# Acute Pancreatitis and Acute Recurrent Pancreatitis in Children: Imaging Findings and Outcomes

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# What is already known on this topic?

- There has been an increasing incidence of acute pancreatitis (AP) in the pediatric population over the last few years.
- Defining the severity of AP in children has been challenging and has lacked a universally accepted diagnostic imaging algorithm.
- Radiological imaging plays a crucial role in the diagnosis, risk factor identification, and detection of complications in these patients.

# What this study adds to this topic?

- This study provides the results of imaging findings at admission and follow-up of the patients with AP and acute recurrent pancreatitis from one of the biggest study populations in Turkey.
- For the diagnosis of acute pancreatitis, magnetic resonance imaging should be preferred as a second option when the initial ultrasound is inconclusive or to reveal the most common causative factor in children, the biliary tract anomalies.
- Computed tomography may only be preferred in trauma patients or to rule out other possible acute abdominal diseases.

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ABSTRACT

**Objective:** The prevalence of acute pancreatitis and acute recurrent pancreatitis in children has increased over the years, and there are limited data about imaging findings. This study aimed to reveal the imaging findings of acute pancreatitis and acute recurrent pancreatitis in children at a tertiary care hospital.

Materials and Methods: The patients with acute pancreatitis and acute recurrent pancreatitis diagnosed between January 2007 and December 2018 were included. Demographic and clinical features, follow-up period, and interventions were noted. Imaging features were evaluated for pancreatic enlargement, peripancreatic fluid, and biliary ducts for initial examination and pancreas parenchymal necrosis, peripancreatic collection, walled-off necrosis, pseudocyst, parenchymal atrophy, and biliary ductal dilatation for follow-up.

**Results:** The study included 74 patients with a mean age of  $9 \pm 4.9$  years. The most common causes of acute pancreatitis and acute recurrent pancreatitis were biliary tract anomalies (n = 21), biliary ductal stones (n = 9), and cystic fibrosis (n = 8). Findings consistent with acute pancreatitis were determined by ultrasound in 40.5% (n = 30/74), whereas by magnetic resonance imaging in 60% (n = 39/65). Forty-one percent of the patients (n = 16) with positive magnetic resonance imaging findings did not show any findings on ultrasound. Acute recurrent pancreatitis was seen in 32 patients (43.2%). Follow-up imaging was performed in 55 patients (74.3%) between 2 months and 11 years. At follow-up, 8 patients had peripancreatic collections (6 walled-off necrosis and 2 pseudocysts).

**Conclusion:** Recognizing the imaging findings of acute pancreatitis and its complications is crucial. Magnetic resonance imaging should be preferred as a second option following ultrasound, with the advantages of biliary ductal system delineation and better characterization of complications.

Keywords: Acute pancreatitis, magnetic resonance cholangiopancreatography, magnetic resonance imaging, computed tomography, ultrasound, biliary tract anomalies, pseudocyst, walled-off-necrosis

# INTRODUCTION

Acute pancreatitis (AP) is defined as an acute inflammatory process of the pancreatic parenchyma with variable involvement of adjacent tissues and remote organs.<sup>1</sup> In recent years, the diagnosis of AP has been increasing in childhood.<sup>2</sup> Despite being less prevalent in children compared to adults, it is the most common disease of the pancreas in the pediatric age group.<sup>3</sup> The estimated annual incidence of AP in the pediatric population ranges between 1 and 13 cases per 100 000 individuals.<sup>4</sup> Nearly 15%-35% of pediatric AP patients present with recurrent attacks.<sup>5-9</sup> Acute recurrent pancreatitis (ARP) is an inflammatory process that is

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characterized by 2 or more distinct attacks divided by asymptomatic periods.<sup>9,10</sup> In case of chronic and irreversible morphological changes in the pancreas, it is defined as chronic pancreatitis.<sup>10</sup>

