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# CLINICOPATHOLOGICAL ASSESSMENT OF PANCREATIC LESIONSIN A SAMPLE OF IRAQI PATIENTS

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## ABSTRACT

Pancreatic lesions are aggressive lesions that usually present late with poor prognosis, indicating a need for early diagnosis. In this study we aim to assess the clinical and pathologic features of most commonly encountered pancreatic lesions in a sample of Iraqi patients. This is a retrospective study, the clinicopathological data of 220 pancreatic lesions, were analyzed. The non-neoplastic lesions contributed to (20.45%) of all pancreatic lesions. Chronic pancreatitis, were 11 cases (24.44%), with same rate in male and female. The neoplastic pancreatic cystic lesions were (49.05%) and all patients were female, and the non-neoplastic cystic lesions were (50.94%). The neoplastic lesions formed 79.54% of all pancreatic lesions, and pancreatic ductal adenocarcinoma (PDAC) was the major component among the malignant epithelial neoplasms (93.38%), PDAC correlated significantly with age groups ($p<0.05$), majority of PDAC patients were at their 50s & 60s. PDAC histological grading was moderately differentiated in 75% and of stage pT2 and T3 in 83%. Radiological images revealed mass in 99% of malignant epithelial lesions and neuroendocrine neoplasm and this correlation was highly significant ($p<0.05$).

**KEYWORDS:** Pancreatic lesions, Chronic pancreatitis, PCLs, Pseudocyst, Mucin producing cysts, PDAC.

## INTRODUCTION

Pancreatic lesions are heterogeneous group of diseases with variable degree of potential malignancy, morbidity and mortality. However early detection has significant prognostic implications.[1,2]

**Pancreatitis** is the commonest lesion affect the pancreas.[1] Chronic pancreatitis is a fibro- inflammatory disease, in patients with genetic and environmental risk factors, leads to persistent tissue damage.[1,2] Early chronic pancreatitis is the reversible pathological condition of a preceding stage of completed chronic pancreatitis and with preserved pancreatic function.[3] Hereditary pancreatitis, seen in patients with autosomal recessive cystic fibrosis and individual with mutations in serine protease 1 (*PRSS1*) or serine peptidase inhibitor kazal type 1 (*SPINK1*).[4]

**Pancreatic cystic lesions (PCLs);** are common pancreatic disease, with different malignant potential, broadly mucinous cystic lesions have higher malignant potential than non-mucinous lesions.[5,6] Many guidelines have been published to assist in the diagnosis and management of PCLs. In 2018 European and non-European, multidisciplinary expert groups performed systematic reviews and an evidence-based guidelines, to improve diagnosis and management of PCNs.[6] In 2019 the WHO updated the definition and classification of PCNs.[5]

**Pancreatic Pseudocysts**; behave indolently, and may never progress into malignancy.[7] Composed of fluid collections inside or around the pancreatic parenchyma, with thick walls, and no lining epithelium. Cyst fluid is rich in pancreatic enzymes. They occur as a complication of acute or chronic pancreatitis, or trauma.[8] Its incidence is low (1.6–4.5%).[20] EUS–FNA cytology, is the preferred diagnostic tool, however correlation of cytology and/or histology with clinical history and radiology isa rule to confirm the diagnosis.[8]

**The Intraductal papillary mucinous neoplasm (IPMNs)**; are neoplastic mucinous epithelium of unclear malignant potential. Have equal sex distribution and presented as solitary or multifocal mass at the head of the pancreas.[9] IPMNs lesions, forming papillary proliferations in the main pancreatic duct and/or its

branches. And categorized into benign, borderline, or malignant depending on the grade of dysplasia and invasiveness.[10] IPMNs consider a well-known precursor of pancreatic ductalcarcinomas, with rates of in situ or invasive carcinoma, varies from 23% to 92%. These rates of carcinoma are high in main duct IPMNs (40-90%), and mixed (main duct and branch duct) type IPMNs (19-68%), and low in branch duct IPMNs (6-46%).[9-10] Therefore surgical resections are recommended for main duct and mixed type IPMNs.[9-10]

