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RESEARCH ARTICLE
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FREQUENCY OF CHOLANGIOCARCINOMA IN PATIENTS OF OBSTRUCTIVE JAUNDICE IN SURGICAL DEPARTMENT OF LADY READING HOSPITAL, PESHAWAR

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ABSTRACT:

INTRODUCTION:

Cholangiocarcinoma is the second most common primary hepatic cancer. Despite advances in diagnostic techniques during the past decade, cholangiocarcinoma is usually encountered at an advanced stage. In this review, we describe the classification, diagnosis, and initial management of cholangiocarcinoma with obstructive jaundice. Cholangiocarcinoma (CC) is an epithelial malignancy with markers of cholangiocyte differentiation arising within the biliary tree. It is characterized by a marked genetic heterogeneity which explains its high therapeutic resistance. CC is rare but related mortality is high because it is most often diagnosed at a locally advanced stage, not amenable to curative surgery.[2] As no such study has been conducted in our population for the last five years so this will provide us the latest and updated information regarding frequency of common causes of obstructive jaundice. More over the results of this study will be compared with other studies conducted on national and international level to observe any significant difference in the disease pattern. The recommendations will be suggested regarding starting baseline treatments of patients with obstructive jaundice keeping in front the results of this study.

OBJECTIVE:

To determine the frequency of cholangiocarcinoma in patients of obstructive jaundice.

METHODOLOGY:

The present study was carried out at the department of General Surgery, Lady Reading Hospital Peshawar. It was a descriptive cross sectional study and duration of study was one year from 1st August 2019 to 30th July 2020. The sample size was 241. All the patients presenting with clinical jaundice having serum bilirubin >3 mg/dl[14], alkaline phosphatase levels > 306 mg/dl, age between 18-60 years and both gender were included The diagnosis in all these cases was based on history, clinical examination and routine laboratory investigations including Liver Function Tests (LFT's). Ultrasound was done in all patients for the diagnosis of cholangiocarcinoma. All these patients were prepared for surgery for 2 to 3 days after admission with injection vitamin K, intravenous

antibiotics and infusion Mannitol, hydration status checked and corrected. After preparation all the patients were operated on the next list and in cases where mass is found biopsy were taken and sent for histopathology to detect cholangiocarinoma. All the data was analyzed in SPSS 20.0

RESULTS:

In the current study a total of 241 patients were observed in which 75(31%) patients were in age range 18-30 years and 166(69%) patients were in age range 31-60 years. 140(58%) patients were male and 101(42%) patients were female. More over 7(3%) patients had cholangicarcinoma and 234(97%) patients didn't had cholangicarcinoma.

CONCLUSION:

Our study concludes that the frequency of cholangiocarcinoma was 3% in patients of obstructive jaundice.

KEYWORDS: Cholangiocarcinoma, Obstructive jaundice**.**

INTRODUCTION:

Cholangiocarcinoma is the second most common primary hepatic cancer. Despite advances in diagnostic techniques during the past decade, cholangiocarcinoma is usually encountered at an advanced stage. In this review, we describe the classification, diagnosis, and initial management of cholangiocarcinoma with obstructive jaundice. Cholangiocarcinoma (CC) is an epithelial malignancy with markers of cholangiocyte differentiation arising within the biliary tree. It is characterized by a marked genetic heterogeneity which explains its high therapeutic resistance. CC is rare but related mortality is high because it is most often diagnosed at a locally advanced stage, not amenable to curative surgery.[2] Although the incidence of CC is rapidly increasing it remains a rare disease. Data about endoscopic therapeutic options are often comprised into large databases of malignant obstructive jaundice mainly due to pancreatic head cancer. This may have influenced the reported outcomes and benefits of endoscopic treatment modalities.[3,4]

