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ORIGINAL ARTICLE

Endoscopic ultrasonography in pediatric patients—Experience from a tertiary care center in India

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Abstract
Background and Aims Although endoscopic ultrasound (EUS) is used in the management of various gastrointestinal (GI) diseases in adults, data on its role in children is limited. This study evaluated the indications, safety, and impact of EUS in children.
Methods Records of children (<18 years age) who underwent EUS between January 2006 and September 2014 were reviewed retrospectively and analyzed.
Results One hundred and twenty-one children (70 males, 51 females) aged 15.2 ± 2.9 years (mean ± SD) underwent 123 diagnostic (including fine needle aspiration cytology (FNAC) in 7) and 2 therapeutic EUS procedures. Conscious sedation was used in 81 procedures (65 %) and general anesthesia in 44 (35 %). The pancreaticobiliary system was evaluated in 114 (118 procedures), mediastinum in 5, and stomach in 2 patients. EUS diagnosed chronic pancreatitis (21 patients), pancreatic necrosis (1), splenic artery pseudoaneurysm (1), gastric varix (1), pseudocysts (3), insulinomas (2), other pancreatic masses (2), choledocholithiasis (2), choledochal cysts (2), portal biliopathy (1), esophageal leiomyoma (1), gastric neuroendocrine tumor (NET) (1), and GI stromal tumor in stomach (1). EUS-guided FNAC was positive in four of seven patients (two had tuberculosis, one pancreatic solid pseudopapillary tumor, and one gastric NET). Three patients had minor adverse events. EUS had a positive clinical impact in 43 (35.5 %) patients.
Conclusions EUS is feasible and safe in children. It provides valuable information that helps in their clinical management.

Keywords Biliary tree · Diagnosis · Endosonography · Imaging · Pancreas · Pediatric

Introduction

Endoscopic ultrasound (EUS) is an endoscopic technique that provides highly accurate imaging of the layers of the bowel wall as well as periluminal structures. Since the first description of EUS in 1980 [1], there has been significant improvement in equipment design in terms of diagnostic and therapeutic capabilities which in turn have contributed to patient management. Though EUS with or without fine needle aspiration cytology (FNAC) has now become an established diagnostic tool in adults, data on its utility in the pediatric population is scant. This is because of the relatively low incidence of pancreatobiliary and luminal gastrointestinal (GI) cancers, absence of dedicated pediatric echoendoscopes, need for deep sedation or general anesthesia, and challenges of esophageal and duodenal intubation in small children [2–4].

This is a retrospective study describing our experience of EUS in pediatric patients and its impact on subsequent management.

Methods

All EUS procedures performed between January 2006 and September 2014 at a tertiary care center (Christian Medical College, Vellore, Tamil Nadu, India) were reviewed. Patients younger than 18 years of age were identified. The demographics, EUS indications, procedural details (instruments

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used, sedation, EUS findings, interventions, adverse events) and clinical impact were retrospectively analyzed.

All EUS procedures were performed by experienced endosonographers using radial echoendoscopes (GF-UE 160, Olympus Corp. Japan; EG-3670 URK, Pentax Corp. Japan) and/or linear echoendoscopes (GF-UCT 140, Olympus Corp. Japan; EG-3870UTK, Pentax Corp. Japan). EUS-guided FNAC was done using a 22 or 25-gauge needle (Echotip® Ultra, Cook Medical, Limerick, Ireland). Intravenous antibiotics were administered prior to the sampling of cystic lesions. Rapid onsite evaluation was performed by trained cytopathologists. The procedures were carried out either under conscious sedation (midazolam and pentazocine) or general anesthesia. The sedation was administered by the endoscopist in case of conscious sedation and by the anesthesiologist in case of general anesthesia. The type of sedation was chosen based on the patient's age, weight, previous experience with sedation, and comorbidities. Procedures were performed with patients in the left lateral decubitus position. Adverse events such as hypotension (systolic blood pressure <90 mm of Hg), bradycardia (heart rate <50 beats/minute), hypoxia (oxygen saturation <94 %), bleeding, perforation, and post-procedure infection were identified. A positive clinical impact was defined as the establishment of a definitive diagnosis or exclusion of a suspected pathology, which subsequently altered management of the patient.