Obstructive biliary tract diseases, anatomic and genetic causes are known to be the most common causes of pediatric AP, but still, 20% of the cases remain idiopathic.<sup>9</sup> Abdominal pain and/ or irritability, nausea, vomiting, and abdominal tenderness are common. However, definition of pediatric pancreatitis is based on not only clinical symptoms but also physical examination, laboratory findings, and radiological assessment.<sup>10</sup> In 2012, International Study Group of Pediatric Pancreatitis: In Search for a Cure (INSPPIRE) study group presented a standardized diagnostic approach for children.<sup>11,12</sup> To diagnose AP in children, at least 2 of the following 3 criteria are required: abdominal pain suggestive of or compatible with the disease, at least a 3-fold increase in serum amylase and/or lipase levels, and imaging findings characteristic of or consistent with AP.<sup>2</sup> Thus, imaging is not an essential tool to make a diagnosis of AP but can contribute in this regard. Furthermore, imaging can be required for the diagnosis of AP in 5% of children in whom pancreatic amylase or lipase is not elevated.<sup>4</sup> In infancy, the symptoms may not be obvious enough for the early diagnosis of AP and it may present with irreversible systemic complications that may be occasionally lethal.<sup>2,13</sup> As a consequence, a high level of suspicion and well-interpreted radiological evaluation are required not only to determine the diagnosis but also the severity of AP in children.3

Over recent decades, several scores for pancreatitis based on clinical and laboratory features [Ranson, Glasgow, modified Glasgow, bedside index of severity in acute pancreatitis and Acute Physiology and Chronic Health Evaluation II (APACHE II)] as well as radiologic features [Balthazar classification, computed tomography severity index (CTSI) and modified CTSI] have been introduced for adult patients to predict adverse outcomes.<sup>14-16</sup> However, the diagnosis and management of AP have been challenging due to discordance between radiologists and clinicians by confusing terminology.<sup>1</sup> To avoid this discrepancy, in 2012, a consortium of adult AP experts revised the Atlanta Classification, which was initially released in 1992 to adapt the latest understanding and severity of the disease.<sup>17,18</sup> Besides confirmation of the diagnosis, noninvasive imaging studies enable to identify potential causes of AP and ARP, disease severity, and complications and to decide therapeutic interventions.<sup>19</sup> There are still insufficient data about the radiological finding,<sup>9</sup> etiology, and outcome of pediatric AP,<sup>4,20-26</sup> and most of the pediatric recommendations are based on the adult literature.<sup>9</sup>

Herein, our objective was to evaluate the role of noninvasive imaging techniques in diagnosis and follow-up of AP and ARP from a single pediatric tertiary referral hospital.

### **MATERIALS AND METHODS**

#### **Patient Selection**

This retrospective study was approved by the Noninterventional Clinical Research Ethical Board of Hacettepe University (decision no: GO 18/838-19), and the informed consent form was waived due to retrospective nature of the study and the anonymous usage of the records. The archive of the department of radiology was reviewed for imaging studies for which one of the discharge diagnoses was AP and ARP, between January 1, 2007, and December 31, 2018. Patients with an AP diagnosis based on at least 2 of the following 3 criteria were included<sup>11</sup>: (1) abdominal pain suggestive of AP, (2) at least 3-fold increase compared to normal values of serum amy-lase or lipase levels, and (3) imaging findings consistent with AP. Acute recurrent pancreatitis is defined as 2 or more distinct attacks with an asymptomatic period lasting at least one month or with the resolution of pain and normalization of pancreatic enzymes regardless of the interval between attacks.<sup>11</sup>

#### **Imaging Parameters**

Computed tomography (CT) examinations were performed with 3 different CT scanners: a 16-slice GE Optima 540 CT system (General Electric Medical Systems, Milwaukee, Wis, USA), a 16-slice Somatom Emotion CT system (Siemens, Erlangen, Germany), and a 64-slice dual-source Somatom Definition CT scanner (Siemens). Postcontrast abdominal CT images were obtained at the venous phase after intravenous contrast injection.

Magnetic resonance imaging (MRI) examinations were performed with 3 different 1.5 Tesla MR scanners; Philips Achieva dStream (Koninklijke Philips N.V., Nederland), Siemens Symphony TIM (Siemens), and Siemens Aera (Siemens). The routine abdominal MRI protocol for pancreatitis in all scanner consisted of coronal T2-weighted, axial T2-weighted fat-suppressed, dual-echo gradient T1-weighted, 3-dimensional MR cholangiopancreatography (MRCP), diffusion-weighted imaging, pre-contrast interpolated gradient echo T1-weighted and dynamic contrast-enhanced (arterial phase, portal venous phase, and 5-min delayed phase) T1-weighted images. Due to the prominent difference in size of our patient cohort, between 1 and 18 years old, fieldof-view was adjusted in each examination according to the patient's size, ranging from 380-280 to 285-160 mm.

