IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 19, Issue 2 Ser.1 (February. 2020), PP 18-24
www.iosrjournals.org

Histopathological spectrum of Pancreatic and Periampullary lesions with special emphasis on malignant lesions and their prognosis based on histomorphology.

Dr. Syamala Rao Moida[1] (PG 3rd year), Dr. P R D Ganesh Basina[2](Assistant professor), Dr. B V V D Kiranmayi[3](Associate professor), Dr. R. Vijaya Bhaskar[4](Professor &HOD).

1 (Postgraduate, Department of pathology, Rangaraya Medical College, India)
2 (Assistant professor, Department of pathology, Rangaraya Medical College, India)
3 (Associate professor, Department of pathology, Rangaraya Medical College, India)
4 (Professor and Head, Department of pathology, Rangaraya Medical College, India)
*2*Corresponding author Dr. P R D Ganesh Basina*

Abstract:
Introduction: *Periampullary region encircles a radius of 2cm diameter around ampulla of Vater, which includes pancreatic head and uncus, lower common bile duct, ampulla of Vater and periampullary duodenum. Pancreatic adenocarcinoma is the most common malignant neoplasm arising from this region and is the 4th most common cause of cancer-related deaths, with the least survival rates ranging from 6.8 to 15%. As malignant lesions are more common than benign counterparts, early diagnosis and management improve survival.*
Aims & Objective: *To analyze the histological spectrum of pancreatic and periampullary lesions in the period between 2015 and 2018.*
Material and methods: *The resected specimens of Pancreaticoduodenectomy (Whipple`s procedure) and small biopsies were adequately sampled, sections stained with H&E for microscopy and classified as per recent CAP guidelines -2017.*
Results & Discussion: *Among 39 cases of pancreatic and periampullary lesions studied, 10 (25%) cases were female and 29(75%) cases were male. Out of 39 cases, 27(69.2%) cases were malignant lesions, 1(2.6%) case was benign, and 11(28.2%) cases were non-neoplastic. The study highlights the histological spectrum of pancreatic and periampullary lesions in our institute.*
Keywords: *Pancreatic lesions, periampullary carcinoma, pancreaticobiliary type, intestinal-type ampullary adenocarcinomas.*

Date of Submission: 17-01-2020 Date of Acceptance: 05-02-2020

I. Introduction

Periampullary region is defined as an area of 2cm diameter around the Ampulla of Vater and Periampullary tumors are defined as tumors arising from head and uncinate process of the pancreas, lower common bile duct, Ampulla of Vater and periampullary duodenum.[1] (fig-1)

Among periampullary lesions, pancreatic ductal adenocarcinomas are the most common. Pancreatic ductal adenocarcinomas constitute 80 – 90% of all pancreatic malignancies and it is the 4th most common cause of cancer-related deaths with least 5yr survival rate.[2]

The ampullary papilla is lined by intestinal mucosa while the other parts are lined by pancreaticobiliary type of simple mucinous epithelium.[3] In consequence, ampullary carcinomas may arise from two different types of mucosa, which thus reflect the broad histomorphological spectrum of these tumors.[4] These were intestinal type& Pancreatico biliary type. Some cases may show both the morphologies which were categorized as mixed type.[5]

In most intestinal-type adenocarcinomas are positive for keratin 20 and only about half are positive for keratin 7, whereas most pancreatobiliary-type adenocarcinomas are keratin 7- positive and keratin 20 negative. The markers of intestinal phenotype, CDX2, and MUC2, label intestinal-type adenocarcinomas, but are negative in those with a pancreatobiliary phenotype, which are MUC1 (EMA) - positive.[5]

II. Materials and Methods

This study was an observational study that was conducted from June 2015 to May 2018, in the Department of pathology, Rangaraya Medical College, Kakinada, Andhra Pradesh. A total of 39 cases were included in the present study with a clinical diagnosis of pancreatic and periampullary pathology. Clinical details like age, sex, biochemical & radiological investigations, and clinical diagnosis were obtained from the hospital records. Whipple`s procedure, distal Pancreatico-splenectomy, and excision biopsy specimens were included in this study. Specimens were grossed strictly according to the Royal College of Pathology protocols and processed. The paraffin-embedded samples were cut to 4µ thick sections and were stained with regular hematoxylin and eosin(H&E) stain. Lesions were classified according to the 2019 WHO classification. The periampullary carcinomas were further subclassified based on histomorphology and were correlated with immune histochemical markers CK20 and MUC1.

