

OBSTRUCTIVE JAUNDICE IN GALL BLADDER CANCER AND CHOLANGIOCARCINOMA: MANAGEMENT AND OUTCOMERajesh Kumar Rathore¹**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: The present study was carried out to study the cases of obstructive jaundice caused by gall bladder cancer and cholangiocarcinoma. Twenty cases were included in the study. The major aims of the study were to delineate the clinical features and laboratory tests to know the extent of liver damage in patients with obstructive jaundice caused by gall bladder cancer and cholangiocarcinoma and to evaluate further the diagnostic accuracy and safety of procedures like ultrasonography, computerized tomography scan, percutaneous transhepatic cholangiography and diagnostic laparoscopy. An attempt was made to evaluate these techniques for the early detection of metastasis and to know the feasibility of surgery, definitive or palliative to relieve obstructive jaundice and its outcome including morbidity and mortality. The study was carried out in MB Government Hospital associated with R.N.T. Medical College, Udaipur. Material and method used in this study include various laboratory investigations including haemogram, blood sugar, urea, creatinine, liver function test, urine examination etc. Investigations like ultrasonography, CT scan, x-ray abdomen and chest and ECG were carried out in hospital. Various procedure e.g., percutaneous transhepatic biliary drainage, diagnostic laparotomy and surgical procedure were performed in hospital. Statistical analysis of various data done which include spectrum of gall bladder cancer and cholangiocarcinoma, distribution of site of pathology in cholangiocarcinoma, age wise distribution, sex wise distribution, area wise distribution, occupation wise distribution, symptomatology, physical findings, laboratory investigation findings, ultrasonography and CT scan reports and various procedures like percutaneous transhepatic biliary drainage, diagnostic laparoscopy and surgery. Jaundice and lump in abdomen were the commonest presenting symptoms in the presenting series. All the twenty patients with gall bladder cancer and cholangiocarcinoma had extreme hyperbilirubinaemia with significant elevation of direct fraction of serum bilirubin level. On ultrasonography and computerized tomography scan 45 percent patients revealed gall bladder stones associated with gall bladder cancer and cholangiocarcinoma. Both of these investigations detected hepatomegaly, dilated intrahepatic biliary radicals and dilated hepatic ducts in 100 percent patients with obstructive jaundice caused by gall bladder cancer and cholangiocarcinoma. In detection of site of mass, liver infiltration, lymph node involvement, ascites and other organ involvement both ultrasonography and CT scan were almost equally effective. Percutaneous transhepatic cholangiography (PTC) was 100 percent effective in showing dilated biliary tree above the level of obstruction in the patients with obstructive jaundice due to gall bladder cancer and cholangiocarcinoma. Diagnostic laparoscopy yielded additional information of the liver and biliary tract and allowed accurate evaluation of extent and degree of neoplasm and involvement of lymph nodes and other organs. Treatment offered was mainly palliative in nature in majority of cases. Non-operative palliation included Percutaneous Transhepatic Biliary Drainage (PTBD) and operative palliation included cholecystectomy along with Roux-en-Y hepatico or choledocho-jejunostomy.

ORIGINAL ARTICLE

Definitive treatment was offered in two patients who included surgical resection of tumour mass, cholecystectomy and Roux-en-Y hepatico or choledocho-jejunostomy. Outcome of patients with obstructive jaundice caused by gall bladder cancer and cholangiocarcinoma were not good in sixty percent of patients as they were discharged with their own request with no treatment. In those patients, who were offered an operative or palliative treatment, 100 percent patients showed a decrease in post-operative serum bilirubin level and were discharged with satisfactory management. One patient expired within 24 hours after operation in whom laparotomy and biopsy was performed. One patient of cholangiocarcinoma died 3 years and 8 months after surgical resection of tumour mass with, cholecystectomy and Roux-en-Y hepatico-jejunostomy.

KEYWORDS: Obstructive Jaundice, Bilirubin, Carcinoma, Gall Bladder, Cholangiocarcinoma, CBD, IHBR, PTC, PTBD.

