

# Diagnostic utility of EUS-guided tissue acquisition in children: A tertiary care center experience

Zaheer Nabi<sup>1</sup>, Sundeep Lakhtakia<sup>1</sup>, Radhika Chavan<sup>1</sup>, Shujaath Asif<sup>1</sup>, Jahangeer Basha<sup>1</sup>, Rajesh Gupta<sup>1</sup>, Raghavendra Yarlagadda<sup>1</sup>, Palle Manohar Reddy<sup>1</sup>, Rakesh Kalapala<sup>1</sup>, D. Nageshwar Reddy<sup>1</sup>

<sup>1</sup>Department of Gastroenterology, Asian Institute of Gastroenterology, Hyderabad, Telangana, India

## Abstract

**Background and Objectives:** EUS is frequently utilized for tissue acquisition in adult patients. However, the literature is limited regarding the utility of EUS-guided fine-needle aspiration or biopsy (FNA or FNB) in children. In this study, we aim to evaluate the feasibility, safety, and diagnostic utility of EUS-FNA/FNB in children with various gastrointestinal diseases.

**Methods:** The data of children ( $\leq 18$  years) who underwent EUS-FNA/FNB from March 2014 to June 2020 were analyzed, retrospectively. The following parameters were analyzed: technical success, adverse events, and impact on the final diagnosis.

**Results:** Sixty-seven children (32 – boys,  $14.8 \pm 2.9$  years, range 8–18 years), underwent EUS-guided tissue acquisition procedures using standard therapeutic echoendoscope during the study period. The indications included solid pancreatic lesions in 29 (43.3%), mediastinal or abdominal lymphadenopathy in 30 (44.7%), cystic pancreatic lesions in 5 (7.5%), subepithelial lesions in 2 (3%), and retroperitoneal mass in 1 (1.5%). EUS-FNA and FNB were performed in 42 and 25 children, respectively. All the procedures could be successfully performed and there was no major procedure-related adverse event. Minor adverse events included self-limiting throat pain (10) and abdominal pain (3), self-limited bleeding at puncture site (3), and transient fever (1). EUS-FNA/FNB provided a histopathological diagnosis in 59 (88.1%) children. **Conclusion:** EUS-guided tissue acquisition using standard echoendoscope is feasible and safe in the pediatric age group. EUS-FNA/FNB establishes diagnosis in majority of the children when performed for appropriate clinical indication.

**Key words:** EUS, fine-needle aspiration, fine-needle biopsy

## INTRODUCTION

EUS-guided tissue acquisition is a major advancement in the field of gastrointestinal (GI) endoscopy. EUS guided tissue acquisition in real time enables the confirmation of the diagnosis of various GI diseases.<sup>[1]</sup> The safety, efficacy, and the diagnostic utility of EUS-FNA or EUS-guided fine-needle biopsy (EUS-FNB) has been

established in adult patients.<sup>[2,3]</sup> Emerging data suggest the utility of EUS as a diagnostic as well as therapeutic modality in pediatric cases.<sup>[4-8]</sup> However, the current literature on EUS in children is sparse and remains limited to noninvasive pure diagnostic applications,

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### Address for correspondence:

Dr. Zaheer Nabi, 6-3-661, Asian Institute of Gastroenterology, Hyderabad - 500 082, Telangana, India.

E-mail: zaheernabi1978@gmail.com

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especially in pancreato-biliary diseases, *e.g.*, recurrent pancreatitis or suspected biliary obstruction.<sup>14,6,7</sup> Therefore, the safety and diagnostic utility of EUS-FNA and -FNB is not well known in children.

In this study, we aim to evaluate the feasibility, safety, and diagnostic accuracy of EUS-FNA or -FNB in various pediatric GI diseases.

## METHODS

The data of consecutive children who underwent EUS-guided tissue acquisition from March 2014 to June 2020 were analyzed, retrospectively.

Children having GI or mediastinal lesions, that appeared amenable for EUS-FNA/FNB on cross-sectional imaging where guided tissue acquisition was likely to alter their management, were included. Contraindications included cardiac or respiratory instability, significant coagulopathy (platelets <100,000/ $\mu$ L and international normalized ratio >1.5), recent use of antiplatelets and anticoagulants, and children weighing <15 kg.