Results

Demographics

From January 2006 to September 2014, 125 EUS examinations were performed on 121 children (70 males and 51 females) aged 15.2 ± 2.9 years (mean ± SD), range being 3–18 years. Out of 119 (98.3 %) patients from India, 61 (51.2 %) were from east, 42 (35.3 %) from south, and 16 (13.5 %) from north India.

Procedure details

The indications for EUS are shown in Table 1. Diagnostic EUS was performed in 119 patients, (EUS guided FNAC in 7) and EUS-guided cystogastrostomy in 2 patients. In two children (age 3 and 6 years), intubation into the second part of duodenum was unsuccessful, while in another patient, presence of food prevented an optimal study. The examination was successfully completed in the remaining patients.

The EUS examination was done under conscious sedation (midazolam and pentazocine) in 81 (65 %) and general anesthesia in 44 (35 %) patients. There were three minor complications related to procedures. One patient had transient desaturation after conscious sedation. Another patient had minor self-limiting bleed during the FNAC. One of the patients who underwent cystogastrostomy had post-procedure fever which settled with higher antibiotics and two sessions of endoscopic necrosectomy. There were no major complications.

Overall EUS had a significant clinical impact on patient management in 43 (35.5 %) of the patients (Table 1).

Evaluation of pancreas

More than 75 % of the EUS examinations were done for assessment of suspected pancreatic pathology. Evaluation of etiology of recurrent acute pancreatitis (RAP) was the most common indication ($n = 71$, 58.7 %). EUS in RAP was performed at least 6 weeks after an episode of acute pancreatitis and when toxic-metabolic evaluation and abdominal imaging studies (abdominal ultrasonography/contrast enhanced computed tomography (CECT)/magnetic resonance imaging (MRI)) were negative. EUS did not detect any pancreatic or biliary etiology for RAP. The pancreas was normal in 20 patients. Twenty patients were diagnosed as chronic pancreatitis (≥5/9 criteria as per the conventional criteria for diagnosis of chronic pancreatitis by the International Working Group for Minimum Standard Terminology for Gastrointestinal Endoscopy) and advised dietary modification and pancreatic enzyme supplements [5, 6].Thirty-one patients had insufficient criteria for chronic pancreatitis (indeterminate chronic pancreatitis) and were advised clinical follow up. Three of them had a repeat EUS examination and one progressed to chronic pancreatitis after 1 year.

Four patients with acute pancreatitis were assessed for etiology and local complications. None of them had biliary stones, sludge, worms, or pancreatic structural abnormalities. Pancreatic necrosis already diagnosed on CT was confirmed by EUS in one patient; no other local complications were detected.

Nine patients with known chronic pancreatitis were assessed for local complications. Two patients presented with GI bleed; EUS confirmed bleeding gastric varix in one who underwent cyanoacrylate glue injection while the other had a splenic artery pseudoaneurysm and underwent surgery. Pseudocyst and splenic vein thrombosis were noted in a patient who presented with persistent abdominal pain, and he was managed conservatively.

EUS was also used for screening of pancreatic mass lesions. Five patients with clinical suspicion of insulinoma and negative findings on abdominal imaging (CECT/MRI) underwent EUS. Lesions detected in two of them were confirmed as insulinomas after surgical resection. In another patient who presented with cholestatic jaundice and a pancreatic head mass, EUS-guided FNAC showed solid pseudopapillary tumor and the patient underwent Whipple surgery. In a child with hypervascular liver metastasis where CT-guided FNAC