Obstruction in the drainage system of bile causes raised levels of bilirubin i.e.>1.2mg/dl[5] in the blood (surgical jaundice)[6]. It could be a partial or complete reduction in secretion or block to flow of bile and /or its components into the duodenum[7]. Normally bile is formed in hepatic canaliculi and is excreted at a rate of 40 ml/hr4, from there it is drained into right and left hepatic ducts[8]. The two ducts unite tofrom common hepatic duct (<2.5cm), which later joins cystic duct (3cm) to form common bile duct (CBD), 7.5cm in length[8]. Injury to common bile duct causes increased levels of serum alkaline phosphatase i.e.>306 mg/dl[8]. The symptoms of obstructive jaundice include jaundice with or without pain, dark urine, pruritis, pale stools, weight loss and anorexia.[15] There are various causes due to which the normal flow of bile is obstructed[7]. Choledocholithiasis is the presence of stones inside the lumen of CBD, and leads to outflow obstruction of bile[8]. Carcinoma Head of pancreas impinges upon the lumen of CBD, where as cholangiocarcinoma and carcinoma gall bladder causes intraluminal obstruction[7,8]. Strictures and pancreatitis are less common causes[7]. The best diagnostic tool to identify the cause and level of obstruction is ultrasound[8,9,]. It is the gold standard investigation for demonstrating gall stones[9,11]and it differentiates obstructive from non obstructive jaundice[10,] Ultrasound can also pick masses in the pancreas, liver and CBD though less sensitive than CT (computed tomography) scan[10,11]. In a study, out of 60 cases of surgical jaundice, overall leading cause was CBD stones (35%)[7]. The second commonest cause was found to be carcinoma head of pancreas (30%)[7]. Carcinoma of common bile duct was 11.66%, and carcinoma gall bladder was 13.33%[7]. In another study, out of 116 patients, the commonest cause was carcinoma head of pancreas 44%, 30% choledocholelthiasis, 8% cholangiocarcinoma and 6% carcinoma gall bladder.[14]

In another, study out of 50 patients, 30% had carcinoma head of pancreas, 22% had choledocholelthiasis, 16% carcinoma of gall bladder, 6% cholangiocarcinoma and post cholecystectomy biliary stricture 8%.[1] In another recently published study, out of 100 patients, the

commonest cause was carcinoma gall bladder 32%, 22% carcinoma head of pancreas, 28% choledocholithiasis, and 4% cholangiocarcinoma.[16]

OBJECTIVE:

To determine the frequency of cholangiocarcinoma in patients of obstructive jaundice.

METHODOLOGY:

The present study was carried out at the department of General Surgery, Lady Reading Hospital Peshawar. It was a descriptive cross sectional study and duration of study was one year from 1st August 2019 to 30th July 2020. The sample size was 241 which was calculated on WHO formula for sample size calculator by keeping 6% prevalence of cholangiocarcinoma in obstructive jaundice [15], confidence interval 95% and margin of error 3%. Non probability consecutive sampling technique was used for sample collection. More over all the patients presenting with clinical jaundice having serum bilirubin >3 mg/dl[14], alkaline phosphatase levels > 306 mg/dl, age between 18-60 years and both gender were included while patients with indirect hyperbilirubinemia or intrahepatic cholestasis of pregnancy, Hepatitis: which is detected by elevated serum bilirubin but alkaline phosphatase levels may be normal. The diagnosis in all these cases was based on history, clinical examination and routine laboratory investigations including Liver Function Tests (LFT's). Ultrasound was done in all patients for the diagnosis of cholangiocarcinoma. All these patients were prepared for surgery for 2 to 3 days after admission with injection vitamin K, intravenous antibiotics and infusion Mannitol, hydration status checked and corrected. After preparation all the patients were operated on the next list and in cases where mass is found biopsy were taken and sent for histopathology to detect cholangiocarinoma. All the data was analyzed in SPSS 20.0 Mean and standard deviations were computed for numerical variable like age where as categorical variable like gender, smoking, family history and diabetes mellitus, cholangicarcinoma were described in term of frequency and percentages. Cholangicarcinoma was stratified with respect to age, gender, smoking, family history and diabetes mellitus to see the effect modifiers. Post stratification chi square test was applied in which P-value ≤0.05 was considered as significant.

