

## "A Study on Incidence, Clinical Presentation & Management of Periapillary Carcinoma"

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### **Abstract :**

#### **Background :**

Periapillary carcinoma accounts for the majority of pancreaticoduodenectomies at our institute. The ampulla of Vater tumors incidence rate is about 0.53 /1 lakh population per year(1). Among the gastrointestinal tract malignancies, periapillary cancers account for 5 %(2).

A periapillary carcinoma is defined as – one that is arising in the region of the ampulla of Vater within 2cm of it, maybe from one of four origins- pancreas, bile duct, the ampulla & it's surrounding duodenal part. Surgical series related to periapillary tumors have demonstrated that patients with ampullary tumors have a better prognosis as compared to those with pancreatic or bile duct tumors(3,4,5,6)

The government general hospital, Kakinada, Andhra Pradesh, India is a tertiary center for two districts, and a lot of sick people attend this hospital with high confidence in the doctors of this institute. As there is no-good number of studies regarding periapillary malignancies from our institution, we have selected this study to evaluate incidence, clinical features and management modalities available for periapillary malignancies.

#### **Materials and methods :**

This descriptive study is conducted prospectively in the department of surgery, GGH Kakinada, between January 2019- May 2020. Included in this study are 30 cases of periapillary carcinomas, which during final histological examination proved to be the ampullary, cholangial, or duodenal origin. All patients had adenocarcinoma of the periapillary region. All patients underwent detailed clinical examination.

Routine investigations like hemogram, renal function test, liver function test, chest x- ray, electrocardiogram were done in all patients. Radiological investigations like USG Abdomen & pelvis, CECT abdomen & pelvis were done as a part of staging evaluation of cancers. ERCP and stenting in selected patients were done either outside or at our institute.

#### **Results :**

In my study, a total of about 30 patients were studied. Out of the 30 patients, 18 had ampullary carcinoma, 2 had cholangiocarcinoma, 4 had duodenal carcinoma, 6 had carcinoma head of the pancreas.

Twenty-seven patients underwent curative resection for periapillary carcinoma out of 30 patients. Tumor in the remaining 3 of them was unresectable & managed with palliative care.

- The mean patient age was 51 years.
- 22 were males, and 8 were females.
- Jaundice was present in 24 patients. 10 patients had bilirubin < 5 mg%
- The average duration of illness was five months, the range being two months to twelve months.
- The mean duration of hospital stay was 14 days that range between 12 days to 35 days.
- All patients had icterus (100%).
- 55% of patients had pain abdomen, of which 42% of patients had a typical colicky type of abdominal pain.
- 44% of patients had a fever, of which 31% of patients were associated with chills and rigors.
- Symptoms of complete biliary tract obstruction, clay-colored stools and high colored urine presented in 30% of patients.
- Cachexia was seen in 29% of patients.
- Gall Bladder was palpable in 52% of patients.
- The mean serum bilirubin value was 12.5 mg%
- The range between 3-24 mg/dl.
- The average ALP value was 530 IU/L, and the range between 108-1230 IU/L.
- Urine examinations showed absent urobilinogen in 42 % of patients.
- The serum albumin range was 2.0-5.5 gm %. In More than 50 % of patients, the A: G ratio was reversed.
- Ultra sonogram revealed IHBR dilatation in 90% of pts.

*Preoperatively all patients received three doses of Vit K and fresh frozen plasma in selective patients. The coagulation profile was monitored by measuring PT and INR.*

- *Standard pancreaticoduodenectomy was done in 21 patients & PPPD in 4 patients & triple bypass done in 2 patients.*
- *The mean transfusion requirement was two units.*
- *The mean operating time was 5 hours.*
- *Major complications were present including pancreatic leak(2 patients), biliary leak(4patients), biliary gastritis(1 patient) & were managed conservatively*
- *Minor wound infections were present in 12 patients(31.9%).*
- *Delayed Gastric emptying was seen in 9 patients(13%).*
- *Relaparotomy was done in 2 patients(6.6%), the indication being post-operative hemorrhage.*
- *Post-operative mortality was 11%(3 patients).*
- *The mean size of the tumor was three cm.*
- *21 patients had the node-negative disease, and 9 patients had node- positive disease.*
- *Biopsy report revealed about five R1 resections who were subsequently sent for adjuvant chemoradiotherapy.*

**Conclusion :**

*Our institutional observational study suggests that periapillary carcinoma is commonly seen in the fifth and sixth decade of life, with males having a greater propensity of developing this disease by 2.7 times more than females.*

*Jaundice and loss of appetite with anorexia are the most common presenting complaints, leading to most patients being diagnosed at early localized and operable stage.*

*Palpable gallbladder with progressive jaundice of waxing & waning type & pruritis & high bilirubin levels usually suggests periapillary carcinoma.*

*Only 16% of patients presented with metastatic disease, with the liver being the most common metastatic involvement site.*

*Post-operative findings suggest that moderately differentiated adenocarcinoma is the most common histopathology observed in these patients, and ampulla being the most common site of primary origin of this disease with a good prognosis compared to others.*

*Early detection of cancer and staging and proper selection of the patient is more important to gain benefit from resection of the tumor, whereas late presentation and those patients not suitable for resection will have a good quality of life with palliative surgery.*

*Improving deranged bilirubin and liver enzymes, correction of anemia, and hepatorenal problem improves the surgical results (morbidity and mortality).*

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## **I. Introduction**

Periapillary tumors originate from the pancreas' head, ampulla of Vater, distal common bile duct, and the duodenum. They constitute 30 % of malignant tumors that arise from the pancreatic head region. Periapillary tumors display unique characteristics due to their specific origin.