Table 1 Indications and impact of endoscopic ultrasound in pediatric patients

Indications	Number of patients (%)	EUS/FNAC findings	Number of patients	Change in management	Positive impact number (%)
Recurrent acute pancreatitis—to assess etiology and/or progression to chronic pancreatitis	71 (58.7)	Chronic pancreatitis	20	Change in diet, pancreatic enzymes	21 (29.6)
		Insufficient criteria to definitely diagnose chronic pancreatitis	31	Kept on close clinical follow up—one of these progressed to chronic pancreatitis	
		Normal pancreas	20	–	
Acute pancreatitis—to assess etiology or rule out complications	4 (3.3)	Pancreatobiliary etiology	0	–	0 (0)
		Pancreatic necrosis	1	–	
Previously diagnosed chronic pancreatitis—to characterise local complications	9 (7.4)	Splenic artery pseudoaneurysm	1	Frey's operation with splenectomy	3 (33.3)
		Gastric varix	1	Cyanoacrylate glue injection	
		Pseudocyst with splenic vein thrombosis	1	Nasoenteral feeding	
Assessment of pancreatic cyst or mass	9 (7.4)	Pseudocyst/WOPN	2	Cystogastrostomy	6 (66.7)
		Pancreatic mass in clinically suspected insulinoma with negative abdominal imaging	2	Surgical enucleation	
		Pancreatic primary detected in patient with liver metastases (CT-guided FNAC from liver lesions suggestive of NET)	1	Octreotide	
		Pancreatic head mass—FNAC:SPT	1	Whipple operation	
Biliary pain	7 (6.6)	Choledocholithiasis	1	ERCP and bile duct clearance done	7 (100)
		Choledochal cyst (one with choledocholithiasis)	2	Cyst excision and Roux-en-Y hepaticojejunostomy	
		Negative for choledocholithiasis	4	Prevented unnecessary ERCP	
Obstructive jaundice	1 (0.8)	Portal biliopathy	1	Biliary stenting	1 (100)
Mediastinal mass	5 (4.1)	Lymph nodal mass: EUS FNAC—tuberculosis	1	Antitubercular therapy	2 (40)
		Esophageal leiomyoma	1	Advised follow up	
Gastric submucosal mass	2 (1.7)	NET (confirmed by EUS FNAC)	1	Distal gastrectomy with lymph node excision	2 (100)
		GIST	1	Surgical resection followed by imatinib	
Peripancreatic mass	1 (0.8)	EUS FNAC: tuberculosis	1	Antitubercular therapy	1 (100)
Evaluation of unexplained upper abdominal pain to rule out pancreatobiliary disease	12 (9.9)	Normal study	12	–	0 (0)
Total	121				43 (35.5)

ERCP endoscopic retrograde cholangiopancreatography, *FNAC* fine needle aspiration cytology, *GIST* gastrointestinal stromal tumor, *WOPN* walled off pancreatic necrosis, *NET* neuroendocrine tumor, *SPT* solid pseudopapillary tumor, *EUS* endoscopic ultrasound

was suggestive of neuroendocrine tumor, EUS aided in confirmation of a pancreatic primary and the patient was started on depot octreotide. EUS-guided cystogastrostomy was performed in two patients with traumatic pseudocyst and walled off pancreatic necrosis (WOPN) respectively avoiding surgery in both of them.

Evaluation of biliary tract

Seven patients with history of biliary pain underwent EUS to assess the biliary tract. One had choledocholithiasis and two had choledochal cysts, one of whom also had choledocholithiasis. Endoscopic retrograde cholangiopancreatography (ERCP) was done for stone clearance in patient with choledocholithiasis, and both patients with choledochal cysts underwent cyst excision and hepaticojejunostomy. A patient with extrahepatic portal venous obstruction who presented with cholestasis was diagnosed to have portal biliopathy on EUS which was managed by biliary stenting. ERCP was avoided in four patients who did not have choledocholithiasis.

Evaluation of mediastinal/abdominal masses

Four patients with mediastinal masses underwent EUS-guided FNAC. In one patient, histology showed granulomatous inflammation with caseation suggestive of tuberculosis. He responded well to antitubercular therapy (ATT). FNAC from mediastinal mass in three other patients was inconclusive as the material was inadequate. Another patient with history of a maxillary tumor underwent EUS for evaluation of a mediastinal mass which showed a well-circumscribed homogeneous and hypoechoic lesion in the fourth layer of the esophageal wall, suggestive of leiomyoma. This patient was advised follow up with EUS.

In two patients who had gastric submucosal masses, EUS diagnosed neuroendocrine tumor (by FNAC) and GI stromal tumor and both underwent surgery. Tuberculosis was detected on FNAC from a peripancreatic mass, and the patient responded well to therapy with ATT.