III. Aims & Objectives

1. To analyze the histopathological spectrum of pancreatic and periampullary lesions.
2. To subcategorize ampullary adenocarcinomas based on the 2019 WHO classification.
3. To know the prognosis of the histomorphological subtypes of ampullary tumors, based on follow up.
4. To evaluate the diagnostic utility of immunohistochemical markers like CK-20 and MUC-1 in correlation with histomorphology.

IV. Results

The total number of cases included in this study wee 39. Based on anatomical location lesions were broadly categorized into pancreatic lesions (lesions arising from body and tail of pancreas) accounting for 13(33.3%) cases and periampullary lesions (head and uncinate process of pancreas, lower common bile duct, Ampulla of Vater and periampullary duodenum) accounting for 26(66.7%) cases.

Figure -1: Anatomy of the periampullary region

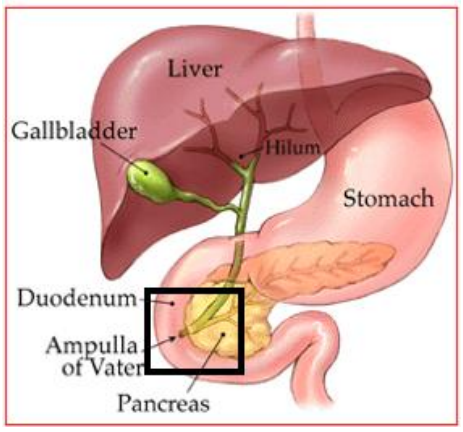
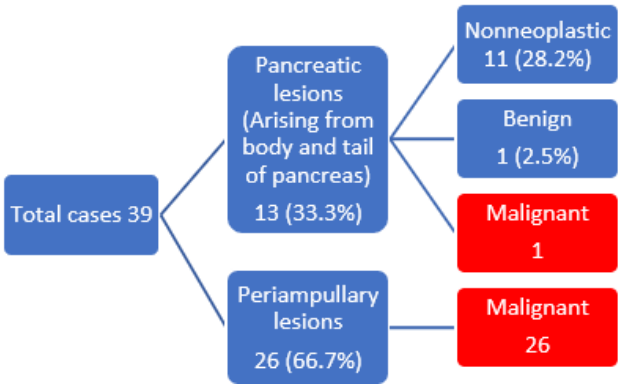


Chart – 1: Case distribution (Anatomical & morphological)



The age distribution in the present study was from 16yrs to 67yrs, where it was a solid pseudopapillary neoplasm in a 16-year female and pancreaticobiliary type of adenocarcinoma in the 67-year-old male. The sixth decade was the most common age group involved with a total of 10 cases of which all the ten cases were malignant lesions in which one case was from the body of the pancreas and the remaining nine cases were from the periampullary region.

Table -1: Age distribution of Non-neoplastic lesions of pancreas (n=11)

Age group	Number of cases
11 – 20yrs	1
21 – 30yrs	5
31 – 40yrs	2
41 – 50yrs	2
51 – 60yrs	0
61 - 70yrs	1

Table- 2: Age distribution of neoplastic lesions of Pancreas & Periampullary tumors (n = 28)

Age group	Number of cases
11 – 20yrs	1
21 – 30yrs	2
31 – 40yrs	5
41 – 50yrs	5
51 – 60yrs	10
61 – 70yrs	5

In the age distribution of non-neoplastic lesions, the 3rd decade was the most commonly affected, whereas in neoplastic lesions 6th-decade group of people affected most commonly, followed by equal frequency of distribution of cases in 4th, 5th & 7th decades with five cases (17.8%) each.
In the present study male to female ratio is approximately 3:1, with males being more commonly affected in both non-neoplastic lesions and neoplastic lesions.