**Mucinous cystic neoplasms (MCNs);** occur almost exclusively in middle age females mainly at the tail and body of the pancreas without communication to the pancreatic duct. Histological sections show cellular ovarian-like stroma, stains positively for estrogen and progesterone receptors and KRAS mutation, and negative for GNAS and CTNNB1 mutations.[7,9,11] Cyst fluid analysis with DNA-based markers, and measurement of cyst fluid glucose level, give promising results in diagnosis of MCNs.[9,12] MCNs have significant risk of high-grade dysplasia and invasive carcinoma ranging from 10% to 39%, increases with the increasing size of the lesion (≥4cm) and/or presence of solid nodule.[7,9,11] In the 5th edition of the WHO classification of digestive system tumors - pancreatic tumors (2019), the IPMNs and mucinous cystic neoplasms are classified into two tiers of dysplasia (Low grade and high grade), rather than the three-tier system used in the 4th edition.[5]

**Solid pseudopapillary neoplasms (SPNs);** are low-grade malignant pancreatic lesions. Form less than3% of all primary pancreatic neoplasms. Occur in young females. SPNs are usually encapsulated and cured with surgical resection. However some (5–15%) have the risk of metastasis, recurrence, and an aggressive biological behavior. Risk factors for the aggressive behavior and poor prognosis are notfully clarified, and they vary among different studies.[8,13]

**Serous cystic neoplasms;** are always found in females younger than 55 year.[7] Unlike mucin producing cystic lesions (MCNs and IPMNs), serous neoplasms have very low or no risk of malignant transformation and can be classified as non-neoplastic PCLs, with no need for further imaging surveillance by most guidelines.[14] The malignant serous cyst, are rare and can only diagnosed in the presence of metastases.[15] Measurement of cyst fluid (CEA) and glucose levels can be used for differentiation between mucinous and serous pancreatic neoplasms.[7,9,14]

**Pancreatic tumors** are a broad spectrum of entity. The WHO classification of pancreatic neoplasms (2019), almost remains unchanged from the 4th edition. Except for the precursor lesions (PIN,IPMN and MCNs) are classified into two tiers of dysplasia, rather than the three-tier system, and the Intraductal tubulopapillary neoplasms and Intraductal oncocytic papillary are distinguished from IPMNs and adenocarcinoma by the absence of KRAS in these lesions.[5] Pancreatic cancer is of low annual incidence over the world. It has ranked the 11th among the most common cancer in the world.[16] In Iraq, it ranks the 16th by cancer site, with an incidence of 1.67/100000.[17] Worldwide, the incidence of pancreatic cancer increases with age and is slightly more in males.[16,17]

Pancreatic ductal adenocarcinoma (PDAC) is the commonest (90%) of all pancreas tumors.[18] Majority of PDACs are sporadic cancer, and less than 10% are hereditary/familial cancer.[18] Smoking, chronic pancreatitis, alcohol consumption, diabetes mellitus, obesity and age are consider as risk factors.[19] MCNs are considered as premalignant lesions and high grade pancreatic intraepithelial neoplasm (PanIN) and IPMNs are precursors of PDAC.[9,19] In the sporadic (non-hereditary) cancer, genomic analysis revealed activating mutations of *KRAS* gene, *TP53*, *CDKN2A* and *SMAD4* in over 90% of cases.[19] Histologically, PDAC is considered as a heterogeneous tumor consisting of many variants (e.g. Colloid carcinoma, signet ring cell carcinoma, medullary carcinoma, adenosquamous carcinoma).[5] Circulating tumor DNA (ctDNA), exosomes, KRAS gene mutations, and other protein markers, can be detected in two-thirds of early stage pancreatic cancer.[19] PDAC has poor prognosis with 5 year survival of 10% in USA and 8.5% in Japan. It ranks the third cause of cancer deaths in USA and the fourth In Japan, and it is expected to be the second cause of cancer related deaths by 2030.[16,17]

**Pancreatic neuroendocrine neoplasms (PNENs);** are slowly progressing tumors.[20] The (WHO) classification (2019) considered the differentiation and proliferation rate of the tumor for assessment.