Unexplained upper abdominal pain

EUS was also performed to rule out pancreatobiliary etiology in 12 patients with unexplained upper abdominal pain. None of these patients showed abnormality in the biliary tract or pancreas. On further work up, two patients had microliths on bile microscopy, one was diagnosed with abdominal epilepsy, one with significant steatorrhea was diagnosed to have malabsorption, and eight patients who had no organic cause were managed as functional abdominal pain.

Discussion

Our study on pediatric endosonography which has the largest number of patients published so far demonstrates the feasibility and safety of endoscopic ultrasonography in evaluation of the pancreatobiliary system, GI tract, and mediastinum in children. All the pediatric EUS procedures were performed by gastroenterologists with experience in pediatric endoscopy and advanced GI endoscopy. The choice of sedation in advanced procedures in children depends on patient factors such as age, weight, comorbidities, procedure complexity, duration, and institutional policies. As seen in Table 2, most of the previous series used general anesthesia for EUS in children. We have however shown that in a large number of children (65 %), EUS could be successfully performed under conscious sedation. A similar observation was made by Cohen et al. [4]. There were three minor adverse events in our patients (with or without FNAC). As in other studies, there were no major adverse events suggesting that EUS can be safely performed in children (Table 2).

In adults, EUS is frequently used for diagnosis and treatment of many benign and malignant conditions. However, EUS is infrequently used in children due to fewer indications and preference for use of other less invasive modalities such as ultrasonography, CT, and MRI. In contrast to adults where EUS (with or without FNAC) is done in considerable numbers for diagnosis and preoperative tumor and nodal staging of a variety of cancers, most of the EUS examinations in children are for benign indications [7]. The most common indication for EUS in all studies including ours was for evaluation of pancreatobiliary disorders (Table 3). Other indications in previous studies include evaluation of mediastinal masses, submucosal lesions in esophagus, stomach, rectum, and unexplained upper abdominal pain. In our study, EUS was performed for diagnosis or therapy of pancreatobiliary disorders in about 94.4 % of patients. Other indications in our study were more or less similar to other series (Table 3). EUS-FNAC which has been shown to have high diagnostic accuracy was done in seven (5.6 %) of our patients [3, 4, 7, 8]. FNAC was positive in four (57 %) (two had tuberculosis, one pancreatic solid pseudopapillary tumor, and one gastric neuroendocrine tumor), making an impact on management of these patients.

EUS has also been used for therapeutic procedures such as pseudocyst drainage, drainage of pancreatic fluid collections, biliary drainage, and celiac plexus block [7–11].Two of our patients underwent EUS-guided cystogastrostomy thereby avoiding surgery.

Most studies of EUS in children showed a high positive impact on management ranging from 44 % to 98 % (Table 2). The overall impact on management in the present study was low (35.5 %). Analysis of the various subgroups in our study showed low impact in RAP, acute pancreatitis, chronic pancreatitis, and

Table 2 Comparison of demographics and procedure details of pediatric endoscopic ultrasound in published studies

Study	Study period	Number of children	Number of procedures	Age range (mean)	Gender	Sedation	Complications	Impact
Roseau et al. [2]	1987–1994	18	23	4-16 (12)	NA	DS (100 %)	Nil	
Varadarajulu et al. [3]	2001–2004	14	15	5-17 (median13)	M 64 % F 36 %	GA (100 %)	Nil	93 %
Bjerring et al. [16]	1992–2006	18	18	0.5-15 (median 12)	M 67 % F 33 %	GA (100 %)	Nil	78 %
Cohen et al. [4]	1999–2005	32	32	1.5-18 (12)	M 65 % F 35 %	GA (38 %) CS (56 %) NS (rectal EUS) (6 %)	Nil	44 %
Attila et al. [7]	2001–2008	38	40	3-17 (13.5)	M 58 % F 42 %	GA (67.5 %) DS (22.5 %) CS (10 %)	Nil	–
Al-Rashdan et al. [8]	2000–2008	56	58	4-18 (median 16)	M 37.5 % F 62.5 %	GA (17 %) DS (73 %), CS (6 %)	Nil	86 %
Scheers et al. [11]	2000–2014	48	52	2-17 (12)	M 39.6 % F 60.4 %	GA (86 %) DS (14 %)	3.8 %	98 %
Present study	2006–2014	121	125	3-18 (15.2)	M 58 % F 42 %	GA (35 %) CS (65 %)	2.4 % (all minor)	35.5 %

