Carcinoma Gallbladder – an overview

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Carcinoma gallbladder is the commonest malignancy of biliary tract, with very poor prognosis. Clinical signs usually appear late, in advance stages. Surgical resection is the only possible curative option, that can also help decrease morbidity. Categorized by Nevin's staging, local infiltration and lymphatic spread are the bad prognostic indicators. Our's is a 24 patients series in West Surgical Ward where we picked three cases incidentally on routine laparoscopic cholecystectomy, three diagnosed on FNAC and three on laparoscopic biopsy. Cholecystectomy was done in four cases and added with hepatic bed resection in two. Obstructive jaundice was palliated by T-tube stenting, hepaticogastrostomy, hepaticojejunostomy or therapeutic PTC. Longest survivor is over two years who underwent laparoscopic cholecystectomy followed by adjuvant chemotherapy in Nevin's II stage.
Keywords: Carcinoma, gall bladder, tissues diagnosis, management

Carcinoma gallbladder is the most common malignancy of biliary tract[1]. Due to early non specific symptoms, and appearance of overt clinical signs only at advanced stages, it has got very poor prognosis[2]. Depth of tumor infiltration and lymphatic invasion are unfavorable prognostic indicators[3].

Carcinoma gallbladder is one of the most fatal malignancies, with very poor survival rates. Sometimes it presents clinically with non-specific upper abdominal symptoms. At other times it is picked during ultrasound abdomen done for some other problem. It may even be diagnosed incidentally during surgery for gallstone disease, and even on histopathology[4]. Therefore, no one surgical option can be advised for all cases.

In early stage disease, operative treatment provides the opportunity for good survival, while in late disease it may be the only chance of relatively prolonged survival and improved quality of life[5].Pre-operative FNAC plays an important role in diagnosis of Carcinoma Gall bladder as it helps in determining the urgency of treatment and planning of the surgical procedure. In advanced cases pre-operative FNAC confirmation would avoid unnecessary laparotomies.

Other treatment options available are chemotherapy, radiotherapy and cryotherapy etc. but all have disappointing results. Which best operative intervention be offered to a given stage of disease has remained the point of controversy.

Material and methods

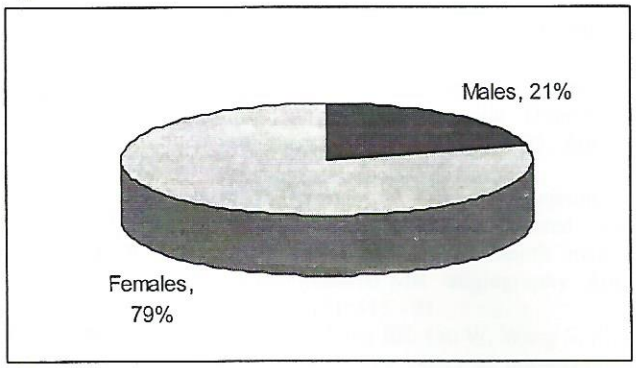
Patients admitted in West Surgical Unit, Mayo Hospital, Lahore with gallbladder disease from January 2001 to December 2004 were included in the study. All patients underwent thorough scrutiny of history and physical signs. Features specially sought included pain upper abdomen, jaundice, loss of weight, history suggestive of upper G.I. obstruction, smoking and any previous interventions. In addition to baseline biochemical and haematological assays patients were investigated by either of abdominal ultrasound, CT scan, PTC, ERCP etc. Ultrasound or CT guided FNAC and diagnostic laparoscopy and biopsy done in cases where applicable. Dictated by preoperative evaluation of stage of disease and general condition of patients, open exploration was done; proceeded by biopsy only, cholecystectomy, extended cholecystectomy, stenting or bypass, as feasible. Oncological advice was sought whenever possible. Patients were followed for post-operative complications, morbidity and mortality.

Results:

This study includes patients with carcinoma gallbladder diagnosed preoperatively on radiological investigations, under ultrasound guided FNAC or laparoscopic biopsy suspected per exploration and diagnosed on histopathology.

A total of 24 cases were diagnosed having carcinoma gallbladder. Five (21%) of them were males and rest 19 (79%) females.

Fig. 1: Gender



Eighteen patients were admitted from Outpatient Department and six from Emergency Department.

Age group was 39-64 years with mean age of 51 years. Most of cases were in 5th & 6th decade of life.

Dominant symptoms were obstructive jaundice (42%), mass upper abdomen (38%), features suggestive of gallstone disease (25%), severe pain right upper quadrant (17%), weight loss (38%), and ascites (17%).