Differentiation is assessed via the histopathological examination of the tumor, and classified into well-differentiated neuroendocrine tumors, or poorly differentiated neuroendocrine carcinomas (NECs). Tumor grading (the proliferation rate), is based on Ki-67 index and mitotic count.[5,21] Most PNENs occur sporadically, less occur with inherited disorders (MEN, von Hippel-Lindau syndrome).[20]

**Other pancreatic Lesions**

**Pancreatic islet hyperplasia**; The reported standard pancreatic islet diameter is about 150 µm, and islet >250 µm in diameter are considered as hyperplastic.[22] The main pathogenic mechanism for pancreatic islet cell hyperplasia is increased cell neogenesis from the exocrine ductal epithelium, and can be diagnosed by histologic examination. It could be focal or diffuse hyperplasia.[21,22]

In this study, we **aim to** assess different types of pancreatic lesions (neoplastic and non-neoplastic) with clinicopathological correlation in a sample of Iraqi patients.

## MATERIALS AND METHODS

We retrospectively analyzed the clinicopathological data of 289 pancreatic lesions, diagnosed at the Dept. of Pathology/Specialized Center for Gastroenterology and Hepatology/Medical City Teaching Hospital/Baghdad, for the period of 2019–2022.

**Inclusion criteria**: Cases with adequate data and materials for histopathological assessment (220 cases) were included in the study. Histopathological sections were reviewed and categorized into non- neoplastic and neoplastic pancreatic lesions, (according to the WHO classification of digestive system tumors (2019)), and a subclass of pancreatic cystic lesions (PCLs). Patients clinical parameters (age, Sex, radiological images, and types of surgical procedure) also included.

**Exclusion criteria**: Cases with insufficient data and/or with inadequate material for histopathological assessment (69 cases) were excluded.

**Statistical analysis;** The results were analyzed using SPSS v25.0 software, and descriptive statistics (frequency, range, mean, mode, and standard error). *P*-value ≤ 0.05 was considered statistically significant.

**Approval for the study**; Obtained from the Committee of Scientific Council of Pathology/Arab Board for Medical Specialization in Pathology.

**Ethical consideration**; Data were collected from archives of Dept. of Pathology/Specialized Center for Gastroenterology and Hepatology / Medical City Teaching Hospital. Patient files from the archives are allowed to be used for research purposes while maintaining the confidentiality of all information. And no costs were borne by the patients.

## RESULTS

The clinicopathological data of 289 pancreatic lesions were reviewed, and that with adequate data and materials for histopathological assessment (220 cases) were enrolled in this study. Among them (97, 44.09%) were male and (123, 55.90%) were female. Age ranged from 45 days (female with islet cell hyperplasia) to 90 years (female with adenocarcinoma) (Figure 1). Endoscopic ultrasound-fine needle biopsies (EUS-FNB) was the most frequent surgical procedure and adequate material were given in 64.43% of FNB specimens (table 1).

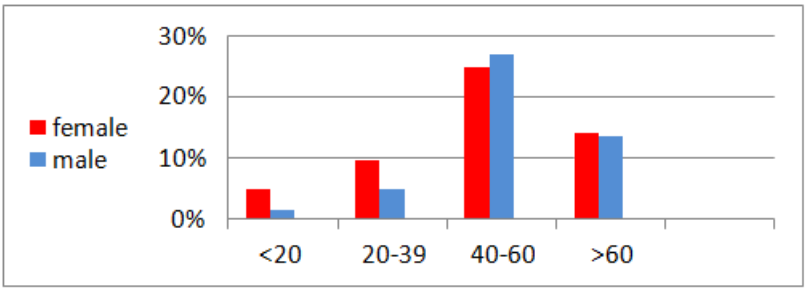



**Figure 1: Age and Sex Distribution of patients with pancreatic lesions in this study.**

**Table 1: Type of Biopsy (Surgical procedure) and Histopathological Results.**

| Type of Biopsy/Frequency & Pathological Results | EUS-FNB* No. | % | Excisional BiopsyNo. | % | Whipple** No. | % |
|---|---|---|---|---|---|---|
| Frequency of the procedure(n=289) | 194 | 67.12 | 52 | 17.99 | 43 | 14.87 |
| Adequate for histopathological assessment(n=220) | 125 | 64.43 | 52 | 100 | 43 | 100 |
| Inadequate for histopathological assessment(n=69) | 69 | 35.56 | 0 | 0 | 0 | 0 |
| Total 289 cases | | | | | | |

***Endoscopic ultrasound-fine needle biopsies, * Whipple procedure (pancreaticoduodenectomy) *P*-value < 0.05 is considered statistically significant**

