

Pancreatic Diseases in Children in a North Indian Referral Hospital

Srikant Das, N.K. Arora, D.K. Gupta*, A.K. Gupta#, Prashant Mathur and Anjali Ahuja

*From the Departments of Pediatrics, *Pediatric Surgery and #Radiodiagnosis, All India Institute of Medical Sciences, New Delhi 110 029, India.*

Correspondence to: Dr. N.K. Arora, Professor, 3063, Department of Pediatrics, All India Institute of Medical Sciences, New Delhi 110 029, India.

E-mail: narendrakumararora@hotmail.com

Manuscript received: January 24, 2002, Initial review completed: April 19, 2002;

Revision accepted: December 29, 2003.

This was a cross-sectional study to determine the profile of pancreatic disorders in 54 children (age <15 years) presenting to a tertiary care center in India. Acute pancreatitis was the most common pancreatic disorder (28/54, 52%). Twenty-three children (43%) were diagnosed to have either chronic calcific (n = 15, 28%) or chronic non-calcific (n = 8, 15%) pancreatitis. Specific etiologic factors could be identified in 64.3% (18/28) of acute pancreatitis and 43.5% (10/23) of chronic pancreatitis patients. At least some of the 13 children with idiopathic chronic pancreatitis had features suggestive of tropical pancreatitis.

Key words: Acute pancreatitis, Chronic pancreatitis.

There is a paucity of literature regarding the profile of pancreatic disorders in children(1-4). Buntain, *et al.*(1) after a review of pancreatitis in childhood over a 15 years period concluded that pancreatitis was not rare in childhood and had a significant over all mortality rate of 30% or greater as compared to 12% in adults(5). At least three other series between 1965 and 1992 reported a mortality rate ranging from 12 to 26% of pancreatitis in childhood(2-4). The divergence of opinion between authors regarding etiology, pathophysiology, definitions and classification of pancreatic disorders and non-uniformity of vocabulary makes it difficult to compare different studies(6-9).

Disease entities like tropical pancreatitis and malnutrition related diabetes mellitus are almost exclusively found in tropical countries, with probably the highest prevalence in India (6,7,10). From our country, only case reports of various pancreatic disorders in children are available(11-14). The present study was

conducted to determine the profile of pancreatic disorders in children presenting to our center, between 1994 and 2001.

Subjects and Methods

This study included children who were diagnosed to have pancreatic disorders at the Division of Pediatric Gastroenterology, Hepatology and Nutrition of AIIMS during the years 1994-2001.

Pancreatic disorders were suspected if the child had abdominal pain associated with raised serum lipase or amylase or/and suggestive ultrasound (USG)/CT scan abdomen/ERCP (endoscopic retrograde cholangio pancreatography) showing altered echogenicity, change in size, shape, duct caliber or calcification of pancreas. These patients were worked up further for assigning etiologic label according to a pre-defined protocol and classified as having acute pancreatitis, chronic pancreatitis, hereditary pancreatitis and congenital anomalies of the

pancreas. Medical / surgical conditions that were / could potentially be causing pancreatic pathology with temporal association were labeled as etiologic factors. Medical / Surgical condition(s) that were present in addition to etiologic factor(s) and/or those conditions which were unlikely to be cause of pancreatic pathology in the specific patient, were labelled as associated conditions.

Patient work up

Children with suspected pancreatic disorders were worked up according to a uniform protocol. The pre-tested form consisted of demographic features, and clinical (history and examination) details of patients. This included a two generation family history, history of trauma to abdomen, existence of other systemic disorders (like cystic fibrosis, celiac disease and others), exposure to drugs, toxins, recent infections (particularly clinical/laboratory evidence of salmonella typhi, mumps and hepatitis B) and metabolic disorders.

Following investigations were undertaken as and when required and feasible to establish presence of pancreatic disorder and its potential etiologies.

Blood: Serum amylase, C-reactive protein, lipid profile, serum calcium, renal and liver function tests, blood sugar and glucose tolerance test (GTT).

Radiologic: Plain X-ray abdomen, abdominal ultrasonography, contrasts enhanced CT-scan of abdomen and magnetic resonance cholangiopancreatography (MRCP).

Endoscopy: Upper gastrointestinal endoscopy and ERCP.