#### **Study Parameters**

Demographic features, symptoms, clinical findings, laboratory tests [serum cholesterol (low-density lipoprotein (LDL), verylow-density lipoprotein (VLDL), and triglyceride) and pancreatic enzyme (amylase, lipase) levels, viral serologic studies for cytomegalovirus, herpes virus, mumps, rubella, varicella, Epstein-Barr virus], duration of the clinical follow-up, the results of invasive procedures (records of endoscopic retrograde cholangiopancreatography (ERCP), surgery, and percutaneous drainage) were noted.

As a first-line imaging modality, ultrasound (US) was used to evaluate the increase in pancreas size, pancreatic echogenicity, peripancreatic fluid collection, vascular complications, anomalies of the biliary tree, pancreatic ductal system, and pancreaticobiliary junction. Follow-up US was performed to evaluate the peripancreatic collection and to reveal whether ARP cases developed the findings of chronic pancreatitis such as parenchymal atrophy and irregular biliary ductal dilatation. On the other hand, CT and MRI images were used as a second-line modality to determine pancreatic parenchymal necrosis and peripancreatic collection within the first week of admission and to reveal potential causes of AP or ARP within the first month. Follow-up CT and MRIs (>1 month) were performed to evaluate local complications such as walled-off necrosis (WON), pseudocyst, and parenchymal atrophy and to reveal biliary and pancreatic ductal system anomalies. For patients with ARP, CT and MRI were used to screen for the development of chronic pancreatitis' indicators (parenchymal atrophy, fat replacement, calcification, and main pancreatic duct dilation<sup>27</sup>).

To determine the increase in size, pancreas thickness from the head, body, and tail was measured and compared with the normal range of the patient's age group. Normal pancreas parenchymal thickness values for age groups were obtained from the recent study of Trout et al<sup>28</sup> to compare and determine the enlargement of the pancreas in our patient cohort. Images were reevaluated from the Picture Archiving and Communication System by 2 radiologists according to the aforementioned imaging features.

#### **Statistical Analysis**

Statistical analyses were performed using International Business Machines' (IBM) Statistical Package for Social Sciences, version 25 software (IBM, Armonk, NY, USA). Continuous variables with normal distribution were expressed by the means  $\pm$  standard deviations (range) and categorical variables were stated as frequencies (numbers with percentages) in descriptive analysis. Related categorical variables were compared by the McNemar test. A significance level of 95% (or  $\alpha$  = 0.05 margin of error) was used to ascertain the presence of significant differences.

### RESULTS

#### **Patient Characteristics and Etiology**

The search yielded 74 patients [32 boys, 42 girls; mean age of diagnosis =  $9 \pm 4.9$  years (range between 1 and 18 years)] with AP or ARP. Presenting symptoms and the etiological distribution of AP and ARP are presented in Table 1. The most common causes in the study population were biliary tract anomalies (n = 21, 28.4%) (Figure 1), followed by gallstones and/or biliary ductal stones (n = 9, 12.2%) and cystic fibrosis (n = 8, 10.8%). In 14 patients (18.9%), the etiology could not be ascertained. Drug-induced pancreatitis was revealed in 6 patients (8.1%); L-asparaginase therapy for acute lymphoblastic leukemia (n = 5) and teriflunomide treatment for multiple sclerosis (n = 1). All of these patients recovered after the cessation of the drugs, but one of them had recurrent pancreatitis due to medication.

The ARP group included 32 patients (43.2%) and the most common three diagnoses are pancreaticobiliary maljunction (n =12, 66.7% among all pancreaticobiliary maljunction cases), followed by gallstones and/or biliary ductal stones (n = 8, 88.9%) and hyperlipidemia (n =3, 60%).

Although clinical and radiological features were compatible with AP, a more than 3-fold increase in amylase or lipase