GA general anesthesia, *CS* conscious sedation, *DS* deep sedation, *NS* no sedation, *NA* not available, *EUS* endoscopic ultrasound

unexplained abdominal pain and high impact in pancreatic cyst/mass, biliary pain, obstructive jaundice, gastric submucosal, and peripancreatic masses. Possible reasons for the low impact in our study are (a) lack of follow up in RAP, the largest subgroup (59 %) with 71 patients. EUS in RAP is performed for evaluation of etiology like microlithiasis, small bile duct stones, pancreas divisum, and ruling out early chronic pancreatitis. Microliths and choledocholithiasis are uncommon in children, and majority of children with negative etiology screen often develop chronic pancreatitis on follow up [12–14]. Lack of follow up in 25 of 27 patients who had indeterminate chronic pancreatitis may be a reason for low impact of EUS in RAP. (b) Most previous studies were reported at a time when ERCP was routinely used as a diagnostic tool for evaluation of pancreatic disease and avoidance of a pancreatogram by EUS was taken as a positive impact in management. Non-invasive radiological investigations such as CT and MRCP have now replaced ERCP as the investigations of choice in suspected pancreatobiliary disorders [15]. (c) Less stringent criteria to define a positive impact in some studies [3, 4, 8, 16].

Our study has some limitations. The data was analyzed retrospectively and few patients had long-term follow up. As

Table 3 Comparison of the indications of pediatric endoscopic ultrasound procedures and the interventions performed in published studies

Study	Pancreatobiliary *n* (%)	Mediastinal masses *n* (%)	Esophagus *n* (%)	Stomach *n* (%)	Rectum *n* (%)	Others *n* (%)	FNAC *n* (%)	Intervention *n* (%)
Roseau et al. [2]	9 (39)	0	1 (4)	6 (26)	6 (26)	1 (4)	0	
Varadarajulu et al. [3]	15 (100)	0	0	0	0	0	3 (20)	
Bjerring et al. [16]	12 (66.7)	1 (5.6)	0	3 (16.7)	0	2 (11.1)	0	
Cohen et al. [4]	19 (59)	0	8 (25)	2 (6.5)	2 (6.5)	1 (3)	7 (22)	
Attila et al. [7]	25 (62.5)	5 (12.5)	1 (2.5)	6 (15)	1 (2.5)	0		2 (5) All celiac blocks
Al-Rashdan et al. [8]	41 (70.7)	Mucosal/submucosal – 8 (13.8)			4 (6.9)	0	15 (25.9)	5 (8.6) 4 - celiac block, 1 - EUS guided pancreatogram
Scheers et al. [11]	52 (100)	0	0	0	0	0	12 (23.1 %)	13 (25) 12- Pancreatic fluid collection/ pseudocyst drainage 1-Transluminal biliary drainage
Present study	118 (94.4)	5 (4)	0 (0)	2 (1.6)	0 (0)	0	7 (5.6)	2 (1.6) Cystogastrostomy

FNAC fine needle aspiration cytology, *EUS* edoscopic ultrasound

in other series, most of our patients were adolescents, with younger children and infants not adequately represented. It is in the latter group that use of an adult EUS scope is technically difficult, and congenital abnormalities are more common.

We conclude that EUS with or without FNAC can safely and successfully be performed in children. EUS provides important information that impacts management in children with pancreatobiliary disease and submucosal lesions of esophagus and stomach. It has replaced diagnostic ERCP in children and has important therapeutic roles as well. The scope of endosonography in pediatric population can be expanded by use of narrow caliber echobronchoscopes [17], ultrasound miniprobes, and development of dedicated EUS scopes.

Compliance with ethical standards

Conflict of interest RM, EGS, AC, DVR, PRK, AJJ, AKD, SDC, and RTK declare that they have no conflict of interest.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975 as revised in 2008. We did not obtain informed consent from individual patients as it was a retrospective study. Institutional ethics committee clearance was obtained.

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