RESEARCH PAPER

Clinical Profile and Outcome of Chronic Pancreatitis in Children

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Received: April 03, 2013; Initial review: May 28, 2013; Accepted: June 03, 2013.

Objective: To evaluate the etiology, presentation, complications and management of chronic pancreatitis in children.

Design: Retrospective chart review.

Setting: Gastroenterology department at Christian Medical College and Hospital, Vellore, India between January 2005 and December 2010.

Participants: 99 Children (<18 yrs) diagnosed with chronic pancreatitis based on clinical and imaging features.

Main outcome measures: Etiology, clinical presentation, complications and management of chronic pancreatitis in children.

Results: Of 3887 children who attended the Gastroenterology department, 99(2.5%) had chronic pancreatitis, of which 60 (60.6%) were males. In 95(95.9%) patients no definite cause was detected and they were labeled as Idiopathic chronic pancreatitis. All patients had abdominal pain, while 9(9.1%) had diabetes mellitus. Of the 22 children tested for stool fat, 10(45.5%) had steatorrhea. Pancreatic calcification was seen in 69 (69.7%). 68 (71.6%) patients with idiopathic chronic pancreatitis had calcification. Calcific idiopathic chronic pancreatitis was more frequent in males (67.6% *vs.* 48.1%, *P*=0.07), and was more commonly associated with diabetes mellitus (13.2% vs. none, *P*=0.047) and steatorrhea (61.5% *vs.* 16.7%, *P*=0.069). Pseudocyst (17.1%) and ascites (9.1%) were the most common complications. All children were treated with pancreatic enzyme supplements for pain relief. 57 patients were followed up. With enzyme supplementation, pain relief was present in 32 (56.1%) patients. Of those who did not improve, 10 underwent endotherapy and 15 underwent surgery. Follow up of 8 patients who underwent endotherapy, showed that 5 (62.5%) had relief. Follow up of 11 patients who underwent surgery showed that only 3 (27 %) had pain relief. There was no death.

Conclusions: Idiopathic chronic pancreatitis is the predominant form of chronic pancreatitis in children and adolescents. It can present with or without calcification. The calcific variety is an aggressive disease characterized by early morphological and functional damage to the pancreas.

Key words: *Chronic pancreatitis, Diabetes mellitus, Pancreatic calcification, Steatorrhea, Tropical chronic pancreatitis.*

Published online: May 5, 2013. PII: S097475591200371

Chronic pancreatitis is a progressive inflammatory disease leading to irreversible damage of the pancreas with resultant exocrine and endocrine insufficiency. Abdominal pain is one of the most distressing symptoms of chronic pancreatitis and leads to significant impairment of quality of life [1]. Steatorrhea and diabetes mellitus develop in the long term [2].

Though the disease is well characterized in adults, there is limited data in children and adolescents; and most of the reported series include small number of subjects [3-5]. We conducted this study to evaluate the etiology, clinical presentation, complications and management of chronic pancreatitis in children.

METHODS

Medical charts of patients attending the Gastroenterology department at the Christian Medical College and Hospital, Vellore, India between January 2005 to December 2010 were retrospectively reviewed. Children diagnosed with chronic pancreatitis, with age of onset of symptoms below 18 years were included.

Chronic pancreatitis was diagnosed on the basis of clinical features (abdominal pain, steatorrhea or diabetes mellitus) and the identification of pancreatic ductal and/or parenchymal changes (calcification, atrophy, ductal dilatation) on imaging [6]. Clinical information, complications and laboratory data were collected by a standardized review of medical charts and the data recorded in data forms. Nutritional status was assessed using WHO growth charts for height for age and body mass index (BMI) for age [7].

Pancreatic exocrine insufficiency was assessed by estimation of 72-hour stool fat using van de Kamer method [8]. Steatorrhea was diagnosed if the stool fat was >18 g in a 72-hour stool collection [9]. Blood sugar was checked in all the children. A fasting plasma glucose of ≥ 126 mg/dL, 2 hr post-prandial plasma glucose >200 mg/dL or HbA1C >6.5% was used to diagnose diabetes

mellitus [10]. Morphological changes in the pancreas were identified by imaging studies of abdomen *viz*. ultrasound abdomen, contrast enhanced computed tomography (CECT), MRI with maganetic resonance cholangio-pancreatography (MRCP), endoscopic retrograde cholangio-pancreatography (ERCP) and / or endoscopic ultrasound (EUS). Main pancreatic duct was considered to be dilated if the duct diameter was more than 3 mm in the head and 2 mm in the body or tail of the pancreas [11].