Written informed consent was obtained from the parents or the legal guardians before all the procedures. The study was approved by the institutional review board committee (AIG/IEC BHR 06/08.2020-01).

### *Devices and accessories*

Linear echoendoscope (GF-UCT 180, Olympus Corp., Tokyo, Japan) with an outer diameter of 14.6 mm and channel diameter of 3.7 mm was used in all the cases. The needle used for FNA had calibers 19G/22G/25G (*EchoTip Ultra*, Cook Medical, Bloomington, Indiana; *Expect*, Boston Scientific Corp., Marlborough, Massachusetts). The FNB needles included 22G/25G (*ProCore*, Cook Medical, Bloomington, Indiana; *Acquire*, Boston Scientific Corp., Marlborough, Massachusetts). The choice of needle caliber and design and method of tissue acquisition was at the discretion of the operating endoscopist. A 19G FNA needle was preferred in pancreatic cystic lesions >2 cm in size.

### *Technique of EUS-FNA and -FNB*

All the procedures were performed under deep sedation (intravenous propofol) under the supervision of an anesthetist. An upper GI gastroscopy was initially performed using a standard gastroscope to look for the feasibility of EUS. The steps of EUS-FNA or -FNB

were as follows: (a) initially, the indication of EUS-guided tissue sampling was confirmed, (b) the lesion was localized with EUS scope and the optimum path chosen for needle puncture, (c) the needle was inserted into the channel of the scope, (d) the sheath of the needle was protruded for a few millimeters outside the scope, (e) Doppler was used to confirm the absence of any intervening vessels, (f) finally, the lesion was punctured and the needle moved back and forth within the lesion. Subsequent needle passes were made in a similar manner if the sample appeared inadequate in the initial attempt [Figure 1].

In the *suction technique*, after puncturing the lesion, the stylet was removed and negative pressure applied using a 5 or 10 cc syringe, whereas, in the *slow pull technique*, the stylet was gradually pulled while the operator performed back and forth motion within the lesion. The use of suction or slow pull technique during FNA/FNB was left to the discretion of the operator performing the procedure. In general, suction was avoided while sampling lymph nodes or a vascular lesion, and in a situation where the initial sample was hemorrhagic.

In cases with the cystic lesion, complete aspiration of the cyst was attempted in one pass to avoid infection. In addition, antibiotic prophylaxis was considered in cases where the FNA of cystic lesions was contemplated.

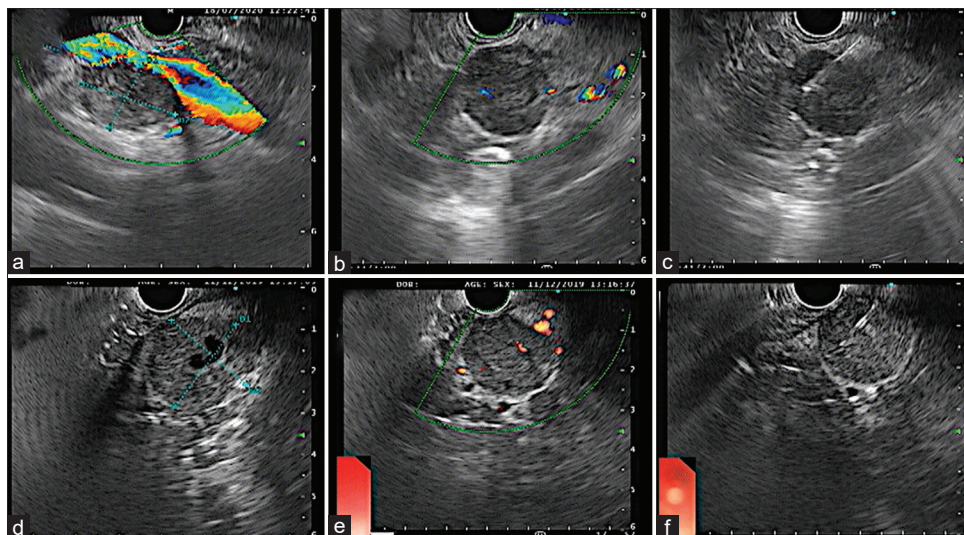
The sample obtained was used for preparing a minimum of four slides and or cell block depending on the indication.

