



## INCIDENTAL GALL BLADDER CANCER AFTER LAPAROSCOPIC CHOLECYSTECTOMY FOR SYMPTOMATIC CHOLELITHIASIS - OUR EXPERIENCE

**Dr. Wormi Sharon**

Assistant Professor Department of General Surgery Jawaharlal Nehru Institute of Medical Sciences Porompat, Imphal-795001

### ABSTRACT

#### Background:

Incidental gall bladder carcinoma (IGBC) is an incidental finding of carcinoma diagnosed on histopathological examination of gall bladder specimen removed for symptomatic cholelithiasis. Laparoscopic cholecystectomy (LC) is the accepted standard management for symptomatic cholelithiasis. Gall bladder carcinoma is a highly malignant tumor with a poor prognosis. The incidence of IGBC is around 0.19 - 3.3% in the literature

#### Aim:

To determine the percentage of gall bladder carcinoma incidentally diagnosed during histopathological examination of cholecystectomy specimens done for gallstone disease.

#### Material and Methods:

We analyzed the medical records of patients with symptomatic gallstone disease of single surgical unit, who underwent laparoscopic cholecystectomies at Jawaharlal Nehru Institute of Medical Sciences (JNIMS) Hospital, Porompat, Imphal, during the period from 1st January 2014 to 31st December 2016.

#### Results:

A total of 480 laparoscopic cholecystectomies were performed at our surgical unit during the study period of two (2) years. In 7 (1.5%) cases, incidental gallbladder carcinoma was discovered. A laparoscopic cholecystectomy which is performed for benign gall bladder disease rarely results in a diagnosis of unexpected gallbladder cancer. IGBC detected after a cholecystectomy due to cholelithiasis is a rare disease. We found IGBC in 1.5% of cases, which is on a comparable scale to the world literature.

#### Conclusion:

With the increase of laparoscopic cholecystectomies both elective and urgent performed in our Centre we also observed an increase of incidentally diagnosed gallbladder neoplasms. Early diagnosis, meticulous peri-operative study and accurate surgical strategy are essential factors to obtain good results in incidental gallbladder cancer. This cancer is more common in females and in people over 60 years of age.

**KEYWORDS :** Incidental gall bladder carcinoma (IGBC), Laparoscopic Cholecystectomy (LC), Symptomatic cholelithiasis, Gallbladder cancer (GBC)

### INTRODUCTION

Laparoscopic Cholecystectomy (LC) is the accepted gold standard management for symptomatic gallstone disease since the past two decades. With the advantages of a shorter hospital stay, decreased post-operative pain and an early resumption of normal activities, this procedure has now become routine in the treatment of benign gallbladder disease in the general surgical units all over the world. A LC which is performed for benign gall bladder disease rarely results in a diagnosis of unexpected gallbladder cancer. From this study, we are reporting our experience with gallbladder cancer which was incidentally diagnosed after a LC which was performed for gallstone disease. Gallbladder cancer (GBC) is a relatively rare neoplasm and is considered to be an aggressive and highly lethal disease. It is the most frequently occurring malignancy of the biliary tract and the fifth most common gastrointestinal cancer<sup>1</sup>. Only 30% of gallbladder carcinomas are suspected preoperatively, and the remaining 70% are usually discovered incidentally by pathological examination during or after surgery<sup>2</sup>.

Although patients with GBC have a poor prognosis, most IGBC tumors tend to be at an early stage of development. Hence, radical second surgery is performed in most patients with IGBC, and improved prognosis is usually reported<sup>3,4</sup>. However management of IGBC is a difficult issue in the absence of established guidelines.

Primary aim of our study is to evaluate incidental gallbladder carcinoma incidence in our experience.

### METHODS

This study includes 480 cholecystectomy specimens in patients undergoing Laparoscopic cholecystectomy, from 1st January 2014 to 31st December 2016 in a single surgical unit of Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. All the cholecystectomy specimens sent for histopathological examination. Out of 480 specimens, 7 have been reported to be carcinoma. All the cases were incidental findings with no preoperative suspicion of a malignancy. All the patients underwent laparoscopic cholecystectomy for symptomatic cholelithiasis as elective procedure.

