# Association of Laboratory and Imaging Parameters in Different Types of Pancreatitis in Children in a Tertiary Care Hospital in Bangladesh

MAIMUNA SAYEED<sup>1</sup>, RAYHAN SHAHREAR<sup>2</sup>, SHARMIN AKTER<sup>3</sup>, NAHID-E-SUBHA<sup>4</sup>, ASM BAZLUL KARIM<sup>5</sup>

# Abstract

**Background:** Pancreatitis is an inflammatory condition of the pancreas, which might extend to local and distant extra-pancreatic tissues. It can be acute, acute recurrent or may be chronic. The diagnosis of different types of pancreatitis is based on a combination of clinical signs and symptoms, laboratory investigations and imaging techniques.

**Objective:** To describe and find out the association of the laboratory and imaging profiles of different variety of pancreatitis in children.

**Methods:** It was a an observational study conducted at the department of Paediatric Gastroenterology and Nutrition of Bangabandhu Sheikh Mujib Medical University from July 2018 through June 2020. A total of 48 cases were included in this study. The diagnosis of acute, acute recurrent and chronic pancreatitis was based on diagnostic criteria made by INSPPIRE group. Clinical characteristics, hematological, biochemical and imaging profile of the different variety of pancreatitis and their hospital outcome were observed.

**Result:** Among 48 cases, acute recurrent pancreatitis were 56.3%. Mean age of the patients at presentation was 10.3 years. Laboratory tests showed serum calcium and *C*-reactive protein was significantly altered among acute, acute recurrent and chronic pancreatitis with characteristic imaging findings. Among imaging modalities, abdominal ultrasonogram showed swollen pancreas (58.3%) was significantly common in acute recurrent pancreatitis than chronic pancreatitis, whereas shrunken pancreas (28%) was significantly common findings in chronic pancreatitis. In addition to ultrasonogram, MRCP aided diagnosis of chronic pancreatitis. Complications developed in 25% of acute pancreatitis cases, which included hypocalcemia (58.3%), ascites (86.7%), pleural effusion (66.7%), pseudocyst (33.3%) and pancreatic necrosis (25%). Hospital stay was significantly prolonged in acute pancreatitis cases, when compared to other types of pancreatitis.

**Conclusion:** Low calcium level and high CRP level were found in acute pancreatitis than in acute recurrent and chronic pancreatitis. Swollen pancreas with beaded and tortuous pancreatic ducts were found in case of chronic pancreatitis.

Key words: Pancreatitis, Pancreatitis in Children.

DOI: https://doi.org/10.3329/bjch.v47i2.77680

5. Professor & Former chairman, Department of Pediatric Gastroenterology & Nutrition, BSMMU, Dhaka.

**Correspondence:** Dr. Maimuna Sayeed, Assistant Professor, Department of Paediatrics, Ad-din Women Medical College Hospital, Dhaka. Email: dr.maimuna.sayeed@gmail.com Contact: +8801728002004

### Introduction

Pancreatitis is an inflammatory condition of the pancreas, which might extend to local and distant extra-pancreatic tissues. It can cause recurrent inflammation and can lead to irreversible damage to the pancreas. The diagnosis of different type of pancreatitis is based on a combination of clinical signs and symptoms, laboratory investigations and imaging techniques.

<sup>1.</sup> Assistant Professor, Department of Paediatrics, Ad-din Women's Medical College Hospital, Dhaka.

<sup>2.</sup> Assistant Professor, Department of Anatomy, Ibrahim Medical College, Dhaka.

<sup>3.</sup> Consultant, Department of Pediatric Gastroenterology & Nutrition, BSMMU, Dhaka.

<sup>4.</sup> Assistant Professor, Pediatric Gastroenterology & Nutrition, BSMMC, Faridpur.

BANGLADESH J CHILD HEALTH 2023; VOL 47 (2) : 96

Overall acute recurrent pancreatitis (ARP) is reported in 15–35% of children following an initial occurrence of AP <sup>1-4</sup> and chronic pancreatitis (CP) is estimated as ~0.5 per 100,000 persons per year <sup>5, 6</sup>.