MESHTERMS: Jaundice, Obstructive (D041781), Gallbladder Neoplasm (D005706), Cholangiocarcinoma (D018281).

INTRODUCTION: Jaundice refers to yellow appearance of the skin, sclera and mucous membranes resulting from an increased bilirubin concentration in the body fluids. It is detectable when the plasma bilirubin concentration exceeds 3 mg/dl. There are four pathological mechanisms giving rise to jaundice.¹ Haemolytic jaundice, congenital nonhemolytic hyperbilirubinaemia, Hepatocellular jaundice and Cholestatic jaundice. In this study the cases of obstructive jaundice caused by biliary tract malignancy are included. With the availability of the technologies at R.N.T. Medical College, Udaipur, the present study was undertaken to know the cause, site and extent of biliary tract obstruction with the help of various investigations especially ultrasonography, CT scan and percutaneous transhepatic cholangiography (PTC): extent of liver damage through biochemical tests and feasibility of surgery.

The goals of diagnostic imaging for biliary tract tumours include assessment of location and extent of tumour in biliary tree, including vascular invasion, hepatic lobar atrophy and presence of metastatic disease. Ultrasonography is noninvasive and standard initial imaging technique for patient presenting with jaundice. It may demonstrate biliary calculi, size of gallbladder, thickness of gallbladder wall, size of common bile duct, malignancy occluding bile duct, liver infiltration, metastasis, ascites, and evaluation of lymph nodes, common bile duct infiltration or peritoneal dissemination. Computerized tomography (CT) is a valuable procedure in the investigation of patients with gallbladder cancer and cholangiocarcinoma and defines its extent, the presence of lymphadenopathy and the presence of metastasis.

Percutaneous transhepatic cholangiography (PTC) conducted under fluoroscopic control in which a needle (the chiba or okuda) is advanced into the liver, contrast is injected and seen entering bile radicals. All the cases investigated for extent of liver damage through biochemical tests. Serum bilirubin is predominantly conjugated bilirubin in obstructive jaundice. Protein synthesis especially serum albumin and prothrombin concentrations are reduced in long standing liver disease. Serum alkaline phosphatase is characteristically greatly elevated in obstructive jaundice. Hepatocellular damage is shown by raised serum level of aminotransferase. Slight elevation is consistent with obstructive jaundice and very high values suggest viral hepatitis or toxic damage.² Malignancies of the biliary tract can be divided into two main groups – gallbladder cancer and cholangiocarcinoma. Malignancies of both the gallbladder and the bile ducts are almost always adenocarcinomas.

ORIGINAL ARTICLE

For both tumours radiologic work up is similar and resection with negative margins is the goal of therapy. Unfortunately, many patients present at an advanced stage and palliation is the only option.³ All the neoplasms share certain common characteristics. They lack specific signs and symptoms, are diagnosed late and cure following resection is rare.⁴

In this study, both patient and tumour related factors considered for feasibility of surgery, definitive or palliative to relieve obstruction and its outcome including morbidity and mortality. Non-operative palliation has management of obstructive jaundice with either percutaneous transhepatic biliary stents or biliary endoprosthesis. Operative palliation includes confirmation of a tissue diagnosis, removal of the gallbladder if possible and palliation of jaundice via one of several forms of biliary enteric anastomosis. Surgical resection therapy is based on pathologic staging and historical survival rates.

METHODS: The present study was conducted in department of surgery, R.N.T. Medical College and Maharana Bhupal Govt. Hospital, Udaipur. Patients from both sex of various age groups having obstructive jaundice caused by gallbladder cancer and cholangiocarcinoma were taken. A detailed history, thorough clinical examination and necessary investigations were performed in each case according to planned proforma. All patients were investigated for hemogram including hemoglobin, bleeding time and clotting time. Blood examinations; sugar, urea, creatinine, bilirubin, albumin, globuline, SGOT, SGPT, alkaline phosphatase, prothrombine time and Urine examination were done. Ultrasonography done on patients with empty stomach placed in supine position.