Periapillary carcinomas are 2 to 3 cm in diameter and are divided into three forms; intramural protruding, exposed protruding, and ulcerating form.

The hallmark clinical presentation for periapillary cancer is jaundice, which results from obstruction of the intrapancreatic portion of the common bile duct. Obstructive jaundice fluctuates when the tumor sloughs off. Jaundice is associated with dark urine, light stool, and pruritis.

Nonspecific symptoms such as nausea, anorexia, weight loss, and fatigue are common in many patients with periapillary cancer. Some may complain of pain in the upper abdomen, emaciation, dark stools, anemia, and upper gastrointestinal obstruction. On initial presentation, jaundice is the most common physical finding. Evidence of cutaneous scratching is commonly present, secondary to pruritis. Abdominal examination reveals hepatomegaly with the palpable gall bladder.

Pruritis is a well-documented manifestation among patients with liver diseases and intrahepatic or posthepatic cholestasis. The pruritis is generalized and mostly noticed on hands, feet, and around tight-fitting clothes, while rarely seen over the face, neck, and genital areas. The pathogenesis is still not clearly understood, as the exact substance responsible for it is still unknown. Some believe it is caused by the bile acids in the blood (cholemia) or skin, but there is a poor correlation between bile salts skin concentration and the intensity of

pruritus.

Recently, the research found an elevation of endogenous opioids in these patients' blood, and treatment with the opiate antagonist naloxone improved pruritus. The itch in patients with cholestatic pruritus can be lessened by treatment with cholestyramine, phototherapy, plasmapheresis, which lower or remove the unknown circulating pruritogen; antihistamines can be used as adjuvants.

Ursodeoxycholic acid has been used (10-15 mg/kg) with success. Interestingly, some serotonin subtype-3-receptor antagonists like ondansetron, given intravenously, have helped treat cholestatic pruritus.

Laboratory analysis often reveals elevated liver function studies, reflecting the degree of biliary obstruction. In deeply jaundiced patients with malabsorption of fat-soluble vitamins, prolongation of the prothrombin time may be seen.

USG, CT, and MRCP are widely used because of their availability and non- invasiveness. The importance of these techniques in diagnosing ampullary carcinoma will continue to evolve with the experience accumulated. In this study we evaluate the incidence ,clinical presentation and management of peri ampullary carcinoma.

## **II. Materials And Methods**

This descriptive study is conducted prospectively in the department of surgery, GGH Kakinada, between January 2019- May 2020.

Included in this study are 30 cases of periampullary carcinomas, which during final histological examination proved to be the ampullary, cholangial, or duodenal origin.

All patients had adenocarcinoma of the periampullary region. All patients underwent detailed clinical examination.

Routine investigations like hemogram, renal function test, liver function test, chest x- ray, electrocardiogram were done in all patients.

Radiological investigations like USG Abdomen & pelvis, CECT abdomen & pelvis were done as a part of staging evaluation of cancers. ERCP and stenting in selected patients were done either outside or at our institute.

The study has received the acceptance of the Institute Ethics Committee and informed written consent was taken from all enrolled patients.

### **Inclusion criteria:**

- 1.Both males & females
- 2.Radiological/Pathologically proven cases of periampullary carcinoma.

### **Exclusion criteria:**

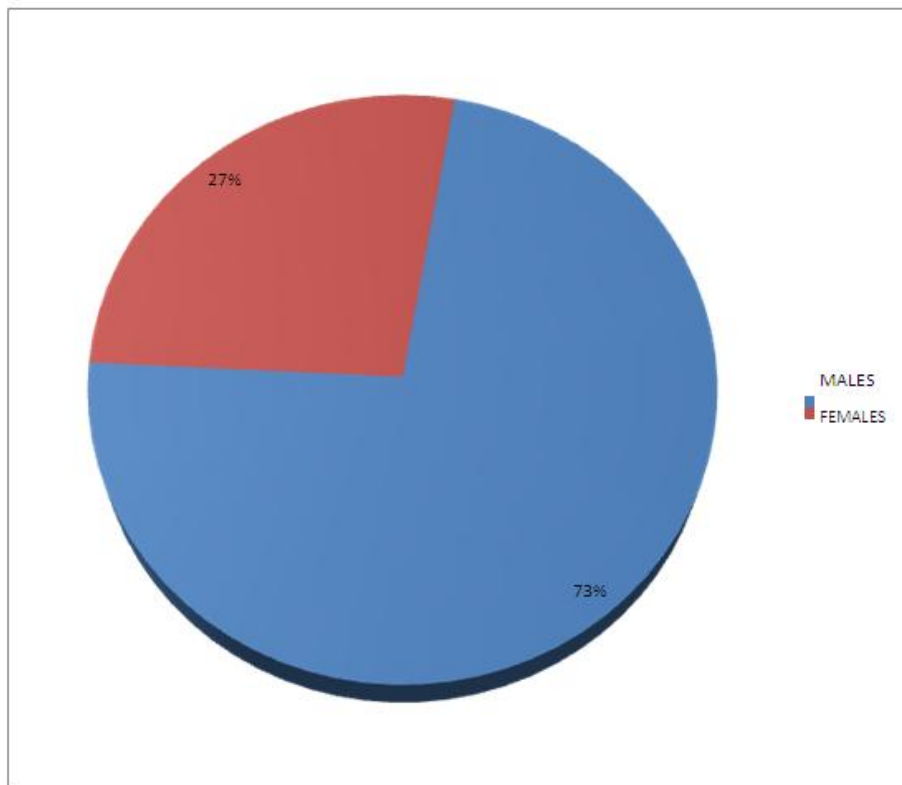
- 1.pregnant women
- 2.benign pathologies

Patients deemed suitable for resection underwent either a standard pancreaticoduodenectomy (21patients) or pylorus-preserving pancreaticoduodenectomy (4 patients).The triple bypass was done in 2 patients. Three of the patients had unresectable disease & were not fit for surgery, So they were managed by palliative care.

