Shrikhande et al,<sup>[20]</sup> in their study observed that abdominal pain was the most common complaint with which patients had presented and this is similar to what we have observed in our current study i.e. 2300 patients (97%).

## CONCLUSION

Incidence of incidental gall bladder carcinoma in our study is 2.5%. Early detection contributes to a higher survival rate. The prognosis of gall bladder cancer is poor, mainly because of the delayed presentation.

## REFERENCES

1. Mittal R, Jesudason MR, Nayak S. Selective histopathology in cholecystectomy for gallstone disease. *Indian J Gastroenterol*. 2010 Jan;29(1):26-30.
2. Ghimire P, Yogi N, Shrestha BB. incidence of incidental carcinoma gall bladder in cases of routine cholecystectomy. *Kathmandu Univ Med J (KUMJ)*. 2011 Apr-Jun;9(34):3-6.
3. Zhang WJ1, Xu GF, Zou XP, Wang WB, Yu JC, Wu GZ, Lu CL. Incidental gallbladder carcinoma diagnosed during or after laparoscopic cholecystectomy.
4. Joon Joon Khoo; Nurul Akmar Misron. A clinicopathological study of nine cases of gallbladder carcinoma in 1122 cholecystectomies in Johor, Malaysia *Malaysian Journal of Pathology*. Jun2008, Vol. 30 Issue 1, p21-26. 6p.
5. Shrestha R, Tiwari M, Ranabhat SK, Aryal G, Rauniyar SK, Shrestha HG. Incidental Gallbladder carcinoma : value of routine histological examination of cholecystectomy specimens. *Nepal Med Coll J*. 2010;12(2):90–94.
6. Jetley Sujata, Rana S, Khan Sabina, Hassan MJ and Zeeba Shamim Jairajpuri. Incidental Gall Bladder Carcinoma in Laparoscopic Cholecystectomy: A Report of 6 Cases and a Review of the Literature *J Clin Diagn Res*. 2013 Jan; 7(1): 85–88.
7. Towfigh S, McFadden DW, Cortina GR, Thompson JE Jr, Tompkins RK, Chandler C, Hines OJ Porcelain gallbladder is not associated with gallbladder carcinoma. *Am Surg*. 2001 Jan; 67(1):7-10.
8. Aldridge MC, Bismuth H. Gall bladder cancer: the polyp cancer sequence. *Br J Surg*. 1990; 77:363–64. [18]. Henson DE, Albores-Saavedra J, Corle D Carcinoma of the gallbladder. Histologic types, stage of disease, grade, and survival rates. *Cancer*. 1992 Sep 15;70(6):1493-7.
9. Hai, A. A., et al. (1994): Carcinoma gallbladder—possible aetiology. In: Rao RS, Deo MG, Sanghvi LD, (Eds). *Proceedings of the XVI International Cancer Congress*, Ed., Monduzzi, 2069–72.
10. Nath G, et al. Association of carcinoma of the gallbladder with typhoid carriage in a typhoid endemic area using nested PCR. *J. Infect.Dev.Ctres*. 2008;2:302–307.
11. Raicht RF, Cohen BI, Fazzini EP, Sarwal AN, Takahashi M. Protective effect of plant sterols against chemically induced Colon tumors in rats. *Cancer Res* 1980; 40:403-5.
12. Henson DE, Albores-Saavedra J, Corle D. Carcinoma of the gallbladder. Histologic types, stage of disease, grade, and survival rates. *Cancer* 992;70: 1493-1497.
13. Ramesh S Waghmare, Rima N Kamat Incidental Gall Bladder Carcinoma in Patients Undergoing Cholecystectomy : A Report of 7 Cases
14. Amanullah MK, Rizwn AK, Shahid S, Veena M. Occult carcinoma of gallbladder: Incidence and role of simple cholecystectomy. *JK- Practitioner* 2007; 14: 22-3.
15. A. Panebianco, A. Volpi, C. Lozito, A. Presteria, P. Ialongo, and N. Palasciano. Incidental gallbladder carcinoma: our experience. *Journal ListG Chirv*.34(5-6); May-Jun 2013 PMC3915589.
16. Lazcano-Ponce EC, Miquel JF, Muñoz N, Herrero R, Ferrecio C, Wistuba II, Alonso de Ruiz P, Aristi Urista G, Nervi F. Epidemiology and molecular pathology of gallbladder cancer. *CA Cancer J Clin*. 2001 Nov-Dec; 51(6):349-64.
17. Shipra Dwivedi, Amit Madeshiya, Devendra Singh, Shraddha Singh, Akhilesh Krishna. Gall Bladder Cancer and some epidemiological factors: A cross sectional study. *Biomedical Research* (2013) Volume 24, Issue 1.
18. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol*. 2014 Mar 7;6:99-109. doi: 10.2147/CLEP.S37357. eCollection 2014.
19. Miller G, Jarnagin WR. Gallbladder carcinoma. *Eur J Surg Oncol*. 2008 Mar;34(3):306-12.
20. Shrikhande SV, Barreto SG, Singh S, Udwardia TE, Agarwal AK. Cholelithiasis in gallbladder cancer: coincidence, cofactor, or cause! *Eur J Surg Oncol*. 2010 Jun;36(6):514-9.

**How to cite this article:** Sarangi CR, Mohanty AK. A Prospective Study of Incidental Gall Bladder Carcinoma in Patients Undergoing Cholecystectomy. *Ann. Int. Med. Den. Res*. 2020; 6(1):SG45-SG48.

**Source of Support:** Nil, **Conflict of Interest:** None declared