### RESULTS

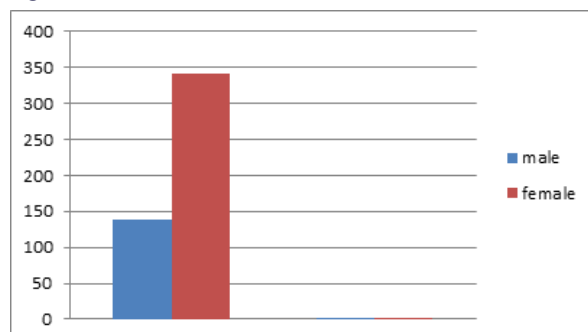
We analyze 480 patients who underwent elective Laparoscopic cholecystectomy for symptomatic cholelithiasis over a period of two (2) years done in a single surgical unit.

Out of the 480 patients, 342 are female patients i.e. 71.30% against 138 male patients i.e. 28.70%.

**Table 1: Sex distribution**

Frequency	No. of patients	Percentage
F	342	71.3
M	138	28.7
Total	480	100

**Figure 1: Sex distribution**



**Table 2: Frequency of carcinoma in relation to sex**

Gender	Frequency	Percent	Valid Percent
Valid	F	5	71.4
	M	2	28.6
	Total	7	100

**Table 3: Standard deviation in relation to sex**

Age			
Gender	Mean	N	Std. Deviation
F	63.80	5	18.68
M	71.50	2	0.70
Total	66.00	7	15.71

Out of the 7 patients diagnosed to have incidentally detected to have Gallbladder carcinoma, 5 of them are females and 2 are males. The mean age group of these patients is 66.0 years with standard deviation of 15.71. Majority of these patients are above 40 years of age.

All Laparoscopic cholecystectomies were performed for symptomatic cholelithiasis in a single surgical unit. The incidence of IGBC detected during laparoscopic cholecystectomy in this single center study was found to be 1.45%.

In view of inadequate facility in our hospital all the 7 patients were referred to a regional cancer center for further evaluation and management. This is one of our main drawbacks of our study as we cannot comment on the type of the surgical intervention and their survival.

### DISCUSSION

Incidental Gallbladder Carcinoma (IGBC) is the carcinoma of the gallbladder which is suspected for the first time during cholecystectomy or which is found on the histological examination of the gallbladder.

The incidence of IGBC during or after LC has been reported to be 0.19–3.3%<sup>4,7,8</sup>. Because of the increased use of LC and difficulty regarding the preoperative diagnosis of GBC, IGBC has become more frequent. Symptoms are non-specific and the diagnosis is often made at an advanced stage at operation for routine cholecystectomy. In the present study, the rate of occurrence of IGBC was 1.5%. Carcinoma of gall bladder is a rare gastrointestinal malignancy however it is reported to be the most frequent carcinoma of the extra hepatic biliary tract. Gallbladder Carcinoma (GBC) is the most common malignancy of the biliary tract and the sixth most common malignancy of the gastrointestinal tract worldwide. It is an aggressive and a late symptomatic disease and most of the patients are treated at advanced stages. The prognosis is usually dismal and the 5 year survival rates have been reported to be less than 5% for the more advanced stages<sup>10</sup>. The countries with a high incidence of gallbladder cancer include Chile, Poland, India and Japan. A very high incidence of this cancer has been reported among women in northern India (21.5/100,000) and among female Native American Indians (14.5/1000,000)<sup>11</sup>.

Gallbladder cancer either remains asymptomatic for a long time or it presents with very non-specific symptoms like pain in the abdomen, vomiting, anorexia, jaundice, a gallbladder mass and fever. The early-stage carcinoma is typically diagnosed incidentally because of the inflammatory symptoms which are related to the coexistent cholelithiasis or cholecystitis. Incidental Gallbladder Carcinoma (IGBC) is the carcinoma of the gallbladder which is suspected for the first time during cholecystectomy or which is found on the histological examination of the gallbladder. Some studies have reported that risk factors for IGBC are as follows: sex (female); obesity; age >65 years; cholelithiasis; polypoid lesions; Asian or African American; and an elevated alkaline phosphatase level<sup>12,13</sup>. With the increasingly widespread acceptance of LC and the difficulties in diagnosing GBC preoperatively, the number of cases of IGBC during and after LCs has increased. The female gender and advanced age are the demographic risk factors for GBC.

The association of GBC with cholelithiasis and chronic gallbladder inflammation is well known. The causes of the gallbladder mucosal inflammation include infection, drugs (such as isoniazid and methyl dopa), congenital anomalies (such as choledochal cysts and the anomalous junction of the pancreaticobiliary ducts) and primary sclerosing cholangitis. It has been presumed that a longstanding chronic inflammation which is caused by cholelithiasis plays a role in the tumour progression and that carcinogenesis and gallstones are seen in 54–97% of the patients of GBC. However, while most of the patients of GBC will have a history of cholelithiasis, only 0.3–3% of the patients with gallstones develops GBC.

