

ACUTE PANCREATITIS IN CHILDREN: EPIDEMIOLOGY AND ETIOLOGY

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Abstract: All cases of pancreatitis examined between 1980 and 2009 were reviewed to determine the etiologic factors and the epidemiology of this disease. Out of 70 patients (49 boys, 21 girls; average age 9 years old; range 2 month-17 years), 52,8% had traumatic **acute pancreatitis** (AP), 11,4% had infectious causes of AP, 7,1% had biliary AP, in 5,7% of the cases AP was associated with systemic illness, 4,2% had drug-associated AP and 1,4 % metabolic, malformative and postoperative problems. However in 14,3% of the patients there was no cause identified after the initial diagnostic evaluation: idiopathic AP. A better management of diagnostic tools by their proper use in proper circumstances will not only improve the well-being of the patient but also reduce the number of idiopathic AP to minimum.

INTRODUCTION

Acute pancreatitis (AP) is the most frequent pancreatic disease, and it is observed in every part of the world. AP is an uncommon condition in children, with published series reporting an incidence of 2-9 cases per year per institution (1). The small number of patients has made it difficult to evaluate outcomes, genetic factors, treatments, prognostic scores, severity and epidemiologic factors in childhood in a prospective fashion.

In recent years, many advances have been made in the diagnosis and management of this disease and this has led to a significant decrease in both morbidity and mortality: however we do not have complete information about its etiology and pathogenesis. Regarding etiology, because most studies have been conducted in single centers, the relative frequency of the various etiologic factors over extensive geographic areas is different. Moreover, the relation between etiology and mortality rates is not well established (2).

Although clinical awareness of AP in children has improved immensely over recent years, AP remains a rare disease in children. Furthermore, there is a significant difference in cause between Western countries and Asian countries. Tonomasa et al. reviewed the cause of AP in Japan. An abnormal biliary tract (47%) was the common cause of AP in Japanese children, and the other causes were infections (12%), trauma (9%) and systemic disease (2%). Mader and McHugh reviewed pediatric cases of AP in Western countries and reported greater diversity with no particular predominant category. Five different groups, trauma (22%), medications (13%), infections (11%), structural anomalies (15%) and systemic illness (13%) share distribution fairly even (2).

MATERIALS AND METHODS

In the present work we intended to make a retrospective study over the frequency, distribution on age groups and gender and on the etiology of the AP cases that were diagnosed in “Sfanta Maria” Children Hospital Iasi, Clinic of Surgery and Pediatric Orthopedics.

The specialists in this field accept the fact that AP is difficult to diagnose in children; most of the times this diagnostic is ignored, so AP is much more frequent in children than we thought.

AP was defined as a serum amylase level >3x normal or the serum lipase level >3x normal, with clinical signs and symptoms consistent with the diagnosis. Although serum lipase testing is reportedly as sensitive as and more specific than serum amylase for pancreatitis, routine use of serum lipase testing has become available only in the past 3 years.

RESULTS AND DISCUSSIONS

Frequency, distribution on age groups and sex (Fig. 1)

The cases were diagnosed on a period of time of 29 years, starting with 1980 until 2009, with a total number of 70 cases:

1986 (1 case), 1989-(5 cases), 1990-(1 case), 1991-(1 case), 1994 -(2 cases), 1996-(1 case), 1997-(1 case), 1999-(2 cases), 2000-(3 cases), 2001-(1 case), 2002-(3 cases), 2003-(3 cases), 2004-(1 case), 2005-(14 cases), 2006- (13 cases), 2007- (5 cases), 2008-(6 cases), 2009- (7 cases).