To the best of knowledge, in Bangladesh very few studies has been carried out so far to find out the relationship of laboratory and imaging profile of acute pancreatitis in children <sup>7, 8</sup>. No studies carried out on different types of pancreatitis in our country till date.

So, The study aims to observe profile of different types of pancreatitis in children in a tertiary care center from hematological, biochemical and imaging point of view.

# Material and method

The study was an observational observational study carried out at the Department of Pediatric Gastroenterology and Nutrition, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh from July 2018 to June 2020. After obtaining ethical clearance from IRB, a total of 48 children attended at the Department of Pediatric Gastroenterology and Nutrition, BSMMU with primarily diagnosed and admitted as a case of Pancreatitis in Children defined as per INSPPIRE definition were selected for the study.

Entity	Clinical definition
AP	Requires at least 2 of 3 criteria:
	<ol> <li>Abdominal pain suggestive of, or compatible with AP (i.e., abdominal pain of acut onset, especially in the epigastric region)</li> </ol>
	<ol> <li>Serum amylase and /or lipase activity at least three times greater than the upper limit of normal (IU/L)</li> </ol>
	<ol> <li>Imaging findings characteristic of, or compatible with AP (e.g., using U/S, CECT EUS, MRI/MRCP)</li> </ol>
Pediatric onset	The first episode of AP occurring before the patient's 19th birthday
ARP	Requires at least two distinct episodes of AP (each as defined above), along with:
	<ul> <li>Complete resolution of pain (≥1-month pain-free interval between the diagnose of AP)</li> </ul>
	OR
	<ul> <li>Complete normalization of serum pancreatic enzyme levels (amylase and lipase before the subsequent episode of AP, is diagnosed, along with a complet resolution of pain symptoms, irrespective of a specific time interval between A episodes</li> </ul>
CP	Requires at least 1 of the following 3:
	<ol> <li>Abdominal pain consistent with pancreatic origin and imaging findings suggestiv of chronic pancreatic damage*</li> </ol>
	<ol> <li>Evidence of exocrine pancreatic insufficiency C" and suggestive pancreatic imagin findings*</li> </ol>
	<ol> <li>Evidence of endocrine pancreatic insufficiencyG" and suggestive pancreatic imagin findings*</li> </ol>
	OR
	Surgical or pancreatic biopsy specimen demonstrating histopathologic feature compatible with CP

Definitions of pancreatitis in children according to INSPPIRE<sup>9</sup>

Children under 18 years were included if they fulfilled INSPPIRE criteria, children were excluded if they had any one of the following: 1) Any other comorbid condition except the consequences of pancreatitis, 2) unwilling to give consent.

Data was collected in a structured questionnaire by the investigator. The guardian of the patients was informed about the study and a written consent was taken. Each patient went under a detail clinical evaluation at entry.

In each case, history was taken in details especially regarding abdominal pain, associated symptoms like vomiting, loss of appetite, fever, abdominal distension, duration and onset of illness were also noted. Examination of each case was done with especial reference to vital signs, hemodynamic stability and abdominal status like tenderness, distension, mass, presence of ascites, pleural effusion and bowel sound. Blood for complete blood count with hematocrit, amylase, lipase, blood glucose, serum calcium, Creactive protein (CRP), urea, BUN were evaluated. Imaging techniques abdominal ultrasonography were done for establishing diagnosis and complications. Imaging findings were documented. MRCP were done when feasible, especially in chronic pancreatitis.

The studied populations were divided into three groups of pancreatitis according to INSPPIRE criteria as AP, ARP and CP. Hospital stay and complications of the enrolled patients were noted.

Statistical analysis was done using Statistical Package of Social Science (SPSS) version 23 (SPSS

Inc, Chicago, IL, USA) for Windows. Results were compared using the Chi-square test for categorical variables, and one way ANOVA for quantitative variables. All data were expressed as mean ± standard deviation (SD) or number or percent as appropriate. For statistical test, p value d"0.05 was considered as significant.

