

Incidence of Carcinoma Gall Bladder in Patients with Cholelithiasis in Tertiary Care Hospital, Hapur

Hardeep Balyan¹, Satwik Nishan², Gyanendra Swaroop Mittal³, Anubhav Arya⁴

¹Resident, General Surgery, Rama Medical College Hospital and Research Centre, Hapur, India

²Resident General Surgery, Rama Medical College Hospital and Research Centre, Hapur, India

³Professor and Head of Department of General Surgery, Rama Medical College Hospital and Research Centre, Hapur, India

⁴Associate Professor, General Surgery, Rama Medical College Hospital and Research Centre, Hapur, India

Received: 25-03-2023 / Revised: 25-04-2023 / Accepted: 22-05-2023

Corresponding author: Dr. Hardeep Balyan

Conflict of interest: Nil

Abstract

Background: Gallbladder carcinoma is a rare complication of cholelithiasis. The aim of this study was to find out the incidence incidental carcinoma gall bladder in patients undergoing cholecystectomy for cholelithiasis.

Methods: A total number of 430 patients who were operated at tertiary care hospital, Hapur over a period of 18 months, starting from July 2020 till December 2021, were included in this study. Cases admitted in various surgical wards were clinically evaluated and confirmed by ultrasonography for cholelithiasis.

Results: Out of the 430 participants, maximum 237 (62.6%) had multiple stone and 161(37.4%) had single calculi, out of which 161 (37.4), 9 (5.50%) participants had Ca gall bladder. In our study, there were 2.8% incidence of ca gall bladder in patients who underwent laparoscopic surgery. In the study, a statistically significant high GB carcinoma was found among the patients who had single stone, stone>3cm, and body mass index (BMI).

Conclusion: This study highlights the importance of considering the risk of Gall Bladder Carcinoma in patients having a simple cholecystectomy.

Keywords: Carcinoma Gall Bladder, Incidental, Cholecystectomy.

This is an Open Access article that uses a funding model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Gall Bladder disease is a very common problem worldwide. According to recent data of the national registry program of India, northern part of India especially the Gangetic belt has the highest incidence. [1] The incidence of gall stone disease has

increased in Asian countries owing to change in their food habits, as diet in Asian countries are high in calories and fat. [2] While Gallbladder carcinoma is the 8th common cancer of the digestive tract in India [3]. The largest incidences have been

documented among Indians, Pakistanis, Chileans, Bolivians, Central Europeans, Israelis, Native Americans, and Americans of Mexican heritage [4]. It is more common in India along the Gangetic plains in northern India [3,5]. Although the global incidence of gallbladder cancer is less than 2/100000 people, there has been a lot of variation in the data [6]. The Indo-Gangetic belt, notably females in northern India (21.5/100000) and south Karachi, Pakistan (13.8/100000), has been identified as one of the most affected areas [7]. Cholelithiasis, inflammatory reasons, infection, exposure, and gall bladder diseases or anomalies are all risk factors. Cholelithiasis affects 70 to 90% of GBC patients, and it is thought that prolonged mucosal irritation by calculi causes dysplasia [8]. Chronic inflammation of the bile duct tissue accumulates consecutive genetic alterations that lead to malignant transformation, according to the current hypothesis. The oncogene K-ras and the tumor suppressor beta-catenin are the most commonly documented mutations (CTNNB1). [9] There has been no evidence of an inherited familial risk. Adenocarcinomas are the most common histopathological abnormalities in gallbladder cancer (90 percent). Following around 15 years of inflammation, this syndrome evolves from pre-neoplastic dysplasia to carcinoma in situ and, eventually, to invasive malignancy. Squamous cell carcinoma of the gallbladder is uncommon. Despite of improved imaging techniques preoperative diagnosis of Gall Bladder carcinoma is not always possible, 80% of cases present in late stages. [10] Such cases cannot be operated and therefore Gall Bladder specimen not available for histopathological diagnosis. The cases which are detected preoperatively are usually in advanced stages, such cases show five year survival rate of less than 5%. [11] Cholecystectomy is the most common major abdominal surgery worldwide which is mostly done for gall

