Yield of Endoscopic Ultrasound in Children and Adolescent With Acute Recurrent Pancreatitis

*Sumit Kumar Singh, *Anshu Srivastava, †Praveer Rai, *Surender K. Yachha, and *Ujjal Poddar

ABSTRACT

Objectives: Endoscopic ultrasound (EUS) is an established tool for evaluation of adults with acute recurrent pancreatitis (ARP) whereas data in pediatrics is limited. Our study assessed the role of EUS in identifying etiology including changes of chronic pancreatitis (CP) in children and adolescents with ARP.

Methods: Children with ARP (≥2 episodes of acute pancreatitis [AP]) were prospectively evaluated with a detailed clinical proforma and EUS. Subjects with known etiology of ARP or CP on ultrasonography/computed tomography and magnetic resonance cholangiopancreatography (MRCP, Cambridge grade ≥3) were excluded. Parenchymal and ductal changes on EUS as per minimal standards terminology (MST) features were noted.

Results: Thirty-two children (22 boys, age 14 [8–18] years) with ARP (median of 3 [2–5] episodes of AP) were enrolled. EUS was safe and technically successful in all. Gall bladder sludge was found in 1 (3%) case and none had other pancreatobiliary structural abnormalities. EUS diagnosis of CP (≥4 features) was made in 10/32 (31%) cases. Subjects with CP on EUS had a longer disease duration than those without CP (45 [10–97] vs 22 [8–78] months; P = ns). MRCP was normal in 28 and showed pancreas divisum in 1 case. Three cases had equivocal (Cambridge II) changes at initial MRCP and 2 of them had repeat MRCP, which showed definite (Cambridge IV) CP. All these 3 cases had CP on EUS.

Conclusions: EUS diagnosed CP (≥4 features) in 31% and biliary abnormality in 3% children with ARP. EUS is safe, sensitive, and useful for early diagnosis of CP in children with ARP.

Key Words: endoscopic ultrasound, pancreatitis, pediatric, recurrent

(*JPGN* 2018;66: 461–465)

What Is Known

- Endoscopic ultrasound is an established tool for evaluation of adults with acute recurrent pancreatitis.
- Data regarding role of endoscopic ultrasound in pediatric acute recurrent pancreatitis is limited.

What Is New

- Endoscopic ultrasound diagnosed chronic pancreatitis in 31% and biliary abnormality in 3% children with idiopathic acute recurrent pancreatitis.
- Endoscopic ultrasound is safe, sensitive and useful for early diagnosis of chronic pancreatitis in children with acute recurrent pancreatitis.

Incidence of acute pancreatitis (AP) in children has increased in recent years (1,2). Nearly one-third of patients with AP have more than 1episode, thus, qualifying for acute recurrent pancreatitis (ARP) (3). Structural abnormalities of pancreatobiliary system and genetic susceptibility are the major causes of ARP in children and etiology remains unknown in one-third of cases (3,4). ARP may also evolve into chronic pancreatitis (CP) in 20% to 25% of children and one-third of adults (2,5,6).

Information about the etiology of ARP and likelihood of progression to CP is important for appropriate therapy and counseling regarding prognosis. Although endoscopic retrograde cholangiopancreatography (ERCP) is the gold standard for diagnosis of CP, magnetic resonance cholangiopancreatography (MRCP) is the preferred diagnostic modality as it is safe, noninvasive, and feasible across all ages (7,8). Both these modalities, however, cannot evaluate certain pancreatic parenchymal abnormalities (9).

EUS is a useful tool for evaluation of ARP patients as it can assess both parenchymal and ductal pancreatic changes as well as the biliary tree (9). EUS scores over ERCP for detection of early changes of CP. In a study of 130 adults, EUS had 100% sensitivity to detect early changes of CP (10). In a landmark study of adults with idiopathic ARP, EUS identified the etiology in 30% and diagnosed presence of CP in another 40% cases (11). Data on EUS for evaluation of children with ARP is scanty, with small patient numbers and mostly retrospective (12–16). The objective of our study was to assess the role of EUS in identifying etiology of idiopathic ARP, both in terms of structural abnormalities and changes of CP. The secondary objective was to evaluate clinical or laboratory features, which can help identify ARP children who are at risk of developing CP.

