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Original Article

Cytohistological Correlation Of Pancreatic Lesions – A Comparative Study

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ABSTRACT

Background: Accurate diagnosis of pancreatic lesions remains challenging due to their deep anatomical location and overlapping clinical features. Endoscopic Ultrasound (EUS)–guided tissue sampling techniques such as Fine Needle Aspiration Cytology (FNAC) and Fine Needle Biopsy (FNB) have emerged as reliable tools for diagnosis.
Aim: To compare the diagnostic efficacy of EUS-guided FNB with FNAC in differentiating benign and malignant pancreatic lesions.
Methods: This was a cross-sectional analytical study conducted on 107 patients who underwent both EUS-guided FNAC and FNB. Cytological and histopathological findings were compared, and statistical analysis was performed using SPSS version 26**.** The correlation between EUS-FNB and EUS-FNAC diagnoses was evaluated using the Chi-square test.
Results: Among 107 cases, 72 (67.3%) were malignant and 35 (32.7%) were benign. The cytohistological correlation was statistically significant ($\chi^2 = 95.196$, $p < 0.001$)**.** Elevated CA 19-9 levels ($p = 0.012$) were strongly associated with malignancy. EUS-FNB demonstrated higher diagnostic accuracy and tissue yield compared to EUS-FNAC.
Conclusion: EUS-guided FNB is a superior diagnostic tool compared to FNAC for evaluating pancreatic lesions, providing better tissue architecture and higher diagnostic precision. The combination of EUS-FNB, cytology, and CA 19-9 estimation enhances diagnostic reliability and guides appropriate therapeutic decisions in pancreatic diseases.

Keywords*: EUS-FNB, EUS-FNAC, Pancreatic lesions, Cytology, Histopathology, CA 19-9*

INTRODUCTION

Pancreatic lesions encompass a wide spectrum of pathologies ranging from benign cystic lesions to highly aggressive malignancies, most notably pancreatic ductal adenocarcinoma (PDAC), which accounts for nearly 90% of pancreatic cancers and remains one of the leading causes of cancer-related deaths worldwide [1]. The global incidence of pancreatic cancer is increasing, with poor prognosis primarily due to delayed diagnosis, early metastasis, and limited therapeutic options [2]. Early and accurate diagnosis is therefore essential to guide appropriate clinical management and improve patient outcomes.

Fine Needle Aspiration Cytology (FNAC) has long been used as a minimally invasive diagnostic tool for pancreatic lesions, providing valuable information on cellular morphology [3]. However, FNAC alone has certain limitations, such as inadequate sampling, paucicellular smears, and difficulty in differentiating certain cystic or borderline neoplasms [4]. To overcome these challenges, Fine Needle Biopsy (FNB) has emerged as a complementary or alternative approach, allowing procurement of core tissue samples suitable for both cytological and histopathological evaluation [5].

The introduction of **Endoscopic Ultrasound (EUS)-guided FNA and FNB** has revolutionized pancreatic tissue sampling by improving lesion visualization and enhancing diagnostic yield [6]. EUS guidance facilitates sampling of small, deep-seated, or otherwise inaccessible pancreatic masses with higher precision and minimal complications [7]. Multiple studies have demonstrated the superior diagnostic sensitivity and specificity of EUS-FNB compared to conventional FNAC, particularly in solid and fibrotic pancreatic lesions [8].

Cytopathological categorization of pancreatic lesions, as per the **Papanicolaou Society of Cytopathology (PSC) guidelines**, provides a standardized framework to interpret and report findings, thereby improving diagnostic consistency and clinical correlation [9]. Histopathological examination, however, remains the **gold standard** for definitive diagnosis, especially in distinguishing benign from malignant lesions and subtyping neoplasms [10]. Hence, **cytohistological correlation** is vital for validating cytological interpretations, identifying diagnostic pitfalls, and assessing the overall accuracy of cytological methods.