stones. Approximately 90% of Gall Bladder cancer have accompanying stone [12] but only 5% to 3% of patients with cholelithiasis will develop Gall Bladder carcinoma. [13] The patients with incidental carcinoma of Gall Bladder in the cholecystectomy specimens are very fortunate to be incidentally found of carcinoma Gall Bladder. Such an early diagnosis is very helpful in reducing mortality due to Gall Bladder carcinoma. In India, Gall Bladder cancer is the fourth commonest cancer overall in the female population. Women are more commonly affected than men. [14,15] Peak age of Gall Bladder carcinoma is 6th and 7th decade. [16] Due to the lack of distinct signs and symptoms and the frequent relationship with chronic cholecystitis and gall stones, diagnosing gall bladder cancer at an early stage is challenging. Today, ultrasonography is regarded as the preferred approach for diagnosing gall bladder disorders. The "gold standard" for surgical therapy of symptomatic cholelithiasis is laparoscopic cholecystectomy. However, there are no established protocols for the care of patients having laparoscopic cholecystectomy for sporadic (intraoperative diagnosis) or occult (postoperative histological diagnosis) gall bladder cancer. It is recognised that the finding of disease at the port sites is a sign of generalised peritoneal disease and carries a very poor prognosis. [16] Because gallbladder carcinoma (GBC) frequently has no symptoms or is asymptomatic in its early stages, it is difficult to detect and diagnose. Patients who arrive with symptoms usually have advanced tumors, with 75% of them being non-resectable [17]. Furthermore, radiation and chemotherapy have no effect on GBC. GBC is an extremely fatal tumor with a 5-year survival rate of fewer than 5% due to all of these factors. Given that T1a illness patients have a near-100 percent survival rate after a simple cholecystectomy, For early identification and improved

outcomes, it is becoming increasingly important to identify patients at high risk of carcinoma.

Aims of the Study : This study was carried out to find out the incidence of Gall Bladder malignancy and the incidental carcinoma in cholecystectomy specimens

Material and Methods:

Study area: Tertiary care hospital, Hapur

Study duration 2020-2021 (18 months)

Study design Prospective observational study

Sample size A total number of 430 patients who were operated for cholelithiasis at tertiary care hospital ,Hapur over a period of 18 months, starting from July 2020 till December 2021.

Study population – Cases admitted in various surgical wards of tertiary care hospital, Hapur diagnosed with cholelithiasis who were clinically evaluated and confirmed by ultrasonography. patients were considered from any socio- economic status, any religion, with no age limit and both genders were included.

Inclusion criteria: All patients who are undergoing laparoscopic and open cholecystectomy for gall stone .

Exclusion criteria: Patients with pre diagnosed Gallbladder malignancy were excluded.

Intervention: Gall bladder specimens collected during laparoscopic or open cholecystectomy are sent for histopathological examination. If HPE report came back positive for malignancy, incidence of Ca-GB is calculated in the sample size taken.

Methodology

All the patients of cholelithiasis were diagnosed via trans-abdominal ultrasound. Known cases of gall bladder carcinoma without any gall stones were excluded. Complete medical history, physical examination was done and routine laboratory investigations were undertaken. After taking informed consent & Pre-anaesthetic check-up, patients were taken for cholecystectomies. After surgery, specimens were sent immediately to the Hospital's pathology laboratory for histopathological examination. The information obtained was collected via self-made proforma.

Data collection methods:

Written and informed consents was taken from the patients. Detailed patient history was taken and patient taken up for either open or laparoscopic cholecystectomy. GB specimens will be extracted and sent for HPE

Results:

In our study, mean age of study participants was 39.5 ± 13.3 years and out of the 430 participants, maximum 147 were belongs to age <30 years followed by 102 in age group of 51-60 years.

