

HISTOPATHOLOGICAL ANALYSIS OF WHIPPLE'S RESECTION SPECIMENS AT A TERTIARY CARE CENTER IN IRAQ

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ABSTRACT

Background: Pancreaticoduodenectomy (Whipple's technique) treats pancreatic, bile duct, duodenal, and periampullary carcinomas. About 5% of gastrointestinal cancers are ampullary and periampullary carcinomas. The research examines Whipple's specimens' tumour incidence by histological diagnosis, age, sex, and other clinicopathological variables. **Method:** We analyse Whipple's material histopathologically to determine these tumours' diagnosis, grade, stage, nodal status, marginal status, prognosis, and incidence. This research analyses the incidence of different tumours in Whipple's material, calculates the sex ratio, then grades and stages the tumours using the WHO grading system. And to compare incidence with other research. **Methods:** Histopathology data of all Whipple's resection patients from January 2019 to October 2013 were examined. We studied the slides and computed parameters. **Results:** Out of 100 Whipple's resection cases, the age range was 26–85, with 46–65 being the most prevalent. 80 percent of sex distribution situations 54% males were affected. Most instances were grade II (40%), T2 (18%), and N0 (26%). Ampullary tumours were the most prevalent lesions at 55%. Pancreatic age, histopathological type, grade, and stage correlated significantly. Age, histopathological type, grade, and stage correlated with pancreatic adenocarcinoma in 17%, 12% grade II, and 8%T2. Among benign lesions, ampullary adenomyoma 4%, chronic pancreatitis 3%, and cholangiocarcinoma 13% were mentioned. **Conclusion:** In the analysis of the Whipple procedure ampullary adenocarcinoma was the commonest neoplasm followed by pancreatic adenocarcinoma and cholangiocarcinoma was the commonest periampullary malignant neoplasm.

KEYWORDS: Histopathological, analysis, Whipple's, resection, specimens, tertiary care center.

INTRODUCTION

The broad portion of the pancreatic head, the duodenum from the pylorus to the Teitz ligament, the proximal jejunum, the distal extrahepatic biliary system, the gallbladder together with the cystic duct, and sometimes the distal portion of the stomach are removed during Whipple's surgery, also known as the pancreaticoduodenectomy.^[1] In 1935, Allen Oldfather Whipple changed the pancreaticoduodenectomy surgery to a one-stage operation that included removing the whole duodenum and the entire head of the pancreas.^[2] Pancreatic cancer ranks fourth among cancer-related deaths in the western hemisphere and is one of the leading causes of mortality in eastern nations. Only 10% to 20% of patients have a decent mass when they first arrive, and the majority of patients have advanced illness.^[3] Whipple's surgery is used to treat duodenal

malignancies, tumours of the common bile duct, pancreatic duct, and periampullary and ampullary carcinomas. This procedure may sometimes be used to treat non-cancerous diseases such as chronic pancreatitis, paraduodenal pancreatitis, and chronic fibrosing pancreatitis. The size of the tumour, its level of differentiation, the involvement of the resected margins, the post-resection CA 19-9 level, and the tumor's DNA content are some of the parameters that may be used to predict the prognosis of pancreatic malignancies.^[4] Although the exact causes of pancreatic cancer are yet unclear, increased tobacco use and prolonged smoke exposure raise the risk. There is some evidence that the use of aspirin, caffeine, and alcohol is one of the risk factors.^[5] **Aim of the study** to analyze Whipple's specimens histopathologically, evaluate the incidence of various tumors encountered, according to

histopathological diagnosis, age, sex, and other clinicopathological parameters.

METHOD

This is a retrospective analysis of one hundred instances of Whipple's operation specimens that were gathered between January 2019 and September 2023 from the gastroenterology and hepatology teaching hospital in Baghdad, Iraq.

- Tissue blocks encased in paraffin and preserved with formalin for Whipple's technique specimens.
- For histopathological review, sections with a thickness of 5 µm were extracted from every block that had been stained with hematoxylin and eosin.
- Age, gender, histological diagnosis, tumour site, grade, and stage were among the histopathological data examined, and they were gathered from archival material.