Table 1. Symptoms and Etiologies of the Patients with	Acute Pancreatitis and Acute Recurrent Pa	Increatitis		
	Number of Patients	(Total: 74), n (%)		
Sex (male/female)	32/42			
Mean age $\pm$ standard deviation (range) (years)	9 ± 4.9 (1-18)			
Symptoms				
Abdominal pain	67 (90.5)			
Nausea	37 (50)			
Vomiting	34 (45.9)			
Failure to thrive	8 (10.8)			
Fever	7 (9.5)			
Diarrhea	5 (6.8)			
Etiology (n = 74)	Acute pancreatitis (no recurrence) (total: 42, 56.8%) n (%)	Acute recurrent pancreatitis (total: 32, 43.2%) n (%)		
Biliary tract anomalies:	9 (21.4)	12 (37.5)		
<ul> <li>pancreaticobiliary maljunction</li> </ul>	6	12		
choledocal cyst	3	0		
Gallstones and/or biliary/pancreatic ductal stones	1 (2.4)	8 (25)		
Cystic fibrosis	5 (11.9)	3 (9.4)		
Medication-induced	5 (11.9)	1 (3.1)		
Hyperlipidemia	2 (4.8)	3 (9.4)		
Trauma	4 (9.5)	0		
IgG4-related pancreatitis	3 (7.1)	0		
After bone marrow transplant	1 (2.4)	0		
Duodenal diverticulum	0	1 (3.1)		
Ectopic pancreas	1 (2.4)	0		
Annular pancreas	0	1 (3.1)		
Not defined	11 (26.1)	3 (9.4)		



Figure 1. Ultrasound (A) and coronal 3-dimensional reconstructed magnetic resonance cholangiopancreatography (B) images of a 2-year-old girl with epigastric pain, pale stool, increased amylase and lipase levels. There is fusiform dilatation of the common bile duct containing bile sludge (asterisk) and mildly dilated intrahepatic bile duct (arrow). After surgical excision, the biopsy confirmed the diagnosis of the Todani type 1 choledochal cyst.

levels was not seen in 16 patients (21.6%). The etiologies of this group were noted as idiopathic (n = 4), type I autoimmune (IgG4-related disease) pancreatitis (n = 3), biliary tract anomalies (n = 3), hyperlipidemia (n = 2), gallstones (n = 2), L-asparaginase (n = 1), and cystic fibrosis (n = 1).

#### **Radiological Findings**

All of the patients were examined with US within the first 3 days of the initial diagnosis and 85% (63/74) of those were examined within the first 24 hours. Seventy-three of 74 patients were evaluated with CT and/or MRI within the first month to delineate etiology more clearly or to search for complications. Fifty-five patients (74.3%) had one or more follow-up radiologic evaluations after one month. Twenty-three patients were evaluated by only US, whereas 32 patients (43.2%) had CT and/ or MRI (26 patients with US and MRI, 3 patients with US and CT, and 3 patients with US, CT, and MRI).

Imaging findings of the initial examination and follow-up are shown in Table 2. Ultrasound, as the first-line imaging modality, demonstrated pancreatic swelling and/or peripancreatic fluid in 30 of 74 patients (40.5%). Among them, 19 had biliary ductal dilatation and 5 had biliary ductal stones. No thrombosis was determined. An MRI was performed in 65 patients (87.8%) within the first month of initial diagnosis and pathological findings were noted in 39 (60%) patients as follows: pancreatic enlargement in 35 (53.8%), peripancreatic fluid collection in 19 (29.2%), biliary ductal dilatation in 24 (36.9%), biliary ductal stones in 5 (7.7%) patients, and lack of contrast enhancement in 1 (1.5%) patient. Twenty-three of 39 (58.9%) patients with positive MRI findings showed positive US findings. Hence, remaining 41% (n = 16) patients with positive MRI findings did not show any clue in US (Table 3). Magnetic resonance imaging revealed more positive findings of AP in our cohort than US, but there was no significant difference between them according to McNemar test (P = .093).

In 3 patients with type I autoimmune pancreatitis, MRI demonstrated diffusion restriction of the pancreatic parenchyma despite previously unremarkable US findings. A CT was performed in 16 patients (21.6%), which revealed pancreatic swelling in 10 (62.5%), peripancreatic fluid collection in 11 (68.8%), biliary ductal dilatation in 3 (18.8%), common bile duct stones in 2 (12.5%), and lack of contrast enhancement in 2 (12.5%) patients. Traumatic laceration was shown as an additional finding on CT in 1 trauma patient. In the remaining 3 trauma patients, peripancreatic fluid collections were revealed at the initial examination.

