

Clinical Study of Carcinoma Gallbladder in a Tertiary Care Hospital

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Abstract:

Background: Carcinoma of the gallbladder is an aggressive disease with a poor prognosis. Gallbladder Carcinoma is more common in females than males. Most of the patients with Gallbladder Carcinoma presents in advanced stage and often unresectable though Surgical resection is the only effective treatment. So, most of the patients receive only palliative therapy.

Aims and Objective : To study the clinical presentation and management of carcinoma gallbladder in the department of Surgery, AMCH, Dibrugarh during the study period.

Materials and Methods: Hospital based observational study, was conducted from 1st June 2018 to 31st May 2019 in the department of Surgery, AMCH, Dibrugarh. 61 patients with carcinoma gallbladder were evaluated during the study period.

Results: Peak incidence was noted in the 51-60 years age group and the mean age was 53.67 ± 12.24 years. Female predominance was seen with 86.89% patients with male: female ratio of 1:6.63. Most of the cases belong to the upper lower class (59.02%). Pain abdomen was the most common symptom and it was present in 83.61% cases followed by Lump Abdomen (62.30%). Ultrasonography findings include Gall bladder mass (72.13%), wall thickening (31.14%), Liver metastasis (47.54%), Dilated CBD (42.62%), Lymphadenopathy (44.26%). Findings in CT abdomen are Gall bladder or gallbladder fossa mass (83.60%), Liver involvement (52.46%), Lymphadenopathy (57.38%), CBD involvement (26.23%). Other adjacent structure involvement (11.48%). Adenocarcinoma was found in 96.72% and Squamous cell carcinoma in 3.28%. 9.84% were diagnosed in Stage I, 58.20% in Stage II, 9.84% in Stage III and 72.13% were in Stage IV. Out of 61 patients 17 (27.86%) underwent curative resection. Among these 9 underwent extended cholecystectomy, 7 underwent radical resection and one underwent simple cholecystectomy, after resection they were given adjuvant chemotherapy. Rest of the patients were given palliative therapy like Segment III HJ or palliative chemotherapy.

Conclusion: Gallbladder carcinoma is more commonly seen in females. Most common presenting symptom is pain abdomen. Most of the patients present at advanced stage but Curative Surgery is possible only when it is diagnosed at an early stage.

Key words: Carcinoma Gallbladder, Chemotherapy, Surgical Resection.

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I. Introduction :

Carcinoma of the gallbladder is an aggressive disease with a poor prognosis¹. It is the fifth most common cancer involving gastrointestinal tract and most common malignancy of biliary tract; it constitutes 80–85% of total biliary tract cancer^{2,3}. GBC is notoriously lethal disease and has a dismal prognosis; mean overall survival and 5-year survival rates are reported as low as 6 months and 5%, respectively³.

Incidence of GBC is high in Asia, South America and some part of central Europe (Hungary, Germany and Poland)³. In India, gallbladder cancer (GBC) is most prevalent in northern and northeastern states mainly in Uttar Pradesh, Bihar, Orissa, West Bengal and Assam. The comparison of different population based cancer registries indicated that GBC was one of the commonest causes of cancer related mortality in women in northern and north-eastern states of India⁴.

Gallbladder Carcinoma is two to six times more common in females than males⁵. Main risk factors for GBC are: female gender, gallstones, gallbladder polyps, chronic inflammation, obesity, environmental exposures, genetics and anomalous junction of the pancreatic and biliary duct^{8,11,12}. Association between gallbladder carcinoma and gallstone was first mentioned by Mayo in 1903⁶.

Most of the patients with Gallbladder Carcinoma presents late and often at an unresectable stage. Locally advanced GBC presents with a varied symptomatology depending on the extent of the adjacent organ or vascular involvement. About 25-50% of the patients of GBC present with jaundice^{1,7}. Prognosis is particularly poor for patients with locally advanced GBC. Both pre-operative jaundice and lymph node metastases are associated with worse outcomes when present in GBC⁹. While positive portal nodes are evidence of a more advanced tumour and stage¹⁰.

The three common radiological patterns of GBC are GB fossa mass (40–65%); GB wall thickening (20–30%) and polypoidal lesion (15–25%)¹³.

Surgical resection is the only effective treatment for gallbladder cancer because effective systemic therapy has not been established. Therefore, accurate preoperative evaluation is important to determine the curability and appropriate extent of surgery. It is well known that the survival outcomes after curative resection of gallbladder cancer are strongly associated with the depth of tumour invasion through the gallbladder wall according to the largest series of patients with gallbladder cancer¹⁴. Patients with T1 gallbladder cancer (tumour limited to the mucosal or lamina propria) had a 5-year survival rate of 85.9%, whereas patients with T3 and T4 tumours (tumour invading beyond the serosa) had dismal 5-year survival rates of 19.2% and 14.1%, respectively. Patients with T2 gallbladder cancer (tumour had reached the subserosal layer) had a moderate 5-year survival rate of 56.1%. Therefore, adequate surgical management for T2 gallbladder cancer has been of major clinical interest to surgeons¹⁵⁻¹⁹.

Attempts have been made to improve local control and survival using adjuvant chemotherapy alone or in combination with radiotherapy. There have been conflicting reports regarding the value of postoperative adjuvant radiotherapy²⁰⁻²⁶. Gemcitabine and cisplatin became the standard chemotherapy for locally advanced GBC based on the results of the drug combination in metastatic and unresectable biliary tract cancer²⁷.

In our study we are trying to focus the various risk factors, the clinical presentations and sequelae of Gallbladder carcinoma in this region and also to look the different modalities of management in our institution.

Aims and Objective : To study the clinical presentation and management of carcinoma gallbladder in the department of Surgery, AMCH, Dibrugarh during the study period.