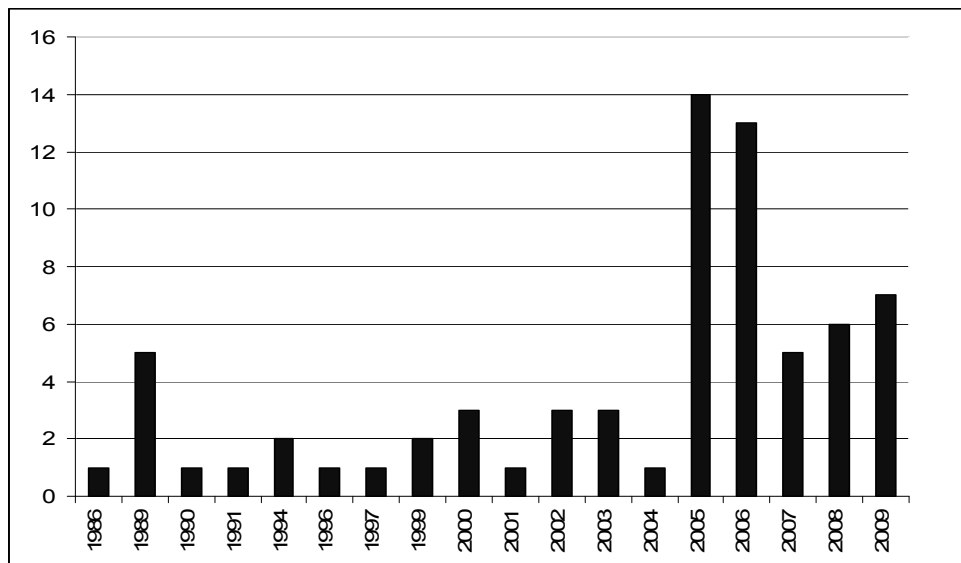


Fig. 1. Distribution of cases on years

Although the study covered a large period of time (29 years) only 6 cases were diagnosed before 1990. In the past 15 years the incidence of AP seems to have increased. The cases were evenly distributed throughout the year. However, it has been suggested that this increase may be explained by improved diagnostic tests and imaging procedures (ultrasound, computed tomographic scan or magnetic resonance imaging of the pancreas and endoscopic retrograde cholangiopancreatography), changes in amylase or lipase testing or improved physician awareness of AP (6). On the other hand, AP etiology in children, being predominantly traumatic, once the number of bicycle road accidents increased, the incidence of posttraumatic AP increased, too.

This thing coincides with the data from the specialized literature. One retrospective study made by DeBanto et al.(4) that included the cases hospitalized in the United States, in 6 centres, between 1976-1997, came to the conclusion that 86% of the children were diagnosed between 1988 and 1997. It's the same with a Swiss study (5) that analyzed 21 cases between 1979 and 1993 and concluded that more than 50% of the cases were diagnosed after 1989.(Fig. 2)

We have diagnosed 45 cases in the last 5 years since we began our study and that represents 63% of the total cases. This phenomenon is not an increase in incidence, but it must be considered that we are getting close to the real epidemiology of acute pancreatitis in children.

Distribution on gender

From a total of 70 cases considered, 49 cases (70%) were boys and 21 (30%) were girls, the bigger ratio of the male gender being probably correlated with the major AP etiology in children, especially the traumatic one: traffic accidents, accidents during play time, sleigh accidents, bike accidents. However, it is unclear whether boys have a higher risk of developing severe AP in comparison with girls. There are speculations that estrogens may be protective with the pancreas, causing a diminished severity of pancreatitis (7).(Fig. 3)