Ultrasonography transducer was placed in contact with abdominal skin and used to scan the liver, biliary tract, gallbladder and adjacent structures. The images were monitored on fluoroscopic screen and recorded on photographic paper. Computerized Tomography scan performed on patients placed in supine position. Patients were asked to take orally Trazogastro oral contrast 30 ml diluted in 1.5 litre water one hour prior to the scan. A series of scans acquired during suspended respiration. The scan taken was NCCT. Then Radiopaque 300 mg percent was injected intravenously and scans taken immediately. These were CECT. Diagnostic laparoscopy was performed in those cases where the general condition of the patient did not allow exploratory laparotomy.

Patients were kept fasting overnight and enema was given in night. Patient in supine position and under general anaesthesia; pneumoperitoneum was created with Veress needle connected to carbon dioxide source. Intra-abdominal pressure maintained around 12 mmHg. Telescopic examination of peritoneum and abdominal cavity was carried out. Liver and gallbladder were visualized and biopsies were taken with biopsy forceps from most representative areas. Percutaneous transhepatic cholangiography (PTC) was performed to see the dilated intrahepatic biliary radicals (IHBR) and site of obstruction in ducts.

Vitamin K 10 mg daily was given for correction of Prothrombin time and was continued even after the procedure was done. Intravenous antibiotic Ceftriaxone was started two days prior to the procedure and was continued for two to three more days. Emergency drugs were kept ready while the procedure was being done. Sedation by ude of 10 mg diazepam intravenously was used in all the cases studied. Constant monitoring of pulse and blood pressure was carried out throughout the procedure. X-ray machine with facility for fluoroscopy was utilized. The patient was placed supine on the table. A lead marker was placed on the xiphisternum, this site was approximately midway between the dome of diaphragm and upper part of the 'C' of duodenum. A point of puncture was selected in the 7th or 8th intercostals space on the right site.

ORIGINAL ARTICLE

1 percent xylocaine was in filtered for local anaesthesia on the selected space. Patient was made to hold the breath midway between the inspiration and expiration at the time of entry of needle. Normal respiration was permitted after introduction of full needle. Fluoroscopy was started and needle with stylet was pushed horizontally to the level of table and its tip was aimed at the lead marker on the xiphisternum. The stylet was removed and 10 ml syringe containing Conray 280 was directly attached to the needle. Half to one ml of contrast was injected at a time and the pattern of dye was followed on fluoroscopy.

X-ray plates were exposed after giving different positions to the patient. Percutaneous transhepatic biliary drainage (PTBD) was planned in patients with evidence of metastatic or locally unresectable disease. A soft Silastic stent advanced over guide wire and placed transhepatic through 7th or 8th intercostals space on the right side under aseptic condition and under local anaesthesia. Exploratory laparotomy planned in some patients. Most of the patients at laparotomy had unresectable disease hence operative palliation planned which included confirmation by tissue diagnosis, removal of the gallbladder if possible and palliation of jaundice via. Biliary-enteric anastomosis e.g., Roux-en-Y choledochojejunostomy was done. In resectable mass; whole mass of CBD removed along with gallbladder and Roux-en-Y hepaticojejunostomy was performed.

STATISTICS: Twenty cases of obstructive jaundice with biliary tract malignancy were included in study and statistical data were obtained. Eight patients (40%) had gallbladder cancer and twelve patients (60%) had cholangiocarcinoma. Out of twelve cases of cholangiocarcinoma, 5 cases(41.6%) had mass at the confluence of right and left hepatic ducts (Klatskin tumour), 1 case(8.3%) had mass in common hepatic duct, 1 case (8.3%) had mass in proximal CBD and 5 cases (41.6%) had mass in distal CBD. Two patients (10%) were in the age group of 31-40 years, three patients (15%) were in 41-50 years, nine patients (45%) in 51-60 years, three patients (15%) in 61-70 years and three patients (15%) were in 71-80 years age group. Gall bladder cancer was found in four male patients and four female patients with male to female ratio of 1:1. Cholangiocarcinoma was found in 10 male patients and 2 female patients with male to female ratio of 5:1.