Table 1: Distribution of study participants according to gallstone number:

Gallstone number	Frequency	Percent
Multiple	269	62.6
Single	161	37.4
Total	430	100.0

In our study, out of the 430 participants, maximum 269 had multiple stone.

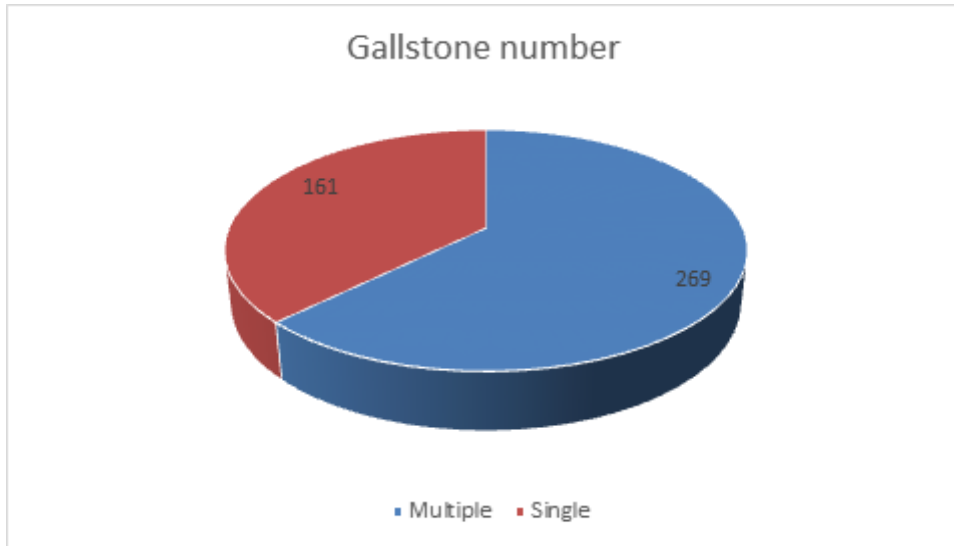


Figure 1: Gallstone number

Table 2: Distribution of study participants according to histopathological findings:

Histopathological findings	Frequency	Percent
Acute on chroniccholecystitis	181	42.1
Chronic cholecystitis	237	55.1
Mucinous adenocarcinoma	8	1.9
Papillary adenocarcinoma	4	.9
Total	430	100.0

In our study, out of the 430 participants, maximum 237 had Chronic cholecystitis followed by 181 had Acute on chroniccholecystitis on histopathological examination.

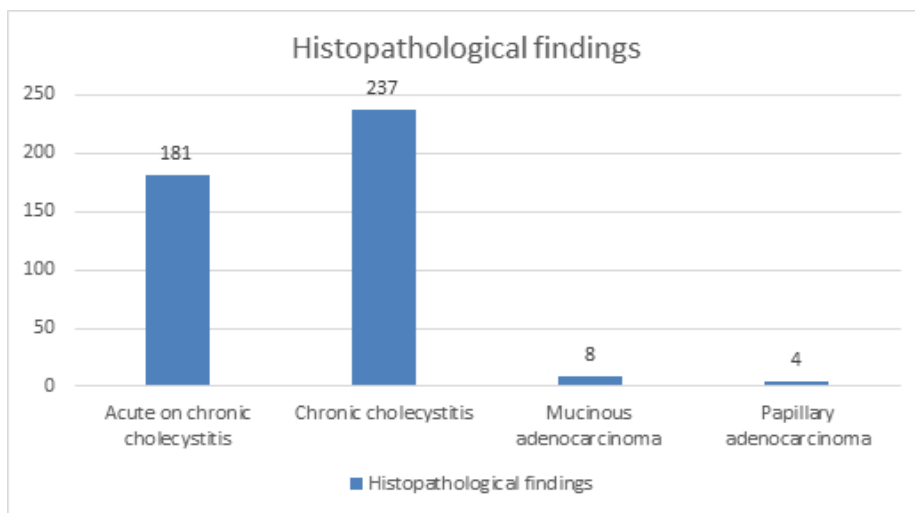


Figure 2: Histopathological findings

Table 3: Incidence of incidental GB Carcinoma:

Incidental GB carcinoma	Frequency	Percent
Yes	12	2.8
No	418	97.2
Total	430	100.0

In our study, incidence of incidental GB carcinoma in cholelithiasis patients was found to be 2.8%.