METHODS

All children (8–18 years) diagnosed as ARP were prospectively enrolled between May 2015 and December 2016. Diagnosis of AP was based on standard criteria, that is, presence of at least 2 of

Received September 6, 2017; accepted November 16, 2017.

From the *Department of Pediatric Gastroenterology, and the †Department of Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India.

Address correspondence and reprint requests to Prof Surender K. Yachha, MD, DM, Department of Pediatric Gastroenterology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226014, Uttar Pradesh, India (e-mail: skyachha@yahoo.co.in).

Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (*www.jpgn.org*).

The authors report no conflicts of interest.

DOI: 10.1097/MPG.0000000000001855

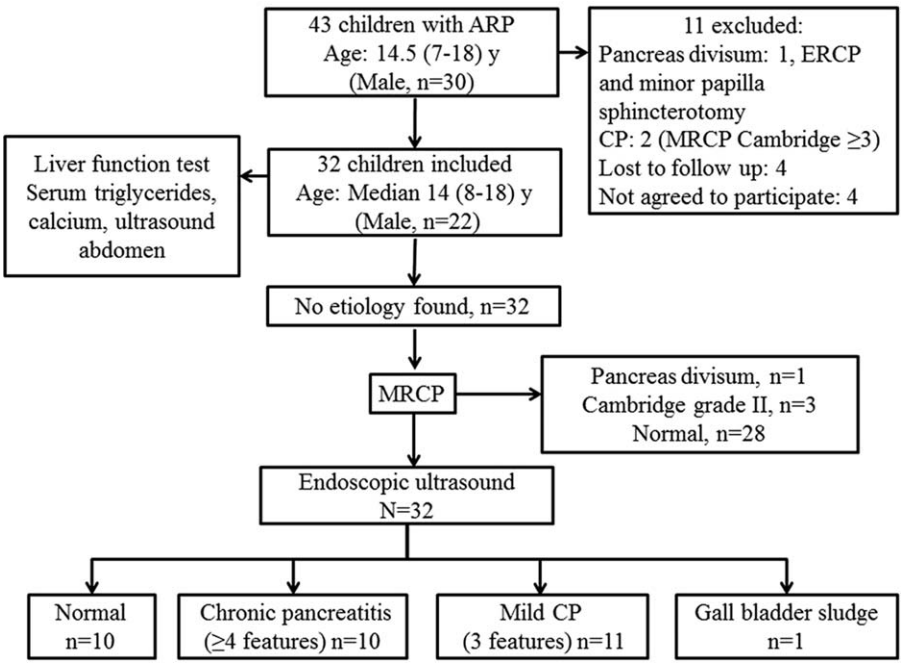

FIGURE 1. Flow chart of the study.

the following: abdominal pain suggestive or compatible with AP, serum amylase and/or lipase activity at least 3 times upper limit of normal (international units/liter), and/or imaging findings characteristic or compatible with AP (17). The episodes of AP should be distinct and with complete resolution of pain (≥1-month pain-free interval between the diagnoses of AP) or complete normalization of serum pancreatic enzyme levels (amylase and lipase), before the subsequent episode of AP is diagnosed, along with complete resolution of pain symptoms, irrespective of a specific time interval between AP episodes (17). The severity of each episode of AP was graded as mild (no organ failure and no local or systemic complications), moderately severe (transient organ failure that resolves within 48 hours and/or local complications without persistent organ failure) and severe acute pancreatitis (persistent organ failure [>48 hours, single or multiple]) as per revised Atlanta classification (18). CP was diagnosed in the presence of typical abdominal pain plus characteristic imaging findings or exocrine insufficiency plus imaging findings or endocrine insufficiency plus imaging findings (17). Detailed information about clinical parameters like age at onset of symptoms, number and duration of acute episodes, severity of each episode, total disease duration (interval between first episode of pancreatitis and EUS), history of drug intake/trauma or infection before episode, family history of pancreatitis or carcinoma pancreas was noted. Obesity was defined as body mass index (BMI) >95th centile, failure to thrive as height for age <3rd centile and underweight as weight for age <3rd centile (19).