**Non-Neoplastic Pancreatic Lesions;** A total of 45 (20.45%) non-neoplastic lesions were included in this study (table 2), among them 11 cases of chronic pancreatitis with a median age of 45.5 years, and a mean of 42.35 years (range, 14–60 years), of them, 6 were male and 5 were female. Histological sections revealed diffuse parenchymal fibrosis, acinar destruction and dilated ducts filled with protein plugs (figure 2). Pseudocysts, 10 were male and 15 were female, with wide age range (11–73 years), histologically the picture was consistent with the diagnosis of pancreatic pseudocyst, revealed cystic spaces without epithelial lining with reactive fibrosis and chronic inflammation), (figure 3).

Out of seven cases of islet cell hyperplasia, six were female with a median age and mode of 1 year.

Hydatid cyst was diagnosed in two cases (table 2). Radiological images were cystic in 60% of non-neoplastic lesions. No statistical significant associations ($P \geq 0.05$) were found between non-neoplastic lesions and other parameters (table 2).

**Table 2: Association of Non-Neoplastic Pancreatic Lesions Histopathology with Age, Sex, andRadiological data.**

| Non Neoplastic Pancreatic lesions (n=45) | | Lesion Histopathology | | | | Total No % | *P* Value* |
|---|---|---|---|---|---|---|---|
| | | Chronic Pancreatitis | Islet cell hyperplasia | Pseudocyst | Hydatid cyst | | |
| Lesions No % | | 11 (24.44%) | 07 (15.55%) | 25 (55.55%) | 02 (4.44%) | 45 (20.45%) | |
| Age Mean ±SE (years) | | 42.352± 3.42 | 3.32± 1.61 | 42.82± 3.67 | 17.5± 1.01 | | >0.05 |
| Age groups (years) | <20 | 1 (8%) | 7 (58%) | 3 (25%) | 1 (8%) | 12 (26.66%) | |
| | 20-39 | 3 (33%) | 0 | 5 (56%) | 1 (11%) | 9 (20.00%) | |
| | 40-59 | 7 (33.33%) | 0 | 14 (66.66%) | 0 | 21 (46.66%) | |
| | ≥60 | 0 | 0 | 3 | 0 | 3 (6.66%) | |
| Age range (years) | | 14 - 60 | 0.12 –12 | 11 - 73 | 10 - 25 | 0.12 –73 | |
| Sex | Male | 6 (33.33%) | 1 (5.5%) | 10 (55.55%) | 1 | 18 (40%) | >0.05 |
| | Female | 5 (18.5%) | 6 (22.22%) | 15 (55.55%) | 1 (3.7%) | 27 (60% | |
| Radiological data | Mass | 11 (61.11%) | 7 (38.88%) | 0 | 0 | 18 (40%) | >0.05 |
| | Cyst | 0 | 0 | 25 (92.6%) | 2 (7.4%) | 27 (60% | |

**P*-value < 0.05 is considered statistically significant

**Neoplastic Pancreatic Lesions;** A total of 175 (79.55%) neoplastic lesions were included in this study (table 3). Benign epithelial neoplasms formed only 17 cases (9.71%), (figure 4-6). Mucinous cystic neoplasms were the most common benign lesions. While the malignant epithelial neoplasms constituted 137 (78.28%) of all neoplastic pancreatic lesions, and ductal adenocarcinoma accounted for 93.38%. Most adenocarcinoma patients (76%) were at their 50s & 60s, with mode of 60 year. Males were nearly equal to females patients (table 3). Solid pseudopapillary neoplasm (SPN) patients were female, and eight out of nine cases (88.88%) were in 2nd and 3rd decade (table 3). Radiological images revealed mass in 99% of malignant epithelial lesions and neuroendocrine neoplasm.

