



Assessment of the Diagnostic Accuracy of EUS-FNAC for Evaluating Intra-Abdominal Lesions

Md. Fazlur Rahman^{1*}, Zannatul Ferdous², AHM Towhidul Alam³, Manir Hossain Khan⁴

¹Resident, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
Email: fazlurr1983@gmail.com,
Orcid ID: 0009-0000-1421-9060

²Radiologist, Department of Radiology and Imaging, Dhaka Medical College Hospital, Dhaka, Bangladesh.
Email: zannatsbmc34@gmail.com,
Orcid ID: 0009-0005-1353-6298

³Professor, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
Email: gsdbsmmu@gmail.com,
Orcid ID: 0000-0002-4355-3516

⁴Associate Professor, Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.
Email: dmanirhk@gmail.com,
Orcid ID: 0009-0008-5084-7484

*Corresponding Author

Received: 15 September 2023

Revised: 22 October 2023

Accepted: 06 November 2023

Published: 31 December 2023

Abstract

Background: The abdominal cavities can develop a wide range of reactive, inflammatory, and neoplastic lesions. Determining prognosis and choosing the best method of treatment require accurate diagnosis. EUS-FNA is now routinely done in many endoscopic centers. This study conducted to assess the diagnostic accuracy of EUS-FNAC for evaluating intra-abdominal lesions. The aim of this study was to evaluate the diagnostic accuracy of EUS-FNAC for evaluating intra-abdominal lesions. **Material & Methods:** The observational analytical study was carried out from January 2016 to February 2017 over a period of 12 months in the general surgery unit in the Department of Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. About twenty-five patients with intra-abdominal lesions were included in this study; the other patients were excluded based on exclusion criteria. The results were given with the use of tables showing mean values, ranges, frequencies, and percentages. **Results:** Out of 25 cases, the maximum number of patients 7 (28.00%) were in the age group >60 years. The mean age was 50.04, within the range of 14–77 years. The male-female ratio was 2.13:1. Most patients have symptoms of abdominal pain 19 (76.00%). The majority of patients presented without abdominal lump (80.00%). Most of the intra-abdominal lesions detected by EUS were in the pancreas 16 (64.00%), followed by intra-abdominal lymphadenopathy 5 (20.00%). Most of the needle passes (17 or 68.00%) were 3–4 passes. Majority of the patients were malignant 18 (72.00%). The EUS-FNAC technique has a high validity (88%) for diagnosing of intra-abdominal lesions, with a perfect specificity (100%) and positive predictive value (100%). **Conclusions:** In surgical practise, intra-abdominal lesions will always remain an enigma. EUS-FNAC is a more recent, safe, and less invasive diagnostic tool for deeply seated intra-abdominal lesions.. The accuracy of EUS-FNAC is really excellent in our study. Therefore, EUS-FNAC can be used as a valuable tool for pathological examination of intra-abdominal lesions.

Keywords:- Endoscopic Ultrasound, Fine Needle Aspiration Cytology, Intra-abdominal Lesions, Pancreatic Lesions, Biopsy.



INTRODUCTION

The abdominal cavities can develop a wide range of reactive, inflammatory, and neoplastic lesions. They are identified as space-occupying lesions through ultrasonography/CT imaging. However, these imaging approaches are ineffective in determining the precise diagnosis of these pathologic processes or distinguishing between inflammatory, benign, and malignant lesions.^[1]

Determining prognosis and choosing the best method of treatment require accurate diagnosis. Up until recently, open laparotomies or laparoscopic tissue samples have been required to get a definitive diagnosis; nevertheless, these procedures are very invasive and cause needless morbidity in patients with benign diseases alone.^[2]

Endoscopic ultrasound system is a novel diagnostic modality that was created in the 1980s by Olympus Medical Systems in Japan to aid in the early diagnosis of pancreatic cancer.^[3] EUS-FNA is now routinely done in many endoscopic centers, and it is clear that this method has a significant influence on patient therapeutic treatment by establishing a definitive tissue diagnosis from lesions indicated by endosonography.^[4,5]

Ultrasonography is a test in which high-frequency sound waves are reflected off the inside tissues of the body and the echoes are turned into a sort of image known as a sonogram. Endoscopic ultrasound (EUS) takes ultrasound technology a step further by merging it with endoscopy.^[3] It has been demonstrated that EUS-FNAC is helpful for

diagnosis, avoiding unnecessary treatments and cutting expenses.^[6]

EUS-FNA has been shown to be useful in diagnosing biliopancreatic and abdominal/mediastinal lymph node mass lesions.^[7,8] EUS-guided FNAC outperforms other modalities in identifying pancreatic lesions, such as computed tomography (CT) or magnetic resonance imaging, because it can detect lesions <3 cm in size and can take cytopathology samples.^[9,10,11]

Unlike traditional endoscopy, which can only show the innermost lining, EUS imaging can see all four layers of the GI wall, namely the mucosa, submucosa, muscularis propria, and serosa or surrounding adventitia.^[3]

However, this technique was held in Bangladesh. It began in 2015 at the BSMMU General Surgery Department.