In our study all the 7 patients diagnosed to have gallbladder cancer are all cases of symptomatic cholelithiasis and has undergone laparoscopic cholecystectomy. 5 out of 7 patients are all females.

Surgical resection is the only potentially curative treatment for GBC. Only 10–30 % of GBC patients have resectable disease on presentation<sup>14</sup>. Radical cholecystectomy is the standard surgical procedure performed for GBC. The management of GBC including IGBC depends on the T stage (depth of invasion)<sup>15,16</sup>.

Given that cholecystectomy for gallstone disease is the second or the third most frequent procedure in digestive surgery, incidental GBC is going to become an increasingly frequent medical entity. The widespread use of laparoscopic cholecystectomy has led to discovery of this deadly disease at an earlier stage, altering the management and the outcome of these patients. GBC is an incidental finding and almost half of these cases are occasionally discovered during or after laparoscopic cholecystectomy for benign disease, such as gallstones and their complications- 47% in the series of Memorial SloanKettering Cancer Centre (MSKCC), 50% in the series of Johns Hopkins<sup>17,18</sup>. The earlier discovery results in an earlier pathological stage, and consequently, increased long-term survival<sup>18,19,20</sup>. Patients with incidental GBC had a significant increase in survival when compared with those who had a preoperative diagnosis (overall 5- year survival 15% vs 33%)<sup>21,22</sup>. Therefore, the surgeon should be prepared to deal with GBC suspected or diagnosed incidentally. It is paramount not to violate oncological principles during the first operation, if a two-stage approach is necessary. For this reason,

the surgeon during a laparoscopic cholecystectomy should always follow these simple rules:

- perform an accurate preoperative diagnosis;
- preserve the integrity of the gallbladder
- use the endobag for the removal of the gallbladder
- When in doubt, give up the laparoscopy to open access
- Carefully inspect the gallbladder once extracted
- perform a histological examination promptly;
- Desufflate the pneumoperitoneum with the trocars in situ

During cholecystectomy, accidental opening of the gallbladder is described in 25–30% of the cases, which clearly have a worse prognosis<sup>23</sup>.

All gallbladders removed for stone disease should always be cut, opened and examined carefully for any suspicious lesions before closing incision. If suspicious lesion is present, the gallbladder should be sent for a timely frozen section for diagnosis and assessment of depth of invasion. If the surgeon is trained, and the team has experience in the management of hepatobiliary disease, radical cholecystectomy should be done. If not, the abdomen should be closed and patient should be referred to a higher Centre for radical surgery.

### CONCLUSION

The importance of a histological examination of the post cholecystectomy specimens cannot be over emphasized. The non-specific clinical features and sonographic findings of early GBC make the preoperative diagnosis difficult and an incidental GBC has been recorded in every reported series of laparoscopic cholecystectomy cases.

Gallstone is one of the commonest diseases in North East India. With the greater availability of ultrasonography, Cholecystectomy has become the commonest procedure performed and hence an increase in the incidence of IGBC also.

The incidence of IGBC detected during laparoscopic cholecystectomy in this single center study was found to be 1.5%. Although the number of patients enrolled was small, our findings further support the suggestion that GB carcinoma may be curable if diagnosed at an early stage as IGBC.

Since our center does not have adequate facilities and expertise to deal with incidentally detected gallbladder cancer, all the patients were referred to the regional cancer center for further evaluation and management.