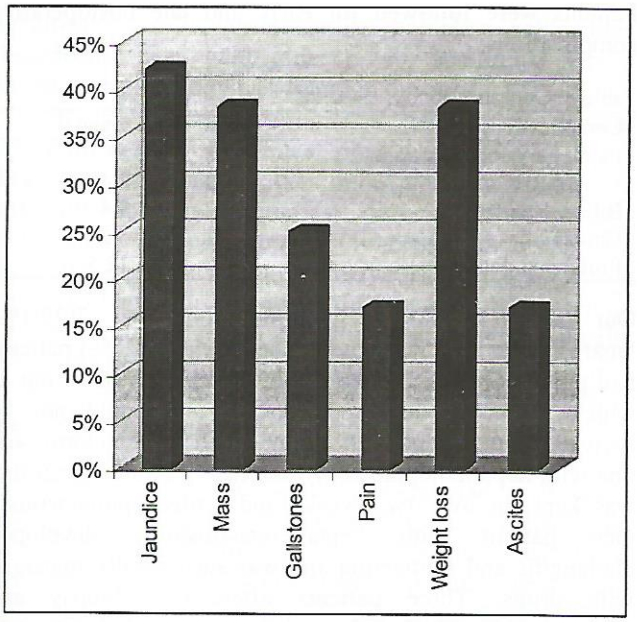


Fig. 2: Symptomatology

In this study gallstones were found in 17(65%) cases picked on ultrasound or per-exploration. Five of them were symptomatic for more than 5 years with recent change in disease pattern. Eight patients of our study were smokers. Among them were 6(25%) females.

There were no known cases of porcelain gallbladder or choledochal cyst. On clinical examination, we picked jaundice in 14 patients, mass (palpable gallbladder, metastatic liver) in 8 cases and ascites in 2 patients. All patients underwent a thorough screening of investigations for preoperative cytological diagnosis and staging.

Ultrasound abdomen was our main investigative tool that was done in all cases. It helped diagnose three cases of mass fundus of gallbladder, enlarged lymph nodes in peri-choledochal area in 7(29%) and para-aortic lymph nodes in 4(16%) cases.

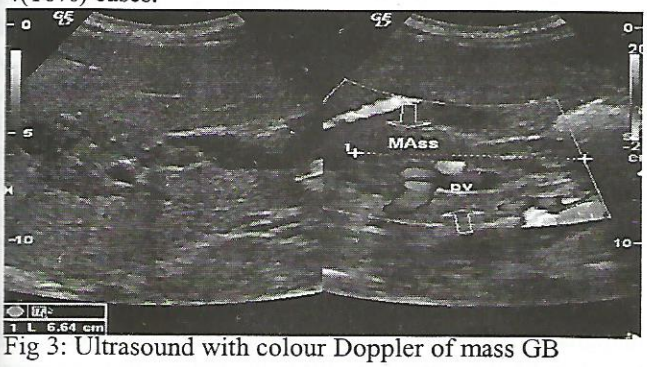


Fig 3: Ultrasound with colour Doppler of mass GB

Contrast CT scan could be done in 4 (16%) cases, of mass in sub hepatic area for metastastic workup. Ultrasound and CT guided FNAC was done in 12 (50%) cases, 3 of them revealed just haemorrhagic back ground. 5 cytologies from masses showed atypical cells with nuclear changes suggestive of adenocarcinoma. In 4(16%) we could get specimen from infiltrated liver mass and proved metastatic adenocarcinoma.

Table 1: FNAC

Pathology	n=	%age
Haemorrhagic aspirate	05	20.8
Adenocarcinoma from mass	03	12.5
Hepatic metastatic adenocarcinoma	04	16.7

Three patients in which FNAC confirmed carcinoma, were in stage IV and no further surgical intervention was offered and referred to Oncologist. Patients were categorized according to Nevin's staging.

Table 2: Nevin's staging.

Stage	
I	Intramucosal
II`	Extends to muscularis.
III	Extends through the serosa
IV	Transmural involvement and cystic left node involved
V	Direct extension to liver and/or distant metastasis.

Laparoscopic cholecystectomy is currently the gold standard technique and routinely done in our ward. Among these cases, 3(12.5%) patients were incidentally discovered having carcinoma on histological diagnosis. Two of them were stage II and one stage I. All were referred to oncologist and followed for a year. Among 5 (20.8%) cases of negative FNAC, laparoscopic biopsy confirmed malignancy in 3 (12.5%) cases; while in 2 (8.4%) we proceeded with open exploration and cholecystectomy. In one patient laparoscopic biopsy was taken from liver secondary and proved metastatic adenocarcinoma.