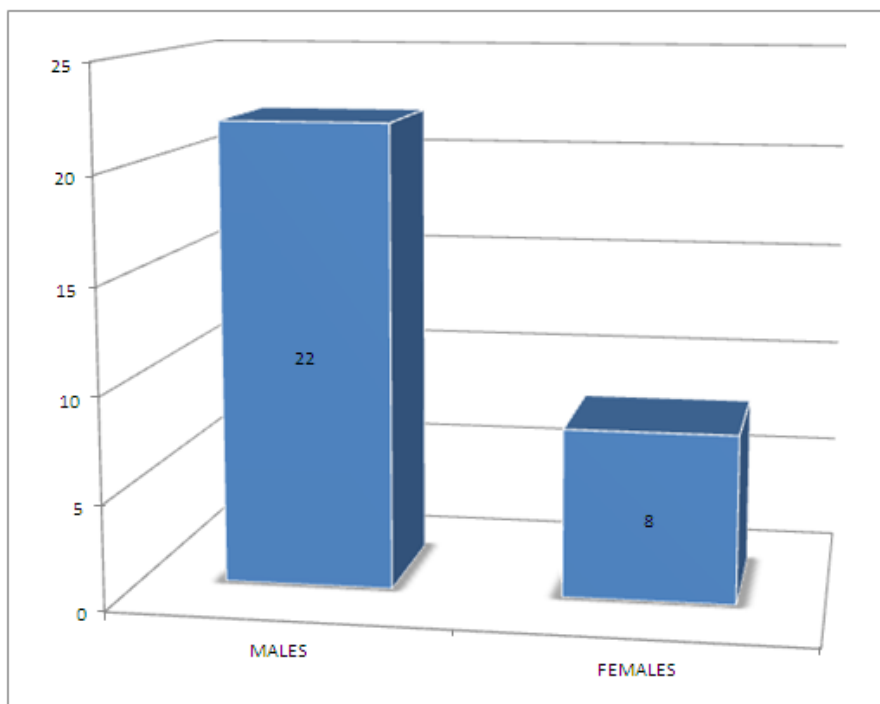
## **III. Observations & Results**

The total number of patients studied is 30, of which 22 were males (73%), and 8 were females (27%), and the male: female ratio was 2.75:1.

Diagrams showing sex incidence



Graph 1- pie diagram showing gender distribution



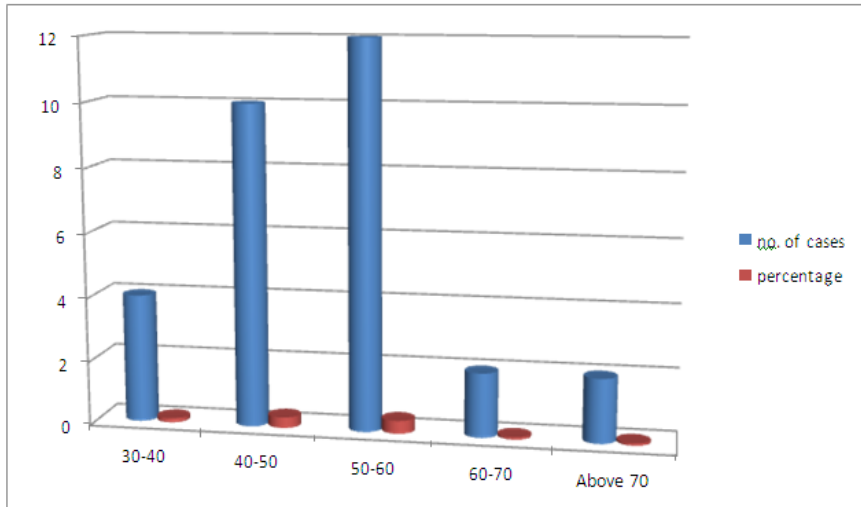
Graph 2-bar chart showing gender variation

Age Incidence:-

Age group	No.of cases	Percentage
30-40	4	13%
40-50	10	33%

50-60	12	40%
60-70	2	7%
Above 70	2	7%

**Table 1 age Incidence.**



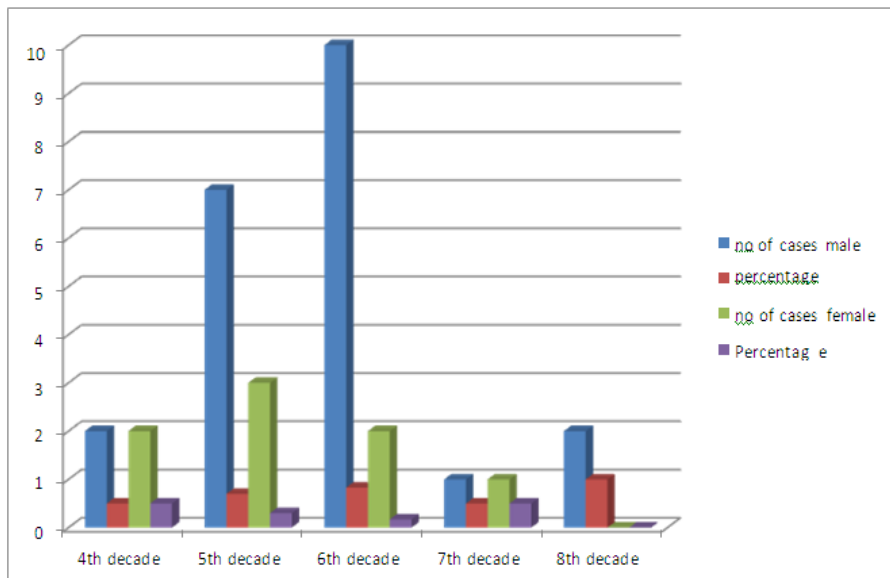
**Graph 3-showing age incidence**

Most patients with periapillary carcinoma have aged 40-60 years.