RESULTS:

In the current study a total of 241 patients were observed in which 75(31%) patients were in age range 18-30 years and 166(69%) patients were in age range 31-60 years. (table no 1). 140(58%) patients were male and 101(42%) patients were female. (Table no 2). 53(22%) patients were smokers and 188(78%) patients were non smokers. (table no 3). 22(9%) patients had positive history of obstructive jaundice and 219(91%) patients had negative history of obstructive jaundice. (table no 4). 80(33%) patients were diabetic and 161(67%) patients were non diabetic. (table no 5). More over 7(3%) patients had cholangicarcinoma and 234(97%) patients didn't had cholangicarcinoma. (Table no 6).

TABLE NO: 1 AGE DISTRIBUTION

AGE	FREQUENCY	PERCENTAGE
18-30 years	75	31%
31-60 years	166	69%
Total	241	100%

TABLE NO: 2 GENDER DISTRIBUTION

Gender	FREQUENCY	PERCENTAGE
Male	140	58%
Female	101	42%
Total	241	100%

TABLE NO: 3 SMOKING STATUS

SMOKING	FREQUENCY	PERCENTAGE
Smokers	53	22%
Non smokers	188	78%
Total	241	100%

TABLE NO: 4 FAMILY HISTORY

Family History	FREQUENCY	PERCENTAGE
Positive	22	9%
Negative	219	91%
Total	241	100%

TABLE NO: 5 DIABETES MELLITUS

Diabetes	FREQUENCY	PERCENTAGE
Yes	80	33%
No	161	67%
Total	241	100%

TABLE NO: 6 CHOLANGICARCINOMA

CHOLANGICARCINOMA	FREQUENCY	PERCENTAGE
Yes	7	3%
No	234	97%
Total	241	100%

TABLE NO: 7 STRATIFICATIONS OF CHOLANGICARCINOMA WITH RESPECT TO AGE DISTRIBUTION

CHOLANGICARCINOMA	18-30 years	31-60 years	Total	P value
Yes	2	5	7	0.8824
No	73	161	234	
Total	75	166	241	

TABLE NO: 8 STRATIFICATION OF CHOLANGICARCINOMA WITH RESPECT TO GENDER DISTRIBUTION

CHOLANGICARCINOMA	Male	Female	Total	P value
Yes	4	3	7	0.9588
No	136	98	234	
Total	140	101	241	

TABLE NO: 9 STRATIFICATION OF CHOLANGICARCINOMA WITH RESPECT TO SMOKING

CHOLANGICARCINOMA	Yes	No	Total	P value
Yes	2	5	7	0.6697
No	51	183	234	
Total	53	188	241	

TABLE NO: 10 STRATIFICATION OF CHOLANGICARCINOMA WITH RESPECT TO FAMILY HISTORY

CHOLANGICARCINOMA	Positive	Negative	Total	P value
Yes	2	5	7	0.0698
No	20	214	234	
Total	22	219	241	

TABLE NO: 11 STRATIFICATION OF CHOLANGICARCINOMA WITH RESPECT TO DIABETES MELLITUS

CHOLANGICARCINOMA	Yes	No	Total	P value
Yes	2	5	7	0.7920
No	78	156	234	
Total	80	161	241	

DISCUSSION:

Cholangiocarcinoma is the second most common primary hepatic cancer. Despite advances in diagnostic techniques during the past decade, cholangiocarcinoma is usually encountered at an advanced stage. In this review, we describe the classification, diagnosis, and initial management of cholangiocarcinoma with obstructive jaundice. Cholangiocarcinoma (CC) is an epithelial malignancy with markers of cholangiocyte differentiation arising within the biliary tree. It is characterized by a marked genetic heterogeneity which explains its high therapeutic resistance. CC is rare but related mortality is high because it is most often diagnosed at a locally advanced stage, not amenable to curative surgery.[2] Although the incidence of CC is rapidly increasing it remains a rare disease. Data about endoscopic therapeutic options are often comprised into large databases of malignant obstructive jaundice mainly due to pancreatic head cancer. This may have influenced the reported outcomes and benefits of endoscopic treatment modalities.[3,4]

In the current study a total of 241 patients were observed in which 75(31%) patients were in age range 18-30 years and 166(69%) patients were in age range 31-60 years. 140(58%) patients were male and 101(42%) patients were female. 53(22%) patients were smokers and 188(78%) patients were non smokers. 22(9%) patients had positive history of obstructive jaundice and 219(91%) patients had negative history of obstructive jaundice. 80(33%) patients were diabetic and 161(67%) patients were non diabetic. More over 7(3%) patients had cholangicarcinoma and 234(97%) patients didn't had cholangicarcinoma.

Similar results were observed in another study conducted by Siddique K et al[101] in which out of 50 patients, 30% had carcinoma head of pancreas, 22% had choledocholelthiasis, 16% carcinoma of gall bladder, 6% cholangiocarcinoma and post cholecystectomy biliary stricture 8%.

Similar results were observed in another study conducted by Kevin C et al[102] in which out of 60 cases of surgical jaundice, overall leading cause was CBD stones (35%). The second commonest cause was found to be carcinoma head of pancreas (30%). Carcinoma of common bile duct was 11.66%, and carcinoma gall bladder was 13.33%

Similar results were observed in another study conducted by Chalya PL et al[103] in which out of 116 patients, the commonest cause was carcinoma head of pancreas 44%, 30% choledocholelthiasis, 8% cholangiocarcinoma and 6% carcinoma gall bladder.

Similar results were observed in another study conducted by Shukla S et al[104] in which out of 100 patients, the commonest cause was carcinoma gall bladder 32%, 22% carcinoma head of pancreas, 28% choledocholelthiasis, and 4% cholangiocarcinoma.

Similar results were observed in another study conducted by Aziz, M et al[105] in which 84 patients (84%) were suffering from malignancy and 16 patients (16%) were suffering from benign diseases. The incidence of various malignancies was CA gall bladder 44 patients (52%), CA Pancreas 26 patients (31%), Cholangiocarcinoma 8(10%) and Hepatoma 6 patients (7%). Incidence of malignancy in obstructive jaundice is 84%, which gradually increases with the increasing age. The

most common malignancy responsible for obstructive jaundice in female patients is CA gall bladder (52%) and in male patients is CA head of pancreas (31%).

Similar results were observed in another study conducted by Björnsso E et al[106] in which seven hundred and forty nine patients were identified, of whom 241 (32%) had OJ (median age 71 years, 129 women). No one was lost to follow up. The biliary obstruction of 154 patients (64%) was a result of a malignancy: 69 patients (46%) had pancreatic cancer, 44 (29%) had cholangiocarcinoma (CC), 5 (3%) had papilla vateri cancers, and 36 patients (23%) had other malignancies. Of the 87 patients with a benign obstruction, 57 (65%) had choledocholithiasis, 7 (8%) had biliary strictures, 6% had PSC, and the obstruction of 16 patients (20.7%) had other causes. A total of 115 of the 242 patients (48%) had abdominal pain associated with jaundice, whereas 52% had painless jaundice. Thirty four percent of patients with a malignant obstruction had abdominal pain versus 71% of patients with a benign obstruction ($P < .05$). At the end of follow up, only 5% (8 patients) with a malignant obstruction were alive versus 78% with a benign obstruction.

CONCLUSION:

Our study concludes that the frequency of cholangiocarcinoma was 3% in patients of obstructive jaundice.

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