II. Material And Methods :

Hospital based observational study was conducted from 1st June 2018 to 31st May 2019 in department of Surgery, AMCH, Dibrugarh. 61 patients with carcinoma gallbladder were evaluated during the study period.

Study design: Hospital based observational study

Place of study: Department of General Surgery, Assam Medical College and Hospital, Dibrugarh, Assam.

Study duration: One year (From 1st June 2018 to 31st May 2019).

Sample size : 61 patients.

Subjects and selection method : All patients of carcinoma gallbladder admitted in the various surgical units at Assam medical college and hospital.

Inclusion criteria:

All patients admitted to Department of Surgery at Assam medical college and hospital with carcinoma gallbladder during the study period.

Exclusion Criteria:-

- a) Suspected carcinoma gallbladder patient without Histopathological evidence.
- b) Patients having secondary biliary carcinoma.
- c) Patients who did not give consent for the study.

Procedure and methodology

After obtaining written informed consent

Patient's information regarding Name, age, sex, religion, address, Hospital numbers were recorded.

Detailed History, General Examination, Systemic Examination.

Required blood investigations and radiological investigations like Ultrasound abdomen, CT scan of abdomen, USG guided FNAC done for diagnosis and treatment of carcinoma gallbladder.

Management of the patient and outcome was recorded.

Follow up.

ETHICAL CLEARENCE: The study has been conducted after approval from Institutional Ethics Committee(H) of Assam Medical College and Hospital, Dibrugarh, and with written consent from each patient after explaining the study procedure to them in their own language.

STATISTICAL ANALYSIS

The data collected was tabulated in Microsoft Excel Worksheet and computer-based analysis was performed using the Statistical product and service solutions (SPSS) 20.0 software (SPSS, Chicago, Illinois, USA) and Microsoft Excel 2010. The categorical variables were summarized as proportions and percentages.

III. Results

The result and observation have been recorded in the following tables and figures.

AGE DISTRIBUTION

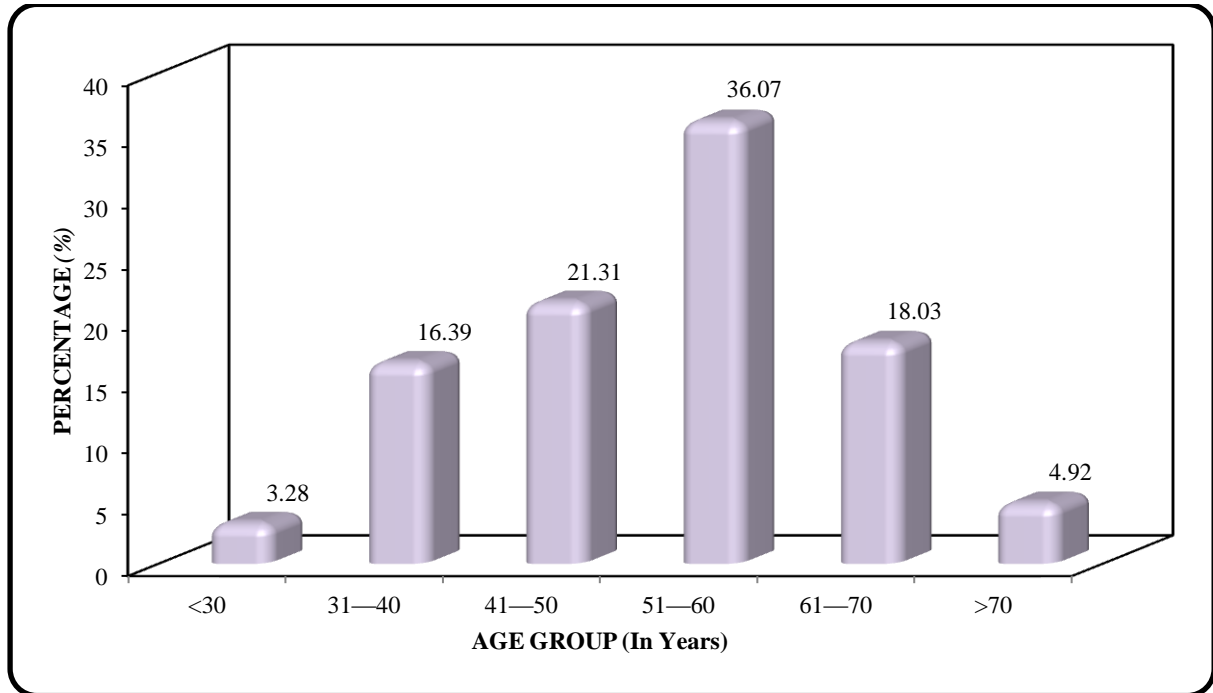


FIGURE- 1 : Bar diagram showing the patients affected with gallbladder carcinoma in different age groups. Out of 61 Patients the youngest patient was of 28 years and the oldest patient was 81 years old. The peak incidence was noted in the 51-60 years age group. The mean age was being 53.67 ± 12.24 years.