This study conducted to assess the diagnostic accuracy of EUS-FNAC for evaluating intra-abdominal lesions.

Objectives

The study was aimed to evaluate the diagnostic accuracy of EUS-FNAC for evaluating intra-abdominal lesions.

MATERIAL AND METHODS

The observational analytical study was carried out from January 2016 to February 2017 over a period of 12 months in the general surgery unit in the Department of Surgery, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. About twenty-five patients with intra-abdominal lesions were included in

this study; the other patients were excluded based on exclusion criteria. All patients with intra-abdominal masses confirmed by CT/USG/endoscopic examination will include the masses that arise from the pancreas, liver, upper GI tract, adrenal gland, and lymph node. Age > 14 years and irrespective of sex were included in the study. Parietal mass, GI tract lesion arising beyond the 3rd part of the duodenum, unfit for sedation anesthesia due to systemic disease (ASA grade 3/4), vascular lesion like hemangioma, and coagulopathy were excluded. The results were given with the use of tables showing mean values, ranges, frequencies, and percentages. The study did not seem to pose any potential risk which was discussed with the patients participating in the study. Statistical analyses were carried out using SPSS-21 and Microsoft.

RESULTS

The observational analytical study was conducted from January 2016 to February 2017 over a period of 12 months in the general surgery unit in the Department of Surgery, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. About twenty-five patients diagnosed with intra-abdominal lesions were included in this study, as some were discarded due to exclusion criteria. The results were reported with the help of tables depicting mean values, ranges, frequencies, and percentages. [Table 1] shows the distribution of patients according to age and gender. The maximum number of patients 7 (28.00%) were in the age group >60 years, followed by 6 (24.00%), 5 (20.00%), 4 (16.00%), and 3 (12.00%) in the groups 50-60 years, ≤30 years, 40-50 years, and 30-40 years, respectively. The mean age was

50.04, within the range of 14–77 years. Male were predominant 17 (68.00%). The male-female ratio was 2.13:1. [Table 2] shows most patients have symptoms of abdominal pain 19 (76.00%), followed by constitutional symptoms 6 (24.00%). Asymptomatic patients were only 1 (4.00%). Pie chart showing patients with intra-abdominal lesions presented with a palpable abdominal lump of only 20.00%; the majority of patients presented without abdominal lump (80.00%) [Figure 1]. [Table 3] shows most of the intra-abdominal lesions detected by EUS were in the pancreas 16 (64.00%), followed by intra-abdominal lymphadenopathy 5 (20.00%), adrenal mass 2 (8.00%), GIT 1 (4.00%), and hepatobiliary mass 1 (4.00%). [Table 4] shows the distribution of patients according to needle pass during EUS-FNAC: 3–4 pass was the majority 17 (68.00%), followed by 1–2 pass 5 (20.00%), and then 5–6 pass 3 (12.00%). [Table 5] shows the FNAC report that the majority were malignant 18 (72.00%), followed by benign 6 (24.00%), and then non-diagnostic 1 (4.00%). Table 6 shows the association of malignancy between EUS-FNAC findings and histopathology findings. 18 (85.70%) patients had positive EUS-FNAC and positive histopathology, 3 (14.30%) patients had positive EUS-FNAC and negative histopathology, 4 (100.00%) patients had negative EUS-FNAC and negative histopathology. The p value was 0.25. [Figure 2] shows bar diagram of the validity test for EUS-FNAC findings. The bar graph shows the following measures of validity: Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), and Accuracy. The bar graph shows the following values: 85.7% for Sensitivity, 100% for Specificity, 100% for PPV, 57.1% for NPV, and 88% for Accuracy.



Table 1: Distribution of the patients by age and gender (N=25).