## Results

A total of 48 patients were enrolled in the study. Mean  $(\pm SD)$  age of the patients at presentation was 10.3±3.6 years among the total cases. Age range at diagnosis was 3-16 years. Among the study population Majority of the cases were acute recurrent pancreatitis (27, 56.3%). (Table-I)

# Table IDistribution of patients by different types ofpancreatitis according to INSPPIRE criteria (N=48)

Variable	Total (N=48)			
	n	%		
Acute pancreatitis (AP)	14	29.2		
Acute recurrent pancreatitis (ARP)	27	56.3		
Chronic pancreatitis (CP)	7	14.6		

Abdominal pain was the most common feature of pancreatitis. All the 48 patients had the complaints of abdominal pain.

On examination, abdominal tenderness was most common sign (43, 89.6%) (table II).

Variables	Total (	(N=48)	AP (	AP (n=14)		ARP (n=27)		(n=7)	p value
	n	%	n	%	n	%	n	%	
Anemia	16	33.3	7	50	9	33.3	0	0	0.072
Dehydration	1	2.1	0	0	1	3.7	0	0	0.672
Tenderness	43	89.6	11	78.6	26	96.3	6	85.7	0.198
Palpable mass	3	6.3	1	7.1	1	3.7	1	14.3	0.580
Ascites	4	8.3	3	21.4	1	3.7	0	0	0.103

Table IIClinical signs of the studied cases (N=48)

Chi-square test was done as a test of significance

Majority of the patients had showed swollen pancreas (58.3%) which was significantly (p=0.024) common in AP and ARP than CP. Significantly common findings in CP were shrunken pancreas (p=0.28). Ascites and pleural effusion were also significant findings in AP (p=.022 and 0.007 respectively). (Table-IV)

In biochemical parameters, significance found in serum calcium (p=0.004) and CRP level (p=0.036). Calcium level was significantly lower and CRP level is significantly higher in AP group in compare to other two groups (post-hoc analysis). (Table III)

Laboratory variables in pancreatitis (IN=48)											
Variable	Total(N=48)	AP(n=14)	ARP(n=27)	CP(n=7)	p value						
	Mean±SD	Mean±SD	Mean±SD	Mean±SD							
Hemoglobin (g/dL)	11.53±1.90	10.61±2.35	11.95±1.72	11.71±0.76	0.096						
Total count (K/mm <sup>3</sup> )	11.06±4.09	11.97±5.34	10.98±3.60	9.54±2.89	0.444						
Platelet (lac/mm <sup>3</sup> )	3.21±1.31	3.55±1.73	3.09±1.03	2.98±1.44	0.516						
Hematocrit (%)	35.21±5.51	32.86±7.55	36.14±4.58	36.29±2.32	0.167						
Lipase (U/L)	2195.94±3246.61	2885.00±3499.70	1955.74±3327.82	1744.29±2536.78	0.643						
Amylase (U/L)	751.00±776.57	1031.00±1199.24	664.00±490.81	526.57±536.96	0.258						
Glucose (mg/dL)	5.55±1.5	6.12±2.22	5.32±1.14	5.33±0.62	0.266						
Urea (mg/dL)	20.04±12.18	16.81±15.45	20.91±10.38	23.13±1.81	0.465						
BUN (mg/dL)	9.40±5.71	7.84±7.37	9.84±4.76	10.79±5.51	0.454						
Calcium (mg/dL)	9.19±0.72	8.73±0.59	9.29±0.60	9.74±0.92	0.004						
CRP (mg/L)	42.71±75.88	85.32±108.93	28.34±54.34	12.95±20.07	0.036						

Table III	
Laboratory variables in pancreatitis	(N=48)