SEX DISTRIBUTION

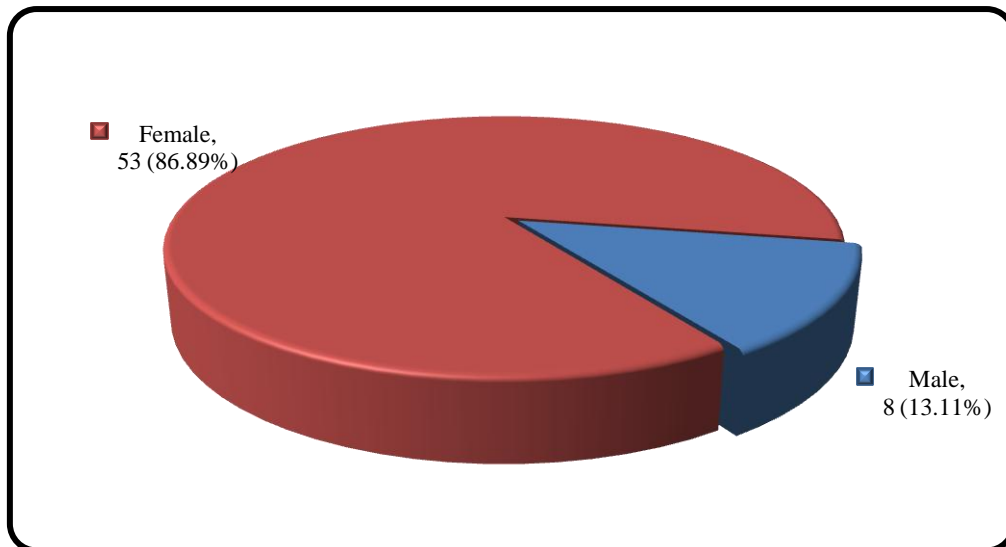


FIGURE- 2 : Pie diagram showing the Sex distribution of patients with gallbladder carcinoma. In our series of 61 cases, there were 53 females (86.89%) and 8 males (13.11%). The male to female ratio was 1:6.63.

SOCIOECONOMIC STATUS

SOCIOECONOMIC CLASS (Kuppuswamy's)		NUMBER (n = 61)	PERCENTAGE (%)
I	Upper	0	0.00
II	Upper Middle	6	9.84
III	Lower Middle	18	29.51
IV	Upper Lower	36	59.02
V	Lower	1	1.64
TOTAL		61	100.00

TABLE- 1 : Table showing the socioeconomic status of patients affected with gallbladder carcinoma. Out of the 61 cases, 6 of the cases belong to upper middle socio economic class (9.84%), 18 belong to lower middle class (29.51%), 36 belong to the upper lower class (59.02%) and 1 belong to lower class (1.64%). So, peak incidence is seen in upper lower class.

CLINICAL FEATURES

CLINICAL FEATURES	NUMBER (n = 61)	PERCENTAGE (%)
Symptoms:		
♦ Pain Abdomen	51	83.61
♦ Lump Abdomen	38	62.30
♦ Anorexia	37	60.66
♦ Weight Loss	35	57.38
♦ Nausea/Vomitting	30	49.18
♦ Jaundice	27	44.26
♦ Fever	14	22.95
♦ Constipation	12	19.67
Signs:		
♦ Pallor	37	60.65
♦ Icterus	27	44.26
♦ Lump in Right Upper Quadrant	41	67.21
♦ Palpable Liver	29	47.54
♦ Tenderness	24	39.34
♦ Ascites	7	11.48

TABLE- 2 : Table showing the clinical features of patients with gallbladder carcinoma

Symptoms:

In the present study we found that the duration of the disease varied from 2 month to 6 years. Long duration of the disease was seen in the cases which presented to hospital with chronic gall bladder disease.

Pain was the most common symptom and it was present in 51cases (83.61%). The pain was mostly confined to the right hypochondrium. In most of the patients the pain was of constant dull aching, radiating to the back. Lump abdomen was the second most common presenting symptom and complained by 38 cases (62.30%). Jaundice was observed in 27 cases (44.26%). In most of the cases it was of short duration. All these patients had features of obstructive jaundice. Anorexia was found in 37 cases (60.66%) and weight loss was found in 35 cases (57.38%).

Signs:

Pallor was found in 37 cases (60.65%), and icterus was found in 27 cases (44.26%). Lump in Right Upper Quadrant was found in 41 cases (67.21%). Most of the lumps were well defined and had irregular margin. In 26 cases it was fixed. The size of the lumps varied from 5 to 11cms in length and 3 to 6 cms in breadth. Liver was Palpable in 29 cases(47.54%). Among them in most of the cases the lump could not be differentiated whether arising from liver or from gallbladder. Tenderness in right hypochondrium was noted in 24 of the cases(39.34%). Ascites was found in 7 cases (11.48%).