Variables		No. of patients	Percentage (%)
Age (years)	≤30	5	20.00
	30-40	3	12.00
	40-50	4	16.00
	50-60	6	24.00
	>60	7	28.00
Mean (Range,Min-Max)		50.04 (14-77)	
Gender	Male	17	68.00
	Female	8	32.00
Male: Female = 2.13: 1			

Table 2: Distribution of patients according to symptoms (N=25).

Symptoms	No. of patients	Percentage (%)
Asymptomatic	1	4.00
Abdominal pain	19	76.00
Constitutional symptoms (Fever, night sweat, Wt loss)	6	24.00

Table 3: Distribution of the patients by EUS finding (N=25).

EUS finding	No. of patients	Percentage (%)
Hepatobiliary masses	1	4.00
Pancreatic masses	16	64.00
GIT masses	1	4.00
Lymphadenopathy	5	20.00
Adrenal mass	2	8.00

Table 4: Distribution of patients according to needle passes during EUS-FNAC (N=25).

Number of needle pass	No. of patients	Percentage (%)
1-2 pass	5	20.00
3-4 pass	17	68.00
5-6 pass	3	12.00

Table 5: Distribution of the patients by FNAC report (N=25).

FNAC report	Frequency	Percentage (%)
Non-diagnostic	1	4.00
Benign	6	24.00
Malignant	18	72.00

Table 6: Association of malignancy between EUS-FNAC findings and histopathology findings (N=25).

EUS-FNAC malignant	Histopathology malignant		P value*
	Positive	Negative	
Positive	18 (85.70%)	0 (.0%)	0.25
Negative	3 (14.30%)	4 (100.00%)	
Total	21 (100.0)	4 (100.00%)	

*McNemar test was done to measure the level of significance.

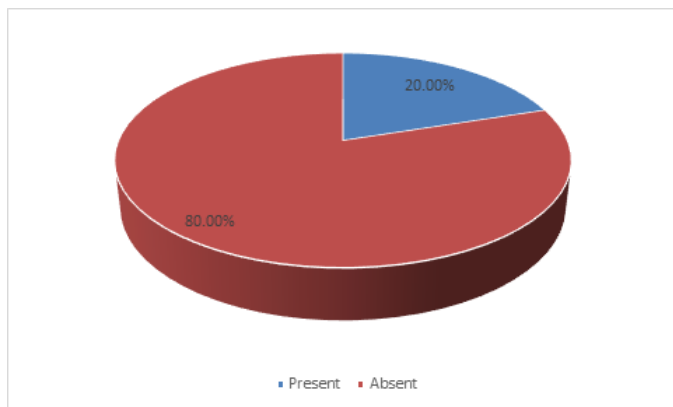


Figure 1: Pie chart of patients according to palpable abdominal lump (N=25).

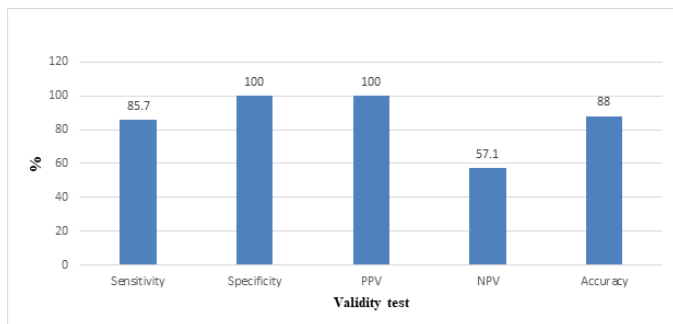


Figure 2: Bar diagram of the validity test for EUS-FNAC findings (N=25).

DISCUSSION

EUS-FNAC for intra-abdominal tumor has recently been conducted and proven to be effective. The relevance and demand for EUS-FNAC are increasing since it is seen as the gold standard for acquiring specimens from intra-

abdominal lesions. The present study sought to determine the diagnostic effectiveness of EUS-FNAC.^[12]