Etiology of chronic pancreatitis was defined as follows: *Metabolic chronic pancreatitis:* Presence of hypercalcemia (>10.5 mg/dL) or hypertriglyceridemia (> 1000 mg/dL); *Hereditary chronic pancreatitis*: ≥2 first degree relatives diagnosed to have chronic pancreatitis with an autosomal dominant pattern of inheritance; *Traumatic chronic pancreatitis*: History of significant abdominal trauma preceding the onset of symptoms; and *Idiopathic chronic pancreatitis*: No definite cause detected [12].

Statistical analysis: Baseline data were presented as mean (SD) for continuous variables and as proportions for categorical variables. For comparison between two groups, chi square test or Fisher's exact test was used for discrete variables and independent sample *t* test was used for continuous variables. Ethical clearance for the study was obtained from the Institutional review board of Christian Medical College, Vellore, India.

RESULTS

A total of 3887 children were seen in the Gastroenterology department between January 2005 and December 2010. Of these children, 99 (2.5%) were diagnosed to have chronic pancreatitis.

No definite etiology was detected in 95 (95.9%) patients and they were labeled as idiopathic chronic pancreatitis. History of blunt abdominal trauma prior to onset of symptoms was present in 4 (4.04%) patients and they were diagnosed as post traumatic chronic pancreatitis. Pancreas divisum was detected in 8 (8.42%) of these patients and family history of chronic pancreatitis was present in 3 patients.

The mean (SD) age at presentation and onset of desease was 15.2 (3.6) and 11 (4) years, respectively. Sixty (60.6%) were males. All patients had abdominal pain requiring an average of two hospitalizations for pain. Diabetes mellitus was detected in 9 (9.1%) children. The blood sugar control in these children was poor as evidenced by mean (SD) HbA1c of 9.5 (2.7). Seven children with diabetes mellitus were treated with insulin for blood sugar control, one child was started on oral hypoglycemic agent and another was on diet control alone.

Elevated stool fat was detected in 10 (45.5%) of 22 children evaluated for the same. Two of these children had symptomatic steatorrhea while 8 had subclinical steatorrhea. Height and weight were recorded in 32 children; height for age was <3rd percentile in 9 (28.1%) and BMI for age was <3rd percentile in 16 (50%) children. Pancreatic morphological abnormalities as identified by imaging studies is shown in ***Table* I**. Dilatation of the main pancreatic duct was seen in 88 (88.9%), pancreatic atrophy in 73 (73.7%) and pancreatic calcification in 69 (69.7%) patients. Intraductal calcification was seen in 16 (23.2%) patients, isolated parenchymal calcification in 30 (43.5%) patients and combined ductal and parenchymal calcification was seen in 23 (33.3%) patients. No pancreatic mass was seen in any patient.

Complications were noted in 30 (30.3%) children. Five children had more than one complication. Pseudocyst 17(17.1%) and ascites 9(9.1%) were the most common complications. In fifteen children, the pseudocyst was managed conservatively with nasojejunal feeds and pancreatic enzyme supplementation. In two children, pseudocysts were drained at surgery. Ascitic fluid examination was done in five children. All had elevated ascitic fluid amylase. Splenic vein thrombosis was detected in 4 (4.04%) cases. Three children had gastrointestinal bleeding in the form of hematemesis and / or melena. In one patient fundal varix was identified as the cause of bleeding and cyanoacrylate glue injection was performed. In another child a pseudoaneurysm involving the splenic artery measuring approximately 5.7 × 5 cm was detected using CT angiogram, and treated by coil embolization. In the third child no definite cause was identified. None of the children had biliary obstruction or fistula formations. Malignancy was not seen in any patient.

TABLE I MORPHOLOGICAL CHANGES OF THE PANCREAS IDENTIFIED BY IMAGING

Morphological Changes	*n (%)*
Pancreatic calcification, duct dilatation and parenchymal atrophy	43 (43.4%)
Pancreatic calcification and duct dilatation	17 (17.2%)
Duct dilatation and parenchymal atrophy	24 (24.2%)
Pancreatic calcification and parenchymal atrophy	6 (6.1%)
Pancreatic calcification	3 (3.0%)
Duct dilatation	6 (6.1%)

Amongst the children with idiopathic chronic pancreatitis, two morphological types were identified, one group with calcification (Calcific idiopathic chronic pancreatitis -CICP) and the other without calcification (Non-Calcific idiopathic chronic pancreatitis-NCICP). Comparison of the clinical profile of the two groups is shown in ***Table* II**.