Among the total cases (n=39), 11(28.2%) cases were non-neoplastic, and all the non-neoplastic lesions are from the body and tail of the pancreas. In which 73% (8/11) cases were chronic pancreatitis and 27 %(3/11) cases were pseudo pancreatic cysts. In the neoplastic category (n=28)71.8%, one (2.5%) case was benign and the remaining 27(69.2%) cases were malignant lesions. The only benign lesion, serous cystadenoma of the pancreas was arising from the body of the pancreas. Among the malignant lesions (n=27) only one case was arising from the body of the pancreas which was diagnosed as pancreatic ductal adenocarcinoma and the remaining 26 malignant cases were from the periampullary region.

These malignant lesions were histologically categorized based on WHO classification of GIT tumors-2019, of which one (3.7%) case was solid pseudopapillary neoplasm of pancreas, one (3.7) case was invasive papillary adenocarcinoma, two (7.4%) cases were mucinous adenocarcinoma, 8(29.6%) cases were pancreatic ductal adenocarcinoma and 15((55.5%) cases were ampullary carcinoma.

Chart -2: Periampullary tumors – histological types

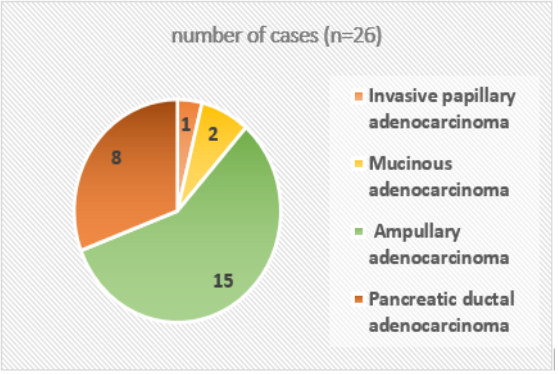
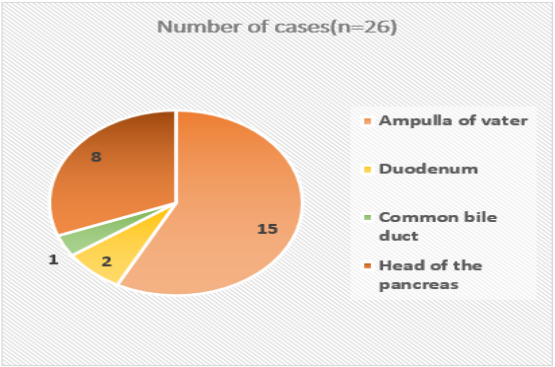


Chart-3: Periampullary tumors – anatomical distribution



This ampullary carcinoma was further sub-classified into intestinal type, pancreaticobiliary type and mixed type based on histomorphology.

Table-3: Ampullary adenocarcinoma histological subtypes (On H&E, n = 15)

Type of lesion	Number of cases
Intestinal type	8
Pancreaticobiliary type	5
Mixed (intestinal + pancreaticobiliary) type	2

Table-4: Ampullary adenocarcinoma subtypes (On IHC, n= 6)

Type of lesion	On H&E N=6	After IHC N=6
Intestinal type (CK20+ / MUC1-)	4	0
Pancreatico biliary type (CK20- / MUC1+)	1	5
Mixed type/Unusual type (CK20-, MUC1 - / CK20 +, MUC1+)	1	1

Among the total ampullary carcinomas morphologically eight cases were diagnosed as an intestinal type of carcinoma, five cases as a pancreaticobiliary type and the remaining two cases were reported as mixed

type. IHC markers with MUC1 (EMA) & CK20 were done for 6 selected cases which include 4 cases of intestinal-type and one case each of Pancreaticobiliary type and mixed type.

IHC showed positive MUC1 and negative CK20 staining in all the cases with a morphological diagnosis of intestinal type, Pancreaticobiliary type, focal staining of mixed type and CK20 staining was observed only focally in the mixed type where the same area was positively stained with MUC1.