INVESTIGATIONS

ULTRASOUND ABDOMEN

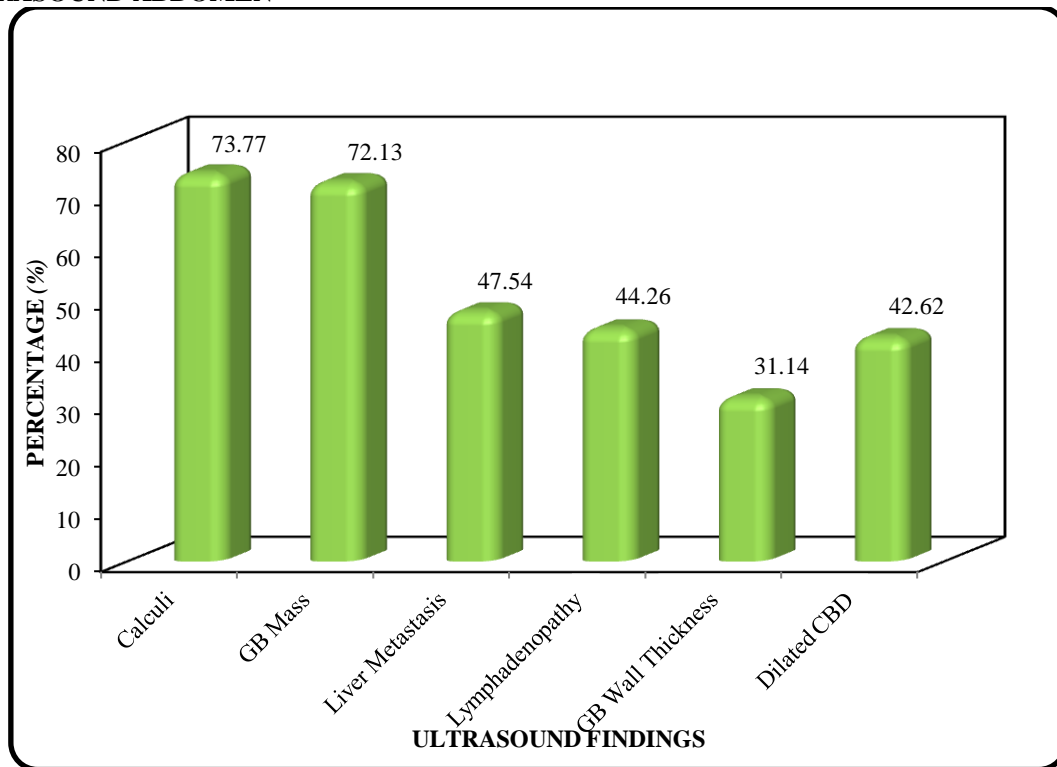


FIGURE- 3 : Bar diagram showing the ultrasonography findings of patients affected with gallbladder carcinoma.

Out of 61 cases during ultrasound evaluation gall stone was found in 45 cases (73.77%). Multiple stones were mostly found. Gall bladder mass was visualized in 44 cases (72.13%). Gall bladder wall thickening was found in 19 cases(31.14%). Liver metastasis was found in 29 cases (47.54%). Lymphadenopathy was found in 27 cases (44.26%). Dilated CBD was found in 26 cases(42.62%).

CT SCAN OF ABDOMEN

CT SCAN FINDINGS	NUMBER (n = 61)	PERCENTAGE (%)
GB or GB fossa Mass	51	83.60
Lymphadenopathy	35	57.38
Liver Involvement	32	52.46
CBD Involvement	16	26.23
Other Organ Involvement	7	11.48

TABLE- 3 : Table showing the CT scan findings of patients affected with gallbladder carcinoma. Out of 61 cases Gall bladder or gallbladder fossa mass was visualized in 51 cases (83.60%), Liver involvement in 32 cases (52.46%), Lymphadenopathy in 35 cases (57.38%). CBD involvement was found in 16 cases(26.23%). Other adjacent structure involvement was found in 7 cases(11.48%). In Chest X Ray of any of the patients no evidence of lung metastasis was noted.

TYPES OF TREATMENT

TREATMENT	NUMBER (n = 61)	PERCENTAGE (%)
Curetive Surgery + Adjuvant Chemotherapy	17	27.86
Palliative Surgery/ Chemotherapy	44	72.13
Concurrent Radiotherapy	3	4.92

TABLE- 4 : Table showing the types of treatments received by patients affected with gallbladder carcinoma Among the 61 cases laparotomy was done in 26 cases (42.62%), out of of these 8 patients has been found unresectable on table and another 1 patient underwent palliative surgery in the form of Segment III HJ. So, 17 patients (27.86%) underwent curative resection and were given adjuvant chemotherapy. The other 35 cases were not put up for curative surgery as the disease was too advanced at presentation to be benefitted from any sort of surgical intervention and also due to the poor health status of the patients. So these 35 cases along with the 9 unresectable laparotomy, total 44 (72.13%) patients were planned for palliative Chemotherapy. 3 patients received Concurrent Radiotherapy.

TYPES OF SURGERY

TYPE	NUMBER (n)	PERCENTAGE (%)
Laparotomy with Biopsy	8	30.77
Extended Cholecystectomy	9	34.61
Cholecystectomy	1	3.85
Radical Resection	7	26.92
Segment III Hepaticojejunostomy	1	3.85
TOTAL	26	100.00

TABLE- 5 : Table showing the types of Surgery done

In the present study, 8 cases (30.77%) were found unresectable during laparotomy, Only Biopsies were taken and abdomen was closed.

9 cases underwent Extended Cholecystectomy. 5 of these cases were planned for cholecystectomy (2 open and 3 laparoscopic cholecystectomy) for presumed benign disease and carcinoma gallbladder was suspected intraoperatively. After confirmation with Frozen section biopsy patients underwent Extended Cholecystectomy. 4 cases were diagnosed carcinoma gallbladder after cholecystectomy on the basis of histopathology of excised gallbladder, CT abdomen was done and these patients too underwent Extended Cholecystectomy with port site excision of the laparoscopic cholecystectomies. All the cases were done in Open procedure (laparoscopy was converted to open procedure). No obvious intraoperative complication was noted.

Among the other cases of curative resection, 6 preoperatively diagnosed cases and one postoperatively diagnosed case (histopathology of excised gallbladder showed perimuscular fibrous tissue involvement) underwent Radical resection. Among them Two cases underwent IVB and V segmentectomy along with removal of the tumour and draining lymph nodes. Along with these structures, 3 cases underwent central hepatectomy including removal of all of segment IV, V and VIII. 2 cases underwent more radical resection. In one case whose part of stomach and hepatic flexure were found to be involved, underwent Subtotal gastrectomy and transverse colon resection along with IVB and V segmentectomy with removal of the tumour and draining lymph nodes. Another case underwent transverse colon resection along with IVB and V segmentectomy with removal of the tumour and draining lymph nodes.

In one patient with Jaundice underwent laparomy for palliative measure whose CBD was found to be involved and he underwent Segment III Hepaticojejunostomy.