Jaundice and pain abdomen was the presenting complaint in 100% cases with gallbladder cancer and cholangiocarcinoma. Three patients (37.5%) out of 8 cases of gallbladder cancer and three patients (25%) out of 12 cases of cholangiocarcinoma were presented with fever. Three patients (37.5%) out of 8 cases of gall bladder cancer and four patients (33.3%) out of 12 cases of cholangiocarcinoma were presented with complaint of vomiting. Abdominal distension was presenting complaint in 1 (12.5%) out of 8 cases of gallbladder cancer and 4 (33.3%) out of 12 cases of cholangiocarcinoma. Pruritus was presenting complaint in 4 (50%) patients out of 8 cases of gallbladder cancer and 4 (33.3%) patients out of 12 cases of cholangiocarcinoma.

Malena was presenting complaint of 3(25%) cases out of 12 cases of cholangiocarcinoma. Four (50%) patients with gallbladder cancer out of 8 cases were smoker. Five cases (41.6%) with cholangiocarcinoma out of 12 cases were smoker, alcoholic and non-vegetarian. Seven patients (87.5%) of gallbladder cancer out of 8 cases and 10 patients (83.3%) of cholangiocarcinoma out of 12 cases were farmer. A palpable mass in the right upper quadrant was present in 100% cases of gallbladder cancer and 75% cases of cholangiocarcinoma. Jaundice, pallor and hepatomegaly were present in 100 % cases studied. Clinically demonstrable ascites was present in 12.5% cases of gallbladder cancer and 16.7% cases of cholangiocarcinoma. Metastatic nodule at umbilicus (Sister Mary Joseph nodule) was present in 1 patient (8.3%) with cholangiocarcinoma.

ORIGINAL ARTICLE

Mean total bilirubin was 20.7 mg% and 20.1 mg%, mean direct bilirubin was 13.9 mg% and 13.3 mg%, mean indirect bilirubin was 6.8 mg% and 6.8 mg% in patients with gallbladder cancer and cholangiocarcinoma respectively. Mean hemoglobin level in patients with gallbladder cancer was 10gm% and in patients with cholangiocarcinoma was 9.7 gm%. Mean serum protein was 6.0 gm% and 5.8 gm% in cases with gallbladder cancer and cholangiocarcinoma respectively. SGOT was ranging from 16-97 IU (mean 64.5 IU) and 27.2-213 IU (mean 80 IU) in cases with gallbladder cancer and cholangiocarcinoma respectively.

SGPT was ranging from 7-180 IU (mean 64.0 IU) and 21-234 IU (mean 88.8 IU) in cases with gallbladder cancer and cholangiocarcinoma respectively. Alkaline phosphatase level SGPT was ranging from 50-685(mean 206) K.A. Units and 25-891 (mean 229) K.A. Units in cases with gallbladder cancer and cholangiocarcinoma respectively. Prothrombin time was ranging from 15-120(mean 35) Seconds and 14-120 (mean 36) Seconds in cases with gallbladder cancer and cholangiocarcinoma respectively.