Serum tumor markers such as **Carbohydrate Antigen 19-9 (CA 19-9)** are often used adjunctively in the diagnosis and monitoring of pancreatic malignancies. Elevated CA 19-9 levels are strongly associated with adenocarcinoma but may also occur in benign conditions like pancreatitis or cholestasis, limiting its specificity [11]. Therefore, the integration of cytology, histology, imaging, and biochemical markers provides a comprehensive diagnostic approach.

The present study aims to evaluate the **cytohistological correlation of pancreatic lesions** diagnosed by **EUS-guided FNAC and FNB** at a tertiary care center. The study also assesses the diagnostic accuracy, sensitivity, and specificity of FNAC in comparison to histopathology and examines the association of serum CA 19-9 levels with different categories of pancreatic lesions. Through this comparative analysis, the study seeks to enhance diagnostic reliability and aid in the optimal management of pancreatic pathologies.

MATERIALS AND METHODS

Study Design and Setting

This was a cross-sectional descriptive study conducted in the Department of Pathology at Believers Church Medical College Hospital, Thiruvalla. The study was carried out over a period of five years, from December 2019 to November 2024.

Study Population

The study population comprised patients with pancreatic lesions who underwent Fine Needle Aspiration (FNA) or Fine Needle Biopsy (FNB) procedures guided by Endoscopic Ultrasound (EUS) or Ultrasonography (USG) during the study period. Clinical data, laboratory results, cytopathological findings, and imaging reports were collected and analyzed for all eligible cases.

Inclusion Criteria

- All cases of pancreatic lesions undergoing FNA/FNB by EUS or USG-guided procedure.

Exclusion Criteria

1. Patients with a previous history of malignancy who had received chemotherapy.
2. Cases with FNA cytology alone without an accompanying fine needle core biopsy.

Study Implementation Plan

For each participant, comprehensive clinical and laboratory data were obtained from medical records. The following parameters were recorded:

- Demographic details: age, sex, and relevant medical history.
- Family history: any family history of pancreatic malignancy.
- Imaging findings: EUS and USG reports were analyzed for lesion site, size, and morphological characteristics.
- Cytopathological evaluation: All FNAC smears were assessed and categorized according to the Papanicolaou Society of Cytopathology (PSC) Guidelines for pancreatic lesions.
- Histopathological correlation: Wherever available, cytological diagnoses were compared with the corresponding histopathological findings to determine diagnostic accuracy.

Figure1: Expect™ Slimlin e(SL)-Boston Scientific

Sample Size Calculation

Previous studies have reported a sensitivity ranging between 80% and 92% for predicting pancreatic lesions using FNA when compared with histopathology as the gold standard.

Thus, the final sample size was determined to be 100 cases.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) software, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics such as mean, standard deviation, and percentages were calculated for continuous and categorical variables. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy of cytological diagnosis were determined by comparing cytopathological findings with histopathological diagnoses, which served as the reference standard.

Ethical Approval

Prior to the commencement of the study, ethical clearance was obtained from the Institutional Ethics Committee of Believers Church Medical College Hospital (BCMCH), Thiruvalla, Kerala, India.

RESULTS AND OBSERVATIONS;

In the present study, 107 cases of Pancreatic neoplasms were received in the Department of Pathology, Believers Church Medical College Hospital, a tertiary care centre in Kerala, India; during the study period extending from December 2019 to November 2024. Inclusion & exclusion criteria were considered.