Methods used during the gross examination

- Ampullary carcinoma is suspected when the majority of the tumour is situated in the ampullary area and protrudes into the duodenal mucosa, straining it. In their research, Adsay V et al. said that if more than 75% of the tumour was located in the ampullary area, the tumour was classified as ampullary carcinoma.
- Periampullary cancer was diagnosed in relation to a tumour involving the ampulla's girth.
- Tumours involving the common bile duct's circumference (CBD) were considered common bile tumours. Granular mucosal surface and longitudinal thickening of the bile duct were considered indicators. According to Gonzalez RS et al.'s research, pancreatoduodenal origin tumours account for 5% of all common bile duct tumours.
- Duodenal carcinoma was the diagnosis made for a tumour whose base or epicentre was located in the duodenum and did not include the ampulla.
- Non-ampullary duodenal cancer differs from its counterpart in the duodenum, and it is linked to

microsatellite instability due to its plaque-like development.

- Other noticeable characteristics were spongy regions in serous cystadenoma of the pancreas and cystic neoplasms of the duct.
- Measurements, gross invasion, colour, and consistency of the tumour were recorded.
- Nodes: Size and number were recorded.
- A homogenous, ghastly white look was thought to be a sign of pseudotumors.
- The periampullary area and the pancreatic head are where the majority of benign lesions are seen. They produce signs of obstruction that resemble cancer and need Whipple's operation.

The slides were evaluated again. Assessments were made of the histopathological classification, nodal status, perineural invasion, angioinvasion, and marginal status.

The proportion of glands visible in the tumour tissue was used to grade adenocarcinomas. Adenocarcinoma with a grade of >95% was considered highly differentiated, 50–95% was considered moderately differentiated, 5–49% was considered poorly differentiated, and 5% was considered undifferentiated.^[10] Statistical analysis done by SPSS 22 was used to conduct statistical analysis on categorical data, using frequency and percentage. Chi-square and DF was used to examine the impact between categorical variables. A significant P-value is less than or equal to 0.05.

RESULTS

Table 1 presents the demographical data of Whipple procedure cases. The results show that the majority of cases were in the 46-65 age group (58.0%) and male (54.0%). Most ampullary tumors were malignant (89.1%), while pancreatic tumors had a higher percentage of malignancy (74.1%). All peri-ampullary tumors were malignant (100.0%).

Table 1: Demographical data of the cases of Whipple procedure.

Parameter	Frequency	Percent %	
Age groups	26-45	27	27.0
	46-65	58	58.0
	66-85	15	15.0
	Total	100	100.0
Gender	Male	54	54.0
	Female	46	46.0
Ampullary tumors	Benign	6	10.9
	Malignant	49	89.1
	Total	55	100.0
Pancreatic tumors	Benign	7	25.9
	Malignant	20	74.1
	Total	27	100.0
Peri-ampullary tumors	Benign	0	0

	Malignant	18	100.0
	Total	18	100

As shown in table 2; there is significant association between site of tumor and diagnosis. So 100% of patients with Periamapullary site diagnosed as malignant tumor

while 89.1% of ampulla site of tumor diagnosed as malignancy. There is no significant association between site of tumor and (age group, gender).

Table 2: association between site of tumor and (age group, gender, diagnosis).