One-way ANOVA was done as a test of significance

Variables	Total(N=46)		AP	AP(n=13)		ARP(n=26)		CP(n=7)	
	n	%	n	%	n	%	n	%	
Swollen pancreas	28	58.3	8	61.5	19	73.1	1	14.3	0.024
Shrunken pancreas	3	6.5	0	0.0	1	3.8	2	28.6	0.028
Pancreatic pseudocyst	4	8.7	3	23.1	1	3.8	0	0.0	0.103
Dilated CBD	1	2.2	0	0.0	1	3.8	0	0.0	0.672
Cystic duct calculi	1	2.2	1	7.7	0	0.0	0	0.0	0.289
GB calculi	1	2.2	1	7.7	0	0.0	0	0.0	0.289
GB sludge	5	10.9	0	0.0	4	15.4	1	14.3	0.317
Ascites	12	26.1	7	53.8	5	19.2	0	0.0	0.022
Pleural effusion	6	13	5	38.5	1	3.8	0	0.0	0.007

 Table IV

 Distribution of sonographic findings of the studied cases (N=46)

Chi-square test was done as a test of significance

CBD= common bile duct, GB=gall bladder

Association of Laboratory and Imaging Parameters in Different Types

Majority of the patients had showed swollen pancreas (58.3%) which was significantly (p=0.024) common in AP and ARP than CP. Significantly common findings in CP were shrunken pancreas (p=0.28). Ascites and pleural effusion were also significant findings in AP (p=.022 and 0.007 respectively). (Table IV).

Over half of the patient performed MRCP (25, 52.1%), among them significant number of cases showed pancreatic and biliary duct abnormalities, which includes beaded pancreatic duct (16%), tortuous pancreatic duct (20%) which was significantly higher in CP (p<0.001 in each). (table V)

Variables	Total(N=46)		AP	AP(n=13)		ARP(n=26)		CP(n=7)	
	n	%	n	%	n	%	n	%	
Swollen pancreas	28	58.3	8	61.5	19	73.1	1	14.3	0.024
Shrunken pancreas	3	6.5	0	0.0	1	3.8	2	28.6	0.028
Pancreatic pseudocyst	4	8.7	3	23.1	1	3.8	0	0.0	0.103
Dilated CBD	1	2.2	0	0.0	1	3.8	0	0.0	0.672
Cystic duct calculi	1	2.2	1	7.7	0	0.0	0	0.0	0.289
GB calculi	1	2.2	1	7.7	0	0.0	0	0.0	0.289
GB sludge	5	10.9	0	0.0	4	15.4	1	14.3	0.317
Ascites	12	26.1	7	53.8	5	19.2	0	0.0	0.022
Pleural effusion	6	13	5	38.5	1	3.8	0	0.0	0.007

Table IV
Distribution of sonographic findings of the studied cases (N=46)

Chi-square test was done as a test of significance

CBD= common bile duct, GB=gall bladder

Variable	Total(N=25)		AP	AP(n=5)		ARP(n=13)		CP(n=7)	
	n	%	n	%	n	%	n	%	
Swollen pancreas	8	16.7	2	40	5	38.5	1	14.3	0.927
Beaded pancreatic duct	4	16	0	0.0	0	0.0	4	57.1	<0.001
Tortuous pancreatic duct	5	20	0	0.0	0	0.0	5	71.4	<0.001
Pancreatic pseudocyst	2	8	1	20.0	1	7.7	0	0.0	0.730
Necrosis	1	4	0	0.0	1	7.7	0	0	0.672
Dilated CBD	1	4	1	20.0	0	0.0	0	0.0	0.289
Cystic duct calculi	1	4	1	20.0	0	0.0	0	0.0	0.289
GB calculi	1	4	0	0.0	1	7.7	0	0.0	0.672
Ascites	4	16	1	20.0	2	15.4	1	14.3	0.827
Pleural effusion	3	12	1	20.0	2	15.4	0	0.0	0.761

Table VDistribution of MRCP finding of the studied cases (N=25)