Pancreatico biliary type

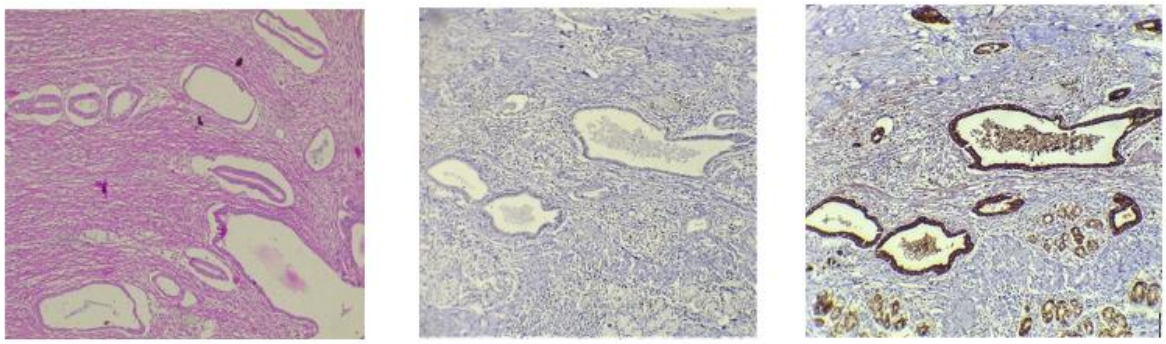


Figure-2a (H&E); fig 2b: CK20 – Negative staining; fig2c – Positive cytoplasmic staining with MUC1.

Mixed type

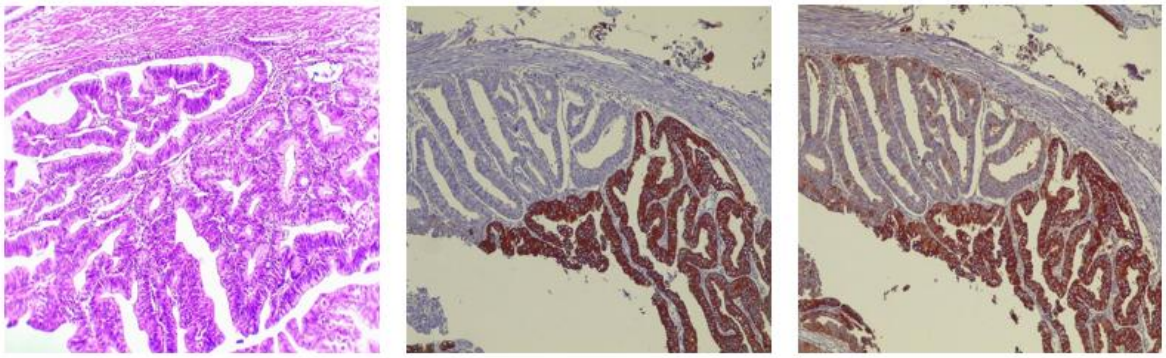


Figure 3a (H&E), fig 3b & 3c: Positive cytoplasmic staining with CK20 & MUC1 respectively

Table-5: Follow up cases of periampullary malignancies (n = 10/26)

Histological type	Survival in months			
	< 6	6 – 12	12 – 18	> 18
Invasive intestinal type (n = 4)	1			3
Pancreatico biliary type (n=2)	2			
Mucinous adenocarcinoma			1	
Pancreatic ductal adenocarcinoma	2			
Invasive papillary adenocarcinoma				1

Follow up could only be done in 10 cases, which include morphological diagnosis of 4 cases of intestinal-type ampullary adenocarcinoma, 2 cases of Pancreaticobiliary type, 2 cases of pancreatic ductal adenocarcinoma, and one case of each mucinous adenocarcinoma and invasive papillary adenocarcinoma.

V. Discussion

The present study was done on 39 cases of pancreatic lesions and periampullary lesions over three years. In the non-neoplastic lesions, chronic pancreatitis and pancreatic pseudocyst was observed in our study, and chronic pancreatitis was the predominant entity in this category, which is similar to study done by Aarthi et al.[6] In the pancreatic malignant lesions ductal adenocarcinoma was constituting 89% in the present study and are more common in the 50 to 60yrs of age group with male preponderance which was correlated with studies done by Aarthi et al[6] and Chang KJ et al.[7]

In the current study male to female with a ratio of 3:1, which is similar to the studies done by M Aarthi et al[6], Chang KJ et al[7].