Other investigations: Appropriate laboratory tests to confirm specific etiologic factors were done according to the clinical indications. Facilities for serum lipase estimation were

available only during later part of the study and hence could be done in 15 patients (7 acute pancreatitis and 8 chronic pancreatitis). As per published evidences, we used a cut off value of upper limit of normal (>165 IU/L) to be suggestive of pancreatitis which is reported to have sensitivity and specificity in the range of 86.5% and 100%(15). Similarly, glucose tolerance test (12 chronic pancreatitis) and 24 hour fecal fat estimation (8 chronic pancreatitis) were systematically done during the last two years of the study only.

Sweat chloride >60mEq/L on two occasions was considered as diagnostic of cystic fibrosis. Alpha-1 antitrypsin (α_1 AT) deficiency was diagnosed on the basis of absence of α -globulin band on simple gel electrophoresis and serum α_1 AT levels below 60 mg/dL. Screening for α_1 AT deficiency was done among patients recruited after 1998, and phenotyping was not available.

Analysis

Stata-6.0 software (STATA Corpn, Texas, USA) was used for statistical analysis. Descriptive statistics were computed for baseline demographic, clinical and laboratory features according to etiology. Frequency tables were generated to reflect the etiology of pancreatic disorders in childhood.

Results

During the study period, 54 cases of pancreatic disorders presented to our center. Acute (28/54, 51.9%) and chronic (23/54, 42.5%) pancreatitis constituted most of the patients with pancreatic disorders. *De novo* presentation as pseudocyst was identified in a single case though pseudocyst was associated as a complicating feature in nearly 25% cases of chronic pancreatitis (6/23) and 41% (11/28) of acute pancreatitis. One girl had pancreatoblastoma while another boy presented with a pancreatic mass due to *Nocardia* infection.

Acute Pancreatitis

Etiology of 28 children with acute pancreatitis is summarized in *Table I*.

Ten children (35.7%) experienced more than one episode of acute pancreatitis over a period of time (0-18 months). Recurrent episodes of acute pancreatitis occurred up to 24 months of follow up in 10 patients. None of these children had manifest clinical or laboratory features of chronic pancreatitis. Three of these cases with recurrent acute pancreatitis were due to underlying α_1 -antitrypsin deficiency, hypertriglyceridemia, and hereditary pancreatitis.

Pulmonary tuberculosis(2), seizure disorder(2), acute leukemia(1), hypertension (1) and HBsAg carrier state without liver dysfunction(1) were the incidental conditions identified in 7 children (25%) that did not appear to have any direct contribution to the development of acute pancreatitis. The child

with acute leukemia developed acute pancreatitis after treatment for one month with steroids and L-asparaginase. No complications were observed in 61 % (17/28) patients. Pseudocyst was the commonest complication (11/28; 39%) of acute pancreatitis. Splenic vein thrombosis was observed in a child who also had pseudocyst formation.

All but one patient required hospitalization. Thirteen children required more than one hospitalization because of acute pancreatitis and/or its complications. Laprotomy was required in 9/28 (32.1 %) patients and in seven of them pancreatic pathology was documented. One child (3.6%) with acute pancreatitis died during the acute phase of illness.

Demographic and clinical profile of these cases is depicted in *Table II*.

The laboratory parameters for acute pancreatitis were fulfilled in most of the patients. Elevated serum amylase (>200 IU/L) and/or ultrasound evidence of pancreatitis was present in 21/22 (95%) cases. Abnormal CT scan and/or amylase >200 IU/L was documented in 19/21 (90%) patients.

Chronic Pancreatitis

Etiology of 23 children with chronic pancreatitis is shown in *Table III*. Both children with hereditary pancreatitis were born out of non-consanguineous marriages. Although no records were available, according to historical details the father and paternal uncle of the first child were also suffering from chronic pancreatitis and were on pancreatic supplements. The mother of second child had chronic pancreatitis and died due to illness. The child with α_1 -AT deficiency was product of a consanguineous marriage and did not have elevated hepatic

TABLE I—*Etiological Factors of Acute Pancreatitis in Children (N = 28)*

Etiology	n	%
Drugs*	4	14.3
Blunt trauma	4	14.3
Bile leak peritonitis / cholecystitis/ cholilithiasis	3	10.7
Tuberculosis	2	7.1
Acute viral hepatitis#	1	3.6
Mumps	1	3.6
Hypertriglyceridemia	1	3.6
α_1 antitrypsin deficiency	1	3.6
Hereditary pancreatitis	1	3.6
Unknown	10	35.7

* Prednisolone, Carbamazepine, Phenytoin, L-Asparaginase

Acute HAV Infection

TABLE II—Demographic and Clinical Profile of Acute Pancreatitis in Children.