OPERATIVE FINDINGS

OPERATIVE FINDINGS	NUMBER	PERCENTAGE (%)
Growth seen in Gallbladder	9	34.61
Calculi	13	76.47
Gallbladder Wall Thickness	20	76.92
Invasion to Adjacent Structures	13	50.00
Liver Metastasis	15	57.69
Peritoneal Metastasis	8	30.76
Ascites	2	7.69

TABLE- 6 : Table showing Operative Findings

Among the operated cases gallbladder calculi could be examined in 17 cases and found in 13 cases (76.47%). Gallbladder Wall Thickness was found in 20 cases (76.92%), Invasion to Adjacent Structures was found in 13 cases (50.00%), Liver Metastasis in 15 cases (57.69%), Peritoneal Metastasis in 8 cases (30.76%), Ascites in 2 cases (7.69%).

HISTOPATHOLOGY

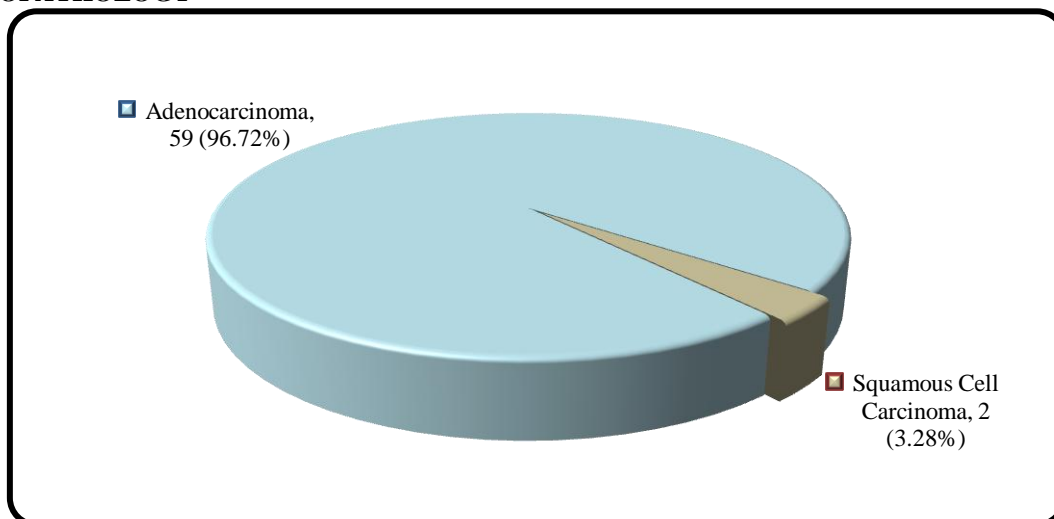


FIGURE- 4 : Bar diagram showing Histopathological Findings.

Among the 61 cases, 35 cases have been found unresectable or inoperable on the basis of clinical examination and radiological findings. USG guided FNAC was done in these cases and all the reports of Histopathology came as Adenocarcinoma of Gallbladder. In the rest 26 patients who underwent laparotomy, excised specimens were sent for Histopathology, Report of 2 patients came as Squamous cell carcinoma. Report of other 24 patients came as Adenocarcinoma. So, total Adenocarcinoma was found in 59 cases (96.72%) and Squamous cell carcinoma in 2 cases (3.28%).

STAGE OF THE PATIENT AT PRESENTATION

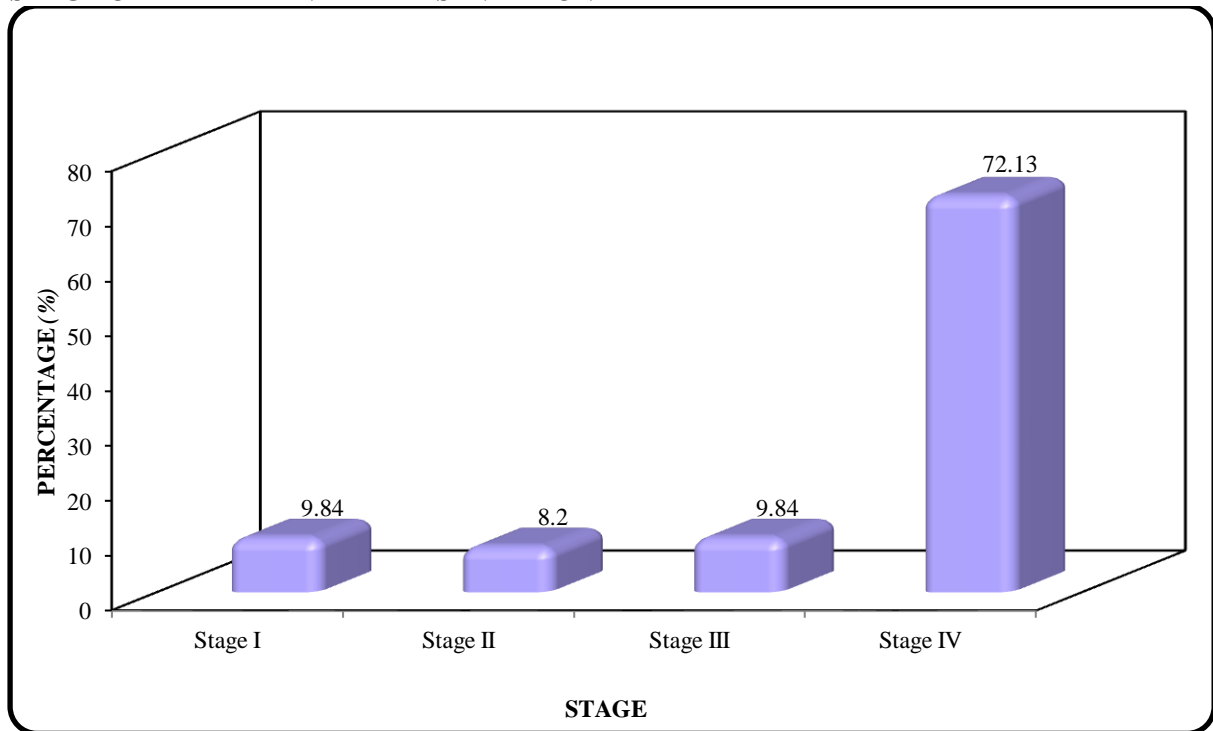


FIGURE- 5 : Bar diagram showing AJCC stage of disease at presentation

Most of the patients presented at advanced stage. All the cases of Stage I and Stage II were diagnosed incidentally. Out of 61 cases, 6 cases(9.84%) were diagnosed in Stage I and 5 cases(8.20%) in Stage II. Another 6 cases(9.84%) presented in Stage III and 44 cases (72.13%) in Stage IV.