### *Statistics*

The data are presented as mean  $\pm$  standard deviation for continuous or parametric variables and median (range) for nonparametric variables. Categorical variables were compared using Chi-square or Fisher exact test. The comparison of two or more nonparametric variables was performed using Mann-Whitney U-test or Kruskal-Wallis test.  $P < 0.05$  was considered as statistically significant. The statistical analysis was performed using SPSS version 26 (SPSS Inc, Chicago, Illinois, USA).

## RESULTS

A total of 67 children (32 males, 47.8%) with mean age  $14.8 \pm 2.9$  years (range 8–18 years) underwent EUS-guided tissue acquisition during the study period.



**Figure 1.** EUS-FNA and -FNB two cases with abdominal lymphadenopathy and pancreatic lesion, respectively. (a) Large hetero-echoic lymph node in the periportal region. Note a large intervening vessel between the transducer and the lymph node. (b) Endosonographic image in the same case focusing a different lymph node. Note the relative absence of the intervening vessels. (c) Puncture of the node with a 25G fine-needle aspiration needle. (d) Endosonographic image in a case with space-occupying lesion in the body of the pancreas. Note a small, anechoic cystic space within the predominantly solid lesion. (e) Color Doppler shows few intervening vessels between the transducer and the SOL. (f) Needle puncture of the lesion with a 22G fine-needle biopsy needle

Of these, EUS-FNA was performed in 42 (62.7%) and EUS-FNB in 25 (37.3%) children. The indications for FNA/FNB were pancreatic lesions in 34 (50.7%), abdominal lymphadenopathy in 18 (26.9%), mediastinal lymphadenopathy in 12 (17.9%), subepithelial lesions in 2 (2.9%), and retroperitoneal mass lesion in 1 child (1.5%). The location of pancreatic lesions was the head of the pancreas (13), body of the pancreas (9), tail of the pancreas (6), uncinete process (4), and genu (2).

#### Technical outcomes

EUS-FNA/FNB was successful in all the children (technical success 100%). EUS-FNA was performed using 19G, 22G, and 25G needles in 6 (14.3%), 21 (50.0%), and 15 (35.7%) children, respectively. EUS-FNB was performed using 22G and 25G needles in 21 (84%) and 4 (16.0%) children, respectively. The distribution of the lesions was not significantly different across types (FNA or FNB) and sizes of the needles (FNA *vs.* FNB needles:  $P = 0.219$ ) (19 *vs.* 22 *vs.* 25G:  $P = 0.713$ ).

The route of EUS-guided tissue acquisition was transesophageal in 13, transgastric in 44, and transduodenal in 15 cases. In five cases having combined mediastinal and abdominal lymphadenopathy, both transesophageal and transgastric routes were used for tissue acquisition. The median number of passes was 3 (1–4) in the EUS-FNA group and 2 (1–4) in the EUS-FNB group. There was no significant difference

in the median number of passes in FNA *versus* FNB groups ( $P = 0.642$ ) [Table 1].

#### Histopathological diagnosis

Overall, a diagnosis could be established in 59 (88.3%) children. In eight cases (11.9%), the diagnosis was not feasible due to the pauci-cellular nature of the sample. The final histopathological diagnosis was established in 83.3% of mediastinal lymphadenopathy/mass, 94.4% of abdominal lymphadenopathy, 86.2% of solid pancreatic lesions, and 100% cases of pancreatic cystic lesions [Table 2].

#### Comparison of diagnostic yield: Location of lesion and needle size/type

The diagnosis was concluded in a similar proportion of cases with solid pancreatic lesions and lymphadenopathy ( $P = 0.706$ ). There was no significant difference in the diagnostic yield between different sizes or type of needles (19 *vs.* 22 *vs.* 25 G,  $P = 0.116$ ). EUS-FNA was equivalent to EUS-FNB in providing adequate specimen for histopathological diagnosis (FNA *vs.* FNB: 88.1% *vs.* 88.0%;  $P = 0.991$ ) [Figure 2].