#### **Follow-Up Results and Outcomes**

The duration of radiological follow-up for 55 patients (74.3%) was between 2 months and 11 years. The imaging findings in

Table 2. Radiological Findings of Acute Pancreatitis in Initial and Follow-Up Imaging Studies						
Radiological Findings/Modality	US CT		MRI			
Initial evaluation (within first month)	74	16	65			
Pancreas enlargement, n (%)	25 (33.8%)	10 (62.5%)	35 (53.8%)			
Peripancreatic fluid, n (%)	22 (29.7%)	11 (68.8%)	19 (29.2%)			
Lack of contrast enhancement, n (%)	N/A	2 (12.5%)	1 (1.54%)			
Biliary ductal dilatation, n (%)	19 (25.7%)	3 (18.8%)	24 (36.9%)			
Gallstone and/or biliary ductal stone, n (%)	5 (6.8%)	2 (12.5%)	5 (7.7%)			
Follow-up imaging (>1 month), n	55	6	29			
Walled-off necrosis, n (%)	4 (7.3%)	3 (50%)	3 (10.3%)			
Pseudocyst, n (%)	2 (3.6%)	1 (16.7%)	2 (6.9%)			
Parenchymal necrosis (lack of contrast enhancement), n (%)	N/A	1 (16.7%)	1 (3.4%)			
Pancreatic ductal dilatation or atrophy, n (%)	12 (21.8%)	1 (16.7%)	7 (24.1%)			
n, number; US, ultrasound; CT, computed tomography; MRI, magnetic resonance in	naging; N/A, not applicable.					

<b>Table 3.</b> Comparison of Positive Findings of Ultrasound andMagnetic Resonance Imaging in Patients with Acute Pancreatitis				
		Magnetic Resonance Imaging Findings		
		Negative	Positive	Total
Ultrasound	Negative	19	16	35

findings Positive 7 23 30

Total 26 65 McNemar test was used to compare 2-paired samples and P value was .093.

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the follow-up period are summarized in Table 2. Eight patients (14.5%) had peripancreatic collections; 6 of them had WON and the remaining 2 patients had pseudocysts. In 1 particular patient, CT demonstrated a homogenous peripancreatic collection that looked like a pseudocyst; however, MRI revealed a necrotic component within the collection, which was diagnosed as WON (Figure 2). Follow-up imaging of ARP patients revealed irregular dilatation of the pancreatic duct along with parenchymal atrophy in 12 patients (n = 4 only US, n = 7 both US and MRI, n = 1 US and CT) and their diagnosis evolved into chronic pancreatitis.

On follow-up, 16 patients required interventional procedures or surgery, and ERCP was performed on 21 patients. The indications for ERCP were ARP without any obstructive finding in 8 patients, biliary duct stone in 3 patients, pancreatic duct stone in 3 patients, biliary tract anomaly in 6 patients, and stent placement for pancreatic necrosis in 1 patient. In a patient with ARP, distal common bile duct stone that was not seen previously in US was detected on ERCP and extracted. In other patients, apart from delineating the biliary anomaly more conspicuously, ERCP had similar diagnostic value as previous radiological examinations. From the therapeutic view, following sphincterotomy in all patients, stent placement was performed via ERCP in 6 patients (in 2 patients due to strictures following stone extraction, in 3 patients with biliary ductal anomalies to maintain bile flow, and in 1 patient with pancreatic necrosis to prevent bile leakage). Eleven (14.9%) patients underwent surgery (3 for posttraumatic distal pancreatectomy, 3 for choledochal cyst excision, 1 for annular pancreas, 1 for ectopic pancreas excision, and 3 for cholecystectomy with hepaticojejunostomy for ARP due to biliary ductal anomalies). Percutaneous drainage was performed 1 month after onset in 5 patients (3 pseudocysts and 2 WON). The indications for percutaneous pseudocyst drainage were gradual increase in size (n = 1), gastric outlet obstruction due to compression of the cyst (n = 1), and main portal vein compression (n = 1). One patient with WON was treated with cystogastrostomy via transgastric approach.

## DISCUSSION

Our study showed 3 major findings: biliary tract anomalies were the most commonly identified cause of AP and ARP in our center, positive findings of AP or ARP in MRI (60%) was higher than US (40.5%), US at diagnosis was negative in 41% of the patients with positive MRI findings. Nevertheless, there was no significant difference between MRI and US regarding positive findings of AP. Biliary and pancreatic ductal system anomalies including bile duct cysts and biliary stones, the most common etiologies in our cohort, can be visualized more obviously with MRI than US. Hence, MRI seems the most useful diagnostic modality to delineate the possible etiology of AP and ARP.