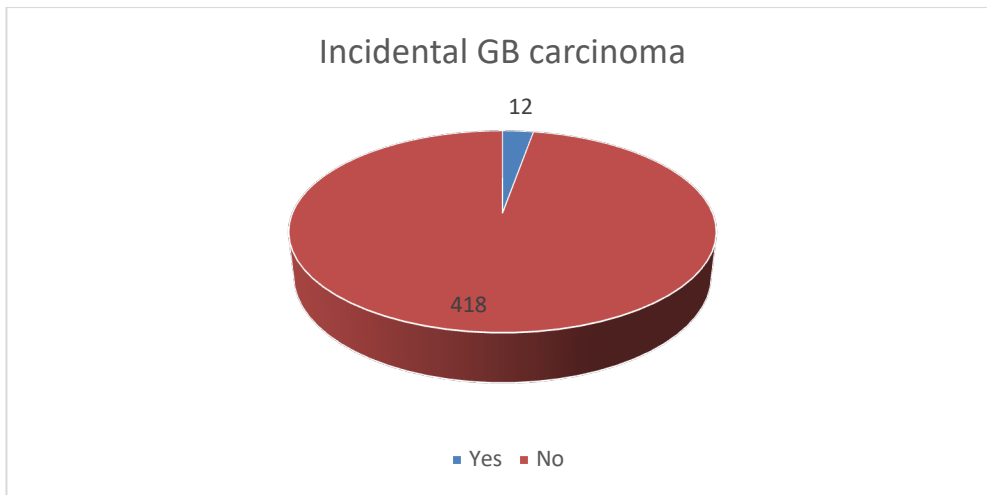


Figure 3: Incidental GB carcinoma

Table 4: Association of age with GB carcinoma

Age	GB carcinoma				p-value
	Yes		No		
	N	%	n	%	
Upto 30 years	0	0.0%	147	35.2%	0.249
31-40 years	2	16.7%	83	19.9%	
41-50 years	3	25.0%	85	20.3%	
51-60 years	4	41.7%	98	23.2%	
>60 years	3	25.0%	5	1.2%	
Total	12	100.0%	418	100.0%	

In our study, no statistically significant age difference were found between GB carcinoma patients and others. However, Incidence of GB carcinoma was increasing as age increases.