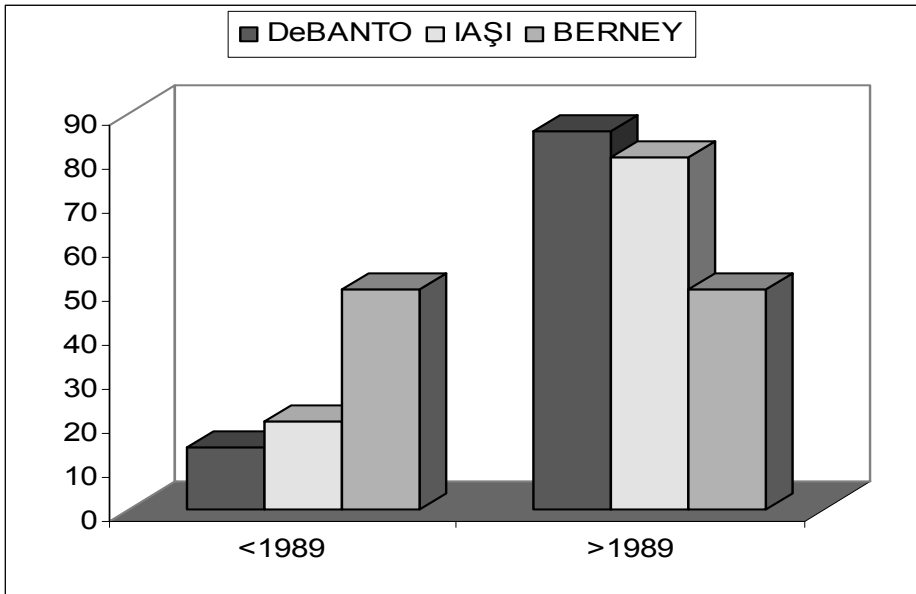


Fig. 2 Comparative incidence of acute pancreatitis

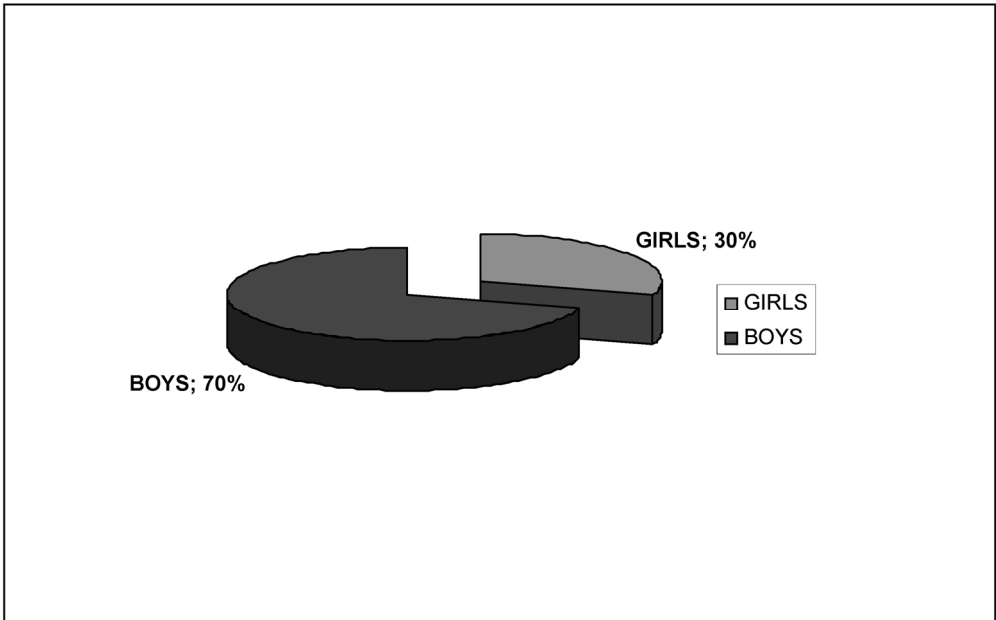


Fig. 3 Patients' distribution on gender

Distribution on age groups and environment

The age of patients range from 2 month to 17 years. There was only one case of AP under 1 year. The average was 9 years.

53% of the patients came from the urban area and 47 % from the rural area. (Fig. 4)

Most patients had a good evolution, without sequelae after leaving the hospital. Only one patient died, the main cause of his death being AP. There have been other deceased patients, but they died because of polytraumatism or severe systemic conditions, so the main cause of death was not AP.