In our study, the majority of patients (28%) were >60 years old, with 24.00%, 16.00%, and 12.00% being 50-60 years old, 40-50 years old, and 30-40 years old, respectively. Within the 14-77 year age group, the mean age was 50.04 ± 18.89 . So, intra-abdominal lesion was substantially more common in the older age group. Shin et al. (2002) found similar statistics, with the mean age of the patients being 65 years for men (range, 20-86) and 64 years for women (range, 35-85). The patients' median age was 60.25 years, ranging from 20 to 82 years.¹³ Also, Mamoon et al. (2011) found that ages ranged from 12 to 85 years, with a mean age of 49 ± 14 years.^[1] According to Qureshi et al. (2011), the mean age of the patients was 58.94 ± 12.84 ranging from 23 to 78 years. So, age is a significant risk factor for the development of intra-abdominal lumps.^[14] In our study, males were predominant (68%) and females were 32%, with a male: female ratio of 2.13:1. A similar result was obtained by Shin et al, (2002), who had 166 patients who underwent EUS-FNA procedures, 103 of whom were men and 63 of whom were women, with a male: female ratio of 1.60:1.^[13] Also, Mamoon et al. (2011) found that in 155 cases of EUS-FNA, 105 patients were males and 50 were females, with a ratio of 2.1:1.

Male sex is therefore an essential preference for the development of intra-abdominal lesion.^[1]

In our study, the majority of patients who had EUS-FNAC had symptoms of abdominal pain (76%) followed by constitutional symptoms (24%) such as low-grade fever, night sweating, and weight loss. Only 4% of patients were asymptomatic. The majority of patients (76%) suffer significant abdominal pain.

Pancreatic carcinoma is usually painless and silent at first. Pancreatic carcinoma has often spread outside the pancreas by the time it is large enough to show symptoms. At this point, symptoms are determined by the location of the malignancy within the pancreas.

Pancreatic cancer at the head of the pancreas causes symptoms such as weight loss, jaundice, dark urine, light stool color, itching, nausea, vomiting, abdominal pain, back pain, and enlarged lymph nodes in the neck. Pancreatic carcinoma in the body or tail of the pancreas frequently causes abdominal and/or back discomfort as well as weight loss.

Another study found that the head of the pancreas has weight loss (92%), jaundice (82%), pain (72%), anorexia (64%), and the body and tail of the pancreas has weight loss (100%), pain (87%), nausea (43%), and jaundice (7%).^[15] In our study, patients with pancreatic lesion experienced similar symptoms.

Lymphoma patients often appear with generalized swollen lymph nodes, fever, sweats, chills, and weight loss.^[16] In our study, patients with lymphoma experienced similar symptoms.

In our study, only 20% of individuals with intra-abdominal lesions had palpable abdominal lumps, whereas the majority (80%) did not. Because trans-abdominal CT/USG guided FNAC is advised for patients with palpable abdominal lumps. EUS-FNAC is required to assess the deep-seated abdominal lesion.

In our study, the pancreas was shown to be the most common intra-abdominal lesion (64%) followed by lymphadenopathy (20%), adrenal mass (8%), GIT (4%) and hepatobiliary mass (4%). The pancreas (162 cases, 91%), ampulla (4 cases, 2%), intra-abdominal lymph nodes (6 cases, 3%), gastric wall (3 cases, 2%), esophagus (2 cases, 1%), and retroperitoneum (2 cases, 1.00%) were all EUS-FNAC sites in Shin H (2002).^[13]

Mamoon et al. (2011) where the most prevalent site of FNA was mediastinal lymph nodes (68 (44%) cases), followed by the pancreas 36 (23.00%) cases. Other sites included abdominal lymph nodes, stomach, ampullary sites, lung, liver, and so forth.^[1]

The cytologic results of the 25 patients who had EUS-FNAC included 6 instances (24.00%) of "benign lesion," 18 cases (72.00%) of "malignant neoplasm," and 1 case (4.00%), of "non-diagnostic."

The statistical data showed that there were 18 (72.00%) true-positive cases, 4 (16%) true-negative cases, 0 (00%) false-positive cases, and 3 (12.00%) false-negative cases. There was a sensitivity of 85.70%, specificity of 100%, and accuracy of 88% in the diagnosis. There was a 100% positive predictive value and a 57.10% negative predictive value.



According to Nakahara et al. (2009), for abdominal lymphadenopathy, the sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy of EUS-FNA were, in that order, 94, 100, 100, 90, and 96%.^[2]

In our study, the following values: 85.70% for Sensitivity, 100% for Specificity, 100% for PPV, 57.10% for NPV, and 88.00% for Accuracy. It established that EUS-FNAC has a high validity for diagnosing pancreatic malignancy, especially for ruling in the disease.

Overall, our results were positive and justify continued application of EUS-FNAC for intra-abdominal masses, despite the fact that they appear to be lower than those from other institutions. This motivates us to seek a reason and pinpoint avenues for development. After confirmation that our study's overall findings were generally positive. Cases exhibiting discrepancy were our main emphasis. Aspiration failures resulting from technical factors, including operator skills, tumor type, and location, may be the source of these, or they may be the result of pathologists' misunderstanding and misdiagnosis.