POSTOPERATIVE COMPLICATIONS

POSTOPERATIVE COMPLICATIONS	NUMBER (n = 26)	PERCENTAGE (%)
Hemorrhage	2	7.69
Wound Infection	4	15.38
Bile Leak	2	7.69
Jaundice	2	7.69
Fever	4	15.38

TABLE- 7 : Table showing Postoperative Complications

Among the patients who underwent curative resection all were discharged satisfactorily except a few patients. Postoperative complications have been shown in the table.

FOLLOWUP IN POSTOPERATIVE PATIENTS (including unresectable laparotomies)

MORBIDITY	AT 3 MONTHS (n)	AT 6 MONTHS (n)
Recurrence of Symptoms	0	0
Recurrence of Lump	0	0
Jaundice	2	4
Weight Loss	9	10
Ascites	2	3

Loss of Appetite	8	9
Chemotherapy related Toxicity	1	1

TABLE– 8 : Table showing Postoperative Followup

The cases were followed up at 3 months and at 6 months. Among the cases who underwent curative resection, at 3 months of follow up, 3 patients presented with Loss of appetite and weight loss. At 6 months follow up 3 cases presented with both Loss of appetite and weight loss. One patient presented only with Loss of appetite. And another patient presented with weight loss. Rest of the patients were in good health without any significant complaints. One patient with incidental carcinoma gallbladder after Open cholecystectomy who refused further Surgery was also followed up, and was free of any symptoms at 3 months and 6 months of follow up. The patient who underwent Segment III Hepaticojejunostomy at 3 months of follow up presented with weight loss and at 6 months of follow up presented with jaundice, weight loss and loss of appetite.

Patients in whom only Laparotomy with Biopsy was done at 3 months of follow up 2 patients presented with Jaundice, 5 patients presented with weight loss, 2 patients presented with Ascites, 5 patients presented with loss of appetite, 1 patient developed chemotoxicity related symptoms. At 6 months of follow up 3 patients presented with Jaundice, 5 patients presented with weight loss, 3 patients presented with Ascites, 4 patients presented with loss of appetite, 1 patient had chemotoxicity related symptoms. 2 patients were lost to follow up at 6 months. The outcome of the patients who underwent curative resection was satisfactory till 6 months as there was no recurrence of symptoms and lump.

The other cases where curative resection was not done were given palliative chemotherapy combination of Gemcitabine and Cisplatin. Many of the cases lost to follow up. 2 Patients developed symptoms related to chemotoxicity after 1 or 2 cycles. And 3 Patients developed symptoms related to chemotoxicity after 4-6 cycles. 3 of the cases who were on chemotherapy were readmitted in debilitated state and, later expired at hospital. Only a few cases showed response to chemotherapy.

IV. Discussion

In our study, the youngest patient was 28 years old and the oldest was 81 years old. Peak incidence was noted in 51-60 years. The mean age was being 53.67 ± 12.24 years. Nearby peak incidence has been noted in the following studies - Sameer Gupta et al (2016)³³, Imran Khan et al (2013)³⁸, Nissar Hussain Hamdani et al (2012)³⁷, Shukla et al (1985)³¹. Kumar S et al (2019) found that mean age was 47.5 years³⁴, Dubey A P et al (2018) reported that majority of the patients (88.23%) were more than 40 years of age⁴³. Madhawi R et al (2018) reported that median age at diagnosis was 55 years⁴⁴, Intiaz A Malik et al (2003) found the mean age was 55 years (± 11 years)³². In Hai's (1994) series the average age incidence is 49.6 years²⁸.

Out of 61 cases, there were 53 females (86.89%) and 8 males (13.11%). The male to female ratio was 1:6.63. Nearby results has been noted in the following studies - Kumar S et al (2019)³⁴, Dubey AP et al (2018)⁴³, Nissar Hussain Hamdani et al (2012)³⁷, IA Malik et al (2003)³², Lazcano-Ponce et al (2001)³⁵, Perpetuo et al (1978)³⁰.

Madhawi R et al (2018) found that Male to female ratio was 0.6 favoring females⁴⁴. Sameer gupta et al (2016) reported that Male to female ratio was 1:4.83³³. Imran khan et al (2013) concluded that Male to female ratio was 1:3.8³⁸. Y Batra et al (2005) found male to female ratio of 0.36:1³⁶. Prakash AT et al 1975 found that female to male ratio of 2 : 1⁴¹.

Among the 61 cases, gall stone was found in 45 cases (73.77%). Multiple small calculi were mostly found on USG of Hepatobiliary system. Sameer gupta et al (2016)³³ reported presence of gallstone in 80% cases of gallbladder carcinoma, Cariati A et al (2014)¹² found gallstone in 96% of the cases. Imran Khan et al (2013)³⁸ found in 71.42% cases, Nissar Hussain Hamdani et al (2012)³⁷ reported in 86% cases, AW Hsing et al (2007)⁴⁰ found in 83.70% cases. Vlad L et al (2003)³⁹, Manoj pandey et al (2001)²⁹ and Perpetuo et al (1978)³⁰ found the association of Carcinoma gallbladder with Cholelithiasis in 100%, 69.7% and 77.33% respectively.