All children with ARP underwent diagnostic workup including hemogram, liver function test, serum calcium, triglycerides, ultrasonography (USG)/contrast-enhanced computed tomography (CECT) abdomen and MRCP. Patients with definite features of CP on USG/CECT and MRCP (Cambridge grade ≥3) or other etiology identified on imaging/biochemistry were excluded. Figure 1 shows the evaluation and exclusion of patients in this study. EUS was performed after 6 hours of fasting, using a linear echoendoscope (Olympus, GFU CT180, 7.5 MHz, Shinjuku-Ku, Tokyo, Japan) by a single experienced endosonographer who was unaware of the other imaging findings. EUS was done under conscious sedation with midazolam and ketamine with continuous monitoring (pulse-oximetry, heart rate). Sedation was given by a trained pediatrician and nurse with monitoring until complete recovery. The gall bladder, biliary tree, and pancreas were evaluated in detail and findings suggestive of CP were described as per the International Working Group for Minimum Standard Terminology (20). EUS was done at least 4 weeks after the last episode of AP.

Biliary sludge was defined as presence of hyperechoic, dependent material within the gallbladder lumen, without acoustic shadowing and stone as hyperechoic structure with acoustic shadow within the bile duct or the gallbladder. Pancreas divisum was diagnosed by EUS whenever there was clear evidence of a dominant dorsal duct with no evidence of communication between the ventral and dorsal ducts. Presence of parenchymal and/or ductal changes suggestive of CP at EUS like hyperechoic foci, hyperechoic strands, parenchymal lobularity, cysts, dilatation of the main pancreatic duct, irregular duct margins, hyperechoic duct margins, dilated side branches, and shadowing calcifications were noted (20). EUS was considered as normal if 2 or less of the above features were present and abnormal if at least 3 features were seen (21–23). EUS diagnosis of CP was made whenever at least 4 features were present (24,25).

Ethics

The study was approved by our institutional review board (IEC: 2015–52-DM-84, dated April 29, 2015) and conforms to the ethical guidelines of the 1975 Helsinki Declaration. Written informed consent was obtained from parents/guardians of all study subjects.

Statistical Analysis

On the basis of the adult studies (11), we presumed the yield of EUS in children with ARP to be 50% for detection of any etiology including CP. A sample size of 24 children was calculated at 50% yield with 95% confidence interval and 20% absolute error in the reported prevalence.

TABLE 1. Endoscopic ultrasound findings in children with acute recurrent pancreatitis

Findings	Number (%)
Hyperechoic foci	31 (97%)
Hyperechoic strands	28 (87.5%)
Lobules	17 (53%)
Cyst	0
Dilated main pancreatic duct	0
Hyperechoic duct wall	13 (41%)
Irregular main pancreatic duct	0
Dilated side branches	1 (3%)
Calculi	0

Continuous data are summarized as median (range) and compared with Mann-Whitney *U* test. Categorical variables were compared by the Chi-square or Fisher exact test as applicable. Statistical package for social sciences, version 23.0 (SPSS-23, IBM, Chicago, IL) was used and $P < 0.05$ was considered significant.

RESULTS

Forty-three children with ARP were managed during the study period and 32 of them were enrolled (Fig. 1). The demographic and clinical characteristics of the 32 enrolled patients are shown in Supplemental Table 1 (Supplemental Digital Content 1, *http://links.lww.com/MPG/B210*). They had a total of 90 episodes of AP, with a median of 3 (2–5) episodes per patient. Thirteen (41%) patients had 2 episodes, 13 (41%) patients had 3, 5 (15%) patients had 4 and 1 (3%) patient had 5 episodes of pancreatitis. Nineteen (60%) children had only mild episodes, 3 (9%) had only moderately severe episodes and 2 (6%) patients had at least 1 episode of severe pancreatitis. In 8 children (25%) the severity of AP varied from mild to moderately severe in different episodes. CECT was available in 23 episodes of pancreatitis and the remaining episodes were assessed by USG. None had exocrine or endocrine insufficiency.