**Table 3: Association of Neoplastic Pancreatic Lesions Histopathology with Age, Sex, andRadiological data.**

| Benign PancreaticLesions (n=17) | | Lesion Histopathology | | | | *P* Value* |
|---|---|---|---|---|---|---|
| | | IPMN | MCN | Serous cystadenomas | TotalNo % | |
| lesions No % | | 2 (11.5%) | 11 (65%) | 4 (23.5%) | 17 | |
| Age (years) Mean ±SE | | 47. 5 ±1.06 | 50.85±4.88 | 33.5±2.87 | | >0.05 |
| Age groups (years) | <20 | 0 | 0 | 0 | 0 | |
| | 20-39 | 1 | 2 | 3 | 6 (35%) | |
| | 40-59 | 0 | 6 | 1 | 7 (41%) | |
| | ≥60 | 1 | 3 | 0 | 4 (23.5%) | |
| Age range (years) | | 35 - 60 | 22 - 64 | 30 - 42 | | |
| Sex | Male | 0 | 0 | 0 | 0 | >0.05 |
| | Female | 2 | 11 | 4 | 17 (100%) | |
| Radiological data | Mass | 2 | 5 | 0 | 7 (41%) | >0.05 |
| | Cyst | 0 | 6 | 4 | 10 (58.9%) | |
| **Malignant Pancreatic lesions(n=137)** | | **Lesion Histopathology** | | | | ***P* value** |
| | | PanIN | PDAC | SPN | TotalNo % | |
| lesions No % | | 1 (0.7%) | 127 (92.7%) | 9 (6.6%) | 137 (78.28%) | |
| Age (years) Mean ±SE | | 52 | 56.24±1.0 | 25.88± 6.23 | | <0.05* |
| Age groups (years) | <20 | 0 | 0 | 4 (44.44%) | 4 (2.9%) | |
| | 20-39 | 0 | 4 (3.14%) | 4 (44.44%) | 8 (5.8%) | |
| | 40-59 | 1 (100%) | 65 (51.18%) | 0 | 66 (48.17%) | |
| | ≥60 | 0 | 58 (45.66%) | 1 (11.11%) | 59 (43%) | |
| Age range (years) | | 52 | 25 -90 | 11 - 73 | | |
| Sex | Male | 1 (100%) | 64 (50.39%) | 0 | 65 (47.44%) | >0.05 |
| | Female | 0 | 63 (49.61%) | 9 (100%) | 72 (52.55%) | |
| Radiological data | Mass | 1 (100%) | 127 (100%) | 1 (11.11%) | 129 (94.16%) | <0.05* |
| | Cyst | 0 | 0 | 8 (88.88%) | 8 (05.84%) | |
| **Neuroendocrine Neoplasms (n=21)** | | | | | | |
| Age (years) Mean ±SE | | 48.42± 2.1 | | | | ***P* value** |
| Age groups(years) | <20 | 0 | | | | >0.05 |
| | 20-39 | 4 (19.04%) | | | | |

| | | | |
|---|---|---|---|
| | 40-59 | 13 (61.90%) | |
| | ≥60 | 4 (19.04%) | |
| Age range (years) | | 32 - 63 | |
| Sex | Male | 12 (57.14%) | >0.05 |
| | Female | 9 (42.86%) | |
| Radiological data | Mass | 21 (100%) | <0.05* |
| | Cyst | 0 | |

**SE (Standard Error), IPMN (Intraductal papillary mucinous carcinoma), MCN (Mucinous cystic neoplasm), PanIN (pancreatic Intraepithelial Neoplasm), SPN (Solid Pseudopapillary Neoplasm). *statistically significant (*P*-value ≤ 0.05)**

Pathological staging were assessed in 35 adenocarcinoma pancreatectomy specimens, pT2 and T3 were the most common stage (83%). Ductal adenocarcinoma grading were assessed in 81 cases, and moderately differentiated was the most common (75%) (figure 7). With respect to location, reported in (55, 25%) of the cases, and the most common was the head (87.27%) followed by the body and tail (7.27% and 5.45% respectively). No significant associations were found between neoplastic lesions and other parameters, except for that of malignant lesions with patients' age and with radiological data ($p$ =0.01), (table 3).

**Pancreatic Cystic Lesions;** Formed 53 cases (24.09%) of pancreatic lesions in this study. Classified according to the WHO criteria into neoplastic cystic lesions in (26 cases, 49.1%) and non-neoplastic cystic lesions in (27 cases, 50.9%). The neoplastic cystic lesions were mucin producing cystic lesions (IPMNs and mucinous cystic neoplasms) and nonmucinous cystic lesions (SPNs, serous cystic neoplasms) (table 4 & figure 4 - 6). Majority of mucin producing cystic lesions (all except one MCN case), were of low grade dysplasia. And all patients with neoplastic cysts were female. The non-neoplastic cystic lesions were pseudocyst (25 cases) and Hydated cyst (two cases) (Table 4). No statistical significant associations were found between pancreatic cystic lesions and other parameters except for that of benign neoplastic lesions with sex ($P \leq 0.05$) (table 3).