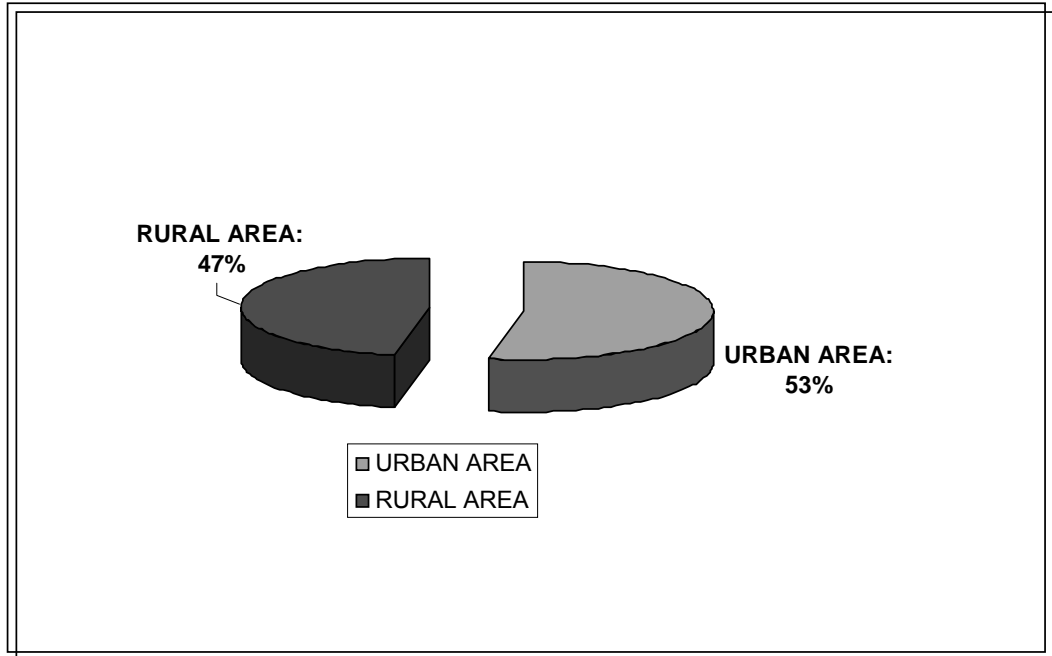


Fig. 4 The patients' environment

Etiology (Fig. 5)

Traumatic – 37 cases: 52,8%; Idiopathic- 10 cases: 14,3%; Biliary-5 cases: 7,1%; Drug related -3 cases: 4,2%; Infectious-8 cases: 11,4%; Metabolic -1 case: 1,4%; Malformations -1 case: 1,4%; Systemic conditions -4 cases: 5,7%; Postoperative - 1 case: 1,4%.

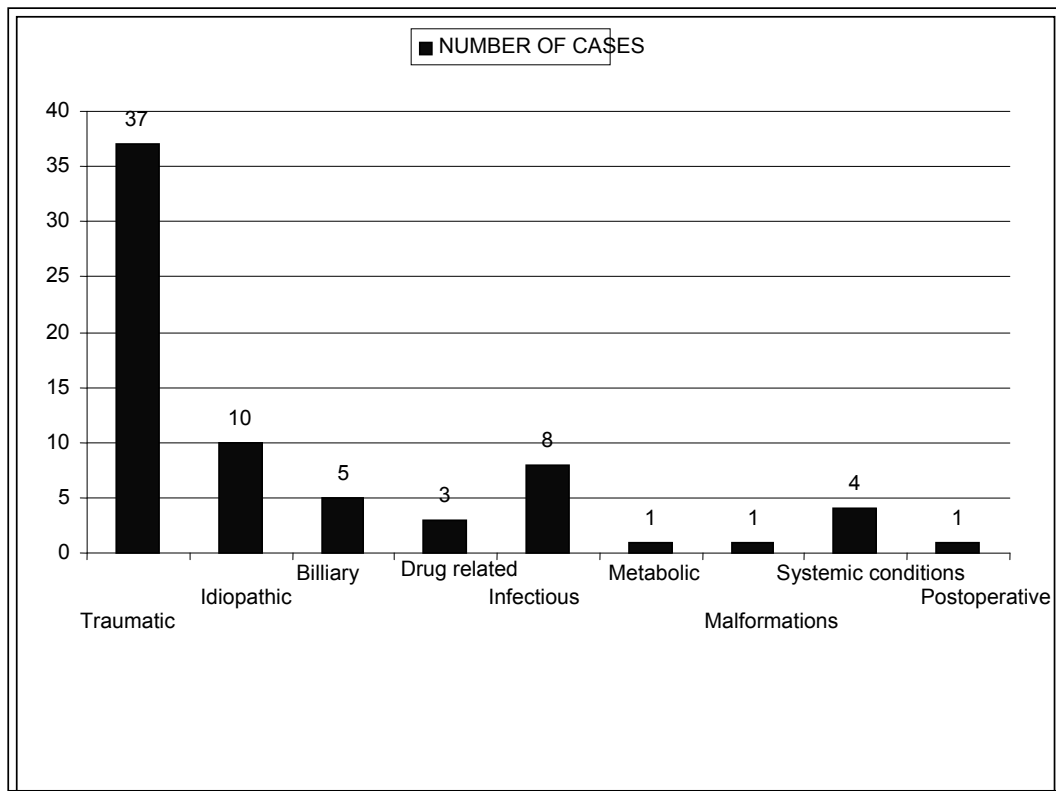


Fig. 5 Etiology

In the case of children, unlike the adult population, acute pancreatitis can very rarely be caused by a biliary condition or alcoholism (no case recorded by our study). But when it comes to pancreatitis etiology in children trauma is on the first place (61%), the second place being credited to idiopathic pancreatitis. Infectious etiology comes on the third place.