Endoscopic Ultrasound Evaluation

EUS was technically successful in all patients. No adverse events related to sedation or EUS were encountered, the youngest child being 8 years old and weighing 21 kg. The median time interval between last episode of AP and EUS was 4 (range, 1.5- 24) months. The average time for EUS examination was ~15 minutes (range 10–20) minutes. EUS showed gallbladder sludge in 1 child who had 4 episodes of ARP over last 2 years. He subsequently underwent ERCP with sphincterotomy and has remained asymptomatic over 16 months of post-sphincterotomy follow-up. Gall bladder or common bile duct stones, pancreas divisum, long common channel, or choledochal cyst were not seen in our patients.

Of the remaining 31 children, EUS was normal in 10 (32%) cases. EUS diagnosed CP (≥4 features) in 10 (31%) children. In another 11 (34%) children, EUS showed 3 features of CP. Parenchymal and ductal changes were seen in 31 (97%) and 13 (41%) children, respectively. The nature and prevalence of the changes suggestive of CP is shown in Table 1. Features of CP, that is, hyperechoic foci, hyperechoic strands, lobules, and hyperechoic duct wall are shown in Figure 2A-D, respectively. Table 2 shows comparison of patients with normal pancreas (n = 10) and CP (n = 10) on EUS. Of the various EUS features of CP, parenchymal lobules, hyperechoic duct wall, and dilated side branches were seen only in CP patients.

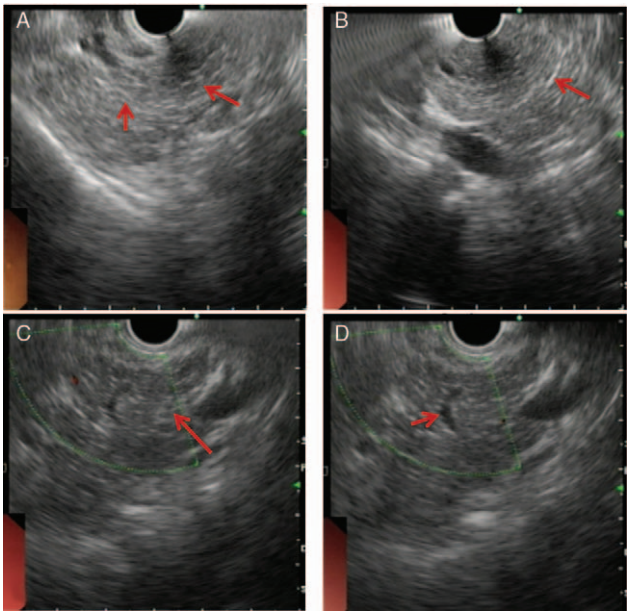

FIGURE 2. (A) EUS image showing hyperechoic foci (arrow). (B) EUS image showing hyperechoic strands (arrow). (C) EUS image showing parenchymal lobules (arrow). (D) EUS image showing hyperechoic duct wall (arrow). EUS = endoscopic ultrasound.

Correlation Between Endoscopic Ultrasound Evaluation and Magnetic Resonance Cholangiopancreatography

MRCP was normal in 28/32 (87.5%) children, 3/32 (9%) cases had equivocal changes of CP (<3 dilated side branches, Cambridge grade II) and one had type 1 pancreas divisum (PD). All 3 children with Cambridge grade II changes had CP on EUS (hyperechoic foci, hyperechoic strands, parenchymal lobules, and hyperechoic duct wall). EUS was not suggestive of PD in the child with PD on MRCP. He is asymptomatic post EUS and planned for ERCP to confirm the diagnosis. All of the 10 patients with normal EUS had normal MRCP.