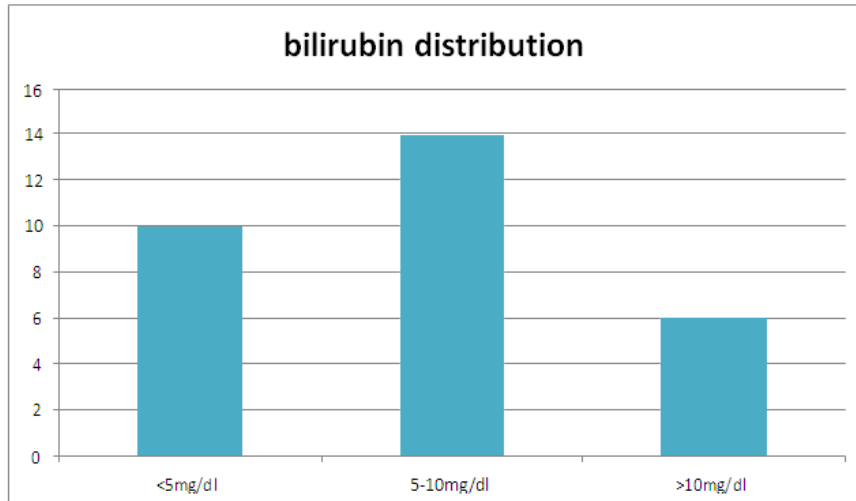
**Relative sex incidence:-**

Age group	No. of cases			
	Male	%	Female	%
4 <sup>th</sup> decade	2	50%	2	50%
5 <sup>th</sup> decade	7	70%	3	30%
6 <sup>th</sup> decade	10	83%	2	17%
7 <sup>th</sup> decade	1	50%	1	50%
8 <sup>th</sup> decade	2	100%	0	0%

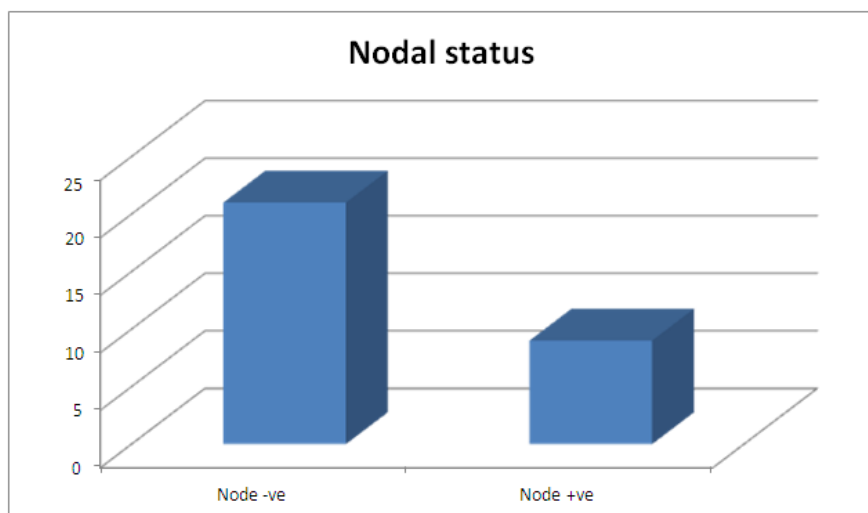
**Table 2- showing relative sex incidence**



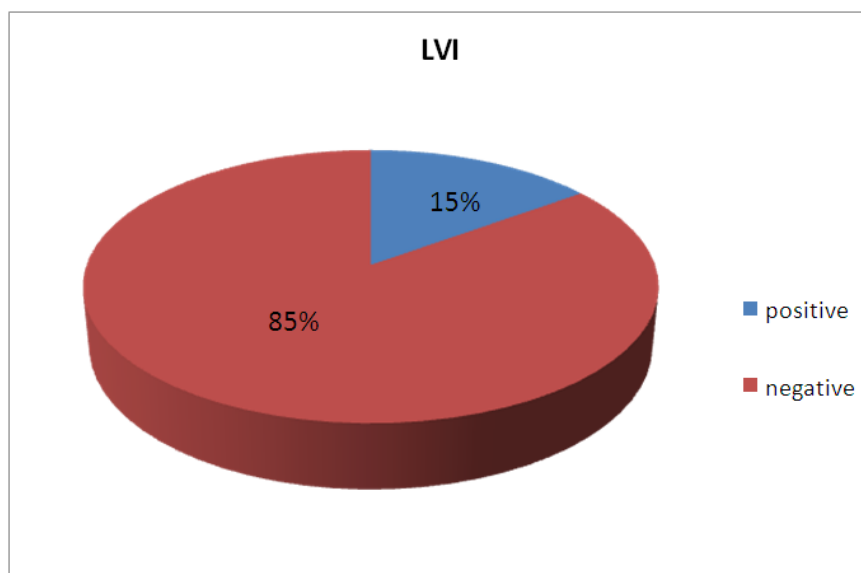
**Graph 4-bar diagram for relative sex incidence**



