Management of Patients with Ampullary and Periampullary Tumors in Gastro-Entrology and Hepatology Teaching Hospital

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ABSTRACT:

BACKGROUND:

Ampullary and periampullary tumors are composed of a group of malignant and benign neoplasms arising in the region of the ampulla of Vater and are a major problem to the patients and surgeons and their management remains a big challenge.

OBJECTIVE:

Study the age, sex distribution, presentation and management of patients with ampullary and periampullary tumors in Iraq and compare it with other world reports

PATIENTS AND METHODS:

prospective study of 50 patients with ampullary and periampullary tumors carried out in GIT hospital (tertiary center) from January 2013 to March 2015 ,risk factors ,age ,sex ,clinical presentation ,images study ,diagnosis and modality of treatments whether curative or palliative are studied.

RESULTS:

29 (58%) were males and 21 (42%) were females , about the age distribution the mean age was 45 ,about the residency they were mainly from Baghdad in (40%) ,the presenting symptom was obstructive jaundice in 43 (86%) ,duration of illness (range from 1-2 months) with the mean period 45 days , abdominal ultrasound study reveal distended Gallbladders in 76 % , dilated CBD in 82% ,dilated pancreatic duct in 56% , Hepatomegaly in 42% , dilated intrahepatic billiary tree in 64% , and liver secondary in 10% .resection surgery was done in 50% ,palliative surgery in 12% and endoscopic palliation in 38%

CONCLUSION:

Ampullary and periampullary tumors are relatively common. The mean age is 45 years, lower than the western studies. Sex: male are affected 1.4 times more than female with male: female ratio = 1.38 . Abdominal ultrasound is very informative but EUS,CT scan and MRI, MRCP is the cornerstone for the diagnosis, Normal looking papilla does not rule out occult ampullary tumor.

KEYWORDS : ampullary tumor , periampullary , pancreatic , whipple procedure .

INTRODUCTION:

Ampullary and periampullary tumors are composed of a group of malignant and benign neoplasms arising in the region of the ampulla of Vater. Ampullary cancers are often discussed as a group based on their similar presentation, workup, and surgical management. Periampullary cancer is cancer arise within 2 cm. around ampulla of vater and the Origin of cancer is difficult to distinguish[1]. The incidence of ampullary carcinoma increases with age, and the majority of patients present in or beyond their sixth decade of life. There is a slight male preponderance. The most common cancer types of the ampullary region are adenocarcinomas. it is likely that pancreas cancer is the site of origin in up to 90% of cases[1]. There are few established risk factors for cancer of the ampullary region.They include tobacco smoking and inherited susceptibility, which account for only 5–10% of cases. Chronic pancreatitis, type 2 diabetes mellitus, and obesity have been consistently associated with pancreatic cancer and are weak risk factors. The diagnosis of ampullary and periampullary cancer is made on the basis of clinical presentation, laboratory data, and radiologic workup. Patients often have only vague

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symptoms early in the course of their disease. Often, it is not appear until the later stages of the disease . . Lesions occurring in or near the bile duct are much more likely to present with obstructive jaundice . The main imaging modalities include right upper quadrant (RUQ) ultrasonography, computed tomography (CT),magnetic resonance imaging (MRI) with or without magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasound (EUS). The "workhorse" in the workup of patients suspected of a periampullary neoplasm is a multidetector spiral CT and is probably the single most useful diagnostic and staging modality[2].

Upper endoscopy is useful as these lesions can be directly viewed through the endoscope. If visualized, it is relatively straightforward to obtain a biopsy and tissue diagnosis. Additionally, EUS may be performed during upper endoscopy,Fine-needle aspiration (FNA) of any suspected lesions can be performed at the same time as EUS(EUS_FNA) if cytological diagnosis is of benefit[3,4]**.** it is often associated with severe pruritus, coagulopathy resulting from the impaired absorption of the fat-soluble vitamin K and less commonly cholangitis. These conditions are often managed preoperatively by biliary decompression through ERCP but billiary decompression is not an absolute requirement prior to resecting a periampullary cancer in jaundiced patients[5,6]**.** With accurate preoperative staging, the resectability rate for periampullary cancers is approximately 80%[7]**.**curative resection can be done by pancreaticoduodenectomy(whipple procedure). the three main problems that need to be palliated include obstructive jaundice, gastric outlet obstruction, and pain. Nonoperative billiary drainage can be achieved through an endoscopic approach (ERCP) [8,9].

AIM OF THE STUDY:

Study the management of ampullary and periampullary tumors in patients who admitted into the Gastro-intestinal &Hepatology Teaching Hospital in Iraq, study the associated and possible risk factors,patients demographic,tumor types and comparing it with other world reports.