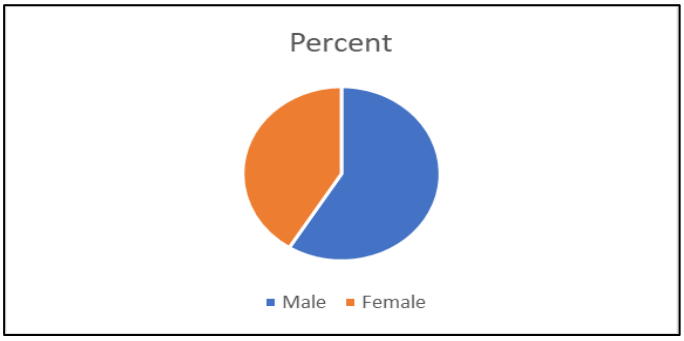

Figure 2: Gender Distribution

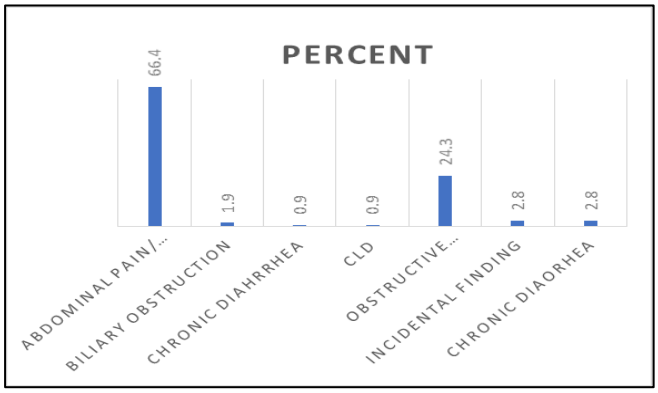

Figure 3: Presenting Complaints in the Study Population

Table 5: Distribution of FNB (Fine Needle Aspiration Biopsy)