Graph 5-Bar chart showing a range of bilirubin distribution in the studiedpatients



Graph 6-Bar chart showing nodal status in the studied patients



Graph 7- Pie diagram showing the no. of lymphovascular invasion

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The mean patient age was 51 years. 22 were males, and 8 were females. Jaundice was present in 24 patients. 10 patients had bilirubin < 5 mg%. The average duration of illness was five months, the range being two months to twelve months. The mean duration of hospital stay was 14 days that range between 12 days to 35 days. All patients had icterus (100%). 55% of patients had pain abdomen, of which 42% of patients had a typical colicky type of abdominal pain.

44% of patients had a fever, of which 31% of patients were associated with chills and rigors. Symptoms of complete biliary tract obstruction, clay-colored stools and high colored urine presented in 30% of patients. Cachexia was seen in 29% of patients. Gall Bladder was palpable in 52% of patients. The mean serum bilirubin value was 2.5 mg%. The range between 3-24 mg/dl. The average ALP value was 530 IU/L, and the range between 108-1230 IU/L. Urine examinations showed absent urobilinogen in 42% of patients. The serum albumin range was 2.0-5.5 gm %. In more than 50% of patients, the A: G ratio was reversed. Ultra sonogram revealed IHBR dilatation in 90% of pts. Preoperatively all patients received three doses of Vit K and fresh frozen plasma in selective patients. The coagulation profile was monitored by measuring PT and INR.

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Post-operative mortality was 11% (3 patients). The mean size of the tumor was three cm. 21 patients had the node-negative disease, and 9 patients had node-positive disease. Biopsy report revealed about five R1 resections who were subsequently sent for adjuvant chemoradiotherapy.

#### **IV. Discussion**

At presentation, most periampullary tumors have grown to involve the pancreas, bile duct, ampulla, and duodenum. This can result in difficulty defining the primary site of origin in many cases except the smallest tumors due to anatomical proximity and architectural distortion. This has led to variation in the reported proportions of resected periampullary cancers.

Generally, periampullary carcinoma displays no particular gender predominance or slightly more in males than females. In this study, the incidence of the disease was more in males than females.

Williamson C et al. (7,8) investigated associations between gender and the decision of surgical resection, as well as the specific outcome for men and women after resection, for periampullary cancer, using a population-based registry. Treatment of the severe disease is influenced by several factors, such as performance level, presence of comorbidity, age, assumed benefits, and the patient's preference. Several have analyzed why patients with early-stage pancreatic cancer do not undergo surgery, showing that patients who are older, female, or have more comorbidities were more likely to refuse surgery (9,10). In this study, the no. of females presented with the disease were less & were mostly in the 4th to 6th decade. The age of incidence of periampullary cancers presents more in the people of age group 50-70 Years, whereas this study shows many of them are in between 40 to 60 years age group.

Futagawa et al. (11) identified age older than 75 years as a negative predictive factor for survival in 340 cases. Only two patients were studied of 8th decade in this study & both of them were not fit for surgery; they underwent ERCP stenting and had poorer outcomes.

Shapiro et al. (12) found the male to present with later-stage periampullary cancers involving pancreatic cancers compared with females, which matched our study. The post-operative outcome regarding both general and pancreatic surgery specific complications was similar for men and women.

In a review from 2008, none out of 20 studies reported that gender was associated with any variation in survival (13), but naturally, refusal of surgery is associated with significantly reduced overall survival. A recent study from England showed no difference in the proportion of given palliative treatment to men and women for stage IV pancreatic cancer (77). Pancreaticoduodenectomy was possible to complete to a similar extent for men and women, with equal morbidity in this study.

The exact etiology of pancreatic and periampullary cancer is unknown, but many risk factors have been identified. The risk factor most commonly identified is cigarette smoking, which may account for almost 25-30% of cases. Other factors like diet (high fat and protein, low fruit and vegetable intake), higher coffee intake, alcohol consumption, occupation, and the effects of other ailments such as diabetes mellitus, pernicious

anemia, chronic pancreatitis, and previous gastric surgery, have also been studied in detail. Of these, only in chronic pancreatitis and adult-onset diabetes with less than two years' duration, there seems to be clear evidence of an increased risk of pancreatic cancer. Chronic pancreatitis is associated with a 5-15 fold increased risk of cancer. In this study, most of the male patients had a history of cigarette smoking, which correlates to the above data.

Pancreatic head cancer can occur in three ways related to the inherited predisposition. Firstly, presence of an inherited component to pancreatic cancer in up to 10% of patients with pancreatic cancer in the absence of other familial pancreatic cancer and other cancer syndromes.

Secondly, an increased presentation of pancreatic cancer in individuals from families having familial pancreatic cancer in which the disease seems to be transmitted in an autosomal dominant fashion and with impaired penetrance. Two latest studies have shown that approximately 17–19% of these families may have disease-causing BRCA2 mutations in both Jewish and non-Jewish populations.

Thirdly, syndromes like Peutz-Jeghers syndrome, hereditary non-polyposis colorectal carcinoma (HNPCC) are associated with a high risk of pancreatic cancer along with familial breast-ovarian cancer syndromes and familial adenomatous polyposis (FAP) but probably not Li-Fraumeni syndrome. The Consensus Guidelines of the International Association of Pancreatology advises that patients with suspicion of an inherited predisposition to pancreatic cancer should be referred to specialist centers.