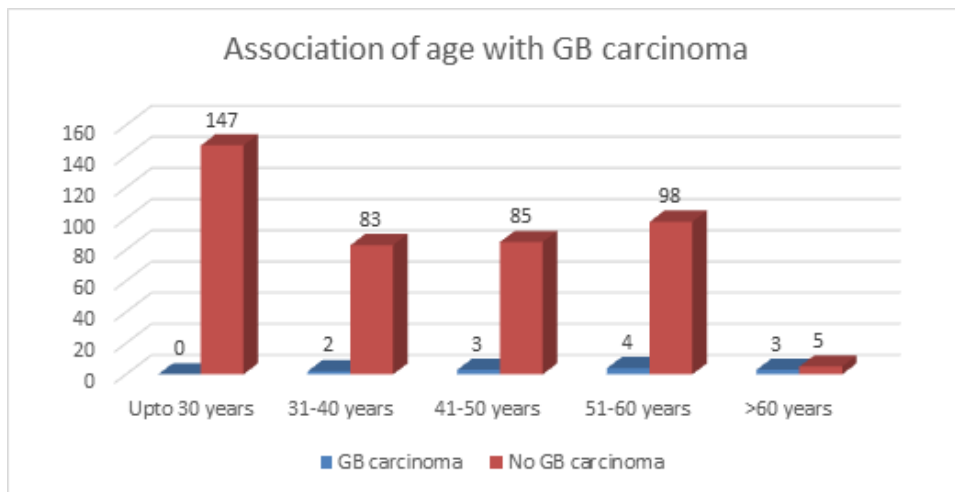


Figure 4: Association age with GB carcinoma

Table 5: Association of gallstone number with GB carcinoma

Gallstone	GB carcinoma				p-value
	Yes		No		
	n	%	n	%	
Multiple	3	25.0%	266	63.6%	0.006
Single	9	75.0%	152	36.4%	
Total	12	100.0%	418	100.0%	

In our study, a statistically significant high GB carcinoma was found among the patients who had single stone.

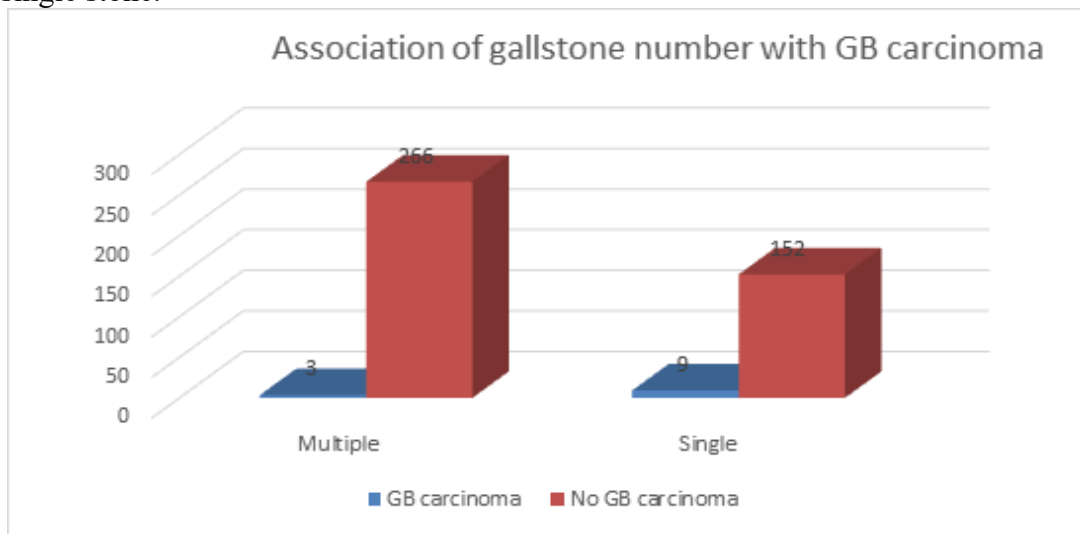


Figure 5: Association of gallstone number with GB carcinoma

Table 6: Association of GB calculi size with GB carcinoma

GB calculi size	GB carcinoma				p-value
	Yes		No		
	n	%	n	%	
<3cm	2	16.7%	373	89.2%	0.0001
>3cm	10	83.3%	45	10.8%	
Total	12	100.0%	418	100.0%	

In our study, a statistically significant diet difference were found between GB carcinoma patients and others.