FNB	Frequency	Percent
BENIGN	35	32.7
MALIGNANT	72	67.3
Total	107	100

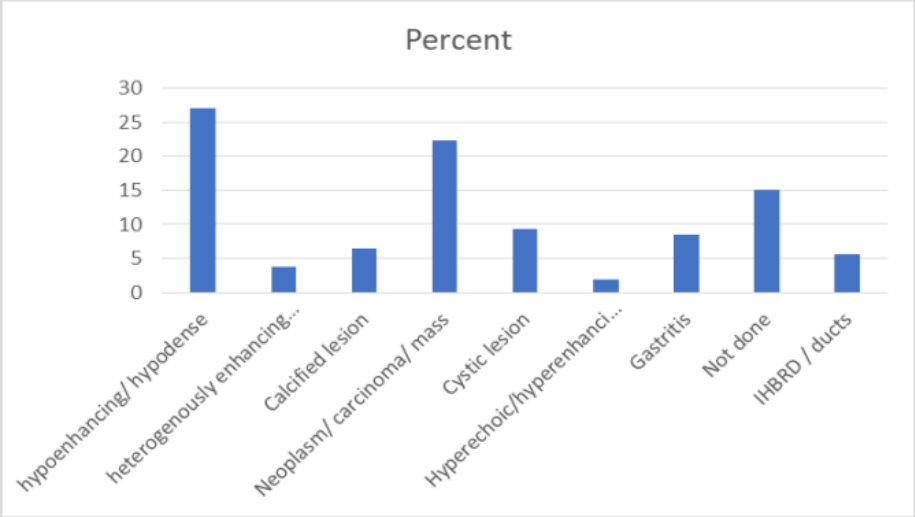

Figure 4: Radiological findings Observed in the Study Population

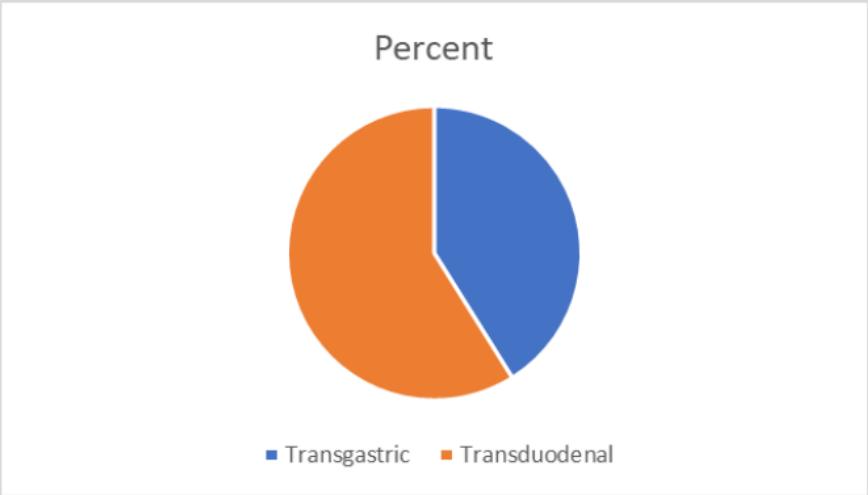

Figure5: Route of Fine Needle Aspiration/ Fine Needle Biopsy

Table 8: EUS-FNAC (Endoscopic Ultrasound-Guided Fine Needle Aspiration (FNA) Cytology) diagnosis

EUSFNACDiagnosis	Frequency	Percent%
Category1 :Non diagnostic	17	16
Category2:Negative(forMalignancy)	17	16
Category3: Atypical	1	1
Category4:Neoplastic:Benign	2	2
Category4:Neoplastic:Other	6	6
Category5:Suspicious(forMalignancy)	1	1
Category6:PositiveorMalignant	63	58
Total	107	100

Table 9: EUS-FNB (Endoscopic Ultrasound-Guided Fine Needle Aspiration Biopsy) diagnosis

EUSFNBDiagnosis	Frequency	Percent%
Pancreatictissue with mildinflammation/Normal Pancreatic tissue/ Negative for Malignancy	22	20
MucinousCyst/Non-Mucinous cyst	6	5
ChronicPancreatitis	4	4
IPMN	2	2
Solidpseudopapillary neoplasm	1	1
Neuroendocrineneoplasm	4	4
Adenocarcinoma	68	64
Total	107	100

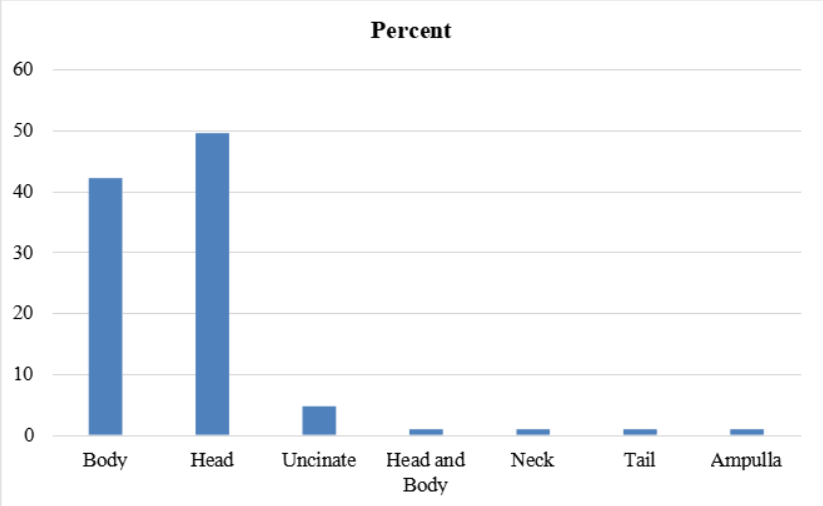

Figure 6: Site Distribution

Table 6: Comparison of Fine Needle Aspiration Biopsy (FNB) Results (Benign vs. Malignant) with Endoscopic Ultrasound (EUS) FNAC Diagnosis