Variables		Site			P-value
		Ampulla	Pancreas	Periamapullary	
Age group	26-45	13 23.6%	6 22.2%	8 44.4%	0.4
	46-65	33 60.0%	16 59.3%	9 50.0%	
	66-85	9 16.4%	5 18.5%	1 5.6%	
	Total	55 100.0%	27 100.0%	18 100.0%	
Gender	Males	26 47.3%	13 48.1%	7 38.9%	0.8
	Females	29 52.7%	14 51.9%	11 61.1%	
	Total	55 100.0%	27 100.0%	18 100.0%	
Diagnosis	Benign	6 10.9%	7 25.9%	0 0.0%	0.032
	Malignant	49 89.1%	20 74.1%	18 100.0%	
	Total	55 100.0%	27 100.0%	18 100.0%	

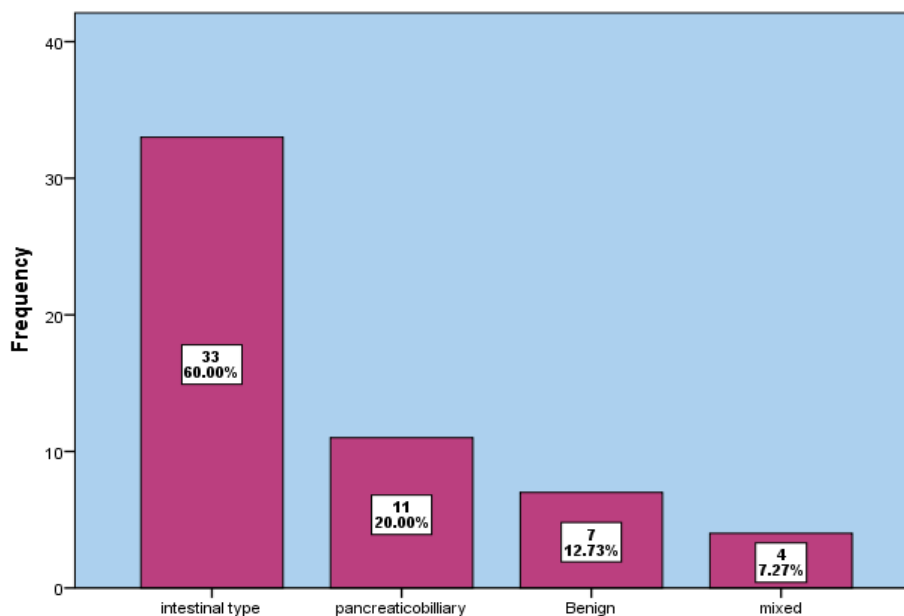


Fig 1: the prevalence of ampullary carcinoma in patients with lesion in ampulla.

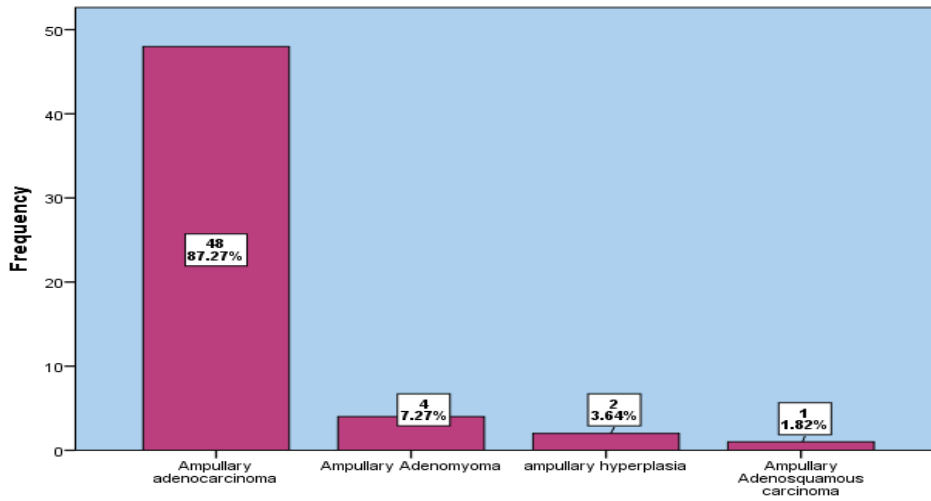


Fig 2: histopathological diagnosis of patients with lesion in ampulla.