There is limited literature about imaging findings of pediatric AP and ARP. The diagnostic imaging features of AP in pediatric patients, which are similar to those seen in adults, are pancreatic swelling due to edema, peripancreatic inflammation and collections, ascites, necrosis of the pancreatic parenchyma,





and peripancreatic fat tissue.<sup>3</sup> Major studies about the diagnostic rate of US and CT findings in pediatric AP are summarized in Table 4.<sup>7,22-25,27,29-35</sup> However, the pediatric studies comparing MRI with other modalities in AP are lacking.<sup>9</sup>

Imaging findings are not only a crucial part of the diagnostic algorithm but are also important for determining the etiology and complications of AP and ARP. Significant number of studies that are mentioned in Table 4 indicate no clear etiology for most of the patients, in contrast to our study, which revealed biliary tract anomalies as the most common cause and only 14 (19.2%) patients had undefined etiology.<sup>21,22,24,25</sup> This is probably due to further evaluation of AP and ARP patients with MRI to reveal biliary ductal anomalies in our center. Because MRI, especially MRCP, is more valuable to delineate biliary etiologies and pancreatic structural abnormalities.<sup>9</sup> Park et al<sup>23</sup> also found that biliary (both ductal anomalies and stones) reasons were more common than in the idiopathic group which correlated with our findings.

Cystic fibrosis (10.8%) was much more common in our cohort than in any other study because our hospital is a referral center for cystic fibrosis.<sup>21-26</sup> In patients with a history of trauma, intravenous contrast-enhanced CT seems to be sufficient, not only for pancreatic parenchyma but also to evaluate other abdominal organs, bowels, and mesentery better than MRI. In our patient cohort, trauma and oncology patients were mostly followed by CT, whereas the patients who had biliary tract anomalies were imaged by MRI when they had recurrent episodes of pancreatitis.

We had 3 patients with type I autoimmune pancreatitis who had normal imaging findings on US and diffusion restriction on MRI which is a specific finding for autoimmune pancreatitis.<sup>5,36</sup> Type I autoimmune pancreatitis is an unusual form of ARP. It is generally associated with immunoglobulin G4 (IgG4)-related disease which is a fibrosing multisystem disease. On the other hand, type II autoimmune pancreatitis is a selective pancreatic disease and is frequently associated with inflammatory bowel disease. Although both forms of autoimmune pancreatitis generally occur in late adulthood, there are a few reports of their occurrence in children.<sup>37</sup> According to The International Association of Pancreatology, radiologic imaging features, serologic tests, and multiorgan involvement and response to steroid treatment are key features for the diagnosis of autoimmune pancreatitis.<sup>38</sup> Characteristic MRI features are diffuse enlargement with a sausage-shaped appearance and restricted diffusion.

Based upon all of our findings and the literature<sup>9,18,39</sup> we recommend MRI and MRCP as a second option when the initial US is inconclusive and in patients with a suspicion of biliary ductal anomalies, bile duct stones, or autoimmune pancreatitis. To reduce edematous compression upon biliary ducts and evaluate biliary tract anomalies more conspicuously, MRCP can be performed after the acute phase of pancreatitis.<sup>2</sup>

There are 2 types of AP according to the revised Atlanta criteria: interstitial edematous pancreatitis and necrotizing pancreatitis.<sup>13</sup> Interstitial edematous pancreatitis has similar imaging findings in US, CT, and MRI, but MRI may show changes earlier due to higher contrast resolution in soft tissue.<sup>18</sup> To identify the type of disease, pancreatic and peripancreatic collections were defined according to the presence of necrosis and the time from the onset of symptoms. In acute edematous pancreas, collections that are seen less than 4 weeks after presentation are called acute peripancreatic fluid collections, and if they persist for more than 4 weeks, they become pseudocysts. These are the most common complications of AP and have been reported as 13%-15% in adults and 8%-41% in pediatric studies.<sup>9</sup> According to the revised Atlanta criteria and INSPPIRE study, CT is not recommended for the diagnosis and in the first