Ultrasonographic examination of all the 20 cases with gallbladder cancer and cholangiocarcinoma revealed gallbladder mass in 8 cases(40%), mass at confluence of right and left hepatic ducts in 5 cases(20%), mass at common hepatic duct in 1 case (5%), mass at proximal CBD in 1 case (5%), mass at distal CBD in 5 cases (20%), cholelithiasis in 9 cases (45%), thick gallbladder wall in 10 cases(50%), hepatomegaly in 20 cases(100%), dilated IHBR and hepatic ducts in 20 cases (100%), dilated CBD in 12 cases (60%), liver infiltration in 7 cases (35%), lymph nodes at porta hepatis in 8 cases (40%), ascites in 4 patients (20%) and involvement of head of pancreas in 3 cases (15%). CT scan findings of all the 20 cases with gallbladder cancer and cholangiocarcinoma revealed gallbladder mass in 8 cases (40%), mass at confluence of right and left hepatic ducts in 5 cases (20%), mass at common hepatic duct in 1 case (5%), mass at proximal CBD in 1 case (5%), mass at distal CBD in 5 cases (20%), cholelithiasis in 9 cases (45%), thick gallbladder wall in 10 cases(50%), hepatomegaly in 20 cases(100%), dilated IHBR and hepatic ducts in 20 cases (100%), dilated CBD in 12 cases (60%), liver infiltration in 7 cases (35%), lymph nodes at porta hepatis in 8 cases (40%), ascites in 4 patients(20%) and involvement of head of pancreas in 3 cases (15%).

Percutaneous transhepatic cholangiography was done in one case (12.5%) out of 8 cases of gallbladder cancer and 2 cases (16.6%) out of 12 cases of cholangiocarcinoma. In all (100%) cases PTC confirmed the site of obstruction in biliary tract. Diagnostic laparoscopy was performed in 2 cases (25%) out of 8 cases of gallbladder cancer and in both (100%) cases it confirmed the diagnosis and metastasis, and biopsy was taken for histopathology. Biopsy was taken in 5 cases (62.5%) out of 8 cases of gallbladder cancer and 1 case (8.3%) out of 12 cases with cholangiocarcinoma.

In both the disease 100% cases showed adenocarcinoma on histopathological examination. Curative treatment offered in 2 cases (25%) out of 8 cases that stayed for treatment in which surgical resection of tumour mass, cholecystectomy, Roux-en-Y hepatico or choledocho-jejunostomy performed. Palliative treatment done in 4 cases (50%) out of 8 cases that stayed for treatment. In 3 cases (37.5) palliation done with cholecystectomy and Roux-en-Y hepatico or choledocho-jejunostomy and in one case (12.5%) percutaneous transhepatic biliary drainage (PTBD) was performed. Laparoscopy was performed in 2 cases (25%) out of 8 cases that stayed for treatment. In both cases disease was found metastatic and biopsy taken for histopathologic examination. Statistics of outcome of patients shows 8 patients (40%) out of 20 patients were stayed for treatment. Twelve patients (60%) out of 20 cases were discharged with no treatment with their own request. Six patients (75%) out of 8 patients showed decrease in post-operative or post palliative bilirubin level.

ORIGINAL ARTICLE

Seven patients (87.5%) out of 8 cases who stayed for treatment were discharged after operative or palliative management. One patient (12.5%) out of 8 cases who stayed for treatment was died postoperative within 24 hours.

RESULTS: The present work was carried out in R.N.T. Medical College, Udaipur. A series of twenty patients presented with clinical jaundice and suffering from gall bladder cancer and cholangiocarcinoma were included in the study group. Out of twenty patients 8 patients had gall bladder cancer and twelve patients had cholangiocarcinoma. In this study maximum incidence of gall bladder cancer and cholangiocarcinoma were seen in sixth decade of life. Males and females are affected with a ratio of 1: 1 in gall bladder cancer. Males are predominantly affected in cholangiocarcinoma with males to female's ratio of 5: 1. Jaundice and lump in abdomen were the commonest presenting symptoms in the present series. Hepatomegaly was present in all the cases of series. Metastatic nodule at umbilicus (Sister Mary Joseph nodule) was present in 1 patient with cholangiocarcinoma.



Fig. 1: Metastatic nodule at umbilicus (Sister Mary Joseph nodule)

Farmers were predominantly affected with a farmer: others ratio of 5.7: 1.