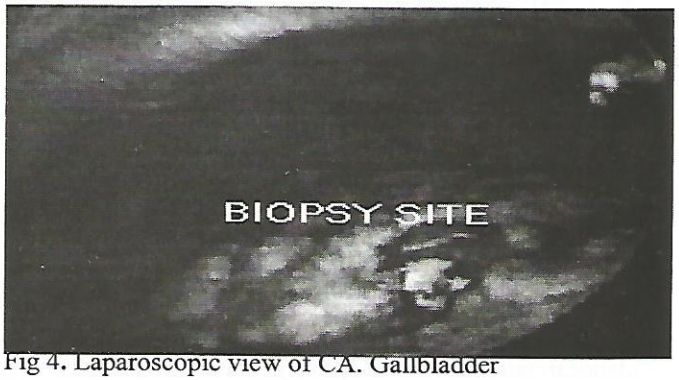


Fig 4. Laparoscopic view of CA. Gallbladder

Table 3: Laparoscopic intervention

	n=	%age
Biopsy only (US guided FNAC negative)	03	12.5
Lap cholecystectomy	03	12.5
Liver biopsy	01	4.2

In 14 (58.3%) patients open exploration was done. In 3 (12.5%) of them we could not proceed because of local infiltration of surrounding structure and wide spread metastasis so opted for open biopsy only.

Table 4: Open exploration

	n=	%age
Biopsy only	03	12.5
Cholecystectomy	04	16.7
Extended cholecystectomy	02	8.4
Cholecystectomy and T-tube placement	02	8.4
Hepaticogastrostomy	02	8.4
Hepaticojejunostomy	01	4.2

Ten (10) of our patients with open exploration had jaundice. In 2(8.4%) patients cholecystectomy was done and T-tube stenting could also be possible. In other 2 (8.4%) cases porta hepatis was totally infiltrated. Feeding tube hepaticogastrostomy was done. In 2(8.4%) patients with multiple secondaries in liver no further intervention was done. In 2(8.4%) patients with tumour infiltrating the liver bed extended cholecystectomy was done in which 3 cm wedge of liver tissue in segment IV & V of gallbladder bed and lymph nodes in porta were removed.

Table 5: Palliation for jaundice

Procedure	n=	%age
T-tube stenting	02	8.4
Hepaticogastrostomy	02	8.4
Hepaticojejunostomy	01	4.2
Therapeutic PTC	03	12.5

In 3 (12.5%) patients with inoperable carcinoma and mass obstructing portahepatis therapeutic PTC was done to decompress dilated intrahepatic biliary channel. The pre-operative confirmation avoided the surgery. Our break up of patients according to Nevin's staging and the treatment offered is as follows:

Table 6: Nevin's stage and operative intervention

Stage	No.	Procedures	No.
I	1	Laparoscopic cholecystectomy	1
II	3	Laparoscopic cholecystectomy	2
		Open cholecystectomy	1
III	0	Laparoscopic cholecystectomy	0
IV	4	Extended cholecystectomy	2
		Cholecystectomy and T-tube placement	2
V	10	FNAC only	3
		Laparoscopic biopsy only	2
		Open biopsy only	3
		Cholecystectomy	2

Histopathology of biopsy specimens was dominated by adenocarcianoma in 23(96%) cases with 1(4.2%) adenosquamous carcinoma

Table 7: Histopathology

	n=	%age
Adenocarcinoma	23	96
Well differentiated	6	27
Moderately differentiated	3	13.5
Poorly differentiated	14	60.9
Adenosquamous carcinoma	1	4.2
Squamous cell carcinoma	0	0
Lymphoma	0	0
Secondary in gallbladder	0	0

Patients were followed for early and late postoperative complications.

Table 8: Complications

Complications	n=	%age
Pulmonary complications	06	25
ARDS	02	8.4
Biliary leakage	02	8.4
Cholangitis	01	4.2
Prolonged ileus	03	12.5

Out of 14(58.3%) open explorations and 7(29.1%) laparoscopies who got general anesthesia, 6 (25%) patients had pulmonary complications with basal atelectasis out of which 2(33.3%) developed ARDS and could not be revived. One patient with extended cholecystectomy and one with hepaticojejunostomy had heavy bilious drain that was kept for over two weeks and settled spontaneously One patient with heptaticogastrostomy developed cholangitis and septicemia and was successfully managed with drugs. Three patients after open biopsy and cholecystectomy had prolonged ileus and settled with suck and drip in 6-9 days.