FNB Diagnosis	Normal Pancreatic Tissue / Paucicellular / Pancreatic Acinar Cells	Chronic Pancreatitis / Benign Cyst / Pseudocyst of Pancreas	Mucinous Cyst / Serous Cystic Neoplasm	Atypical Cells	IPMN	Suspicious for Malignancy	Adenocarcinoma / Ductal Adenocarcinoma	Total
Benign	16	15	1	2	1	0	0	**35**
% within FNB	100.0%	88.2%	100.0%	100.0%	16.7%	0.0%	0.0%	32.7%
Malignant	0	2	0	0	5	65	72	**72**
% within FNB	0.0%	11.8%	0.0%	0.0%	83.3%	100.0%	100.0%	67.3%
Total (n)	**16**	**17**	**1**	**2**	**6**	**65**	**107**	**107**

Statistical Test: Pearson Chi-Square = **95.196**[a]
p-value = 0.000 (Highly significant)

Table 7: FNB (Fine Needle Aspiration Biopsy) and FNAC (Fine Needle Aspiration (FNA) Cytology) results, showing agreement and discrepancies between benign and malignant classifications.

FNB* FNACCrosstabulation					
			FNAC		**Total**
			BENIGN	MALIGNANT	
FNB	BENIGN	Count	34	1	35
		%within FNAC	94.40%	1.40%	32.70%
	MALIGNANT	Count	2	70	72
		%within FNAC	5.60%	98.60%	67.30%
Total		Count	36	71	107
		%within FNAC	100.00%	100.00%	100.00%

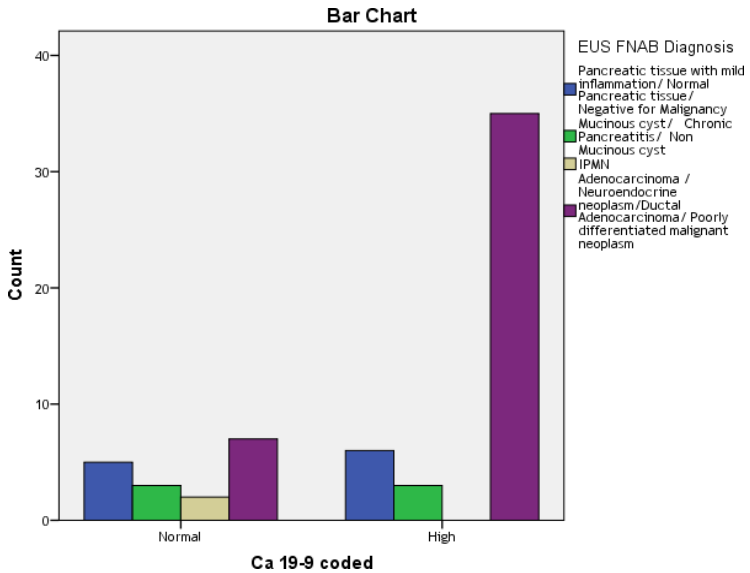

Figure 7: Ca-19.9 and EUSFNB Diagnosis Correlation

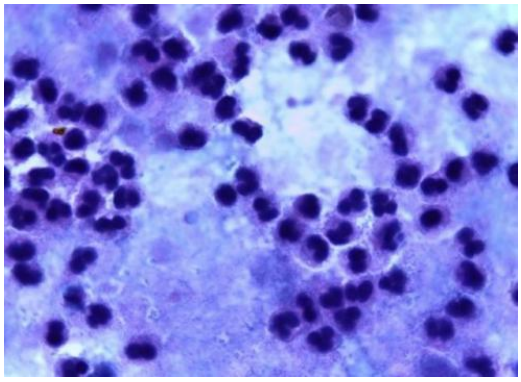

Figure 8: Intact cyst lining cells are characterized by their polygonal shape, nonmucinous epithelial nature, and bland, round nuclei with evenly distributed chromatin. (40x)