PATIENTS AND METHODS:

With prior approval of the local Institutional Committee for Human Investigation, prospective study of 50 patients with ampullary and periampullary tumors carried out in Gastro-intestinal & Hepatology teaching hospital (the main GIT tertiary center) from January 2013 to March 2015 .Their ages, sex, residence, clinical presentation ,Laboratory data ,imaging study, diagnosis and treatments are studied , during that period total admission was 5464 cases, 604 of them were having GIT malignancies. Preoperative laboratory studies included complete blood picture, blood urea, serum creatinine, fasting blood sugar, prothrombin time, partial thromboplastin time , INR and liver function tests, blood group and Hepatitis screening , tumor markers measurement ,we measure CA 19-9 in 32 patients .

Abdominal ultrasound was done for all the patients; review of gall bladders if normal, removed, distended or gall bladder stones were present. Common bile duct also checked if normal, dilated and if containing stones.

CT was done in all patients . We study the immediately adjacent vascular structures such as the portal vein, superior mesenteric vein, and splenic vein, as well as the superior mesenteric artery (SMA) and celiac axis. MRI and MRCP was done in 38 patients and used to image the biliary tree and the pancreatic duct.

Upper endoscopy is used in all patients and we use it in the diagnosis of amp. and periamp. tumor as these lesions can be directly viewed through the endoscope and in 20 patients it help us to obtain a biopsy and tissue diagnosis.

EUS performed during upper endoscopy in all patients and we search details about the tumor size ,location ,CBD, pancreatic duct , invasion of vascular structures and lymph nodes enlargement . Fine-needle aspiration (FNA) of suspected lesions was performed in 30 patients at the same time as EUS(EUS guided FNA) especially in patients with locally advanced or metastatic disease as tissue diagnosis is of benefit if the patients referred to the oncologist .

Preoperative Billiary Decompression was performed in 15 patients presented with acute cholangitis ,severe pruritus or severe coagluopathy in whom they need further evaluation and stabilization to proceed to major surgical operation .this procedure performed by ERCP and EST with plastic stent insertion .

Patients are staged clinically according to the American Joint Committee on Cancer (AJCC) staging system. These staging criteria are based on the size and extent of the primary tumor (T stage), lymph node involvement (N stage), and the presence of distant metastases (M stage). Based on these criteria, patients are stratified to the different clinical stages that guide prognosis and treatment.

Inclusion Criteria : (1)
patient referred to Gastroenterology and Hepatology Teaching Hospital with ampullary and periampullary tumor. (2)Patients with obstructive jaundice during investigation diagnosed with ampullary and periampullary tumor .
Exclusion criteria : patients diagnosed with ampullary and periampullary tumors who travel outside our country .

RESULTS :

50 patients with Ampullary and periampullary tumor were included .They represented 0.9% of the total admissions to the GIT Center during the period of study (5464 patients) , and 8.2% of the GIT malignancies (604 patients). Demographic characteristic; 29 of them were males (58%) and 21 were females (42%) with male to female ratio equal to 1.38/1 .

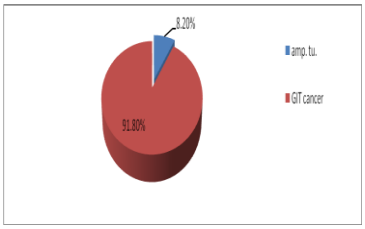

Figure 1 : Percentage of ampullary tu. In relation to other GIT cancer.

In our study 29(58%) were males(mean age 47 year, ranging between 38 year to 74 year) and 21 (42%) were females(mean age 43 year ,ranging between 34 year to 75 year) , about the age distribution they were from 34 to 75 years old and the mean age was 45,the peak age were in between 50-60 year as there are 15 patients (30%) within this range as in figure 3 .

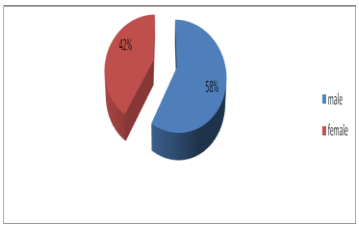

Figure 2: Sex distribution.

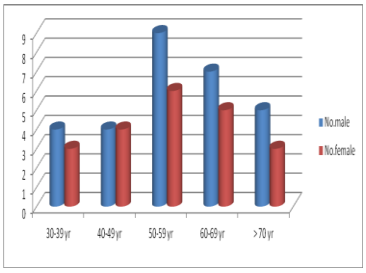

Figure 3: Ages distribution of each sex.