 Table 4. Major Reports That Include Ultrasound and Computed Tomography Findings in Childhood Acute Pancreatitis Between 1996

 and 2018

						Diagnostic		
			Age Range,	Most Common	Number of	Rate of US,	Number of	Diagnostic Rate
	Patients, n	Location, Year	Year	Etiologies	Performed US	n (%)	Performed CT	of CT, n (%)
Yeung et al <sup>29</sup>	43	Taiwan, 1986-1996	2-18	Trauma	-	86	-	100
Tiao et al <sup>30</sup>	61	Taiwan, 1986-2000	2-18	Trauma	51	40 (78.4 %)	21	21 (100%)
Werlin et al <sup>7</sup>	180	USA, 1996-2001	0-18	Systemic	91	22 (24 %)	83	43 (54%)
Chen et al <sup>31</sup>	75	Taiwan, 1992-2002	0-17	Idiopathic	-	57 %	-	74%
Kandula et al <sup>32</sup>	87	USA, 1995-2004	0-3	Systemic	49	25 (51 %)	30	14 (47%)
Park et al <sup>23</sup>	215	USA, 1994-2007	0-20	Biliary	178	51 (28,6 %)	94	-, 59.3%
Chang et al <sup>33</sup>	180	Taiwan, 1993-2008	0-18	Biliary	162	111 (68.5 %)	93	72 (77.4%)
Minen et al <sup>34</sup>	34	Italy, 2007–2012	2-18	Medication	34	25 (73.5 %)	7	4 (57.1%)
								(performed only
								in pts with normal
								US)
Coffey et al <sup>35</sup>	97	Australia, 2000–2011	9.5-15.1	-	77	21 (27 %)	42	28 (67%)
Antunes et al <sup>25</sup>	37	Portugal, 2002–2012	7-17	Biliary	34	22 (79 %)	22	22 (100%)
Fayyaz et al <sup>22</sup>	43	Pakistan, 2014	2-15	Idiopathic	43	- (71 %)	43	- (89%)
Grzybowska	76	Poland, 2004-2013	1.6-18	Idiopathic	76	51 (67 %)	56	34 (60%)
-Chlebowczyk et al <sup>24</sup>								
Khan et al <sup>27</sup>	45	India, 2003-2014	6-14	Idiopathic	-	-	45	31 (69%) (patients
								with CTSI > 3)
Current study	74	xxx, 2007-2018	1–18	Biliary	74	30 (40.5 %)	16	15 (93.75%)
US, ultrasound; CT, computed tomography; CTSI, computed tomography severity index.								





Figure 3. Our diagnostic algorithm for acute pancreatitis in children. AP, acute pancreatitis; CT, computed tomography; US, ultrasound; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography.

phase of acute edematous pancreatitis; however, it can be performed when pancreatic necrosis is suspected.<sup>18,39</sup> For severe pancreatitis, pancreatic necrosis is a well-known risk factor for morbidity and mortality.<sup>40</sup> Early detection of pancreatic necrosis is challenging because both necrotic and edematous parenchyma exhibit heterogeneous enhancement on contrastenhanced imaging.<sup>13</sup> Although US can be performed as soon as possible to determine the etiology, contrast-enhanced CT or MRI should be performed at least 72 hours after initial symptoms in severe cases.

In necrotizing pancreatitis, collections within 4 weeks of onset are defined as acute necrotic collections, and collections that are seen more than 4 weeks after onset are called WON.<sup>17</sup> The late phase occurs only in moderate and severe diseases that are characterized by systemic or local complications. Imaging is crucial for the assessment and management of complications during this phase.<sup>13</sup> Furthermore, contrast-enhanced US (CEUS) seems to have promising results in revealing necrotic tissue as well as contrast-enhanced CT imaging.<sup>41</sup> As none of the US-contrast agents were approved officially in our country, we were not able to perform CEUS.

In patients who recovered from acute edematous pancreatitis, follow-up imaging is not required. However, in patients with complicated pancreatitis, or ARP, US should be performed at least 3-6 months after the initial diagnosis. In patients with necrotizing pancreatitis or WON, follow-up imaging should be performed with MRI with the advantage of dynamic contrastenhanced imaging. Additionally, CT may be inconclusive to delineate the content of peripancreatic collections.<sup>9</sup> In one of our patients, CT revealed a pure homogeneous peripancreatic fluid collection called a pseudocyst; however, MRI demonstrated necrotic content in the same collection which is called WON and altered the severity of the disease. In necrotizing pancreatitis, the follow-up duration should be extended until the lesions disappear.