From Socioeconomic point of view 36 (59.02%) of the cases belonged to Upper Lower class (kuppuswamy's class IV) followed by 18 (29.51%) belonged to lower middle class (kuppuswamy's class III), 6 (9.84%) cases belonged to upper middle class ((kuppuswamy's class II), 1 case (1.64%) belonged to lower class ((kuppuswamy's class V). Dubey AP et al (2018) in their study of demographic and clinicopathological profile of 68 patients of gallbladder carcinoma 75% (51) of patients belonged to either lower-middle or lower socioeconomic class⁴³. Sameer gupta et al (2016) reported that majority of patients were from low socioeconomic strata (68 %) (Kuppuswamy classes IV, V (lower class)³³. Imran khan et al (2013) found in their prospective study that Out of 63 cases, 44 patients (69.84 %) were in class IV (Kuppuswamy.scale)³⁸. Ivan serra et al (2002) stated that a very low socioeconomic status was significant independent risk factors for gallbladder cancer⁵¹.

In our study Pain abdomen was the most common symptom and it was present in 51 cases (83.61%), Lump in Right Upper Quadrant found in 41 cases (67.21%), Tenderness in right hypochondrium was noted in 24 of the cases (39.34%), Jaundice was observed in 27 cases (44.26%), Anorexia was found in 37 cases (60.66%) and Weight loss was found in 35 cases (57.38%), Nausea/Vomiting was noted in 30 cases (49.18%), Fever was present in 14 cases (22.95%) and Constipation was present in 12 cases (19.67%), Pallor found in 37 cases (60.65%), and Ascites in 7 cases (11.48%). Mishra PK (2017) found that Abdominal pain was the most common presenting symptom (89%) followed by weight loss (63%) and loss of appetite (60%). Thirty-one (8%) patients presented with gastric outlet obstruction⁵⁰. Sameer gupta et al (2016) found pain abdomen as the most common presenting complaint (98%)³³. Imran khan et al (2013) reported that out of 63 cases, Pain abdomen was present in 55 cases (87.30%), Jaundice in 20 cases (31.74%), Pallor in 45 cases (71.42%), nausea and vomiting in 42 cases (66.66%), Fever in 11 cases (17.46%), Bowel obstruction present in 10 cases (15.87%), Weight loss in 40 cases (63.49%), Lump in right hypochondrium in 4 cases (6.34%), Ascites was present in 14 cases (22.22%)³⁸. Nissar Hussain Hamdani et al (2012) stated that in his study Abdominal pain was present in 176 cases (88.9%), anorexia in 119 cases (60%), Dyspepsia in 106 cases (53.5%), weight loss in 89 cases (44.9%), Jaundice in 65 cases (32.8%), Nausea and vomiting in 61 cases (30.8%), Malaise in 53 cases (26.8%) and pruritus in 51 cases (25.7%). Clinical signs revealed abdominal mass in 151 cases (76.3%), tenderness in 103 cases (52%), ascites in 44 cases (22.2%) and fever in 22 cases (11.1%)³⁷. Batra Y et al (2005) stated that in his study of 634 patients of carcinoma gallbladder, pain and jaundice were the most common presenting features present in 516 (81%) and 462 (73%) patients respectively³⁶. IA Malik et al (2003) found that the commonest presenting symptom was pain abdomen (89%) followed by nausea and vomiting (52%), weight loss (42%), jaundice (33%) and 25% had a palpable abdominal lump³².

Among the 61 cases during ultrasound evaluation, gall stone was found in 45 cases (73.77%). Multiple stones were mostly found. Gall bladder mass was visualized in 44 cases (72.13%). Gall bladder wall thickening was found in 19 cases (31.14%). Liver metastasis was found in 29 cases (47.54%). Lymphadenopathy was found in 27 cases (44.26%). Dilated CBD was found in 26 cases (42.62%). Garg PK et al (2015) stated that ultrasonographic features of GBC include heterogeneous, predominantly hypoechoic tumour filling the gallbladder lumen fully or partially with irregular margins and presence of intraluminal mass, Features in advanced GBC are Direct invasion of liver and/or other adjacent organs, hepatoduodenal ligament, lymphadenopathy or ascites⁴². Nissar Humdani et al (2012) found gallbladder mass in 184 patients (92.9%) which was associated with gallstones in 145 patients (73.2%). There was evidence of lymph node enlargement in 52 patients (26.3%) and involvement of liver in 105 patients (53%)³⁷. Furlan A et al (2008) stated that the three common radiological patterns of GBC are GB fossa mass (40–65%); focal or diffuse wall thickening (20–30%) and polypoidal lesion (15–25%)¹³.

In Computed tomography of abdomen, out of 61 cases Gall bladder or gallbladder fossa mass was visualized in 51 cases (83.60%). Liver involvement was found in 32 cases (52.46%). Lymphadenopathy was found in 35 cases (57.38%). CBD involvement was found in 16 cases (26.23%). Other adjacent structure involvement was found in 7 cases (11.48%). Ahmed Hafez Afifi et al (2013) examined the twenty-five patients and found Infiltrating masses in fifteen patients (60%), Intraluminal polypoidal masses in nine patients (36%) while one patient (4%) presented with mural thickening of the gall bladder wall. Mild intrahepatic biliary dilatation was detected in six patients (24%)⁴⁶. Kalra et al (2006) found Gallbladder masses, asymmetric wall thickening in 45% of patients, mass replacing the gallbladder was found in 35%, and an intraluminal mass was found in 20%. CT had a sensitivity of 72.7%, a specificity of 100%, and an accuracy of 85% for determining resectability of gallbladder carcinoma⁴⁵.