#### Adverse events

There were no major procedure-related adverse events. Minor adverse events included self-limiting throat pain (10, 14.9%) and abdominal pain (3, 4.5%), self-limited bleeding at the puncture site (3, 4.5%), and transient fever (1, 1.5%).

**DISCUSSION**

In this study, we confirmed the utility of EUS-guided tissue sampling in pediatric patients with various GI lesions. EUS-FNA/FNB was found to be safe and provided with a diagnosis in majority of the cases.

EUS is being utilized for diagnostic and therapeutic indications in adult patients for several decades now. Since the initial reports of EUS-FNA FNA nearly three decades ago, multiple studies have established the role of EUS-FNA/FNB in various neoplastic and nonneoplastic GI lesions in adults.<sup>[2,3,9]</sup> However, the data regarding the safety and efficacy of

EUS-FNA in the pediatric population are limited to small case series.<sup>[10-13]</sup>

In this study, we included a large and homogenous group of the pediatric population in whom EUS was

**Table 1. Characteristics of lesions and needle used for EUS guided tissue acquisition**

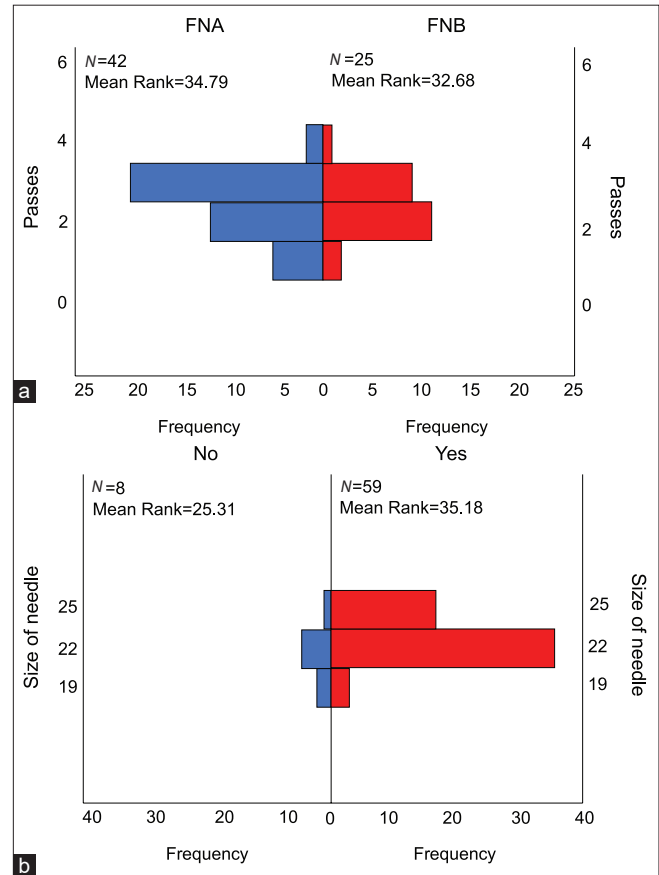
	FNA group (n=42)	FNB group (n=25)
<b>Indication:</b>		
Pancreatic lesion	23	11
Mediastinal lymph node/mass	6	6
Abdominal lymph node	11	7
Sub-epithelial lesion	1	1
Retropancreatic mass	1	0
<b>Size of needle</b>		
: 19G	6	0
: 22G	21	21
: 25G	15	4
<b>Number of passes, median (range)</b>		
Trans-esophageal	3 (1-4)	2 (1-4)
Trans-gastric	8	5
Trans-duodenal	25	19
<b>Adverse events</b>		
Throat pain	7	3
Abdominal pain	2	1
Bleeding (self-limiting)	2	1
Fever	1	0

FNA: fine needle aspiration; FNB: fine needle biopsy

**Table 2. Diagnostic accuracy of EUS-FNA and -FNB**

Lesion	Diagnostic	Non-diagnostic	Diagnostic Yield
Mediastinal lymphadenopathy/mass	Granulomatous lymphadenitis -6	2	83.3%
	Round cell tumor - 2		
	Reactive -2		
Abdominal lymphadenopathy	Granulomatous lymphadenitis- 10	1	94.4%
	NHL-1		
	Reactive-6		
Solid Pancreatic lesions	SPEN - 21	4	86.2%
	Pancreatoblastoma-1		
	Round cell tumor -1		
	Benign/Inflammatory mass -2		
Cystic pancreatic lesion	Pseudocyst-3	0	100%
	Lymphoepithelial cyst - 1		
	Epithelial cyst-1		
Subepithelial lesion	Esophageal leiomyoma-1	0	100%
	Gastric GIST - 1		
Retroperitoneal mass	Paucicellular-1	1	0%