Several studies have stated that 15%-35% of pediatric AP eventually progress to ARP.<sup>5-9</sup> Chronic pancreatitis is a persistent inflammation of the pancreas tissue and a subset of ARP will progress to chronic pancreatitis. Twelve patients (16.2%) in our cohort had imaging findings consistent with chronic pancreatitis on follow-up. The diagnosis and distinction of ARP and chronic pancreatitis are based on clinical findings and biochemical tests (exocrine and endocrine pancreatic function), especially imaging studies.<sup>27</sup> Histopathological evaluation cannot be performed in the majority of cases; therefore, MRCP has paramount importance in both determining the cause and following the clinical course of ARP and chronic pancreatitis. In our study, the indications for ERCP were ARP without any obstructive findings, biliary duct stone, pancreatic duct stone, biliary tract anomaly, and stent placement for pancreatic necrosis. Beyond biliary tract mapping, ERCP added diagnostic value to any radiological evaluation in only 1 patient. Following sphincterotomy in all patients, stent implementation was done in 6 patients. The most common reasons for pediatric ERCP are biliary tract obstruction and chronic/recurrent pancreatitis. In adulthood, ERCP is recommended within 48 hours of symptom occurrence in cases of cholestasis or cholangitis. Otherwise, elective ERCP is advised. In childhood, ERCP has limitations. In addition to the indications reported in our study, pancreatic duct leakage requires ERCP.<sup>2</sup>

In 2021, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, and Society for Pediatric Radiology released a joint position paper as noninvasive imaging studies play a significant role in diagnosis, revealing causative etiology, staging the disease, follow-up, and managing interventions. This joint paper stated that transabdominal US is recommended as the first choice for suspected AP, and either CT or MRI is recommended as a diagnostic modality if US is negative and an imaging diagnosis is needed. Besides, CT or MRI is needed to find out or follow the complications of AP, while US can be used for following known pancreatic fluid collections. However, a caution note was added as CT may underestimate the complexity of peripancreatic fluids. Before any intervention for AP-related complications, CT or MRI is highly recommended. For ARP, MRI is highly recommended to reveal anatomic and obstructive causes as well as screen for progression to chronic pancreatitis if clinically needed. For patients needing sedation, alternating MRI with CT and US is acceptable.9

Based on our experiences regarding various etiologies and long-term follow-up of AP and ARP in children, we recommend an imaging algorithm for the diagnosis and follow-up (Figure 3). If AP was confirmed by INSPPIRE criteria," etiological investigations including imaging should be performed. The first imaging option can be US and if the underlying cause is revealed, no further imaging is necessary for initial diagnosis. Only CT is recommended for traumatic patients. Additionally, with known probable causes such as medication, hyperlipidemia, or cystic fibrosis, US imaging is sufficient unless it becomes complicated. Moreover, follow-up imaging is unnecessary for patients with a unique episode of AP. However, in patients with ARP without any known underlying etiology or in complicated patients, such as peripancreatic collections and abnormal ductal findings on US, MRI should be performed to reveal the extent of the complications or concomitant ductal anomalies. To delineate the biliary anatomy, MRI with MRCP should also be considered in patients who require surgery, ERCP, or percutaneous interventions. When the etiology is proven, US may be sufficient for follow-up imaging in recurrent pancreatitis or postprocedural imaging. Magnetic resonance imaging should be reserved for an unexpected clinical course or unexplained US findings. Contrastenhanced CT or MRI can be performed in severe cases.

Our study has some limitations. This study represents the data of one tertiary hospital. Genetic analysis for hereditary pancreatitis could not be done for each participant due to the retrospective design of the study. Although not affecting the imaging approach, a nationwide multicenter study including detailed genetic studies would represent more generalizable data for the etiology of AP.

#### CONCLUSION

With increasing prevalence over the years and growing treatment opportunities, recognizing the spectrum of imaging findings of acute pancreatitis and complications is crucial. Ultrasound is the first-line imaging technique in pediatric AP. Although CT is accepted as more sensitive than US for the diagnosis of acute pancreatitis in adults, it has limited potential for evaluation of the biliary ductal system which is one of the most common causes of pediatric AP. For ARP, MRI is strongly recommended to reveal anatomic and obstructive causes of pancreatitis as well as screening for progression to chronic pancreatitis. Moreover, radiation exposure limits the usage of CT for severe diseases and complications, such as necrosis and peripancreatic collections, especially in children. We suggest that MRI should be preferred as a second option when the initial US is inconclusive, with the advantages of biliary ductal system delineation and better characterization of cyst content.

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