In this study, out of the six pancreatic head carcinomas, only one had a history of similar complaints in the first-degree relative. Still, due to lack of genetic testing in our institute & patient non-compliance, no further evaluation was done.

Many of the difficulties in the treatment of ampullary carcinoma can be traced to the physician's inefficiency to diagnose the disease in its early stage because the vague early symptoms of ampullary carcinoma are often minimized by both the patient and physicians. It is ordinarily not until the patient manifests jaundice that the diagnosis is made. Fortunately, ampullary carcinoma will lead to jaundice at an early stage that might be seen in tumors arising from the pancreas.

Obstructive jaundice is the most constant symptom and sign and is present in about 70% of cases. Jaundice may fluctuate initially and is often associated with pruritis. Many patients have constitutional symptoms such as malaise and/or anorexia for several weeks or months prior to the appearance of jaundice .

Abdominal pain and loss of weight are also common and occur in about half of patients . Other general signs of malignant diseases are malaise, anorexia, nausea, vomiting, melena, anemia, and occult blood in the feces.

The triad of fluctuating painless jaundice, anemia, with or without gastrointestinal bleeding symptoms, and a palpable gallbladder has been considered relatively specific for an ampullary tumor . Unfortunately, this classic triad is seldom observed—some patients with ampullary carcinoma present with pancreatitis. Acute pancreatitis was reported as the presenting picture in 5–18% of cases .

Cholangitis is an uncommon presentation of ampullary carcinoma, reported in only 6 out of 102 cases (6%) . However, several authors report fever and chills without specifically mentioning cholangitis. It is reported that those patients with ampullary carcinoma who present without jaundice have a better outcome compared with those who present with jaundice.

Almost all the patients with periampullary carcinoma come with the complaint of jaundice, mostly With the yellowish discoloration of the eyes. In this study, all of them presented with jaundice complaints (including waxing and waning type in 18 of them) along with some of the associated features like abdominal pain, malaise, palpable mass, fever, which matched the data mentioned above.

Dr. Mayank Aggarwal et al. (14) studied Patients with Periapillary Carcinoma at the department of radiotherapy and oncology at Maulana Azad Medical College and Lok Nayak Hospital dated from January 2013 till 31 August 2017. Patients included in this study were those who had histologically proven chemotherapy naïve carcinoma, arising out or within 1 cm of the papilla of Vater - including ampullary, pancreatic, distal CBD, and duodenal cancer. Patients with refractory or relapsed disease status at the time of presentation or who had a history of chemotherapy/ radiotherapy were excluded from this study. A total of 114 patients were studied from 01 January 2013 till 31 August 2017. A pattern of male predominance was seen after the statistical analysis. Out of 114 patients, 82 patients were male, constituting 71.9% of the study population. The Median Age of the presentation was 47 years. Jaundice (87.7%) was the most common presenting symptom, followed by loss of appetite (72.8%) and weight loss (66.7%). The pain was present in 64% of patients.

Other common presenting complaints were fever and vomiting—however, only 3 out of 114 patients presented with the features of intestinal obstruction. Most of the parameters are similar to this study except that no patient presented with luminal obstruction.

The common bile duct (38.6%) was the most common site of primary origin, followed by the duodenum (30.7%) and ampulla of vater (14.9%). Pancreatic origin was seen only in 14% of the study group. The histopathologic pattern revealed that moderately differentiated adenocarcinoma was the most common



occurrence pattern, constituting 86.8% of the total. One patient had adenosquamous histology, and one patient had a well-differentiated neuroendocrine tumor. In contradiction to the above results, the present study had ampullary carcinomas in more no. Followed by pancreatic head cancers, and all of them were adenocarcinomas.

The following Table 3 depicts the comparison of different symptoms with which the patients presented as compared to the other studies.

Present study	Other studies
Jaundice(100%)	Jaundice(80-90%)
Abdominal pain(60%)	Abdominal pain(about 50-60%)
Loss of appetite(50%)	Loss of appetite(60%)
Pruritis(70%)	Pruritis(60-70%)
Malaise and/or anorexia(60%)	Constitutional symptoms like anorexia,malaise(60-70%)
Palpable gallbladder(50%)	Palpable gallbladder(60-70%)
Fever with chills and rigors(15%)	Fever with chills and rigors(in advanced diseases with cholangitis)

S D Mansfield et al. (15) studied 111 patients with periampullary carcinoma. Median serum bilirubin on presentation was 160 micromol/l. The median increase was 13.1 micromol/l/day or approximately 100 micromol/l/week.Surgery may be performed in jaundiced patients with pancreatic and periampullary malignancy to avoid biliary drainage procedures, depending on their threshold.

Only ten patients presented with bilirubin levels less than 5mg/dl.rest of them with more than 5mg/dl up to levels of 24mg/dl. About 16 patients had palpable gallbladder on presentation. Early and Accurate staging is important for selecting patients with ampullary and periampullary carcinoma in whom it may be appropriate to attempt pancreatoduodenectomy with curative intent.

The TNM stage of the palliative patients is based on a radiological evaluation. Staging based on imaging may not be consistent with what would have been reviewed pathologically, which might result in an inappropriate correlation between resected and unresected patients. Staging of the ampullary carcinomas done by the following criteria

**Primary tumor (T)**

- TX Primary tumor cannot be assessed. T0 No evidence of primary tumor
- Tis carcinoma in situ
- T1 Tumour limited only to the ampulla of Vater or sphincter of Oddi.
- T2 Tumour invades duodenal wall
- T3 Tumour invades the pancreas.
- T4 Tumour invades peripancreatic soft tissues or other adjacent organs or structures other than the pancreas.