The residency of the patients were taken and the distributions of them on different cities shown in table 1;they were mainly from Baghdad ,followed by Dhi Qar .

Table 1:The residency of the patients.

Residence	No. of patients	Percentages
Baghdad	20	40%
Dhi Qar	7	14%
Al-Diwaniyah	5	10%
Al-Amarah	4	8%
Al-Basra	3	6%
Al-Najaf	3	6%
Diyala	3	6%
Al-Ramadi	2	4%
Al-Samawah	2	4%
Al-Kut	1	2%

The main presenting symptoms and signs of the patients were studied and shown in table 2; the main symptom and sign was jaundice followed by palpable gallbladder .

Table 2 : The presenting symptoms and signs of the patients.

Presenting symptoms and signs	No. of patients	Percentages
jaundice	43	86%
Pruritus	24	48%
Palpable gallbladder	32	64%
Anorexia	23	46%
Weight loss	15	30%
Abdominal pain	10	20%
Cholangitis	8	16%
Vomiting	7	14%
Haematomesis&\or malena	4	8%
Abdominal mass	4	8%

The total serum billirubin (TSB) was increased in 43 patients (86%) and 17 patients (34%) was between 5.1- 10 mg \dl and the elevation was mainly of direct type (the conjugated billirubin) which indicate extra hepatic cholestasis. TSB was normal in 7 patients (14%) .

Table 3 : Total serum billirubin in our patients.

Level of TSB	No. of patients	Percentages
Normal (below 2 mg\dl)	7	14%
2 - 5 mg\dl	10	20%
5.1 – 10 mg\dl	17	34%
10.1 – 20 mg\dl	11	22%
More than 20 mg\dl	5	10%

The possible risk factors and other associated patients factors were studied and the results shown in table 4 ; we found smoking as an associated factor in 58% of patients .

Table 4 : Associated factors in our patients .

Associated factors	No. of patients	Percentages
Smoking	29	58 %
Gallstone disease	13	26%
Family history of GIT malignancy	12	24%
Diabetes mellitus	9	18 %
Alcoholism	6	12 %
History of pancreatitis	4	8%
Previous GIT surgery	3	6%
Familial adenomatous polyposis(FAP)	2	4%

Pre operative billiary decompression was done to relieve the obstruction in 15 patients (30%) by endoscopic retrograde cholangiopancreatography (ERCP) and endoscopicSphincterotomy (EST) done with plastic stents insertion , shown in table 9.

Table 9: Indication of Pre operative billiary decompression.

Preoperative billiary decompression (indication)	15 patients	Percentage (30%)
Acute cholangitis	8	53%
Severe pruritus	6	40%
Impair liver function(e.x severe coagluopathy)	1	7%

Clinical staging of the patients was done according to the the American Joint Committee on Cancer (AJCC) staging system and the results was shown in table10, most of our patients were in stage II or above .

Table 10 : The clinical stages of the patients.

Clinical stage	Stage criteria	No. patients	Percentage
Stage IA	T1,N0,M0	0	0%
Stage I B	T2,No,M0	9	18%
Stage II A	T3,N0,M0	14	28%
Stage II B	T1\2\3 ,N1 ,M0	10	20%
Stage III	T4,any N,M0	12	24%
Stage IV	anyT,anyN,M1	5	10%

In our study 31 patients (62%) do surgery and the other 19 patients (38%) do endoscopic palliation by ERCP ,EST and insertion of self expandable metallic stenting (SEMS) . Those patients, who underwent endoscopic metallic stenting, are in advanced stage or unfit for general anesthesia or both. 4 patients from them refused surgery.

Table 11: Types of procedures done for the patients.

Types of procedure	No. of patients	Percentage
Pancreaticoduodenectomy (whipple procedure)	22	44%
Local excision (Ampullectomy)	3	6%
Bypass-surgery(choledochojeujunostomy and Gastrojeujunostomy)	6	12%
Chemical splanchnicectomy	5	10%
Gastroduodenal stenting	4	8%
Plastic billiary stenting	15	30%
Metallic billiary stenting	19	38%

The results of histopathology examinations of the 25 (50%) surgically removed specimens were studied and shown in table 12 ; and 76% of them was adenocarcinomas .

Table 12 : The results of histopathology of resected tumors.

Histopathology	No. of patients(total 25)	Percentages
Adenocarcinomas	19	76%
Gastrointestinal stromal tumor (GIST)	4	16%
Neuroendocrine tumors	2	8%

DISCUSSION :

The ages of our patients were compared with other studies (Table 13) outside Iraq. In our study, the ages distribution of the patients were between 34-75 year (38-74 year for male patients and 34-75 year for female patients) and the peak were in between 50-60 year as there are 15 patients (30%) with their ages between 50-60 year .