Parameters	N*	n	%
Sex (Male)	28	16	57
Median age at onset (95% CI)	28	125 (84-153) months	
Age categories			
<2 years		1	3.6
2-5 years		4	14.3
5-10 years		8	28.6
> 10 years		15	53.6
Median duration of illness (95% CI)	28	0 (0-4) months	
Duration categories (months)			
<1		17	60.7
1-3		2	7.1
3-6		3	10.7
> 6		6	21.5
Abdominal pain	28	27	96.5
>Epigastric pain	27	16	57.2
>Radiating pain	27	8	28.6
Associated nausea/vomiting	27	23	82.0
Abdominal distension/lump	28	9	32.2
Fever	27	9	33.0
Jaundice	26	4	15.4
Failure to thrive	27	3	11.1
Hematemesis/melena	26	1	3.9
Ascites	26	2	7.7
Amylase (IU/L)			
<200	26	7	26.7
200-800	26	13	50.0
>800	26	6	23.1
Lipase (IU/L) > 165	7	5	71.4
Positive USG findings	24	20	83.3
Positive CT scan findings	22	16	72.7
Anemia (Hb \leq 10.9 g/dL)	25	10	40

*No. of patients in whom information was available.

transaminases. No liver biopsy was done in this child.

In 4 out of 23 patients (17.4%), there were associated conditions viz., tuberculosis,

seizure disorder and hepatitis B. However there was no evidence that these could be contributing to the development of chronic pancreatitis.

TABLE III—*Etiological Factors of Chronic Pancreatitis in Children (N = 23).*

Etiological factors	Chronic calcific pancreatitis (N = 15)		Chronic non-calcific pancreatitis (N = 8)	
	n	%	n	%
Trauma	2	13.3	0	0
Hereditary	2	13.3	0	0
Pancreas divisum	1	6.7	0	0
Annular pancreas	0	0	1	12.5
Tuberculosis	0	0	1	12.5
Cystic fibrosis	0	0	1	12.5
Cholelithiasis	1	6.7	0	0
Drugs*	0	0	1*	12.5
Unknown	9	60.0	4	50.0

Comparison between the categories of Chronic Calcific and Chronic Non-calcific Pancreatitis: Fischer's Exact Test = 0.134, * Valproate intake for more than 6 years.

Pseudocysts were identified in six children (25%), four of whom were having chronic non-calcific pancreatitis. Vascular complications *viz.*, mesenteric vein thrombosis(1), splenic vein thrombosis, splenic artery aneurysm(2) and gastroduodenal artery aneurysm(1) were observed in four children with chronic pancreatitis.

The clinical and demographic profile of calcific and non-calcific chronic pancreatitis was similar (*Table IV*). Weight for age z-scores of ≤ 2 were also comparable in the two groups. Steatorrhea (24 hour fecal fat >6g) was documented in one out of eight consecutive patients in whom the test was done. Similarly, abnormal GTT was present in 33.3% (4/12) patients.

Discussion

The profile of pancreatic disorders as

reported in this study was similar to that reported by Vane, *et al.*(16) and from Boston Children's Hospital (17). In both these studies, trauma, congenital malformations and pseudocyst were listed separate from pancreatitis as etiologic categories. We however included these as factors contributing to development of pancreatitis. In both these case series(16,17) tumors contributed to 10% of all pancreatic disorders. This was higher than that reported in the present study (3.8%). At our institution, there is a separate center for cancers and hence pancreatic tumors were likely to be under represented. Our findings of acute pancreatitis resulting from diverse etiology are similar to that reported earlier(2-4, 18-20). Two of our patients had generalized tuberculosis with lymph nodes around pancreatic head. One of them also had ascites which showed evidence of tuberculous antigen on PCR. During follow up, these patients recovered completely on anti-tuberculous therapy. Mortality due to acute pancreatitis in the present study was 3.6%-as compared to 0-26% reported earlier (1-4,18,19). Increased prevalence of pseudocyst in our series (41%) as compared to 16-22% reported by others (18-20) may be explained by delay in seeking care and or referral to a tertiary center of patients with severe disease or on development of complications.

Recurrent episodes of acute pancreatitis occurred in ten patients (35.7%). It is possible that on follow up some of these patients might develop overt features of chronic pancreatitis. Three of these cases were due to underlying alpha-1 antitrypsin deficiency, hypertriglyceridemia and hereditary pancreatitis, all of which have been reported to cause repeated episodes of acute pancreatitis(20). In remaining seven patients, no etiology could be determined.