**Regional lymph nodes (N)**

- NX Regional lymph nodes cannot be assessed. N0 No regional lymph node metastasis
- N1 Regional lymph node metastasis

**Distant metastasis (M)**

- M0 No distant metastasis
- M1 Distant metastasis

All the 18 ampullary carcinomas in this study were localized and were mostly T2 stage, with 1 of them with N1.none of them had metastases.

The preoperative assessment should include investigations that are sensitive in detecting localized and potentially curable lesions and also at the same time, specific enough to identify factors that render the tumor unresectable. The possibilities of endoscopic or percutaneous transtemporal stenting justify appropriate patient selection to avoid unnecessary laparotomies in those with unresectable lesions.

The role of different methods of diagnosis for staging is to give information on:

1. Tumor size and location
2. The presence or absence of hepatic peritoneal metastasis or ascites
3. Presence of extrahepatic tumor extension
4. Presence or absence of lymph nodes
5. peripancreatic, periportal, or celiac Vascular encasement.

In this study, ultrasound was the primary non-invasive radiological investigation that was used initially. USG abdomen identifies biliary obstruction and, more importantly, the level of obstruction. It can miss a pancreatic head mass but shows advanced disease with liver metastases. It was done in all patients & most of the reports commented on the status of IHBD, dilatation of CBD, the status of the pancreatic duct, and any suspicious lesion if noted.

CECT abdomen was the next frequent investigation done to confirm the mass & to know its extent, presence of any CBD stones, lymph nodes, encasement of the surrounding vasculature by the tumor, metastases. CT is especially useful in borderline resectable cases. If it was not enough for the confirmation, then the patients were further evaluated with investigations like EUS (endoscopic ultrasonography), ERCP, MRCP.

EUS is superior for detecting tumors and predicting vascular invasion. Thus, EUS should be used for patients in whom CT does not detect a mass and for those with an identifiable mass on CT in whom vascular invasion is still in doubt. For pancreatic head carcinoma suspected patients, a Pancreas protocol CECT abdomen is very helpful.

Some patients need preoperative biliary stenting for reasons like very high bilirubin levels, features suggestive of cholangitis. In such patients, ERCP's role is significant & also helps to take a brush biopsy of the lesion, which eventually helps in preoperative HPE report. Pathological confirmation was usually required when suspicion of a benign lesion was present. In this study, ERCP was done in 12 patients, out of which 3 were patients of unresectable disease and unfit for surgery/did not accept the risk of the surgery. No one in this study presented with the features of luminal obstruction.

The periapillary region is a difficult area to evaluate radiologically because of its anatomic location within the retroperitoneum and its relationship with adjacent viscera and major vascular structures. The imaging modalities such as ultrasonography, computed tomography (CT), magnetic resonance imaging have been recognized not always be sufficiently accurate in staging periapillary tumors, even when used in combination.

The use of laparoscopy allows a detailed view of the peritoneal cavity to detect tiny peritoneal tumor deposits and liver metastasis. Here, staging laparoscopy was not done in any of the cases. PTBD was done in one patient who required urgent biliary decompression in the emergency ward to relieve the cholangitis.

All the patients were assessed in view of the performance status, comorbidities, presence of anemia, dehydration, renal failure, liver failure & other investigations like coagulation profile were done. As these patients usually have a low glycogen reserve, dextrose is given preoperatively & any dehydration present was corrected before surgery. Blood transfusions were given to some of the patients to correct anemia. Injection vitamin K was given intramuscularly for five days & in some patients, corrected by transfusion of FFP's for correction of coagulation profile.

Indications for TPN were a reduction of body weight of >5 % in three months and/or a long-term reduced nutritional status and clinical symptoms like severe diarrhea/vomitus, preventing adequate oral nutrition for weeks. TPN was given to 6 patients in the preoperative patients in view of malnourishment & in 3 post-operative patients. Although recent studies have suggested enteral nutrition than TPN, parenteral nutrition is helpful in severely debilitated cachexia patients. Adequate serum albumin levels in the preoperative period helps in early post-operative recovery & decreased complications.

Gilliland et al. (16) assumed that patients with an albumin level of less than 2.5 mg/dL or weight loss > 10% required intense nutritional intervention to decrease post-operative complications. Surgery should be postponed until the functional status is improved. Those with decreased albumin levels (<3.0 mg/dL) or weight loss of > 5% should still receive some form of nutritional supplementation before surgery to avoid undesirable patient outcomes associated with an insufficient nutritional intervention.

Other preoperative screening parameters that can bring further insight into patient nutritional and metabolic status are prealbumin, C-reactive protein, fasting blood glucose, hemoglobin A1C, along fecal elastase. Screening of all the above will aid at the beginning of appropriate enzyme supplementation, glucose management and may predict worsening function after surgery.

Table 4-Factors considered for surgery:

RESECTABLE	BORDERLINE	UNRESECTABLE
No tumor abutment with the vessels	RESECTABLE <180° tumor abutment with PV or SMV	>180° tumor abutment with PV or SMV
No distant metastasis	<1.5cm length encasement/occlusion of PV/SMV	Presence of ascites, liver metastasis, peritoneal metastasis, and other distant metastasis
Clear fat planes around the celiac axis, hepatic artery, and superior mesenteric artery (SMA)	<180° tumor abutment of SMA	No clear planes around the celiac axis, hepatic artery & SMA

Yeo CJ et al. (17) studied 650 consecutive patients with resected periampullary cancers & enumerated the prevalences as follows cancer of the head of the pancreas accounts for 50% to 70%, ampullary cancer for 15% to 25%, biliary cancer for 10%, and duodenal cancer for 10%.