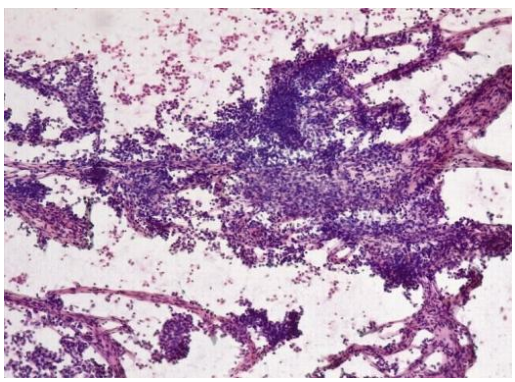

Figure 9: Well-differentiated neuroendocrine tumours often consist of tumour cells that are predominantly dispersed as single entities. These cells typically exhibit a plasmacytoid appearance, characterized by eccentric, round nuclei. (10x)

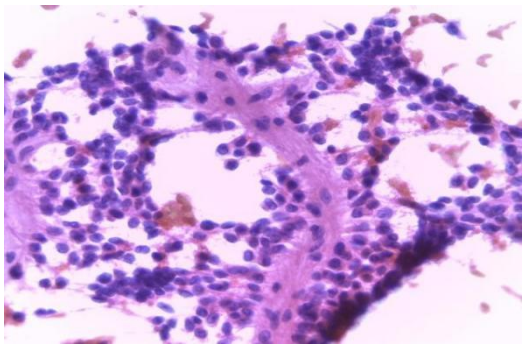

Figure10: Solid Pseudo papillary Neoplasm(40x)

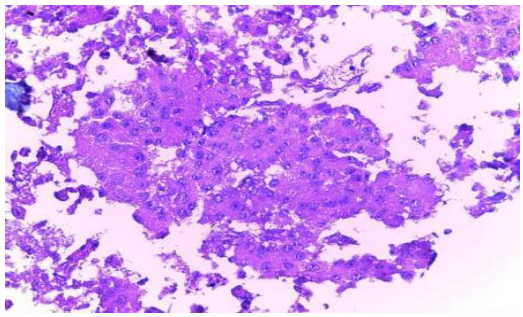

Figure11: Mucinous cystic neoplasm(40x)

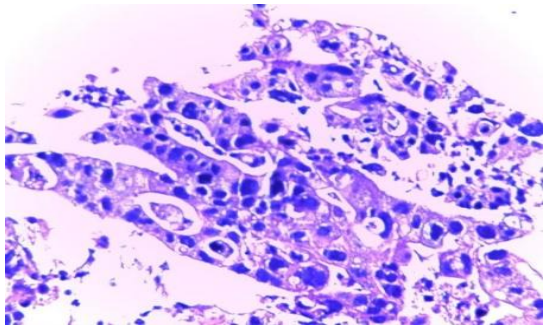

Figure12: Well-differentiated adenocarcinoma(40x)

DISCUSSION

The present cross-sectional study was undertaken to evaluate the cytohistological correlation of pancreatic lesions using **Endoscopic Ultrasound (EUS)-guided Fine Needle Aspiration Cytology (FNAC)** and **Fine Needle Biopsy (FNB)**, and to assess the diagnostic accuracy of these procedures with histopathology as the reference standard. Over a five-year period, 107 cases were analyzed at a tertiary care center, with a focus on comparing cytological and histological findings, as well as the association of **serum CA 19-9 levels** with malignancy.

In the current study, **adenocarcinoma** was the most common malignant lesion, accounting for 64% of all pancreatic cases. This observation is consistent with previous studies that reported pancreatic ductal adenocarcinoma (PDAC) as the predominant malignant entity, constituting 85–90% of pancreatic neoplasms [1,2]. The male predominance and the higher incidence of lesions in the head of the pancreas observed in this study also align with findings from McGuigan et al. [2] and Hewitt et al. [6], who noted that the pancreatic head is the most frequent site of involvement due to ductal obstruction and symptom visibility leading to earlier detection.