**Table 4: Distribution of (53) Pancreatic Cystic Lesions Histopathology Associated with Age & Sex.**

| Pancreatic Cystic LesionsHistopathology | | | Cystic Lesions No. | % | Male/ Female Ratio | Age Mean ±SE |
|---|---|---|---|---|---|---|
| Epithelial Neoplastic Cystic Lesions | Mucin Producing Cystic Lesions | IPMN with lowgrade dysplasia | 2 | 7.69 | 0/2 | 47, 50 |
| | | IPMN with high grade dysplasia | 0 | 0 | 0 | 0 |
| | | MCN with lowgrade dysplasia | 10 | 38.46 | 0/10 | 50.85±4.88 |
| | | MCN with highgrade dysplasia | 1 | 3.84 | 0/1 | 64 |
| | NonmucinousCystic Lesions | Serous cystadenomas | 4 | 15.38 | 0/4 | 33.5±2.87 |
| | | SPN | 9 | 34.61 | 0/9 | 25.88± 6.23 |
| | Total | | 26 | 49.1 | 0/26 | --- |
| Non-Epithelial Non-Neoplastic Cystic Lesions | Pseudocyst | | 25 | 92.59 | 10/15 | 42.82± 3.67 |
| | Hydatid Cyst | | 2 | 7.40 | 1/1 | 17.5 |
| | Total | | 27 | 50.9 | 11/16 | --- |

**SE (Standard Error), IPMN (Intraductal papillary mucinous neoplasm), MCN (Mucinous cystic neoplasm), SPN (SolidPseudopapillary Neoplasm). * statistically significant (*P*-value ≤ 0.05)**

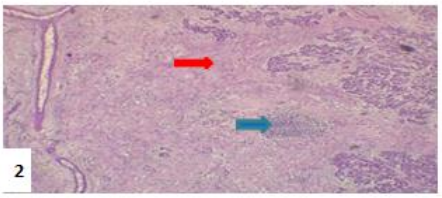


**Figure 2: Chronic pancreatitis shows loss of acini with irregular periductal fibrosis (red arrow) & chronic inflammation (blue arrow). (H&E, 10x).**

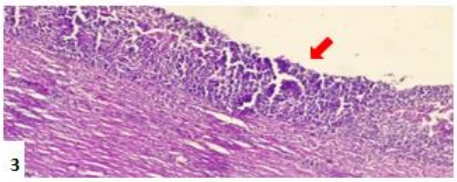


**Figure 3. Pseudocyst. Shows lining of necrotic debris (red arrow), surrounded by thick fibrotic wall. No lining epithelium. (H&E, 10x).**

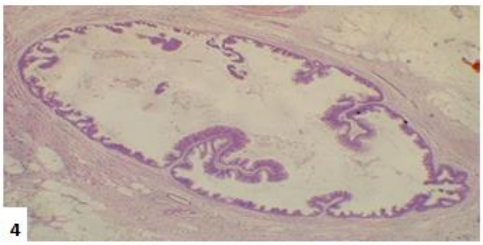


**Figure 4: IPMN proliferation of mucinous epithelium with low grade dysplasia and papillae formation. No ovarian type stroma (H&E, 10x).**

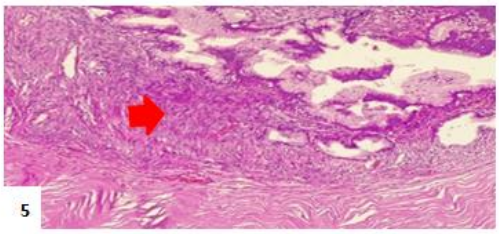
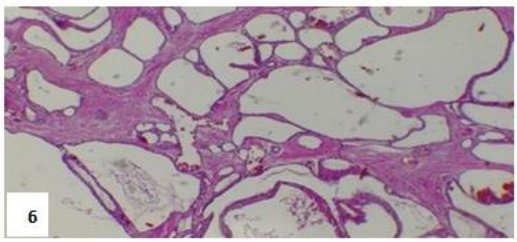