In the present study, 65% (15/23) of

TABLE IV—*Demographic and Baseline Features of Children with Chronic Pancreatitis*

Parameters	Chronic calcific pancreatitis			Chronic non-calcific pancreatitis			*P value
	No.†	n	%	No.†	n	%	
Male	15	10	66.7	8	7	87.5	0.37
Median age at onset (95% CI)	15	15	72(44-118) months	8	8	82 (40-144) months	0.16-0.87
Age at onset							
<2 years	15	2	13.3	8	1	12.5	1.00
2-5 years	15	5	33.3	8	2	25.0	
5-10 years	15	5	33.3	8	3	37.5	
> 10 years	15	3	20.0	8	2	25.0	
Median duration of illness (months) before contact (95% CI)	15	15	48 (14-69) months	8	8	24 (11-121) months	0.49-0.63
Duration (months)							
<24	15	5	33.3	8	5	62.5	0.18
≥24	15	2	66.7	8	3	37.5	
Abdominal pain	15	15	100	8	8	100	1.00
Epigastric pain	15	11	73.3	8	5	62.5	0.64
Radiating pain	15	1	6.7	8	2	25	0.64
Colicky pain	15	6	40	8	4	50	0.84
Nausea/vomiting	15	11	73.3	8	6	75	1.00
Greasy stools	15	5	33.3	8	3	37.5	1.00
Failure to thrive	15	5	33.3	8	2	25	1.00
Fever	15	4	26.7	8	2	25	1.00
Jaundice	15	1	6.7	8	2	25	0.53
Abdominal distension	15	2	13.3	8	0	0	0.53
Ascites	15	1	6.7	8	0	0	1.00
Amylase (IU/L)							
<200	12	8	66.7	7	1	14.3	
200-800	12	3	25	7	5	71.4	0.06
>800	12	1	8.3	7	1	14.3	
Lipase (IU/L) > 165	5	5	100	3	2	66.7	0.38
USG positive	14	13	92.9	7	7	100	1.00
CT scan positive	10	10	100	6	4	66.7	0.13
MRCP positive	4	4	100	5	4	80	1.00
ERCP positive	5	5	100	1	1	100	1.00

† No. of patients in whom information available; *Fisher's Exact Test and Mann Whitney U Rank Sum Test used for comparison.

Key Messages

- Acute (52%) and chronic (43%) pancreatitis were the most common pancreatic disorders.
- Etiology could be determined in 64.3% of acute and 43.5% of chronic pancreatitis.
- There is a need for more detailed workup for metabolic and infectious etiologies to reduce the proportion of patients in indeterminate category.
- At least some patients of chronic pancreatitis had features suggestive of tropical pancreatitis.

chronic pancreatitis patients had pancreatic calcification and remaining 35% without any calcification in pancreas. Etiology in our series was comparable to that reported by Prasad, *et al.*(21). Two of our patients developed chronic pancreatitis due to prolonged pressure on pancreatic ducts/pancreas, caused by tuberculous lymph nodes and cholelithiasis in one case each.

In one of the early studies on chronic pancreatitis from India, Mehta, *et al.*(22) reported six cases of cystic fibrosis. All these patients had gastrointestinal symptoms. In the present study there was a single child with non-calcific chronic pancreatitis and high sweat chloride on two occasions (68 mEq/L and 75 mEq/L). This child had predominantly gastrointestinal symptoms and no respiratory involvement. Our study was undertaken in the gastroenterology division hence it was possible that cystic fibrosis patients with predominant pulmonary symptoms and pancreatic involvement but without gastrointestinal manifestations were missed in the current study.

Both acute and chronic pancreatitis appeared to be diseases of older children. In previous studies also most of the children were in the age ranges of 3-16 years (18-20) with mean age varying between 7.4 years to 10.2 years. The proportion of children below 5 years was small in most previous studies.

It was possible that 13 (56.5%) idiopathic

chronic pancreatitis patients including 9 with calcification might have included children with tropical pancreatitis. The etiology of tropical pancreatitis remains unknown(23) but in India and other geographic regions where the condition has been described it could be a distinct possibility if other known metabolic as well as acquired conditions causing chronic pancreatitis have been ruled out. Our youngest patient was an 11-month-old girl who did not have any identifiable congenital pancreatobiliary or metabolic abnormalities and was labeled as idiopathic chronic pancreatitis. More extensive work up for known infectious diseases and metabolic disorders is necessary to reduce the proportion of patients with indeterminate etiology.

Contributors: NKA designed and coordinated the study. NKA, SD, PM, AA and DKG were responsible for data collection. AKG provided the radiological support. Data were analyzed by NKA and SD. NKA, SD and PM were involved in the manuscript preparation and editing. NKA will be the guarantor.