Table 13: Age incidence in different studies.

Items	Our study	Philippines society study(10)	Blumgart study(11)
Mean age	45	61	65
Peak	50-60	61-70	61-70

Concerning sex, we compared our study with Philippines society of Gastroenterology (PSG), Blumgart study and Mehta study[12]**.** As shown in table(14)

Table 14: The gender incidence in different studies.

	Our study	PSG study	Blumgart study	Mehta study
M/F	1.38	1.27	1.2	1/1

Elevated level of TSB and alkaline phosphatase were more dependable than liver enzymes in assessing these tumors, such finding were also reported in the western literatures[13]**.**
ESR was elevated in 56% of the patients with about 30% of them were above 50 , and this finding is higher than what reported in other studies like PSG ,Euro J. 2000[14] and Blumgart .
We compare the associated factors of our study with study of Mark A. Talamini et al**.** which is published in ANNALS OF SURGERY and shown in table 18,

Table 18 :Comparison of associated factors in our patients with Talamini study.

Associated factors	Our study	Mark A. Talamini study
Smoking	58 %	30%
Gallstone disease	26%	18%
Alcoholism	12 %	16%
History of pancreatitis	8%	5%
Familial adenomatous polyposis(FAP)	4%	7%

We also do comparison between the types of procedure done for our patients with that of *Mark A. Talamini study,* showing lower percentage of whipple procedure and higher percentage of palliative self expandable metallic stenting (SEMS) because most of our patients presented in late stages ,, table 19.

Table 19: Types of procedures done for our patients compared with Talamini.

Types of procedure	Our study	Mark A. Talamini study
Pancreaticoduodenectomy (whipple procedure)	44%	87%
Local excision (Ampullectomy)	6%	1%
Bypass surgery (choledochojeujunostomy and Gastrojeujunostomy)	12%	4%
Chemical splanchnicectomy	10%	12%
Gastroduodenal stenting	8%	3%
Plastic billiary stenting	30%	23%
Metallic billiary stenting	38%	8%

The results of histopathology examinations of the 25 (50%) surgically removed specimens were compared to Charles J. Yeo et al study published *in ANNALS OF SURGERY* ;

Table 20 : Histopathology of our study compared with Charles J Yeo study.

Histopathology	Our study	Charles J. Yeo study
Adenocarcinomas	76%	68%
Gastrointestinal stromal tumor (GIST)	16%	2%
Neuroendocrine tumors	8%	5%
Chronic pancreatitis	0%	11%

CONCLUSION:

1-) Ampullary carcinoma is not a rare cancer. It represents 0.9% of total admissions and 8.2% of the GIT malignancies referred to the GIT Center.

2-) Demographic variables show age incidence(the mean age was 45 years) lower than the western studies. gender: male are affected about 1.4 times more than female . Residency: they are mainly from Baghdad followed by Dhi Qar.

3-) obstructive Jaundice is the main presenting symptom, which is fluctuating in nature with pruritis to a lesser degree. Average duration of symptoms was 45 days.

4-) Abdominal ultrasound is informative but it need further evaluation by CT scan ,MRI ,MRCP,EUS ,EUS-FNAC .

5-) any gastroenterologist should be aware about the possibility of ampullary and periampullary tumor when dealing with patients with CBD stones.

6-) An aggressive surgical approach to ampullary tumours is justified by the low proportion of benign lesions, the low postoperative mortality and improved long-term survival, so Whipple operation become the standard treatment while Local resection is preserved for selected cases.

Recommendation;

1-) patients with ampullary and periampullary tumors need referral to high volume subspecialty center where facilities to do sophisticated laboratory investigations ,imaging studies and interventions that are not available in other general hospitals or even when they are available there is no sufficient experiment to deal with such diseases

2-) improvement in patients management and outcome can be achieved by introduction of positron emission tomography (PET scan) . The role of PET in the preoperative staging of periampullary cancers is evolving. One of its advantage is the ability to differentiate between benign and malignant lesions, and there are reports of PET scans identifying CT occult primary pancreatic cancers in patients with unclear etiology of painless jaundice**.**

3-) Tissue diagnosis of adenocarcinomas is not required prior to an attempt at a curative resection in most cases. The presentation of jaundice and weight loss along with mass or stricture of the distal bile duct should be considered carcinoma until proven otherwise in a patient with appropriate risk factors**.**

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