**Figure 5: Mucinous Cystic neoplasms with low grade dysplasia, lined by mucinous epithelium and surrounded by ovarian type stroma (red arrow). (H&E, 10x)**



**6: Serous Cystadenoma, mass of small cystic spaces lined by cuboidal epithelial with fibrotic stroma and capillary network. (H&E, 10x).**

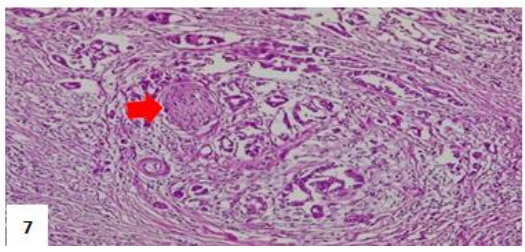


**Figure 7: Pancreatic Adenocarcinoma moderately differentiated. Tumor shows perineural invasion (red arrow).**

## DISCUSSION

A variety of pancreatic lesions are diagnosed in clinical practice, and the distinction of these lesions contributed in disease management and prognosis. Interest has emerged on EUS-FNB, as sensitive procedure for diagnosing pancreatic diseases. In this study EUS–FNB contributed to (67.12%) ofpancreatic specimens, and gave relevant pathological findings in (64.43%) of the cases. Publishedstudies proved that EUS-FNB have superior diagnostic yield in PCLs, compared to FNA cytology (74% Vs. 38.1%). However, further research work is necessary to determine their safety applications,and the optimal sampling with FNB.[23]

**Pancreatitis;** Broadly chronic pancreatitis is a disease of middle age male.[1-4] Our results revealed 11 cases of chronic pancreatitis, six males and five females. The mean age was 42 years. Histological sections revealed diffuse fibrosis with foci of chronic inflammation, loss of acini and dilated ducts. Published results vary in the reported mean age and sex ratio. These variation can be related to the differences in life styles, exposure to risk factors and genetic susceptibility.[4,24]

**Pancreatic cystic lesions (PCLs);** In this study, there were 53 cases of PCLs. Twenty seven (50.94%) were non-neoplastic, and 26 (49.05%) were epithelial neoplastic cystic lesions. The reported prevalencerates of incidental PCLs (in asymptomatic adult population), varies from 0.2% to more than 20%, with different imaging techniques.[7,25]

**Pseudocysts** contributed to 93% of non-neoplastic cystic lesions, diagnosed from histological sections in correlation with the clinical and radiological data. The reported pseudocysts is that with a prevalenceof 10–26% in acute pancreatitis and 20–40% in chronic pancreatitis.[7-9] No significant associations were found between non -neoplastic lesions and other parameters ($p > 0.05$).

**The Intraductal papillary mucinous neoplasm (IPMNs);** In this study two cases IPMN were diagnosed (1.14% of neoplastic lesions). Both were females with mean age of 47.5 years. Histological sections revealed proliferation of mucinous epithelium with low grade dysplasia and papillae formation. In a larger study by Peisl *et al*. (2023), a total of 56 cases of IPMN were diagnosed over 14 year period.[26] This high incidence may related to the broad application of imaging techniques (CT & MRI) in their study design. Various guidelines discuss absolute and relative indications for surgery. The absolute indications includes presence of high risk lesions (main duct IPMNs and mixed type IPMNs, enhancing nodule, dilated main pancreatic duct≥10mm, cytology with high grade dysplastic or malignant cells and jaundice). [25,26] Peisl *et al* (2023), suggested panel analyses of cyst fluid for several biomarkers (PG E, interleukin 1β, telomere fusion status, and analysis of driver genes, KRAS, GNAS, or KLF4, miRNA), to predict IPMNs with high malignant potential.[26]

**Mucinous cystic neoplasms (MCNs);** Our study revealed 11 cases of MCNs, all were females, with mean age of 51 years. Location was reported only in 3 cases, two were in the body and one in the tail ofthe pancreas. Radiological data revealed cystic lesions in 6 cases and mass in 5 cases. Histological sections showed columnar epithelium with dense ovarian type stroma. No invasive malignancy. Similar findings were published in other studies, that reported female gender in 95% of the cases with average age of 47 years, and 90% of the lesions were in the body and tail of the pancreas. Diagnosis of MCNs in male is seldom in most published data.[11,27] MCNs with low grade dysplasia formed the majority in our study as well other studies.[11,27] Published articles reported, that most MCNs are non- invasive, slow growing, and have an excellent prognosis, even with invasive disease.[7,9,27]