Chi-square test was done as a test of significance

Variable	Total(N=48)		AP(n=14)		ARP(n=27)		CP(n=7)		p value
	n	%	n	%	n	%	n	%	
Recovery	37	77.1	11	7.6	22	81.5	4	57.1	0.389
Development of complication	15	31.3	8	57.1	6	22.2	1	14.3	0.042
Hypocalcemia	7	46.7	5	62.5	1	16.7	1	100	0.023
Ascites	13	86.7	7	87.5	5	83.3	1	100	0.070
Pleural effusion	8	53.3	4	50	4	66.7	0	0	0.235
Pseudocyst	4	26.7	3	37.5	1	16.7	0	0	0.103
Pancreatic necrosis	2	13.3	0	0	2	33.3	0	0	0.761
	Mean±SD		Mean±SD		Mean±SD		Mean±SD		
Hospital stays (days)*	9.81±6.10		13.00±6.97		7.70±3.30		11.57±9.55		0.018

Table VIHospital outcome of studied population (N=48)

Chi-square test was done as a test of significance

(\*) Result was expressed in Mean±SD and significant test done by One-way ANOVA

Most of the patients recovered during their stay in the hospital, and significant number of patients developed disease related complications (p=0.042), among which hypocalcemia was significantly common in AP than other two groups (p=0.023 and post-hoc analysis). The duration of hospital stay was significantly higher in AP group (p=0.018) than APR group but not significant with the CP group (post-hoc analysis). (Table VI)

### Discussion

The incidence of acute pancreatitis in the pediatric population have been rising during the past 10 to 15 years <sup>10, 11</sup>, and it is estimated to be 3.6 - 13.2 cases per 100,000 per year <sup>9, 12</sup>. Overall ARP is reported in 15–35% of children following an initial occurrence of AP <sup>1-4</sup> and CP is estimated as ~0.5 per 100,000 persons per year <sup>5, 6</sup>. However, a very few studies have been done so far on pancreatitis in Bangladesh among children. So, the actual incidence and prevalence of this treatable disease are yet unknown. In this respect The current study findings in our country can help pediatricians to clarify some clinical aspects of the disease.

The mean age at presentation in the present study was 10.3 years. Similar findings were seen in a study performed in Bangladesh, which showed their mean age at presentation was 10.2 years <sup>7</sup>. But, the mean age was found to be different in different studies performed abroad. Suzuki, Saito <sup>13</sup> found 7.3 years, Benifla and Weizman<sup>14</sup> showed patients with a mean

age of 9.2 years. On the other hand, Szabo, Hornung<sup>12</sup> found a mean age of 12.7 years in their study. No cases of pancreatitis were observed in children under the age of three years (range 3.0 - 16.0 years) in this study. In a study by Pezzilli, Morselli-Labate<sup>4</sup>, the lowest age at presentation was two years.

The diagnosis of pancreatitis can be made with reasonable certainty on the basis of clinical, radiological and laboratory findings. In this study, laboratory and imaging parameters were observed in different types of pancreatitis.

Regarding the laboratory evaluation, serum amylase and lipase was the most common serum assays for the diagnosis of acute pancreatitis in children. But there was no significant difference found in serum amylase and lipase level between acute, chronic and acute recurrent pancreatitis. Other hematological and biochemical parameters such as hemoglobin, white blood cells, platelet count, hematocrit, blood glucose, BUN and urea levels were found to be nonsignificant among acute, chronic and acute recurrent pancreatitis in the studied cases. But serum calcium and CRP was statistically significant in AP than in ARP and CP groups (p=0.004 and 0.036 respectively). Decreased level of serum calcium was commonly seen in critical illness. Hypocalcemia was significantly more frequent in patients with severe form of acute pancreatitis, hence may serve as a potential prognostic factor <sup>15</sup>. CRP is an acute-phase protein that was first described in 1930. In the mid-1980s, several

studies showed that the hepatic production of CRP was increased after any inflammation, and subsequently, the protein was proposed as a prognostic factor of severe pancreatitis <sup>16</sup>. It is the most widely available, low-cost, and well-studied marker of severity in AP <sup>17</sup>.