All the patients with gall bladder cancer and cholangiocarcinoma had extreme hyperbilirubinaemia with significant elevation of direct fraction of serum bilirubin level. Anaemia was detected in 55 percent of patients. All the patients with carcinoma gallbladder and cholangiocarcinoma had extreme hyperbilirubinaemia with significant elevation of direct fraction of serum bilirubin level. Patients in both groups had minimal depression of total protein levels. There was little elevation of serum alkaline phosphatase in patients with gallbladder cancer and moderate elevation was seen in patients with cholangiocarcinoma.

Similarly there was little elevation of serum transaminases in patients with gallbladder cancer and moderate elevation was seen in the patients with cholangiocarcinoma. Patients in both the groups showed elevation in the prothrombin time. The diagnostic value of the liver function tests were enhanced when more than one test showed abnormal results. Liver function tests were not of any use in distinguishing between gallbladder cancer and cholangiocarcinoma.

On ultrasonography and computerized tomography scan 9 patients i.e. 45 % revealed associated gall stones. Both of these investigations detected hepatomegaly, dilated IHBR and dilated

ORIGINAL ARTICLE

hepatic ducts in 100% patients with obstructive jaundice caused by gallbladder cancer and cholangiocarcinoma. In detection of mass site, liver infiltration, lymph node involvement, ascites and other organ involvement both ultrasonography and CT Scan were equally effective.



Fig. 2: Ultrasonography showing mass in gallbladder

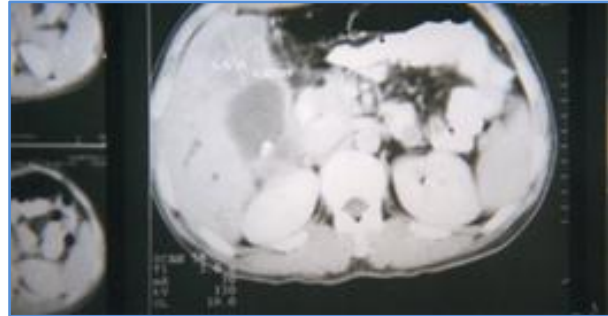


Fig. 3: CT Scan showing mass in fundal region of gallbladder

Percutaneous transhepatic cholangiography (PTC) was 100 per cent effective in showing dilated biliary tree above the level of obstruction in the patients with obstructive jaundice due to biliary tract malignancy.

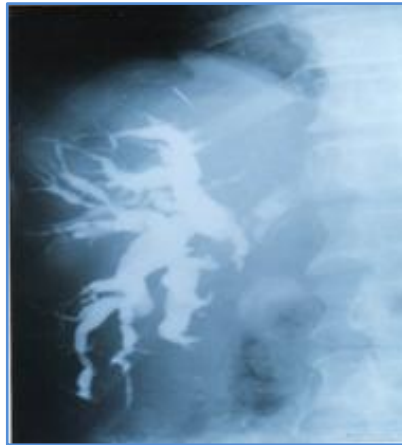


Fig. 4: PTC in a case of cholangiocarcinoma showing dilated IHBR and dilated left and right hepatic ducts

Diagnostic laparoscopy yielded additional information of the liver and biliary tract and allowed accurate evaluation of extent and degree of neoplasm and involvement of lymph nodes and other organs. Target organ biopsy was successfully obtained under vision. Two patients who underwent laparoscopy had gallbladder mass with lymph nodes at porta hepatis and one patient had in addition to it, liver metastasis and peritoneal seeding. No major surgical treatment was planned in these patients.

Treatment offered was mainly palliative in nature in majority of cases. Non-operative palliation included Percutaneous Transhepatic Biliary Drainage (PTBD) and operative palliation included cholecystectomy along with Roux-en-Y hepatico or choledocho-jejunostomy.

ORIGINAL ARTICLE



Fig. 5: PTBD performed in a patient with cholangiocarcinoma as a palliative management

Definitive treatment was offered in 2 patients who included surgical resection of tumour mass, cholecystectomy and Roux-en-Y hepatico or choledocho-jejunostomy.