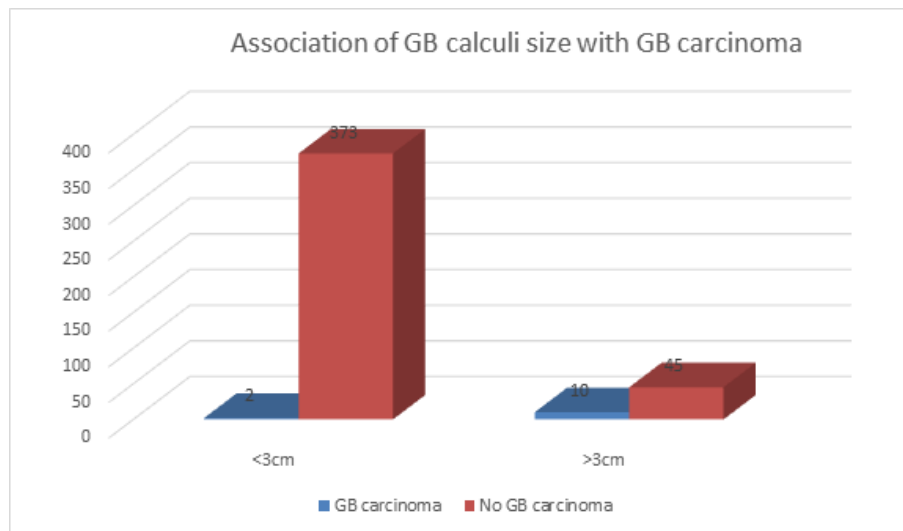


Figure 6: Association of GB calculi size with GB carcinoma

Discussion

Sutradhar PK et al revealed that Eight (eight) of the 150 patients who underwent surgery for gall bladder stone disease later turned out to have gall bladder cancer, making the prevalence 5.3%. Only three

(37.5%) individuals had gall bladder cancer preoperatively suspected based on ultrasonography. This condition affects women more often than men. [18]

Poudel R et al determined that 1.67% of cases of gallbladder cancer are incidental.

It is advised that routine histology of cholecystectomy specimen be sent for early diagnosis and to increase the patient's chance of surviving gall bladder cancer. [19]

Faik Tatli, Abdullah Ozgönül, and others did a study to assess the prevalence of gallbladder cancer among patients having cholecystectomies because of gallbladder illness. They analyzed the records of 341 patients who had undergone regular cholecystectomy procedures between January 2013 and March 2016 and reported the pathological findings. Seven of the patients (2.05%), with an average age of 67.71 years old and six female and one male patients, had gallbladder tumors. [20]

In our study, incidence of incidental GB carcinoma in cholelithiasis patients was found to be 2.8%, that is 12 out of 430 patients.

In our study, out of the 430 participants, maximum 269(62.6%) had multiple stone and 161(37.4%) had single calculi, out of single calculi that is 161(37.4%), 9 (5.50%) participants had Ca GB.

In our study out of 430 participants, 375 (87.20%) had calculi size <3cm and 55(12.8%) had calculi size >3cm, out of these 55(12.8%) >3cm, 10(18.18%) participants had Ca gallbladder.

Remaining 375 (87.20%) participants had calculi size <3cm, 2 (0.53%) had ca gall bladder.

Limitation: The limitations of the study include its single-center nature, small sample size, potential selection bias, failure to consider confounding factors, and the absence of standardized protocols. These limitations restrict the generalizability of the findings and may affect the statistical power and reliability of the study. Additionally, the study did not provide comprehensive insights into patient outcomes and factors influencing the development of gallbladder carcinoma.

Further research addressing these limitations is necessary to obtain a more comprehensive understanding of gallbladder malignancy and incidental carcinoma.

Conclusion

The conclusion of our study, there were 2.8% incidence of ca gb in patients with cholelithiasis and a statistically significant high GB carcinoma was found among the patients who had single stone, stone>3cm.

Implementing early screening for cases of Cholelithiasis that display associations with single stones, stones larger than 3cm. This proactive approach holds the potential to significantly improve the prognosis and outcomes for affected patients.

This study highlights the importance of considering the risk of gallbladder carcinoma in patients undergoing cholecystectomy for cholelithiasis. By detecting incidental carcinomas and implementing appropriate treatment strategies, it is possible to improve patient outcomes and reduce mortality associated with gallbladder carcinoma.