Out of 61 cases, total Adenocarcinoma was found in 59 cases (96.72%) and Squamous cell carcinoma in 2 cases (3.28%). Dubey A P et al (2018) found that Poorly differentiated adenocarcinoma was the predominant histology seen⁴³. Sameer gupta et al (2016) found that the most common histological subtype was adenocarcinoma (78%)³³. Rajni Yadav et al (2013) found that Adenocarcinoma was the most frequent diagnosis in 86.7% of cases⁴⁸. Iqbal et al (2009) conducted a ultrasound guided fine needle aspiration cytology in 50 cases of gallbladder mass. Smears showed adenocarcinoma 23, undifferentiated carcinoma in 7⁴⁷.

In the present study, most of the patients presented at advanced stage. All the cases of Stage I and Stage II were diagnosed incidentally. Out of 61 cases, 6 cases (9.84%) were diagnosed in Stage I and 5 cases (8.20%) in Stage II. Another 6 cases (9.84%) presented in Stage III and 44 cases (72.13%) were in Stage IV. Creasy JM et al (2017) found that majority were stage IVB (58%)⁵⁹. Yamamoto Y et al (2017) found that among 114 patients of their study, 18 had stage I disease. Among the remaining 96 patients 28 patients had stage II, 14 had stage IIIA, 35 had stage IIIB, 11 had stage IVA, and 8 had stage IVB disease⁵⁸. Henley SJ et al (2015) mentioned that about 11% of gallbladder cancers were diagnosed at an early stage, 43% after spread to regional organs or regional lymph nodes, and 42% after spread to distant organs or distant lymph nodes⁵².

In the present study, among the 61 cases, laparotomy was done in 26 cases (42.62%), out of these 8 patients has been found unresectable and only Biopsies were taken and abdomen was closed on table and

another 1 patient underwent palliative surgery in the form of Segment III HJ. So, 17 patients (27.86%) underwent curative resection and were given adjuvant chemotherapy; among them 9 cases underwent Extended Cholecystectomy, 7 cases underwent Radical Resection. Another case of carcinoma gallbladder after open cholecystectomy whose histopathology showed invasion upto muscular layer(T1b) was advised for Extended Cholecystectomy but the patient party refused further operation. So only Cholecystectomy was done in that patient. The other 35 cases were not put for curative surgery as the disease was too advanced at presentation to be benefitted from any sort of surgical intervention and also due to the poor health status of the patients. So these 35 cases along with the 9 unresectable laparotomy, total 44 (72.13%) patients were planned for palliative Chemotherapy. 3 patients received Concurrent Radiotherapy. Mishra PK et al (2017) conducted a study in which, total patients after exclusion criteria was 385. Out of these 154 patients (40%) underwent curative resection⁵⁰. Ishii H et al (2004) stated that out of 335 patients, 139 patients (41.49%) underwent surgical resection with curative intent, and 57 with locally advanced disease were treated with radiotherapy. Of the remaining 141, 57 who met the eligibility criteria below were treated with systemic chemotherapy in a phase 2 setting, and the other 82 received best supportive care⁶⁰.

The cases were followed up at 3 months and at 6 months. Among the patients who underwent curative resection, outcome was satisfactory till 6 months of follow up as no recurrences occurred within that period.

All the 17 patients who underwent Curative Surgical Resection received adjuvant chemotherapy. All of them were given the regimen of Gemcitabine and Cisplatin for 6 cycles. Kasumova GG et al (2017) found that Adjuvant therapy increase the median survival rate⁴⁹. Mantripragada KC et al (2016) mentioned that Adjuvant therapy increase the survival benefit⁵⁴. Ma N et al (2015) found that a significant improvement was observed in Overall Survival with chemotherapy compared with surgery alone⁵⁷.

In the present study of 61 cases, 35 patients were inoperable due to advanced stage of presentation diagnosed on the basis of clinical examination and radiological findings. USG guided FNAC was performed and all the reports came as Adenocarcinoma of gallbladder. After the confirmed tissue diagnosis of the 35 inoperable patients and 9 unresectable laparotomy, total 44 (72.13%) were given with Gemcitabine with Cisplatin regimen as palliative Chemotherapy, but only little response was seen. Su You M et al (2019) conducted a study in which combination therapy with gemcitabine and cisplatin has been widely used as first-line palliative chemotherapy for advanced GBC Patients (most of the patients were in stage IVB) and benefit was noticed⁵⁶. Aloia TA (2015) stated that in advanced stage of carcinoma gallbladder systemic agents remain the mainstay of therapy, with gemcitabine–cisplatin chemotherapy being the treatment of choice in patients with good performance status⁵⁵. Iqbal S et al (2011) found that Gemcitabine plus Capecitabine as a possible treatment option in a phase 2 study and No complete responses were seen⁵³.

In our study, most of the patients did not give consent for radiotherapy. Only 3 patients(all were inoperable cases who were receiving only chemotherapy) received External Beam Radiotherapy. No significant benefit noted in this group of patients in comparison to other patients who didnot receive Radiotherapy.

V. Conclusion

Gallbladder carcinoma is commonly seen among females with peak incidence in 51-60 years of age. Etiologically related to many factors, among them most important is cholelithiasis and more common in lower socioeconomic classes. Most common presenting symptom is pain abdomen followed by lump abdomen. Diagnosis is based on Radiological features like gallbladder or gallbladder fossa mass, asymmetrical wall thickening, surrounding structure involvement or diagnosed histopathologically. Curative Surgery is possible only when it is diagnosed at an early stage, but most of the patients present in advanced stage, who can only be given palliative therapy.

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Dr Sunmoni Bhuyan, et. al. "Clinical Study of Carcinoma Gallbladder in a Tertiary Care Hospital." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 20(06), 2021, pp. 25-36.