Table 5 comparing types of periampullary carcinoma

Type of periampullary Carcinoma	Yeo CJ et al	Present study
1)Head of the pancreas	50-70%	20%
2)Ampullary Carcinoma	15-25%	60%
3)Duodenal	10%	13%
4)Distal bile duct	10%	7%

The majority of the patients, i.e., 18 patients in this study, were diagnosed with ampullary carcinoma & then head of the pancreas carcinoma, followed by duodenal carcinoma, cholangiocarcinoma. This was in contrast to the above findings. All of them were adenocarcinomas on HPE report varying from poor to well-differentiated types.

In the intraoperative period, 2 patients among the 27 were found to have liver & peritoneal metastasis & a consecutive triple bypass procedure was done in them.21 patients underwent standard pancreaticoduodenectomy while four patients underwent PPPD. There was no much difference in the post-operative morbidity in both groups of patients.

Complications like a pancreatic anastomotic leak, biliary gastritis were seen in the carcinoma head of pancreas patients & biliary leak was seen in cholangiocarcinoma, ampullary carcinoma patients & were managed conservatively. In the post-operative period, two patients had frank blood in the abdominal drains and were taken up for relaparotomy because of post-operative hemorrhage complication. one patient was resuscitated and operated but could not survive later.

Giorgio Romano et al. (18) studied between January 2010 and December 2014 & performed a total of 97 pancreaticoduodenectomies. They considered only resectable pancreatic cancer and periampullary neoplasms with no distant metastases and no local tumor invasion to the celiac axis and hepatic artery, along with the lack of involvement of the superior mesenteric vasculature. None of these patients received neoadjuvant chemotherapy. Post-operative pancreatic fistula occurred in 4 patients. 2 patients developed a post pancreatectomy hemorrhage. Perioperative mortality was 4.1%.As pancreaticoduodenectomy is a complex surgical technique and the associated high morbidity and mortality resulted in an initial reluctance to adopt this surgery for the management of pancreatic and periampullary tumors.

Surgical outcomes of pancreatic surgery are better at a high-volume experienced center reporting mortality rates below 5%.This study had a mortality rate of 11%(3patients), of which one expired after the relaparotomy & the other two patients expired due to cardiac arrest in the post-operative period.

The following Table-6 shows the comparison of various studies showing mortality rates post pancreaticoduodenectomy in periampullary carcinomas (19)

Study	year	Patients	Mortality rate(%)
Yamaguchi & enjoji et al	1987	107	5.8%
Monsoon et al	1991	104	5.7%
Yamaguchi et al	1993	36	7.5%
Klempnaueur et al	1995	85	9%
Talamini et al	1997	106	3.8%
Berger et al	1999	98	3.2%
De Castro	2004	107	5.7%
Present study	2021	30	11%

The mortality rate here seems to be high due to the small sample size. Over the decades, due to improvement in the imaging & various staging methods, the mortality rates have decreased significantly & still decreased in high volume centers due to high expertise.

CA 19-9 was done in 9 patients out of the 30, and all the values were elevated above 37 U/ml. CA 19-9 and CEA lack specificity in the diagnosis of tumors and cannot be solely used as the diagnostic tool for tumors.

However, they are sometimes useful in screening high-risk patients with nonspecific symptoms or signs of some particular tumors, predicting the prognosis, and monitoring the tumor recurrence. CA 19-9 is superior to CEA in the diagnosis of pancreatic cancers and is often considered the standard marker for pancreatic cancer, with which other markers are compared.

Shi-Yi Kau et al. (20) showed by the study that CA 19-9 has been reported to be able to predict the resectability of pancreatic cancer. In this study, marked elevation of serum CA 19-9, but not CEA, tended to associate with advanced and unresectable periampullary cancers. Both CA 19-9 and CEA levels had a positive correlation with tumor size.

When applied to periampullary cancers, both tumor markers could provide valuable prognostic information. Low CA 19-9 level (<35 U/mL) was associated with favorable outcomes for both resectable and unresectable periampullary cancers, and low CEA level (<6 ng/mL) predicted favorable prognosis only for resectable cancers.

Their role in periampullary carcinoma still needs to be studied in multiple demographics & larger sample populations to attain valid conclusions. In this study, we did CA 19-9 investigation only when we suspected ahead of pancreas tumor due to its high specificity.

## V. Conclusion

Our institutional observation suggests that periampullary carcinoma is commonly seen in the fifth and sixth decade of life, with males having a greater propensity of developing this disease by 2.7 times more than females.

Jaundice and loss of appetite with anorexia are the most common presenting complaints, leading to most patients being diagnosed at early localized and operable stage.

Palpable gallbladder with progressive jaundice of waxing & waning type & pruritis & high bilirubin levels usually suggests periampullary carcinoma.

Only 16% of patients presented with metastatic disease, with the liver being the most common metastatic involvement site.

Post-operative findings suggest that moderately differentiated adenocarcinoma is the most common histopathology observed in these patients, and ampulla being the most common site of primary origin of this disease with a good prognosis compared to others.

Early detection of cancer and staging and proper selection of the patient is more important to gain benefit from resection of the tumor, whereas late presentation and those patients not suitable for resection will have a good quality of life with palliative surgery.

Improving deranged bilirubin and liver enzymes, correction of anemia, and hepatorenal problem improves the surgical results (morbidity and mortality).

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