FNA was performed with 22G needles. Pawlowski et al. (2010) presented a randomized controlled trial that examined results obtained with needles of different diameters. All of these studies were conducted in the setting of pancreatic masses. Although thinner needles give less cellular material than bigger needles, it has been suggested that the specimens from the former are less contaminated by blood and hence simpler to analyze.^[17]

Hussain et al. reported that in order to verify that the EUS-FNA samples are adequate, a cytopathologist or an advanced trainee in cytopathology should be present. The presence of a cytopathologist during EUS-FNA enhances diagnostic yield by lowering unsatisfactory samples, the requirement for further passes, and, as a result, procedure time. As a result, onsite cytopathological assessment is widely acknowledged as a quality control measure for EUS and is the standard of treatment at the majority of academic EUS centers.^[18]

In our study, most patients reported no discomfort during the EUS-FNA treatment while under general anesthesia in the form of TIVA (total intravenous anesthesia), while a few individuals (20.00%) experienced slight abdomen pain after the surgery. There were no significant problems like bleeding, infection, or visceral damage.

O'Toole et al. (2001) reported that the total risk of complications with EUS-FNA was quite low (1.6%), with no serious or fatal incidences, although the risk seemed to be slightly higher than that for normal EUS alone.^[19]

This study's design was limited by the fact that it was a single-center study with a small number of consecutive patients during a 12-month period. It is impossible to determine the effectiveness of EUS-FNAC. Technical difficulties, inexperienced operators, and pathologists can all lead to incorrect findings. Being aware of such risks is vital since it boosts diagnostic confidence, which leads to higher accuracy.

So, we conclude that EUS-FNAC is reliable and accurate diagnostic technique. Based on these



results, pathologists can be assured that EUS-FNAC provides a desirable representation of the specimen. However, particular attention to adequacy assessment and meticulous observation of samples are critical in order to reduce the discrepancy between cytology-histological diagnoses. Though the percentage of correct diagnoses in EUS-FNAC results is relatively inferior compared to that from histological diagnosis but statistical results, such as diagnostic accuracy were satisfactory in several studies including ours.

EUS-FNAC, thus, can be suggested as a crucial pathologic assessment for intra-abdominal lesions where patient safety and cost effectiveness are the top priorities.

Limitations of the study

This Observational analytical study was performed on small group of people, which is too small to represent the burden of intra-abdominal lesions in the community. Higher number of sample size could give better information. Data was collected from patients of

Bangabandhu Sheikh Mujib Medical University (BSMMU). If samples were collected from the patients of different hospital that may give more precise information. Therefore, in future further study may be under taken with large sample size.

CONCLUSIONS

In surgical practise, intra-abdominal lesions will always remain an enigma. Documentary proof about the kind of pathology behind these masses is necessary for both the prognosis and the start of therapy. Until open laparotomy or laparoscopic tissue sample is required, a definitive diagnosis of this lesion may not be possible. However, both procedures are highly invasive and not cost-effective. A more recent, safe, and less invasive diagnostic method for deeply seated intra-abdominal lesions is EUS-FNAC. The accuracy of EUS-FNAC is really excellent in our study. Therefore, EUS-FNAC can be used as a valuable tool for pathologic examination of intra-abdominal lesions.

REFERENCES

1. Mamoon N, Mushtaq S, Rathore MU. Endoscopic ultrasound guided aspiration cytology--a useful diagnostic tool. *J Pak Med Assoc.* 2011;61(4):367-71.
2. Tanisaka Y, Ryozaawa S, Kobayashi M, Harada M, Kobatake T, Omiya K, et al. Usefulness of endoscopic ultrasound-guided fine needle aspiration for lymphadenopathy. *Oncol Lett.* 2018;15(4):4759-4766. doi: 10.3892/ol.2018.7939.
3. Eloubeidi MA, Wallace MB, Reed CE, Hadzijahic N, Lewin DN, Van Velse A, et al. The utility of EUS and EUS-guided fine needle aspiration in detecting celiac lymph node metastasis in patients with esophageal cancer: a single-center experience. *Gastrointest Endosc.* 2001;54(6):714-9. doi: 10.1067/mge.2001.119873.
4. Chhieng DC, Jhala D, Jhala N, Eltoun I, Chen VK, Vickers S, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy: a study of 103 cases. *Cancer.* 2002;96(4):232-9. doi: 10.1002/cncr.10714.
5. Heintz A, Mildenerberger P, Georg M, Braunstein S, Junginger T. Endoscopic ultrasonography in the diagnosis of regional lymph nodes in esophageal and gastric cancer--results of studies in vitro. *Endoscopy.* 1993;25(3):231-5. doi: 10.1055/s-2007-1010298.
6. Bluen BE, Lachter J, Khamaysi I, Kamal Y, Malkin L, Keren R, et al. Accuracy and quality assessment of EUS-FNA: A single-center large cohort of biopsies. *Diagn Ther Endosc.* 2012;2012:139563.