TABLE 2. Comparison of children with normal and chronic pancreatitis on endoscopic ultrasound

Features	Normal (n = 10; ≤2 features)	CP (n = 10; ≥4 features)
Age at onset of symptoms, y	12 (6–14)	9 (6–16)
Age at time of EUS, y	14 (8–18)	14 (8–17)
Male	7 (70%)	6 (60%)
Duration of illness at EUS, mo	22 (8–78)	45 (10–97)
Number of acute episodes	2 (2–5)	3 (2–4)
Family history of pancreatitis	1 (10%)	0
Hyperechoic foci	10 (100%)	10 (100%)
Hyperechoic strands	7 (70%)	10 (100%)
Lobularity	0	9 (90%)*
Hyperechoic duct wall	0	10 (100%)*
Dilated side branches	0	1 (10%)

CECT = contrast-enhanced CT scan; CP = chronic pancreatitis; EUS = endoscopic ultrasound.
*$P < 0.05$.

Follow-up Evaluation

Over a median follow-up of 14.5 (4–22) months post EUS, 4/10 (40%) patients with CP, 4/11 (36%) patients with 3 features of CP and 2/10 (20%) with normal EUS continued to have pain. Although the percentage is higher in those with abnormal EUS, the difference was not significant. In 2 children with CP on EUS, a repeat MRCP was done after 12 and 16 months of EUS. Both cases showed disease progression (Cambridge II–IV) compared with initial MRCP. Three patients underwent repeat EUS after 18–24 months of previous EUS and all had persistence of same 4 features (hyperechoic foci, strands, lobules, and hyperechoic duct wall). In follow-up, 2/10 (20%) children with CP were found to have pancreatic exocrine insufficiency (low fecal elastase $<200\,\mu g/g$ faeces) and none had endocrine insufficiency (fasting plasma glucose ≥ 126 mg/dL, 2 h post-prandial plasma glucose ≥ 200 mg/dL, or HbA1C $>6.5\%$). One of these children showed progression of disease on repeat MRCP as described above.

DISCUSSION

We found EUS to be a safe, technically feasible, and effective modality for evaluation of etiology in children with ARP. Previous studies have also showed 100% technical success and excellent safety profile of EUS as a diagnostic modality in children with pancreatobiliary disorders, with most subjects being older children (12–14 years) but also in as young as 1.5 years (12–16). There were no adverse events related to sedation, which is similar to previous reports (26).

Only 1/32 (3%) child had gallbladder sludge on EUS and no other biliary abnormality was detected. Overall, biliary etiology (including microlithiasis and structural abnormalities) accounts for ~25% of all cases with ARP in children (4). The lower detection rate of biliary abnormalities in our study could be because of the fact that we included patients with idiopathic ARP, thereby excluding patients with etiologies like choledochal cyst, gall stone, common bile duct (CBD) stone, and so forth, identified on imaging with USG and MRCP in all patients. No comparative study of etiology in idiopathic ARP is available in children. In a study of adults with idiopathic ARP, however, biliary microlithiasis was seen only in 13% cases (27). In the limited pediatric literature on EUS (Supplemental Table 2, Supplemental Digital Content 2, *http://links.lww.com/MPG/B211*), microlithiasis was found to be the most common cause (4/9 cases) (12) followed by pancreas divisum and duplication cyst in 1 case each in a series of 6 cases (13). There is, however, no information whether MRCP was done and those detected with biliary abnormalities were excluded or not in these studies before EUS.

The debate regarding the number of features as per minimal standards terminology (MST), which are required for making a diagnosis of CP on EUS is still ongoing (28) with most experts suggesting that less than 2 changes should be taken as normal. Wiersema et al (21) showed that presence of at least 3 EUS features had a sensitivity of 100%, specificity of 79%, and accuracy of 85% as compared with ERCP. If the number of EUS features is increased to at least 4, the specificity and accuracy increase to 85% and 88%, respectively with pancreatic histology showing CP as the gold standard (24). Similarly, increased specificity and accuracy to the tune of 93% was reported by Pungpapong et al (29) with at least 4 EUS features versus ERCP as gold standard. There is no information about this aspect in the pediatric literature. In view of higher specificity and histopathological correlation with CP, we have taken at least 4 EUS features for diagnosis of CP in children.