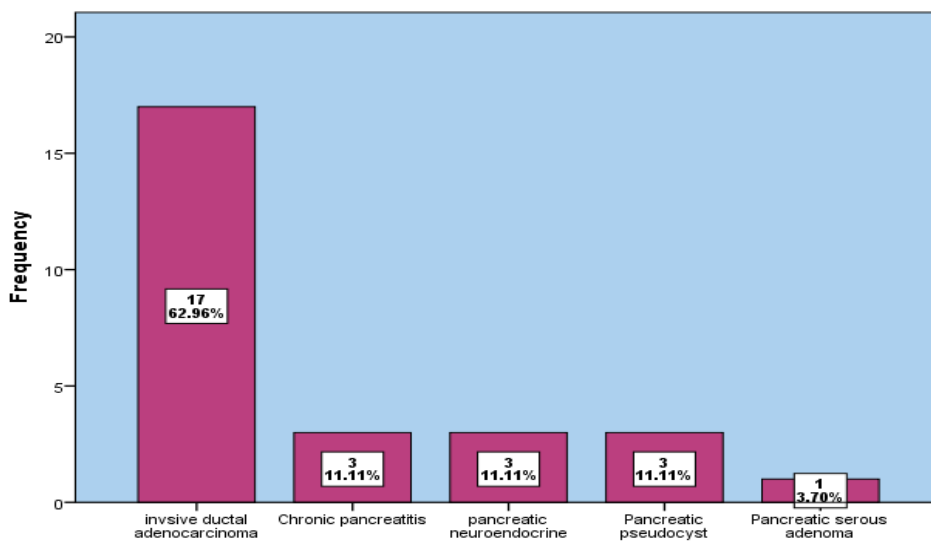


Fig 3: histopathological diagnosis of patients with lesion in pancreas.

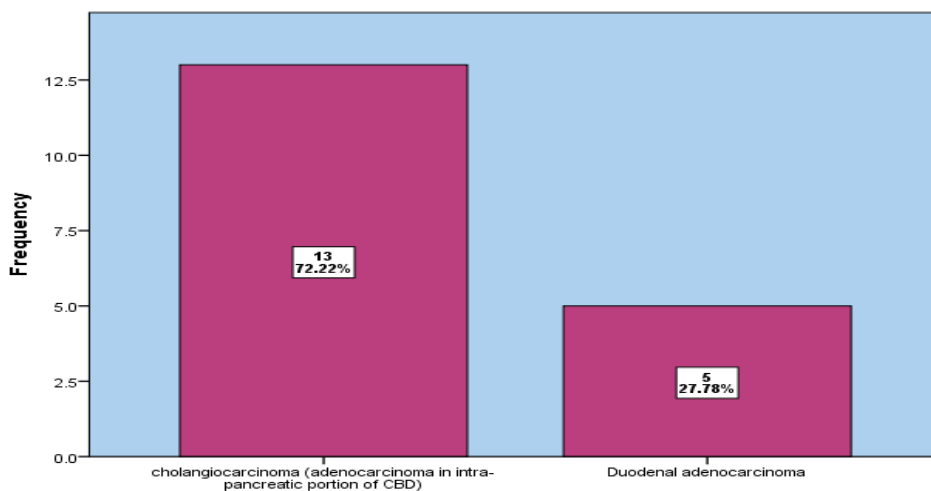


Fig 4: histopathological diagnosis of patients with lesion in Periamapullary.

Table 3 displays histological type, 67.3% were intestinal type, 22.4% were pancreaticobiliary, 8.2% were mixed, and 2.0% were adenosquamous, indicating significant variation. The total number of cases analyzed was 49. For tumor grade, 6.1% were Grade I, 81.6% were Grade II, and 12.2% were Grade III, indicating significant

variation. In terms of tumor stage, T1 accounted for 26.5%, T2 for 36.7%, T3 for 32.7%, and T4 for 4.1%. For lymph node involvement (N), 53.1% were N0, 26.5% were N1, 18.4% were N2, and 2.0% were Nx, indicating significant variation. The M category had a value of Mx for all cases analyzed.