References

1. Shukla VK, Khandelwal C, Roy SK, Vaidya MP. Primary carcinoma of the gallbladder: A review of a 16-year period at the university hospital. *J Surg Oncol.* 1985; 28:32–35.
2. Huang J, Chang CH, Wang JL, Kuo HK, Lin JW, Shau WY, et al. Nationwide epidemiological study of severe gallstone disease in Taiwan. *BMC Gastroenterol.* 2017;27:45
3. Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, Santhappan S, Nallasamy V, John A, Narasimhan S, Roselind FS; ICMR-NCDIR-NCRP Investigator Group. Cancer Statistics, 2020: Report From National Cancer Registry Programme, India. *JCO Glob Oncol.* 2020 Jul;6:1063-1075.
4. Kalita D, Pant L, Singh S, Jain G, Kudesia M, Gupta K, Kaur C: Impact

- of routine histopathological examination of gall bladder specimens on early detection of malignancy - a study of 4,115 cholecystectomy specimens. *Asian Pac J Cancer Prev.* 2013;14:3315-8.
5. Gulwani HV, Gupta S, Kaur S: Incidental detection of carcinoma gall bladder in laparoscopic cholecystectomy specimens: a thirteen year study of 23 cases and literature review. *Indian J Surg Oncol.* 2015; 6:30-5.
 6. Shaffer EA. Gallbladder cancer: the basics. *Gastroenterol Hepatol (N Y)* 2008; 4:737–741.
 7. Randi G, Franceschi S, La Vecchia C. Gallbladder cancer worldwide: geographical distribution and risk factors. *Int J Cancer.* 2006; 118:1591–1602.
 8. Hundal R, Shaffer EA. Gallbladder cancer: epidemiology and outcome. *Clin Epidemiol.* 2014; 6:99–109
 9. Rahnamai-Azar AA, Weisbrod A, Dillhoff M, Schmidt C, Pawlik TM. Intrahepatic cholangiocarcinoma: Molecular markers for diagnosis and prognosis. *Surg Oncol.* 2017 Jun;26 (2):125-137.
 10. Kapoor VK, Pradeep R, Haribhakti SP, Sikora SS, Kaushik SP. Early carcinoma of the gall bladder: an elusive disease. *J Surg Oncol.* 1996; 62 :284-7.
 11. Mittal R, Jesudasan MR, Nayak S. Selective histopathology in cholecystectomy for gallstone disease. *Indian J Gastroenterol.* 2010; 29:26–30.
 12. Oddsdottir M, Hunter JG. Gall Bladder and the extrahepatic system. In: Brunicaardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Pollock RE, editors. *Schwartz's principle of surgery* (8th ed.). New York: McGraw Hill; 2005.1187-1219. 2009; 9:63.
 13. Whang EE, Zinner MJ. Cancer of the Gall Bladder and the bile ducts. In: Zinner MJ, Ashley SW, editors. *Maingot's abdominal operations* (11th ed.). New York: McGraw Hill. 2007 .921-35.
 14. Samad A. Gallbladder carcinoma in patients undergoing cholecystectomy for cholelithiasis. *J Pak Med Assoc.* 2005; 55:497-9.
 15. Lohana D et al. Frequency of Gall Bladder carcinoma in patients undergoing surgery for cholelithiasis. *Isra Med J.* 2009; 1:13-8
 16. Norman S. Williams, P.Ronono' Connell, Andrew W. McCaskie, Bailey and Love's Short Practice of Surgery, Ed 27 CRS Press 2018, 1211
 17. Zeman RK. Cholelithiasis and cholecystitis. In: Gore RM, Levine MS, Laufer I, eds. *Textbook of gastrointestinal radiology.* Philadelphia, Pa: Saunders, 1994;1636-1674.
 18. Sutradhar PK, Saha S, Saha D, Das J, Anik SS, Saha A, Saha E, Saha S. Association of gallbladder carcinoma with gallstone and its prevalence in a tertiary care teaching hospital. *Mediscope [Internet].* 2021 Oct. 4 [cited 2022 Sep. 16];8(2):87-93.
 19. 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 Nov 14;18(3) :547-550.
 20. Tatli F, Ozgönül A, Yucel Y, Yalcin HC, Ciftci R, Gümer M, Erkmen F, Altuntas R, Uzunkoy A. Incidental gallbladder cancer at cholecystectomy. *Ann Ital Chir.* 2017; 6:399-402.