Funding: Nil.

Competing interests: None stated.

REFERENCES

1. Buntain WL, Wood JB, Wooley MM. Pancreatitis in childhood. *J Pediatr Surg* 1978; 13: 143-149.
2. Jordan SC, Ament ME. Pancreatitis in children and adolescents. *J Pediatr* 1977; 91: 211-216.
3. Synn AY, Mulvihill SJ, Fomkalsrud EW. Surgical management of pancreatitis in childhood. *J Pediatr Surg* 1987; 22: 628-632.

BRIEF REPORTS

4. Weizman Z, Durie FR. Acute pancreatitis in childhood. *J Pediatr* 1988; 113: 24-29.
5. Paloyan E. The forms of pancreatitis. *Cuff Probl Surg* 1967; 6: 3-4.
6. Shaper AG. Aetiology of chronic fibrosis of pancreas with calcification seen in Uganda. *BMJ* 1964; 1: 1607-1609.
7. Vishwanathan M, Sampath KS, Subramanyam S, Krishnaswami CV. Etiopathologic and clinical angle of pancreatic diabetes from Madras. *J Assoc Physicians India* 1973; 21: 753-759.
8. Sarles H, Sarles JC, Camattee R, Muratore R, Gaini M, Guien C, *et al.* Observations of 205 confirmed cases of acute pancreatitis, recurring pancreatitis and chronic pancreatitis. *Gut* 1965; 6: 545-559.
9. Sarner M, Cotton PB. Classification of pancreatitis. *Gut* 1984; 25: 756-759.
10. Balaji LN, Tandon RK, Tandon BN, Banks FA. Prevalence and clinical features of chronic pancreatitis in Southern India. *Int J Pancreatol* 1994; 15: 29-34.
11. Choudhary VP, Srivastava RN, Ghai OP. Familial pancreatitis. *Indian Pediatr* 1971; 8: 466-468.
12. Raghuvver TS, Rama Rao, Yashwanth M. Tropical chronic calcific pancreatitis in children. *J Trop Pediatr* 1990; 36: 206-207.
13. Reddy CR, Sita Devi C, Anees AM. Cystic fibrosis of pancreas in India. *J Trop Med Hyg* 1970; 73: 59-62.
14. Dhar A, Goenka MK, Kochar R, Nagi B, Bhasin DK, Singh KJ. Pancreas divisum: Five years experience in a teaching hospital. *Indian J Gastroenterol* 1996; 15: 7-9.
15. Ventrucri M, Pezzilli A, Naldoni P. A rapid assay for serum immuno-reactive lipase as a screening test for acute pancreatitis. *Pancreas* 1986; 4: 320-323.
16. Vane DW, Grosfeld JL, West KW, Rescoria FJ. Pancreatic disorders in infancy and childhood: experience with 92 cases. *J Ped Surg* 1989; 24: 771- 776.
17. Welch KJ. The Pancreas. *In: Welch KJ, Randolph JG, Ravitch MM, O'Neill JA, Rowe MI (eds). Pediatric Surgery IV Edn. 1986; Vol 2 Year Book Med Pub, Chicago, USA. pp 1 086-1 091.*
18. Yeung C, Lee H, Huang F, Ho M, Kao H, Liang D, *et al.* Pancreatitis in children: experience in 43 cases. *Eur J Pediatr* 1996; 155: 458-463.
19. Haddock G, Coupar G, Youngson GG, MacKinlay GA, Raine PAM. Acute pancreatitis in children: A 15 year review. *J Pediatr Surg* 1994; 29: 719-722.
20. Uretsky G, Goldschmied M, James K. Childhood pancreatitis. *Am Fam Phys* 1999; 59: 2507-2512.
21. Prasad M, Wijllie R, Caulfield M, Steffen R, Kay M. Chronic pancreatitis in late childhood and adolescence. *Clinical Pediatr* 1994; 88-94.
22. Mehta S, Wadhwa UN, Mehta SK, Chuttanni PN. Fibrocystic disease of pancreas in India. *Indian Pediatr* 1968; 5:185-191.
23. Tandon RK. Tropical calcific pancreatitis. *J Gastroenterol Hepatol*1998; 13 (suppl): 284-288.
24. Riccardi VM, Shih VE, Holmes LB, Nardi GL. Hereditary pancreatitis: Non-specificity of aminoaciduria and diagnosis of occult disease. *Arch Intern Med* 1975; 135: 822-825.