Trauma is the leading cause of death in children between the age of 1 and 18, injuries to the abdomen can occur in up to 8% of injured children, and the pancreatic lesions appear in 4% of the traumatic lesions of the abdomen. The pancreas is seldom affected because of its deep retroperitoneal anatomical position (8-9).

Penetrant injuries (shot wounds, stabbing) are responsible for 70% of the pancreatic trauma in adults, but they are much more rare in children; the statistics show no recorded case of a penetrant injury in the pancreas.

Children are at increased risk of getting injuries to intra-abdominal organs after blunt abdominal trauma, because: compared with the adult patient, the child's intra-abdominal organs are proportionally larger, are in relatively close proximity to each other, the small size of a child results in a greater degree of force per body surface area, which can lead to significant injury to multiple organs, there is little fat or connective tissue to cushion the organs and the abdominal wall is less muscular, providing little protection to the viscera (8).

The mechanisms that cause posttraumatic AP in children in our study were: road accidents - 11 cases -29,7%; bicycle accidents – 6 cases -16,2%; downfall – 8

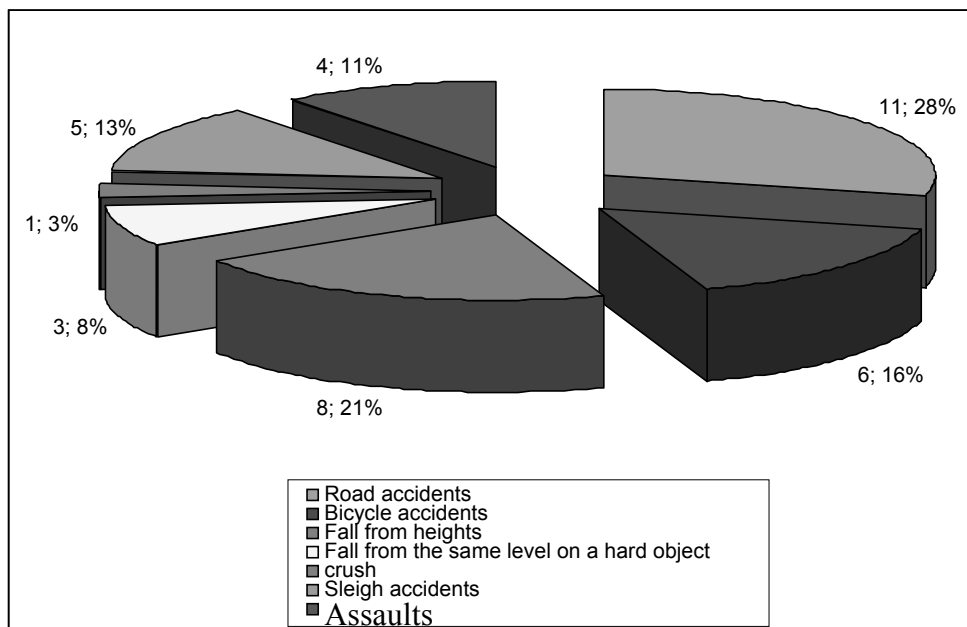


Fig. 6 Traumatic etiology – causing mechanisms

cases – 21,6%; stumbling and fall on a hard object- 3 cases - 8,1%; crushing -1 case -2,7%; sleigh accidents - 5 cases – 13,5%; assault - 4 cases - 10,8%, and a Silverman battered child syndrome. **(Fig. 6)**

One of the classic that cause the pancreatic trauma followed by AP is getting hit by the bicycle handlebars, when the child fall over the bicycle and hits himself with the handle bars in the epigastrium(10).

Pseudocyst formation is the main complication of nonoperative management of pancreatic injuries.