Abdominal ultrasonography has been shown to have 80% accuracy in the diagnosis of pancreatitis, usually shows decreased echogenicity of the pancreas <sup>18</sup>. Unlike other imaging studies, it was a noninvasive imaging technique, having no radiation hazard and cost-effective, that helps not only for the diagnosis of the disease but also for monitoring its course and for identifying local complications of pancreatitis<sup>19</sup>. In this present study, an abdominal ultrasonogram was carried out in majority of the patients (95.8%), it aided in establishing the diagnosis, identifying the complications, such as pseudocyst (8.7%), pleural effusion (13%) or gall bladder sludge (10.9%). Swollen pancreas was found to be significant finding (p=0.024) among acute, chronic and acute recurrent pancreatitis. Enlarged and edematous pancreas are classic sonographic features of acute pancreatitis<sup>20</sup>. Ascites and pleural effusion were also significant finding among acute and acute recurrent pancreatitis. Md. Al Mamun et al. observed, USG was found effective in detecting pancreatitis in 61.5% case 8.

Novel diagnostic modalities, such as magnetic resonance cholangiopancreatography (MRCP) is a safer technique, which may help better to define pancreatitis and its complications<sup>14</sup>. MRCP carries an additional advantage of diagnosing abnormalities of the biliary tree including duplication, choledochal cyst, pancreas divisum and cholangiocarcinoma<sup>21</sup>. MRCP can enable accurate evaluation of the condition of the pancreatic duct and its changes in patients with chronic pancreatitis<sup>22</sup>. In this study, only about half of the patient (52.1%) performed this test. Among them beaded and tortuous pancreatic duct were significant for CP. Thus, it is suggested that MRCP is a better imaging modality for diagnosis of chronic pancreatitis and identify the etiology when result of abdominal ultrasound is not clear. Recent studies demonstrate the higher sensitivity of CT and magnetic resonance imaging when compared with ultrasonography (78%-90% vs 52%-70%) and that these they are most likely beneficial in those patients with a complicated clinical course<sup>23</sup>.

Majority of the patients recovered (77.1%) during the hospital course. About one third (31.3%) of the patients developed significant (p=0.042) disease related complications such as ascites (86.7%), pleural effusion (53.3%), hypocalcemia (46.7%). pseudocyst (26.7%) and pancreatic necrosis (13.3%). Among them hypocalcemia was significant in acute pancreatitis than acute recurrent and chronic pancreatitis. Previous study showed, in children, only a small percentage of patients were reported to have severe complication as opposed to adults. Fewer than 6% of children developed pancreatic necrosis<sup>10</sup>, Pseudocysts developed in 10-20% of cases<sup>19</sup>. Patients were managed with supportive therapy such as bowel rest when needed, proper hydration by intravenous fluid, injectable analgesics and antibiotic in case of suspected infection. Consultation with the hepatobiliary surgeon and done when needed. None of the patient showed adverse outcome during hospital course.

The mean duration of hospital stay was 9.8 days. But it was significantly prolong (p=0.018) in acute pancreatitis cases (13.0 days) than in ARP and CP. Musabbir et al.<sup>7</sup> found the mean duration of hospital stay was 7.9 days in their study. And other study showed that those who develop severe complications of acute pancreatitis have longer hospital stay<sup>24</sup>.

### Conclusion

In this study, low calcium level and high CRP level were important biochemical abnormalities found in acute pancreatitis than in acute recurrent and chronic pancreatitis. Among the imaging modalities, swollen pancreas was found significant in abdominal ultrasound in case of acute recurrent pancreatitis. In MRCP beaded and tortuous pancreatic ducts were found in case of chronic pancreatitis. So MRCP is a better imaging modality for diagnosis of chronic pancreatitis and identify the etiology when result of abdominal ultrasound is not clear.

### Funding: None

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