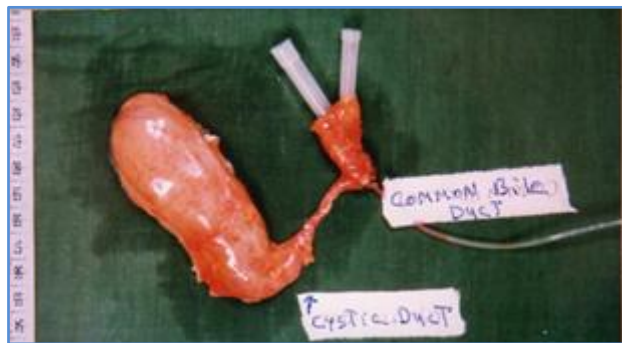


Fig. 6: Gallbladder, common hepatic duct

Outcome of patients with gallbladder cancer and cholangiocarcinoma were not good in 60 per cent cases as they were discharged with their own request with no treatment.

In those patients, who were offered an operative or palliative treatment, 100 percent patients showed a decrease in post-operative serum bilirubin level and were discharged with satisfactory management.

One patient expired within 24 hours after operation in whom laparotomy and biopsy was performed.

One patient of cholangiocarcinoma died 3 years and 8 months after surgical resection of tumour mass with cholecystectomy and Roux-en-Y hepaticojejunostomy.

DISCUSSION: Biliary tract malignancy continues to disappoint the surgeons and patients despite improved diagnostic capabilities, better perioperative care and more aggressive surgical approach based on improved knowledge of the natural history of these malignancies. Overall 5 years survival remains below 5 percent.^{5,6,7}

ORIGINAL ARTICLE

This poor survival is due to late diagnosis, as biliary tract malignancies progress to inoperable stage relatively early in the course of the disease. Even at advanced centres where radical surgical treatment has been advocated, 60-90 percent of tumours are wide spread at operation.^{8,9} In this study all 20 patients i.e. 100 percent patients with biliary tract malignancy were presented with jaundice. Kelly, Chamberlain¹⁰ reported the incidence of jaundice in carcinoma of gallbladder to be 34 percent while that reported by Shukla¹¹ was 72 per cent. In the present series, out of 20 patients, 17 patients i.e. 85 percent patients had a mass in upper right quadrant.

Shukla reported an incidence of 80 per cent of palpable mass in right hypochondrium which is close to the present study. Being economically affordable and non-invasive, ultrasonography was the first line screening investigation in all patients with gallbladder cancer and cholangiocarcinoma in our study.) Dalla¹² are of the view that ultrasonography is 88 percent sensitive in detecting carcinoma of gall bladder. CT scan provided similar information as ultrasonography and it is consistent with view of Thompson.¹³ Success of delineation of dilated biliary tree was 100 percent cases and it is consistent with view of Okuda¹⁴ and Pereras.¹⁵ In our study laparoscopy was used as a final investigation in selected patients of biliary tract malignancy and 100 percent yielded additional information about metastasis to the liver and lymph nodes at porta hepatis.

Biopsy was taken in all cases. Easter¹⁶ reporting on the experience of 120 patients, who had diagnostic laparoscopy reported that a diagnostic yield of about 95 per cent can be expected. Jori and Peschle¹⁷ reported a positive yield of 69 per cent for laparoscopic biopsy as opposed to 39 per cent for the blind percutaneous procedure. In all patients of gallbladder cancer and cholangiocarcinoma in whom biopsy were taken, the histopathology showed adenocarcinoma. Malignancy of both gall bladder and the bile ducts are almost always adenocarcinomas.¹⁸

In those patients, who were offered an operative or palliative treatment in our study, 100 per cent patients showed a decrease in post-operative serum bilirubin level and were discharged with satisfactory management. One patient expired within 24 hours after operation in whom laparotomy and biopsy was performed. One patient of cholangiocarcinoma died 3 years and 8 months after surgical resection of tumour mass with cholecystectomy and Roux-en-Y hepaticojejunostomy.

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ORIGINAL ARTICLE

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