In our study, EUS detected CP in 31% of children with ARP. This is comparable with the adult study by Yusoff et al (11), where 42% of ARP patients with intact gall bladder had CP ($\geq$5 features) at EUS. In the small pediatric series with 2 to 10 ARP cases, changes of CP were found in 33% to 50% of cases at EUS, which is similar to our observation, although the exact diagnostic features for CP are not provided in these studies (Supplemental Table 2, Supplemental Digital Content 2, *http://links.lww.com/MPG/B211*) (12–16). We found abnormal EUS (3 features) in 11/32 (34%) of our patients. This is consistent with mild or early CP as per adult experience (21,22). Follow-up with repeat evaluation is required to determine the risk of progression to overt CP in these cases.

Of the various features suggesting CP on EUS, presence of calculi has the maximum positive predictive value (PPV) of 100% followed by features like side branch dilatation, echogenic foci, and hyperechoic duct wall (PPV ~80%) (30). None of our patients had calculi. Dilated side branches, hyperechoic duct wall, and lobularity were more specific being seen only in CP patients. The interval between the last episode of AP and EUS was 4 (1.5–24) months in our study, which excludes the possibility that these changes could be because of resolving AP.

In our study, 31% cases ($\geq$4 features) with ARP had CP on EUS with median disease duration of 45 months (range, 10–97). This is similar to the risk of progression of ARP to CP of 32%–47% in 2 adult studies (28,31) and of 22%–26% in 2 pediatric studies over a follow-up of 23.2 ± 28.9 months and 1 to 5 years, respectively (2,5). ''Idiopathic etiology'' of ARP was the only independent predictor of progression to CP in the adult study (27) whereas ''idiopathic etiology'' and ''disease duration'' were significant in the pediatric study (2). Ahmed et al (31) showed that idiopathic/alcohol etiology, current smoking, and necrotizing pancreatitis were the independent risk factors on multivariate analysis for developing CP in adult patients with ARP whereas biliary etiology had the lowest risk. Our study is similar as none of our CP cases had a biliary etiology and all were idiopathic.

Operator dependence and inter-observer disagreement are thought to be the limitations of EUS. Duct dilation, lobularity, hyperechoic strands, and parenchymal cysts have been demonstrated to have the highest interobserver agreement (32,33). In addition, the EUS changes in ARP patients were shown to be consistent on repeat EUS after 4 to 6 months in all patients and 22.2% (2/9) cases had progressive disease with parenchymal calcification on follow-up (34). Similarly, repeat EUS in 3/10 cases with CP in our study showed same findings as the previous EUS. This suggests that EUS whenever done carefully and by experts can be a useful tool both for detection of CP and monitoring disease progression.

EUS has been shown to be more sensitive for detection of CP than ERCP in adults (100% and 80.7%; $P < 0.001$) (10). We also feel that EUS was more sensitive than MRCP for diagnosis of CP as EUS diagnosed CP in 7 children with normal and 3 children with equivocal CP (Cambridge II) on MRCP. Further, in 2 cases with CP on EUS, MRCP confirmed the diagnosis of CP by showing progression of changes from Cambridge grade II to IV. EUS also scores over MRCP as it is more convenient in smaller children (does not require breath holding, no issues with claustrophobia) and picks up both ductal and parenchymal changes. It is safe, quick, and has a definite place in evaluation of children with ARP. Identification of patients with CP amongst the ARP cases is useful for counseling.

In follow-up, 2/10 (20%) children with CP were found to have pancreatic exocrine insufficiency and none had endocrine insufficiency. Two pediatric studies of CP from China and India have shown exocrine insufficiency in 9% and 45% and endocrine insufficiency in 0% and 9% cases (35,36). Almost 70% of children in both the studies had calcific CP on imaging (35,36). The patients in our study were detected to have CP at an earlier stage of disease by EUS and this may explain the lower prevalence of exocrine and

endocrine insufficiency. It is known that longer disease duration and presence of calcifications and ductal dilatation increases the risk of exocrine and/or endocrine insufficiency (37,38). Also, the method of diagnosis of exocrine insufficiency was different in these studies; clinical steatorrhea in Chinese study (35), raised 72 h fecal fat (>18 g) in Indian study (36). These methods have different sensitivities and may explain the variation in frequency of exocrine insufficiency across the studies. Our study was limited by lack of genetic testing in our patients.