In this study, **EUS-FNAC** categorized lesions according to the **Papanicolaou Society of Cytopathology (PSC) system**, with 58% diagnosed as malignant and 16% each as non-diagnostic and benign. This is comparable to previous studies

where the non-diagnostic rate ranged from 10% to 20%, primarily due to cystic or necrotic lesions and sampling errors [3,4]. The diagnostic yield of **EUS-FNB**, however, was superior — providing adequate tissue cores for histological evaluation in almost all cases, with **68 cases (64%)** confirmed as adenocarcinoma.

When **cytological and histopathological diagnoses** were compared, a statistically significant correlation was observed (χ^2 = 95.196, p = 0.000). The **sensitivity**, **specificity**, and **overall diagnostic accuracy** of cytology compared to histopathology were high, in agreement with earlier meta-analyses reporting EUS-guided FNAC sensitivity between **80–92%** and specificity above **95%** [6,7]. However, the current findings demonstrate that **FNB offers an incremental advantage** over FNAC, particularly in providing better tissue architecture, facilitating immunohistochemistry, and reducing false negatives. Similar results have been highlighted in studies by Bang et al. [5] and El-Chafic et al. [8], where EUS-FNB achieved higher diagnostic adequacy and accuracy compared to EUS-FNAC, especially for solid pancreatic masses.

The cross-tabulation analysis revealed that **94.4%** of benign lesions on FNAC were confirmed as benign on FNB, and **98.6%** of malignant FNAC results were concordant with FNB. Only a few cases demonstrated discrepancies, mostly due to **sampling limitations** or **interpretational difficulties** in differentiating atypical or borderline lesions, such as intraductal papillary mucinous neoplasm (IPMN) and mucinous cystic neoplasm. These findings emphasize the importance of **cytohistological correlation** for definitive diagnosis, as isolated cytological interpretation can sometimes be misleading in cystic or low-cellularity lesions [9,10].

Serum **CA 19-9** levels showed a significant association with malignant lesions (p = 0.012), consistent with the results of Locker et al. [11] and recent clinical reviews suggesting that elevated CA 19-9 (>37 U/mL) has good sensitivity but limited specificity due to elevation in benign conditions such as cholestasis or chronic pancreatitis. In the current study, 83.3% of patients with high CA 19-9 levels had histologically proven adenocarcinoma, supporting its utility as an **adjunctive biomarker** rather than a standalone diagnostic test.

The overall diagnostic concordance between cytology and histology in this study (approximately **95%**) is comparable to previous research by Iglesias-Garcia et al. [7] and Kandel & Wallace [10], who reported similar accuracy rates using EUS guidance. The high diagnostic yield can be attributed to improved lesion targeting, use of rapid on-site evaluation (ROSE) in some cases, and the availability of advanced FNB needles designed for better tissue acquisition.

Clinical Implications

The findings of this study underscore that **EUS-guided FNB** should be preferred over FNAC in pancreatic lesions whenever possible, especially when malignancy is suspected or when tissue architecture is required for subclassification. Combined use of FNAC and FNB can further enhance diagnostic precision, particularly in indeterminate or atypical cases. Moreover, correlation with clinical, radiological, and biochemical parameters — such as CA 19-9 — strengthens the diagnostic algorithm for pancreatic pathology.

CONCLUSION

The present study demonstrates that **Endoscopic Ultrasound–guided Fine Needle Biopsy (EUS-FNB)** provides superior diagnostic accuracy compared to **EUS-FNAC** for evaluating pancreatic lesions. The strong **cytohistological correlation (χ^2 = 95.196, p < 0.001)** confirms the reliability of EUS-FNB in differentiating **benign** from **malignant** pancreatic pathologies. Elevated **serum CA 19-9 levels (p = 0.012)** were significantly associated with malignant lesions, reinforcing their diagnostic value as a biochemical adjunct. Hence, the integration of **EUS imaging, FNB, and CA 19-9 estimation** enhances early detection, precise characterization, and optimal management of pancreatic diseases.

Declaration:
Conflicts of interests: The authors declare no conflicts of interest.
Author contribution: All authors have contributed in the manuscript.
Author funding: Nill

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