Table-6: Comparison of pancreatic lesions

Comparison entity	Present study (n=39)	M Aarthi et al[6] (n=45)	Chang KJ et al[7] (n=56)
Non neoplastic lesion	Chronic pancreatitis	Chronic pancreatitis	----------
Sex predominance in pancreatic ductal adenocarcinoma	Male	Male	Male
Common age group for pancreatic ductal adenocarcinoma	50 – 60yrs	40 – 60yrs	50 – 70yrs
Histological type of malignant lesion	Ductal adenocarcinoma (89%)	Ductal adenocarcinoma (95%)	Ductal adenocarcinoma (95%)

In the present study, ampullary lesions showed male predominance which was similar to the studies done by Kimura et al [8] and Michelle et al, whereas mean age was 56yrs in the present study which was lesser than the studies of Kimura et al and Michelle et al with their observations of mean age was 63.8yrs and 65yrs respectively. In the current study intestinal type of adenocarcinoma was the most common histological type in contrast to other studies, which showed pancreaticobiliary type as the most common histological entity.

In the current study location-wise distribution of periampullary carcinomas, Ampulla of Vater occupies major portion with 57.7% (n=15/26) followed by pancreas, duodenum and common bile duct with 30.8%, 7.7%, & 3.8% respectively, in contrast, to study done by Piorkowski et al [9], where majority of malignant lesions are arising from the pancreas with 58%(n=32/55), followed by common bile duct, Ampulla of Vater, duodenum and miscellaneous with 16%, 11%, 7.5%, and 7.5% respectively.

Table 7,8 & 9 Comparison of IHC & histological classification with other studies.

Present study (n= 6)	Intestinal type (CK20 +)	Pancreaticobiliary type (MUC1 +)	Unusual type CK20 -, MUC1 - or CK20+, MUC1+
Intestinal type (n = 4)	0	3	1
Pancreaticobiliary type (n = 1)	-	1	-
Mixed type (n = 1)	-	1	-

Yasunari et al [10] (n = 45)	Intestinal type	Pancreaticobiliary type	Unusual type
Intestinal type (n = 16)	**10(62.5%)**	**0**	**6**
Pancreaticobiliary type (n = 18)	**0**	**13(72%)**	**5**
Unusual type (n =1 1)	**1**	**2**	**6 (54%)**

Hui Zhou et al [3] (n = 55)	Intestinal type	Pancreaticobiliary type	Unusual type
Intestinal type (n = 15)	9(60%)	1	5
Pancreaticobiliary type (n = 24)	0	21(87.5%)	3(12.5%)
Unusual type (n =16)	4(25%)	8(50%)	4(25%)

In the present study, based on IHC staining pattern, four cases with histopathological diagnosis of the intestinal type of ampullary adenocarcinoma were turned out to be a pancreaticobiliary type with positive MUC1staining and negative CK20 staining in three cases and one case as the mixed type where both the markers CK20 & MUC1 were positive. The histologically diagnosed mixed type was turned out as pancreaticobiliary type with only MUC1 positivity. Histologically diagnosed pancreaticobiliary type of adenocarcinoma showed a staining pattern as expected in this study with positive staining for MUC1 and negative staining for CK20. Similar studies were done by Yasunari et al[10] and Hui Zhou et al[3] where comparable observations in the conspiracy between histological diagnosis and IHC staining pattern were noticed.

We could able to do follow up in only 10 cases. Follow up study revealed morphologically classified intestinal-type showed prolonged survival rate beyond 18 months than compared to Pancreaticobiliary type of ampullary carcinoma and pancreatic ductal adenocarcinoma. Among 4 cases of intestinal-type of ampullary adenocarcinoma, one case succumbed within 6 months after surgery due to an associated comorbid cardiac ailment, and the rest of the three cases showed a mean survival rate of more than 18 months. In the case of the pancreaticobiliary type, the survival rate after surgery was less than six months.