All patients with abdominal pain were given a trial of enteric coated pancreatic enzyme supplements along with proton pump inhibitors or H_2 receptor antagonist. Follow-up data on 57 patients (median 18 months (2-72 months)) showed that 32 (56.1%) patients had subjective relief of abdominal pain with pancreatic enzymes. Endotherapy or surgery was performed in patients who did not have pain relief with enzyme supplements. Ten patients underwent endotherapy (Extracorporeal shock wave lithotripsy (ESWL) and stone clearance: 2, ERCP with sphincterotomy and stenting: 8). Follow-up data available for 8 patients, (median follow up 36 months (6-102 months) showed that 5 (62.5%) patients (1–ESWL and stone clearance; and 4 – ERCP with sphincterotomy and stenting) had relief of pain following endotherapy. Fifteen patients underwent surgery for management of abdominal pain, (lateral pancreatic jejunostomy: 10, Frey's procedure: 5). Follow up available for 11 patients (median 24 months (12 -60), showed that only 3 (27 %) had pain relief post surgery.

DISCUSSION

The predominant cause of chronic pancreatitis in our study was Idiopathic chronic pancreatitis. Three children with family history of chronic pancreatitis and 8 children with pancreas divisum were included in the idiopathic chronic pancreatitis group as the 3 children did not have a dominant inheritance pattern and association of pancreas divisum with chronic pancreatitis is suspect [13].

TABLE II CLINICAL PROFILE OF CALCIFIC AND NON CALCIFIC IDIOPATHIC CHRONIC PANCREATITIS

Clinical Chracteristics	*Calcific Idiopathic Chronic Pancreatitis (n =68)*	*Non -Calcific Idiopathic Chronic Pancreatitis (n =27)*	*P Value*
Age of onset	11 ± 4.6	11 ± 4.03	1.00
Sex (M:F)	46:22	13:14	0.07
Pain	68 (100%)	27 (100%)	-
Diabetes mellitus	9 (13.23%)	0	0.047
Steatorrhea (n = 19)	8/13 (61.5%)	1/6 (16.7%)	0.069

Complications were seen in one-third cases, the most common being pseudocyst and ascites. Pain was the presenting symptom in all patients.

Studies from China have also reported Idiopathic chronic pancreatitis as the predominant cause of chronic pancreatitis among children [5]. Data on prevalence of exocrine and endocrine insufficiency amongst children with chronic pancreatitis are limited [14]. The prevalence of symptomatic steatorrhea was lower (2.02% *vs.* 9.5%) and diabetes mellitus higher (9.1% *vs.* 0%) in the present study as compared to the study by Wang, *et al*. [5]. The study from China found that BMI of children with chronic pancreatitis was similar to that of healthy children and adolescents [5]. In contrast, we identified nutritional impairment in a significant proportion of Indian children with chronic pancreatitis. Possible reasons could be high prevalence of sub-clinical steatorrhea and diabetes mellitus as well as fat restricted diet [15]. The rate of complications in the present study was similar to that reported in a large prospective nationwide study of adult chronic pancreatitis from India [16].

An interesting observation was failure of surgery to provide sustained relief of pain as opposed to studies on adults with chronic pancreatitis where surgery was effective for short and long term relief of pain [17]. The reason for discrepancy in pain relief with surgery and endotherapy is not clear. A possible reason could be that patients selected for surgery had more aggressive disease where relief of duct obstruction alone did not provide adequate relief of pain.

Two subsets of idiopathic chronic pancreatitis were identified a large group with pancreatic calcification (CICP) and a smaller group without pancreatic calcification (NCICP). Patients with Calcific idiopathic chronic pancreatitis had higher prevalence of diabetes mellitus. Calcific idiopathic chronic pancreatitis is phenotypically similar to 'Tropical Calcific pancreatitis' and differs from 'early onset (juvenile) idiopathic chronic pancreatitis' of the West as it is characterized by male predominance, early calcification and a high frequency of endocrine insufficiency. Non-calcific idiopathic chronic pancreatitis on the other hand has an equal sex distribution, no calcification and low incidence of endocrine insufficiency. This group needs to be followed up for a longer period of time to ascertain whether it is phenotypically similar to 'Early onset (juvenile) idiopathic chronic 'pancreatitis' of the West.

The present study has several limitations: a retrospective study in which assessment of pain was subjective and evaluation and management were not protocol based; data on growth parameters and

steatorrhoea were not available for all patients; and genetic mutation analysis was not performed for etiology evaluation.

Contributors: AC and SDC: conceived and designed the study, and along with BSR and AJJ: revised the manuscript for important intellectual content; AC: will act as the guarantor of the article; SDC, AKK and JA: collected the data and drafted the paper; EGS and AKD: analyzed the data and helped in manuscript writing.
Funding: None; *Competing interests*: None stated.

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