7. Anand D, Barroeta JE, Gupta PK, Kochman M, Baloch ZW. Endoscopic ultrasound guided fine needle aspiration of non-pancreatic lesions: an institutional experience. *J Clin Pathol*. 2007;60(11):1254-62. doi: 10.1136/jcp.2006.045955.
8. Srinivasan R, Bhutani MS, Thosani N, Săftoiu A, Rice DC, Ionciă AM, et al. Clinical impact of EUS-FNA of mediastinal lymph nodes in patients with known or suspected lung cancer or mediastinal lymph nodes of unknown etiology. *J Gastrointest Liver Dis*. 2012;21(2):145-52.
9. Jhala NC, Jhala DN, Chhieng DC, Eloubeidi MA, Eltoum IA. Endoscopic ultrasound-guided fine-needle aspiration. A cytopathologist's perspective. *Am J Clin Pathol*. 2003;120(3):351-67. doi: 10.1309/MFRF-J0XY-JLN8-NVDP.
10. Horwhat JD, Paulson EK, McGrath K, Branch MS, Baillie J, Tyler D, et al. A randomized comparison of EUS-guided FNA versus CT or US-guided FNA for the evaluation of pancreatic mass lesions. *Gastrointest Endosc*. 2006;63:966-75.
11. Pannala R, Hallberg-Wallace KM, Smith AL, Nassar A, Zhang J, Zarka M, et al. Endoscopic ultrasound-guided fine needle aspiration cytology of metastatic renal cell carcinoma to the pancreas: A multi-center experience. *Cytojournal*. 2016;13:24.
12. Baek HW, Park MJ, Rhee Y-Y, Lee KB, Kim MA, Park IA. Diagnostic accuracy of endoscopic ultrasound-guided fine needle aspiration cytology of pancreatic lesions. *J Pathol Transl Med*. 2015;49(1):52-60.
13. Shin HJC, Lahoti S, Sneige N. Endoscopic ultrasound-guided fine-needle aspiration in 179 cases: the M. D. Anderson Cancer Center experience. *The M. D. Anderson Cancer Center experience*. *Cancer*. 2002;96(3):174-80.
14. Qureshi A, Hassan U, Loya A, Akhter N, Najam-ud-Din, Yusuf A. Diagnostic utility of endoscopic ultrasound guided aspiration cytology in evaluation of pancreatic masses. *J Coll Physicians Surg Pak*. 2013;23(7):484-6.
15. De La Cruz MS, Young AP, Ruffin MT. Diagnosis and management of pancreatic cancer. *Am Fam Physician*. 2014;89(8):626-32.
16. Freelove R, Walling AD. Pancreatic cancer: diagnosis and management. *Am Fam Physician*. 2006;73(3):485-92.
17. Polkowski M, Larghi A, Weynand B, Boustière C, Giovannini M, Pujol B, et al. Learning, techniques, and complications of endoscopic ultrasound (EUS)-guided sampling in gastroenterology: European Society of Gastrointestinal Endoscopy (ESGE) Technical Guideline. *Endoscopy*. 2012;44(2):190-206. doi: 10.1055/s-0031-1291543.
18. Hussain T, Salamat A, Farooq MA, Hassan F, Hafeez M. Indications for endoscopic ultrasound and diagnosis on fine-needle aspiration and cytology. *J Coll Physicians Surg Pak*. 2009;19(4):223-7.
19. Jenssen C, Alvarez-Sánchez MV, Napoléon B, Faiss S. Diagnostic endoscopic ultrasonography: assessment of safety and prevention of complications. *World J Gastroenterol*. 2012;18(34):4659-76. doi: 10.3748/wjg.v18.i34.4659.

Source of Support: Nil, Conflict of Interest: None declared