CONCLUSION

In this large prospective study of EUS in children with idiopathic ARP, we have shown that about one-third of cases with ARP have CP. EUS is safe, feasible, and more sensitive than MRCP for diagnosis of CP in children and adolescents with ARP. Our findings need to be confirmed by other larger studies.

REFERENCES

1. Nydegger A, Heine RG, Ranuh R, et al. Changing incidence of acute pancreatitis: 10-year experience at the Royal Children's Hospital, Melbourne. *J Gastroenterol Hepatol* 2007;22:1313–6.
2. Poddar U, Yachha SK, Borkar V, et al. A report of 320 cases of childhood pancreatitis: increasing incidence, etiologic categorization, dynamics, severity assessment, and outcome. *Pancreas* 2017;46:110–5.
3. Sánchez-Ramírez CA, Larrosa-Haro A, Flores-Martínez S, et al. Acute and recurrent pancreatitis in children: etiological factors. *Acta Paediatr* 2007;96:534–7.
4. Lucidi V, Alghisi F, Dall'Oglio L, et al. The etiology of acute recurrent pancreatitis in children: a challenge for pediatricians. *Pancreas* 2011; 40:517–21.
5. Geetha M, Saumya M, Balakrishnan V. Spectrum of pancreatitis in children and adolescents. *Indian J Gastroenterol* 2012;31:175–8.
6. Yadav D, O'Connell M, Papachristou GI. Natural history following the first attack of acute pancreatitis. *Am J Gastroenterol* 2012;107:1096–103.
7. Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. *Gastrointest Endosc* 2001; 54:425–34.
8. Calvo MM, Bujanda L, Calderón A, et al. Comparison between magnetic resonance cholangiopancreatography and ERCP for evaluation of the pancreatic duct. *Am J Gastroenterol* 2002;97:347–53.
9. Petrone MC, Arcidiacono PG, Testoni PA. Endoscopic ultrasonography for evaluating patients with recurrent pancreatitis. *World J Gastroenterol* 2008;14:1016–22.
10. Kahl S, Glasbrenner B, Leodolter A, et al. EUS in the diagnosis of early chronic pancreatitis: a prospective follow-up study. *Gastrointest Endosc* 2002;55:507–11.
11. Yusoff IF, Raymond G, Sahai AV. A prospective comparison of the yield of EUS in primary vs. recurrent idiopathic acute pancreatitis. *Gastrointest Endosc* 2004;60:673–8.
12. Cohen S, Kalinin M, Yaron A, et al. Endoscopic ultrasonography in pediatric patients with gastrointestinal disorders. *J Pediatr Gastroenterol Nutr* 2008;46:551–4.
13. Varadarajulu S, Wilcox CM, Eloubeidi MA. Impact of EUS in the evaluation of pancreaticobiliary disorders in children. *Gastrointest Endosc* 2005;62:239–44.
14. Attila T, Adler DG, Hilden K, et al. EUS in pediatric patients. *Gastrointest Endosc* 2009;70:892–8.
15. Bjerring OS, Durup J, Qvist N, et al. Impact of upper gastrointestinal endoscopic ultrasound in children. *J Pediatr Gastroenterol Nutr* 2008;47:110–3.
16. Fujii LL, Chari ST, El-Youssef M, et al. Pediatric pancreatic EUS-guided trucut biopsy for evaluation of autoimmune pancreatitis. *Gastrointest Endosc* 2013;77:824–8.
17. Morinville VD, Husain SZ, Bai H, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. *J Pediatr Gastroenterol Nutr* 2012;55:261–5.
18. Zaheer A, Singh VK, Qureshi RO, et al. The revised Atlanta classification for acute pancreatitis: updates in imaging terminology and guidelines. *Abdom Imaging* 2013;38:125–36.
19. Khadilkar VV, Khadilkar AV. Revised Indian Academy of Pediatrics 2015 growth charts for height, weight and body mass index for 5–18-year-old Indian children. *Indian J Endocrinol Metab* 2015;19:470–6.