Table 3: Ampullary malignant tumors.

variables		No.	percentage
Histological type	intestinal type	33	67.3
	pancreatic biliary	11	22.4
	mixed	4	8.2
	Adenosquamous	1	2.0
	Total	49	100.0
Grade	I	3	6.1
	II	40	81.6
	III	6	12.2
Stages	T1	13	26.5
	T2	18	36.7
	T3	16	32.7
	T4	2	4.1
	N0	26	53.1
	N1	13	26.5
	N2	9	18.4
	Nx	1	2.0
	Mx	49	100.0

The histological types of the tumors were as follows: 85.0% invasive ductal adenocarcinoma, 5.6% pancreatic neuroendocrine, 5.6% solid pseudo papillary tumor, and 3.8% mucinous tumor. The total number of cases included in the analysis was 20. For tumor grade, 30.0% were Grade I, 60.0% were Grade II, and 10.0% were

Grade III. In terms of tumor stage, 15.0% were classified as T1, 40.0% as T2, 30.0% as T3, and 15.0% as T4. Regarding lymph node involvement (N), 85.0% were N0 and 15.0% were N1. The M staging showed that 85.0% of cases had an Mx value and 15.0% had an M0 value.

Table 4: Pancreatic malignant tumors.

variables		No.	percentage
Histological type	invasive ductal adenocarcinoma	17	85.0
	pancreatic neuroendocrine	1	5.6
	Solid pseudo papillary tumor	1	5.6
	Mucinous tumor	1	3.8
Grade	I	6	30.0
	II	12	60.0
	III	2	10.0
Stages	T1	3	15.0
	T2	8	40.0
	T3	6	30.0
	T4	3	15.0
	N0	17	85.0
	N1	3	15.0
	Mx	17	85.0
M0	3	15.0	

The histological types of the tumors were as follows: 72.2% cholangiocarcinoma and 27.8% duodenal adenocarcinoma. The total number of Pari-ampullary malignant tumors included in the analysis was 18. For tumor grade, 5.6% were Grade I, 88.9% were Grade II, and 5.6% were Grade III. In terms of tumor stage, 22.2%

were classified as T1, 61.1% as T2, 11.1% as T3, and 5.6% as T4. Regarding lymph node involvement (N), 5.6% were Nx, 55.6% were N0, 27.8% were N1, and 11.1% were N2. The M staging showed that all cases had an Mx value.

Table5: Peri-Ampullary Malignant Tumors.

	variables	No.	percentage
Histological type	cholangiocarcinoma	13	72.2
	Duodenal adenocarcinoma	5	27.8
Grade	I	1	5.6
	II	16	88.9
	III	1	5.6
Stages	T1	4	22.2
	T2	11	61.1
	T3	2	11.1
	T4	1	5.6
	Nx	1	5.6
	N0	10	55.6
	N1	5	27.8
	N2	2	11.1
	Mx	18	100.0

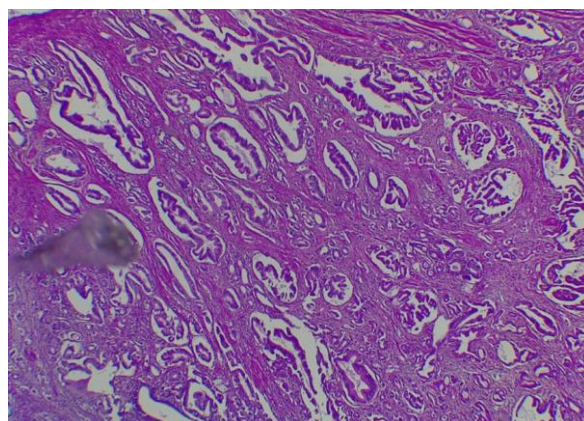


Figure 5: Photomicrograph of adenocarcinoma, pancreatobiliary (moderate differentiated) infiltrating into the submucosa (H and E 4x).