Pancreatic ductal adenocarcinoma also showed a survival rate of fewer than six months. Mucinous adenocarcinoma showed a survival rate of 16 months and invasive papillary adenocarcinoma showed more than 18 months survival rate after surgery. The survival rate of patients correlated well with the histological diagnosis compared with diagnoses on the IHC pattern. This conflicting variation between the histopathological and IHC studies is mainly due to the low specificity of expression of MUC1 in some intestinal-type tumors.[11]

In the present study, the mean survival rate of different entities was correlated well with the study done by Kimura et al.[8] with a better survival rate in the intestinal type of adenocarcinoma than the pancreaticobiliary type of adenocarcinoma.

VI. Conclusion

Though there are conflicting studies regarding the significance of IHC in classifying, assessing the prognosis of ampullary adenocarcinomas, histological subclassification still holds good as they correlated well with clinical outcome.

References

[1]. Verma A, Shukla S, Verma N. Diagnosis, Preoperative Evaluation, and Assessment of Resectability of Pancreatic and Periampullary Cancer. The Indian Journal of Surgery. 2015;77(5):362-370. doi:10.1007/s12262-015-1370-0.

[2]. Tempero MA, Malafa MP, Chiorean EG, Czito B, Scaife C, Narang AK, Fountzilas C, Wolpin BM, Al-Hawary M, Asbun H, Behrman SW. Pancreatic Adenocarcinoma, Version 1.2019. Journal of the National Comprehensive Cancer Network. 2019 Mar 1;17(3):202-10.

[3]. Zhou H, Schaefer N, Wolff M, Fischer HP. Carcinoma of the ampulla of Vater: comparative histologic/immunohistochemical classification and follow-up. Am J Surg Pathol. 2004;28:875-82.

[4]. Fischer HP, Zhou H. Pathogenesis and histomorphology of ampullary carcinomas and their precursor lesions. Review and individual findings. Pathologe. 2003;24:196-203.

[5]. Fred T. Bosman, Fatima Carneiro, Ralph H. Hruban, Neil D. Theise World Health Organization Classification of Digestive system tumors. 5th ed. IARC Press, Lyon; 2019.

[6]. Arthi M, Rajendiran S, Cruze LD, Kumar KA. Spectrum of pancreatic lesions in a tertiary care center in South India. MedPulse – International Medical Journal. December 2016; 3(12): 1034-1037.

[7]. Chang KJ, Nguyen P, Erickson RA, Durbin TE, Katz KD. The clinical utility of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis and staging of pancreatic carcinoma. Gastrointestinal endoscopy. 1997 May 31;45(5):387-93

[8]. Kimura W, Futakawa N, Yamagata S, Wada Y, Kuroda A, Muto T, Esaki Y. Different clinicopathologic findings in two histologic types of carcinoma of papilla of Vater. Japanese journal of cancer research. 1994 Feb;85(2):161-6.

[9]. Piorkowski RJ, Blievernicht SW, Lawrence Jr W, Madarlaga J, Horsley III JS, Neifeld JP, Terz JJ. Pancreatic and periampullary carcinoma: Experience with 200 patients over a 12 year period. The American Journal of Surgery. 1982 Feb 1;143(2):189-93.

[10]. Kawabata Y, Tanaka T, Nishisaka T, Inao T, Nishi T, Yano S. Cytokeratin 20 (CK20) and apomucin 1 (MUC1) expression in ampullary carcinoma: Correlation with tumor progression and prognosis. Diagnostic pathology. 2010 Dec;5(1):75.

[11]. Ang DC, Shia J, Tang LH, Katabi N, Klimstra DS. The utility of immunohistochemistry in subtyping adenocarcinoma of the ampulla of Vater. The American journal of surgical pathology. 2014 Oct 1;38(10):1371-9.

Dr. P R D Ganesh Basina, etal. "Histopathological spectrum of Pancreatic and Periampullary lesions with special emphasis on malignant lesions and their prognosis based on histomorphology." *IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)*, 19(2), 2020, pp. 18-24.