20. Aabakken L, Rembacken B, LeMoine O, et al. Minimal standard terminology for gastrointestinal endoscopy - MST 3.0. *Endoscopy* 2009;41:727–8.
21. Wiersema MJ, Hawes RH, Lehman GA, et al. Prospective evaluation of endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in patients with chronic abdominal pain of suspected pancreatic origin. *Endoscopy* 1993;25:555–64.
22. Sahai AV, Zimmerman M, Aabakken, et al. Prospective assessment of the ability of endoscopic ultrasound to diagnose, exclude, or establish the severity of chronic pancreatitis found by endoscopic retrograde cholangiopancreatography. *Gastrointest Endosc* 1998;48:18–25.
23. Catalano MF, Lahoti S, Geenen JE, et al. Prospective evaluation of endoscopic ultrasonography, endoscopic retrograde pancreatography, and secretin test in the diagnosis of chronic pancreatitis. *Gastrointest Endosc* 1998;48:11–7.
24. Varadarajulu S, Eltoum I, Tamhane A, et al. Histopathologic correlates of noncalcific chronic pancreatitis by EUS: a prospective tissue characterization study. *Gastrointest Endosc* 2007;66:501–9.
25. Wallace MB, Hawes HR. Endoscopic ultrasound in the evaluation and treatment of chronic pancreatitis. *Pancreas* 2001;23:26–35.
26. Miqdady MI, Hayajneh WA, Abdelhadi R, et al. Ketamine and midazolam sedation for pediatric gastrointestinal endoscopy in the Arab world. *World J Gastroenterol* 2011;17:3630–5.
27. Garg PK, Tandon RK, Madan K. Is biliary microlithiasis a significant cause of idiopathic recurrent acute pancreatitis? A long-term follow-up study. *Clin Gastroenterol Hepatol* 2007;5:75–9.
28. Gardner TB, Levy MJ. EUS diagnosis of chronic pancreatitis. *Gastrointest Endosc* 2010;71:1280–9.
29. Pungpapong S, Wallace MB, Woodward TA, et al. Accuracy of endoscopic ultrasonography and magnetic resonance cholangiopancreatography for the diagnosis of chronic pancreatitis: a prospective comparison study. *J Clin Gastroenterol* 2007;41:88–93.
30. Catalano MF. Diagnosing early-stage chronic pancreatitis: is endoscopic ultrasound a reliable modality? *J Gastroenterol* 2007;42:78–84.
31. Ahmed Ali U, Issa Y, Hagenaars JC, et al. Risk of recurrent pancreatitis and progression to chronic pancreatitis after a first episode of acute pancreatitis. *Clin Gastroenterol Hepatol* 2016;14:738–46.
32. Wallace MB, Hawes RH, Durkalski V, et al. The reliability of EUS for the diagnosis of chronic pancreatitis: interobserver agreement among experienced endosonographers. *Gastrointest Endosc* 2001;53:294–9.
33. Gardner TB, Gordon SR. Interobserver agreement for pancreatic endoscopic ultrasonography determined by same day back-to-back examinations. *J Clin Gastroenterol* 2011;45:542–5.
34. Rana SS, Bhasin DK, Rao C, et al. Role of endoscopic ultrasound in idiopathic acute pancreatitis with negative ultrasound, computed tomography, and magnetic resonance cholangiopancreatography. *Ann Gastroenterol* 2012;25:133–7.
35. Wang W, Liao Z, Li Z-S, et al. Chronic pancreatitis in Chinese children: etiology, clinical presentation and imaging diagnosis. *J Gastroenterol Hepatol* 2009;24:1862–8.
36. Chowdhury SD, Chacko A, Ramakrishna BS, et al. Clinical profile and outcome of chronic pancreatitis in children. *Indian Pediatr* 2013;50: 1016–9.
37. Layer P, Yamamoto H, Kalthoff L, et al. The different courses of early- and late-onset idiopathic and alcoholic chronic pancreatitis. *Gastroenterology* 1994;107:1481–7.
38. Lindkvist B. Diagnosis and treatment of pancreatic exocrine insufficiency. *World J Gastroenterol* 2013;19:7258–66.