**Solid Pseudopapillary Neoplasm (SPNs);** In this study nine cases of SPNs, formed 5.14% of all neoplastic lesions. All were females, with a median age of 22 years. Radiological images were solid mass in 8 cases. These results were in accordance with other studies,[7,9] There are no specific diagnostic biomarkers for SPNs, and the characteristic findings for the malignant behavior have not been fully cleared. Although published articles have suggested that tumor size, proliferative index, and lymph node metastasis may be indicators for an aggressive and poor prognosis SPN.[9,13]

**Serous cystadenomas**; Our results revealed four cases of serous cystadenomas, all were females, in their 30s. Histological sections show cysts lined by cuboidal cells. Serous cystadenomas form less than 1% of all primary pancreatic cystic lesions, majority are incidental finding, in women between the 5$^{th}$ and 7$^{th}$ decades, and located in the body or tail of the pancreas.[14,25] Except for large symptomatic cyst, management is conservative, by most guidelines. Malignant serous cystadenocarcinomas, are rare lesions, and defined by the presence of liver and/or lymph nodes metastasis.[15]

**Pancreatic Ductal Adenocarcinoma (PDAC):** Pancreatic cancer, as one of the most fatal cancers, remains a critical lesion in the global burden of disease.[28] Based on results from this study, PDAC formed (93.38%) of malignant epithelial lesions, equally distributed in males and females. Majority of the patients are in 6th & 7th decades and this correlation was significant, and the appearance as mass in radiological images was highly significant ($p$ <0.05). In terms of anatomical site, 87.27% of the cases were at the head of the pancreas. Increasing in pancreatic cancer incidence in both sexes and most age groups were observed in many countries, in the last few decades.[16,17] Published studies reported highest incidence of PDAC in male older than70 year.[16,17,28] The differences in published results concerning patients' age and sex, may related to the exposure to certain risk factors, or the variety of radiological techniques, or even the accuracy of registration may be responsible for the observed variation. Similar studies data explored that aging and male gender may be risk factors for pancreatic cancer, and considered women are less exposing to environmental risk factors.[28] Moderately differentiated grade was the commonest grade in our results assigned in (75.30%) of the cases, and 85.71% were pT2 and pT3. Most published data agree that that moderately differentiated, advanced stage PDAC are the commonest in clinical practice.[18,23]

**Neuroendocrine tumors**; In our study there were 21 cases of pancreatic neuroendocrine tumors (12% of neoplastic pancreatic lesions). The histologic H&E sections showed solid nest of small malignant cells. Male to female ratio was 12/9, and the mean age was 48.42 years. The reported incidence rate ranging from (2.5 – 8.35%).[20] the heterogeneity in the reported incidence rate, may related to the non-standardized categorization protocol, and as well, the role of the biomarkers for applying the WHO grading system. This heterogeneity

hinders the development of an accurate summary of the epidemiology, sub classification and extent of NENs.[21]

**Islet hyperplasia;** were diagnosed via histologic examination in 7 cases, six were females, their age ranged from 45d –12y. Pancreatic islet hyperplasia should be considered in diagnosis and treatment of hypoglycemia, increased islet hormone, and neuroendocrine tumors.[22]

**Hydated cyst;** In our study there were two cases of pancreatic hydatid cyst. Pancreatic hydatid cyst has been reported in other studies.[7,29] Serological testing and (ELISA) for echinococcal antigens are common method for diagnosis.[29]

Despite our findings, this study had some **limitations**. Being retrospective study in a single center, poses some limitations. Furthermore, not all lesions included were precisely described (i.e. tumor location, type, grading or staging). However the **strengths** of our study are the detailed analysis of relatively representative large number of pancreatic lesions (220 cases), including 127 cases PDAC.

In **conclusion**, pancreatic lesions are commonly encountered in clinical practice and in pathological laboratories, tend to occur in men and women and in young age group. The neoplastic lesions form the majority of all and PDAC was the major component.

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