## REFERENCES

1. Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin.* 2014;64(2):104–17.
2. Goetze T, Paolucci V. Does laparoscopy worsen the prognosis for incidental gallbladder Cancer? *Surg Endosc.* 2006;20(2):286–93.
3. Tian YH, Ji X, Liu B, Yang GY, Meng XF, Xia HT, Wang J, Huang ZQ, Dong JH. Surgical treatment of incidental gallbladder cancer discovered during or following laparoscopic cholecystectomy. *World J Surg.* 2015;39(3):746–52.
4. Choi SB, Han HJ, Kim CY, Kim WB, Song TJ, Suh SO, Kim YC, Choi SY. Incidental Gallbladder cancer diagnosed following laparoscopic cholecystectomy. *World J Surg.* 2009;33(12):2657–63.
5. Singh S, Agarwal AK. Gallbladder cancer: the role of laparoscopy and radical resection. *Ann Surg.* 2009;250(3):494–5.
6. Ferrarese AG, Solej M, Enrico S, Falcone A, Catalano S, Pozzi G, Marola S, Martino V. Diagnosis of incidental gallbladder cancer after laparoscopic cholecystectomy: our Experience. *BMC Surg.* 2013;13(Suppl 2):S20.
7. Zhang WJ, Xu GF, Zou XP, Wang WB, Yu JC, Wu GZ, Lu CL. Incidental gallbladder Carcinoma diagnosed during or after laparoscopic cholecystectomy. *World J Surg.* 2009;33(12):2651–6.
8. 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):90–4.
9. Tantia O, Jain M, Khanna S, Sen B. Incidental carcinoma gall bladder during Laparoscopic cholecystectomy for symptomatic gall stone disease. *Surg Endosc.* 2009;23(9):2041–6.
10. Jemal A, Tiwari RC, Murray T, Ghafoor A, Samuels A, et al. Cancer statistics 2004. *CA Cancer J Clin.* 2004;54:8–29.
11. Lai CH, Lau WY. Gallbladder cancer -a comprehensive review. *Surgeon.* 2008;6:101–10.
12. Bertran E, Heise K, Andia ME, Ferreccio C. Gallbladder cancer: incidence and survival in a high-risk area of Chile. *Int J Cancer.* 2010;127(10):2446–54.
13. Solani L, Sharma A, Watt J, Iosifidou S, Chin Aleong JA, Kochev HM. Predictive factors for incidental gallbladder dysplasia and carcinoma. *J Surg Res.* 2014;189(1):17–21.
14. Misra S, Chaturvedi A, Misra NC (2006) Gallbladder cancer. *Curr Treat Options Gastroenterol* 9:95–106
15. Yamaguchi K, Tsuncyoshi M (1992) Subclinical gallbladder carcinoma. *Am J Surg* 16:382–386
16. Onoyama H, Yamamoto M, Tseng A, Ajiki T, Saitoh Y (1995) Extended cholecystectomy for carcinoma of the gallbladder. *World J Surg* 19:758–763
17. A. Duffy, M. Capanu, G.K. Abou-Alfa, D. Huitzil, W. Jarnagin, Y. Fong, M. D'Angelica, R.P. Dematteo, L.H. Blumgart, E.M. O'Reilly, Gallbladder cancer (GBC): 10-year experience at memorial Sloan-Kettering Cancer Centre (MSKCC), *J. Surg. Oncol.* 98 (2008) 485e489, (PMID: 18802958).
18. S.P. Shih, R.D. Schulick, J.L. Cameron, K.D. Lillemoe, H.A. Pitt, M.A. Choti, K.A. Campbell, C.J. Yeo, M.A. Talamini, Gallbladder cancer: the role of laparoscopy and radical resection, *Ann. Surg.* 245 (2007) 893e901, (PMID: 17522515).
19. E.H. Jensen, A. Abraham, E.B. Habermann, W.B. Al-Refaie, S.M. Vickers, B.A. Virnig, T.M. Tuttle, A critical analysis of the surgical management of early stage Gallbladder cancer in the United States, *J. Gastrointest. Surg.* 13 (2009) 722e727, (PMID: 19083068).
20. W.J. Zhang, G.F. Xu, X.P. Zou, W.B. Wang, J.C. Yu, G.Z. Wu, C.L. Lu, Incidental gallbladder carcinoma diagnosed during or after laparoscopic cholecystectomy, *World J. Surg.* 33 (2009) 2651e2656, (PMID: 19760311).
21. M.T. Hueman, C.M. Vollmer, T.M. Pawlik, Evolving treatment strategies for gallbladder Cancer, *Ann. Surg. Oncol.* 16 (2009) 2101e2115, (PMID: 19495882).
22. E.H. Jensen, A. Abraham, E.B. Habermann, W.B. Al-Refaie, S.M. Vickers, B.A. Virnig, T.M. Tuttle, A critical analysis of the surgical management of early stage Gallbladder cancer in the United States, *J. Gastrointest. Surg.* 13 (2009) 722e727, (PMID: 19083068).
23. T.M. Pawlik, A.L. Gleisner, L. Vigano, D.A. Kooby, T.W. Bauer, A. Frilling, R.B. Adams, C.A. Staley, E.N. Trindade, R.D. Schulick, M.A. Choti, L. Capussotti, Incidence of finding residual disease for incidental gallbladder carcinoma: implications for resection, *J. Gastrointest. Surg.* 11 (2007) 1478e1486, (PMID: 17846848).