NHL: non-Hodgkin's lymphoma; SPEN: solid papillary epithelial neoplasm; GIST: gastrointestinal stromal tumor



**Figure 2.** Impact of the needle type and size on the number of passes and diagnostic yield. (a) Comparison of fine-needle aspiration and fine-needle biopsy needle with regards to the number of passes. (b) Comparison of the diagnostic yield according to the size of the needles

performed exclusively for tissue acquisition. Majority of the children had pancreatic lesions (solid or cystic) or mediastinal and abdominal lymphadenopathy. Histopathological confirmation of the diagnosis was obtained in majority (88%). There was no significant difference in the diagnostic accuracy between pancreatic and nonpancreatic lesions. The overall results are similar to previous reported studies on the utility of EUS-FNA in the pediatric age group,<sup>[11-14]</sup> that had heterogenous indications (*e.g.*, pseudocyst drainage and cyst aspiration) in a small numbers.

The other major finding of our study was that the yield of EUS was not significantly different according to the type and caliber of the FNA/FNB needles. In concordance with our results, the systemic review by Bang *et al.* (nine studies, 576 adult patients) concluded that there is no significant difference in the diagnostic accuracy between ProCore needle (FNB) as compared to the conventional FNA needle (85.8% *vs.* 86.2%).<sup>[15]</sup> Similarly, the caliber of the FNA needle did not significantly affect the overall diagnostic yield and accuracy in several randomized trials.<sup>[16-19]</sup> In contrast to our results, a more recent systematic review and meta-analysis concluded that FNB is superior to FNA in sampling pancreatic or nonpancreatic solid lesions.<sup>[20]</sup> We acknowledge that our study may not be adequately powered for a meaningful comparison between different types and sizes of needles.

There were no major complications in our study suggesting that EUS-FNA or -FNB is a safe procedure in the pediatric population even while using adult echoendoscope. However, caution is advised as major complications including acute pancreatitis, severe pain, and fever requiring antibiotics have been reported in adult patients who underwent EUS-FNA of solid pancreatic masses.<sup>[10]</sup> In addition, some complications may be unique to pediatric cases such as airway compression due to the large size of the EUS scope. Since our study included older children ( $\geq 8$  years), we did not encounter this particular adverse event. The guidelines by the European society recommend the use of mini-probe or endobronchial ultrasound in smaller ( $<15$  kg) children.<sup>[21]</sup>

There are several strengths of our study. To the best of our knowledge, this is the largest study evaluating the role of EUS-FNA/FNB in children. We compared the yield of EUS-guided sampling according to the type of lesions and size of the needle. However,

certain drawbacks are noteworthy. These include the retrospective design of the study and relatively small number of children with subepithelial ( $n = 2$ ) and cystic pancreatic lesions ( $n = 5$ ). We performed EUS in the selected group of children and there were no children  $<8$  years age or  $<15$  kg weight. Therefore, the caution is advised while interpreting the technical success of performing EUS in children. The safety and feasibility of EUS-guided sampling remains to be seen in smaller children. We did not compare the diagnostic yield between slow pull and suction technique as a combination of these methods was utilized in majority of the cases. However, a recent meta-analysis of randomized trials concluded nonsuperiority of one approach over the another.<sup>[22]</sup> In addition, our study was not adequately powered to assess the difference in the diagnostic yield among different types or sizes of needles.

## CONCLUSION

EUS-guided tissue acquisition is feasible and safe and has a major impact on the final diagnosis in children.

### *Financial support and sponsorship*

Nil.

### *Conflicts of interest*

Sundeep Lakhtakia is an Editorial Board Member of Endoscopic Ultrasound. The article was subject to the journal's standard procedures, with peer review handled independently of this Member and his research groups. There are no other conflicts of interest.

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