In the etiology of infectious AP in children viruses, bacteria and parasites were involved, too. Our statistics recorded 4 cases of viral AP and 4 probably bacterial AP cases.

In the etiology of viral AP, 3 cases involved the mumps virus (we did not detect antibodies, but the epidemiologic context is suggestive) and in one case AP appeared during a severe meningoencephalitis of viral etiology(10).

HIV infection that is often mentioned in literature (studies show that AP appears in HIV infected people with a frequency that is 35-800 times bigger than its incidence in uninfected people) was not incriminated for any of our cases. The reason is the precaution taken by the medical staff when it comes to these patients, and in most HIV infection cases amylase dosage is not considered a priority (11).

The mechanism by which viruses precipitate AP is unknown and might be multifactor. Apart from the virus per se, pancreatitis was supposed to be a complication of either acute liver failure, its treatment by drugs such as corticosteroids or intra- pancreatic hemorrhage (13).

The recorded statistics showed 4 cases of AP where the etiologic agent involved could be a bacterial agent: a case of AP appeared within a generalized peritonitis after acute appendicitis,

another case of AP was seen following an enterocolitis with toxic-septic shock and 2 cases of pneumonia complicated with multiple organ failure. The pathogenic mechanisms involved can be the ascendant infections in the small intestine, the biliary tree or the hematogenic or lymphatic infection (14).

No pancreatic malformation could be evidenced in the series we studied, although *pancreas divisum* has an incidence of almost 10% of the population and it may be one of the causes of idiopathic recurrent AP.

Only one case of AP presented a multicystic disease that affected the pancreas and the left kidney.

Biliary etiology was seldom described for children, although it is one of the most frequent causes in adults. It includes congenital anomalies (the choledochal cyst, pancreatic-biliary maljunction and Oddi sphincter dysfunction) and biliary lithiasis (15).

In the study we made we found 5 cases of biliary AP: 3 by means of biliary lithiasis, one of them associated with Minkowski-Chauffard anemia and 2 cases of choledochal congenital cyst.

There are 525 drug related AP cases in children that are reported in literature, the most frequent involvement being: valproic acid, cortisone (16).

We identified 3 cases of drug related AP; in 2 of them the valproic acid was involved and in one case the hydrazide.

The metabolic anomalies are rare conditions: they either affect only the pancreas or they are a part of a multiorganic process. They can increase the risk of an AP or pancreatic diabetes incidence (17).

During our study we also identified a case of AP associates with type IV familial hyperlipemia. It is considered to be one of the most frequent inherited causes of recurrent AP.

Postoperative pancreatitis is very often associated with the procedures that imply pancreas and/or periampular area manipulation and the decrease of the intraoperative vascular perfusion. The real incidence of postoperative AP is hard to establish, because the postoperative hyperamylasemia is frequent without being accompanied by clinical signs of AP.

During our study there was only one case of diagnosed postoperative AP, after an intervention of esophagoplasty with the colon.

From time to time we diagnosed a case of AP associated with:

- chronic renal failure during the programme of hemodialysis: kidney failure means supplementary risk factors for AP (uremic toxins, secondary hyperparathyroidism, hypertriglyceridemia, drug toxicity);
- acute lymphoblastic leukemia
- Reye syndrome
- Henoch - Schönlein nephrite

After routine investigations, including a thorough history, routine laboratory study and noninvasive imaging with transcutaneous ultrasonogram, in our study 14,3% of cases (10 patients) have no readily identifiable cause and are called idiopathic.

CONCLUSIONS

AP is an acute inflammatory condition which is fatal in 10 -15 % of cases.

The number of admissions for AP has increased steadily over the last years. Despite these increases, pancreatic disease remains relatively uncommon. However, the hospital management of patients with AP demand o disproportionate amount of time and resourses compared to most other conditions.

Clinically, the cause of AP may be discernable from the history and few standard investigations, less obvious and requiring more detailed studies, or obscure and even speculative.

In children trauma and infectious diseases were the main etiologic factors.

Modern medicine has made notable advances in uncovering various causes of AP and several new diagnostic tools that allow clinicians to approach the patient less invasively and without sacrificing the diagnostic yield have been introduced lately. So clinicians will be able to find the cause more accurately and earlier.

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