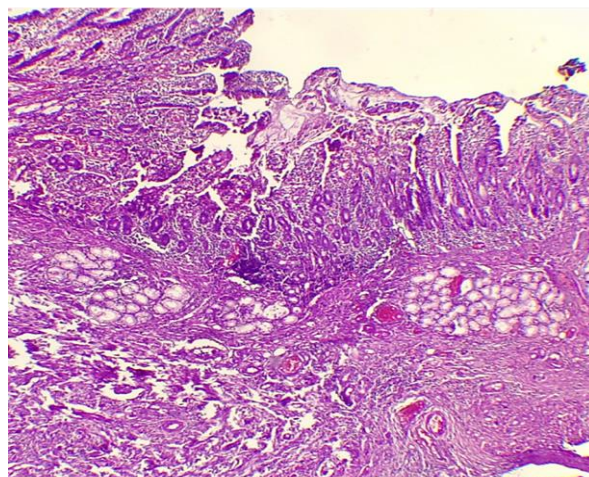


Figure 6: Photomicrograph of Duodenal adenocarcinoma, Grade II (H and E 4x).

DISCUSSION

Whipple's surgical procedure targets tumors located in the ampulla, pancreas, common bile duct, and duodenum. In a study analyzing Whipple's specimens, ampullary carcinoma was predominant in 89.1% of 100 cases, in line with other studies.^[1,2] Ampullary tumors primarily present in males around their sixth decade,

although our study found an equal sex incidence and a younger mean age of 55.5 years.^[6] Histopathologically, ampullary carcinomas manifest in various types: intestinal, pancreatobiliary, and mixed and poor undifferentiated type, the intestinal type has a better prognosis.^[6] In line with Onkendi EO et al.^[7], our study indicated a predominance of the intestinal type and moderately differentiated graded tumors. On the other

hand, Williams JL *et al.*'s research noted uncommon occurrences of well-differentiated tumors, consistent with our findings.^[8] Proper examination of pancreaticoduodenectomy specimens demands a minimum of 12 lymph nodes for evaluation.^[9] Our study averaged 12 lymph nodes, signifying adequate nodal dissection.^[10] Discrepancies in tumor size and nodal involvement were noted when comparing our findings with Onkendi EO *et al.*^[7] Pancreatic head tumors were the second most common, with an equal sex incidence. The PDAC primarily appears in males around their sixth decade, mirroring findings by Tempero MA *et al.*^[11] Our study's histological assessment found that 85% were invasive ductal adenocarcinomas, which matches the incidence data provided by Grundmann RT *et al.*^[12] Meanwhile, Solid Pseudopapillary tumors primarily affect young to middle-aged females, which was concurrent with studies by Lubezky N *et al.* and Antoniou EA *et al.*^[13,14] Our findings on mucinous tumors showed a very low incidence, consistent with Mattiolo P *et al.*'s observations.^[15] In terms of tumor grade, our study predominantly found moderately differentiated tumors (grade II).^[6] However, when compared to McGee EE *et al.*^[6], our study had a lower incidence of poorly differentiated tumors. Peri-ampullary malignant tumors made up 18 cases in our research, with all being malignant. Cholangiocarcinoma was the predominant histological type, contrasting with Mekki SO *et al.*'s findings.^[16] In benign conditions, adenomyomas and papillary hyperplasias were identified as potential mimics for ampullary carcinomas. They are distinguished by their structure and lack of dysplasia and mitosis.^[17] Finally, our study on benign pancreatic tumors revealed that chronic pancreatitis and pancreatic pseudocysts were the primary types, contrasting with Naciri I *et al.*'s study which solely reported chronic pancreatitis.^[17]

CONCLUSION

In the evaluation of the Whipple's procedure:

- The majority of lesions removed via the Whipple's procedure were malignant tumors.
- The most prevalent lesion was ampullary adenocarcinoma, particularly of the pancreatobiliary type, succeeded by pancreatic adenocarcinoma.
- Among the benign lesions, ampullary adenomyoma was the most frequent, with chronic pancreatitis coming next.

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