Patients with feeding tube hepaticogastrostomy were followed upto 5 months. One of them, a 47 years female died after nine weeks, of non-resolving cholangitis. Other patient survived upto 5 months and died of renal failure.

Patients were directed for oncological consultation. Two patients in stage II, one patient in stage III and two in stage IV got chemotherapy. All were given 5-FU, Adriamycin and Mitomycin. Patients with stage I & II survived more than 11 months. One longest survival is over 2 years now,a Nevin II diagnosed after routine laparoscopic cholecystectomy and also received adjuvant chemotherapy.

Discussion:

Gallbladder is a columnar cell lined derivative of foregut that act as a reservoir for and concentrates bile. Carcinoma gallbladder outnumbers malignancies in other portions of biliary tree. Adenocarcinoma is the commonest pathology followed by adenosquamous, squamous cell carcinoma, lymphoma and metastasis in gallbladder. It starts with thickening of wall and polypoid or cauliflower like fronds project into the lumen forming fungating mass. At other times tumour invades wall and infiltrates the surrounding structures. Carcinoma gallbladder is highly lethal disease with bad prognosis[4].

Gallstones have been blamed aetiological factor for malignancy. Whether cause or just association, these are found in 65-90% cases in different studies. In our series, stones were present in 65% cases. Long standing history and increasing size of stones is directly proportional to risk of malignancy. Therefore cholecystectomy should be advised in all cases of gall bladder stones. Now there is established trend for cholecystectomy even in the asymptomatic gall stones. Many other factors have been

documented as precancerous like porcelain gallbladder, choledochal cyst, gallbladder polyp, adenomyometosis[7] but no such pathology was found in our series.

In early stage, carcinoma gallbladder remains asymptomatic with no clinical signs while many cases are diagnosed incidentally either on exploration or later on *histopathology. In* our series three (12.5%) patients undergoing laparoscopic cholecystectomy for cholelithiasis were diagnosed harbouring malignancy on histopathology. This incidental diagnosis has been seen on different series from 6-14%. This phenomenon typically shows obscurity of symptoms in the initial phase. It also signifies importance of sending all operative resection specimens for histopathology.

Laparoscopy is now not a contraindication for cholecystectomy in early carcinoma gallbladder if safely possible. It is also a good technique for taking biopsy from advanced primary lesion or from hepatic metastasis & the tissue reveal is good with higher positive results for confirmation of malignancy. In our series three (12.5%) patients with negative FNAC proved malignant on laparoscopic biopsy. Thus laparoscopy is now proved to be beneficial in assessing local disease, its spread and taking adequate biopsy tissue.

Ultrasound abdomen is a noninvasive investigation that gives good information about primary lesion, lymph node status, liver secondaries and ascites etc. In this series it helped us in diagnosis of 21 cases pre-operatively and in taking FNAC specimens in 12 cases.

Surgical treatment is the only possible curative option. It also provides palliation in cases of jaundice. Cholecystectomy takes away the disease if it is limited to the gall bladder wall. If disease is limited to serosa, second intervention with resection of liver bed and pericholedochal lymph node dissection has been recommended. In our series no second intervention was done. Three of our patients had disease picked on histopathology and all were taken up by oncologist.

For palliation of obstructive jaundice we performed three bypasses one with jejunum and two with stomach. One patient had tumour in gall bladder fundus infiltrating liver sparing the porta. After successful resection of whole mass including cholecystectomy, Roux-en-Y hepatico-jejunostomy was done. This patient had biliary leakage initially that settled with conservative treatment. Two other patients with obstruction had tumour involving porta. A slice of hepatic tissue over the left lobe of the liver was excised exposing the left hepatic duct. A feeding tube was placed in the left hepatic duct and opened in the stomach. This provided good palliation although one patient developed cholangitis and septicemia. Two patients were decompressed by permanent T-tubes, both survived upto four months. We also took help pf radiologist, who did external drainage with PTC in three cases.

In majority of our patients presenting late where we just confirmed histology, oncological advice was taken. Three of them got chemotherapy but median survival in all these cases was 2.8 months.

Thus carcinoma gall bladder remains a challenge for the surgeons with a high morbidity and mortality rates. It signifies thorough evaluation of all cases with upper abdominal symptoms keeping in mind rare pathologies and use of a good ultrasound eye to pick early lesions. FNAC greatly helps in formulating management plan in many cases. Advanced cases can only be helped by improved quality of life by palliation of jaundice and good pain control.

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