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RESEARCH ARTICLE

ACUTE PANCREATITIS IN CHILDREN; INCIDENCE AND COMPLICATIONS; SYSTEMATIC REVIEW

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ABSTRACT

Acute pancreatitis in children is a costly and increasingly recognized disease. As in grownups, the occurrence of intense pancreatitis in children likewise appears to be growing. Several studies have actually documented an increase throughout the past 10 to 15 years. The aim of this systematic review study was to review complications and incidence of acute pancreatitis in children, also we aimed to discuss the etiology regarding AP all these are based on evidence of human population studies from the pediatrics literature. We performed an electronic search of MEDLINE, EMBASE, and SciELO databases. These databases were searched for eligible studies discussing the complications, etiology and epidemiology of acute pancreatitis in children population. Our search had no limit period of studies publication, therefore, we searched through December 2016 Relevant references and historical quotes, as well as extremely important studies within the context of the review were analyzed in the same way, regardless of the publication dates. The incidence of intense pancreatitis in children has actually been increasing for the past 2 years, most likely as a result of multifactorial causes. AP is a disease of great significance in children, due to its tough medical diagnosis and severity of symptoms and associated complications; besides, it has a significantly higher occurrence because of a growing suspicion and better knowledge of its clinical qualities. The main causes of AP in children are biliary disease and medication, however as much as 1/3 of patients might not have a defined etiology at diagnosis. Issues of severe pancreatitis in children are sterilized and infected collections, fistulas, and vascular complications.

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INTRODUCTION

Acute Pancreatitis (AP) is the most typical pathologic entity affecting the pancreas among children (Koizumi *et al*., 2006). According to the INSPPIRE (International Study Group of Pediatric Pancreatitis: In Search for a Cure) Group, intense pancreatitis is defined as reversible inflammation of the pancreatic parenchyma when 2 of the 3 following requirements exist: abdominal pain suitable with severe pancreatitis, serum amylase or lipase worth ≥ 3 times the upper limit of normal, and imaging findings constant with acute pancreatitis (Koizumi *et al*., 2006; Morinville *et al*., 2012). Acute pancreatitis in children is a costly and increasingly recognized disease. As in grownups, the occurrence of intense pancreatitis in children likewise appears to be growing. Several studies have actually documented an increase throughout the past 10 to 15 years. Lopez (2002) first reported an increase in admissions for severe pancreatitis at the Children's Hospital of Dallas from 5 to 113 patients between 1993 and 1998. This was followed by Werlin *et al*. (2003), who showed a 64% boost from 1996 to 2000. Similar studies from Mexico, Australia, New Haven, and Pittsburgh have actually corroborated this pattern (Morinville *et al*., 2010; Park *et al*., 2009; Sanchez-Ramirez *et al*., 2007; Nydegger *et al*., 2007). Pediatricians have actually applied requirements for the diagnosis of pancreatitis in grownups to children. Adults normally present with queasiness, vomiting, and stomach pain. Classically, pain is localized to the epigastrium but can become scattered as well as turn into rebound inflammation. Other functions consist of fever, jaundice, and ileus. The most frequently utilized biochemical requirement for acute pancreatitis is a ≥ 3-fold elevation in the serum of the pancreatic secretory enzymes amylase and lipase (Nydegger *et al*., 2007; Bai *et al*., 2011). By radiography, cross-sectional imaging by computed tomography (CT) scan or magnetic resonance imaging or ultrasound of the pancreas might reveal edema with fluid collection, peripancreatic fat stranding, or necrosis (Bai *et al*., 2011). Alcohol and gallstones

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are the etiology of severe pancreatitis in many adults, and although some distinctions exist based upon sex and ethnic background, these two etiologies account for more than 60% of cases of intense pancreatitis in grownups (Banks, 2002; Yadav and Lowenfels, 2006). The etiology in children is frequently drugs, infections, injury, and anatomic anomalies such as choledochal cysts and unusual union of the pancreatobiliary junction (Table 1) (Benifla and Weizman, 2003; Chen *et al*., 2006; DeBanto *et al*., 2002; Nydegger *et al*., 2006).

Table 1. Etiology of childhood acute pancreatitis (Benifla and Weizman, 2003; Chen *et al*., 2006; DeBanto *et al*., 2002; Nydegger *et al*., 2006)

Congenital anomalies, periampullary obstruction:
Choledochal cyst, abnormal union of the pancreaticobiliary junction, gallstone, cholecystitis, pancreatic divisum, tumor, ascaris aberrant
Infectious: Mumps, measles, coxsackie, echo, lota, influenza, epstein-barr virus, Mycoplasma, salmonella, gram-negative bacteria
Drugs: L-asparaginase, steroid, valproic acid, azathioprine, Mercaptopurine, mesalazine, Cytarabine, Salicylic acid, indomethacin, tetracycline, chlorothiazide, isoniazid, anticoagulant drug, borate, alcohol
Trauma: Blunt injury, child abuse, ERCR, After surgery
Systemic disease: Reye syndrom, systemic lupus erythematosus, polyarteritisnodosa, Juvenile rheumatoid arthritis, sepsis, multiple organ failure, Organ transplantation, hemolytic-uremic syndrome, henoch-schoenlein purpura, kawasaki disease, inflammatory bowel disease, chronic intestinal pseudo-obstruction, gastric ulcer, anorexia nervosa, food allergy, cystic fibrosis
Metabolic: Hyperlipoproteinemia (I, IV, V), hypercalcemia, diabetes, α1 antitrypsin deficiency
Nutrition: Malnutrition, high-calorie infusion, vitamin A and D deficiency
Others: Familial, idiopathic

ERCP: Endoscopic retrograde cholangiopancreatography.

The aim of this systematic review study was to review complications and incidence of acute pancreatitis in children, also we aimed to discuss the etiology regarding AP all these are based on evidence of human population studies from the pediatrics literature.

MATERIALS AND METHODS

Study design

We conducted a systematic review study on childhood acute pancreatitis, and this review performed was according to the systematic reviews guidelines.

Search Strategies

We performed an electronic search of MEDLINE, EMBASE, and SciELO databases. These databases were searched for eligible studies discussing the complications, etiology and epidemiology of acute pancreatitis in children population. Our search had no limit period of studies publication, therefore, we searched through December 2016 Relevant references and historical quotes, as well as extremely important studies within the context of the review were analyzed in the same way, regardless of the publication dates. The review included prospective and retrospective cohort studies, systematic and nonsystematic reviews and clinical trials, containing a description of clinical aspects of AP in patients with up to 18 years old completed; we excluded case reports in our review. We restricted our search for only English language published articles and only to human subject trails, thus any animal trail was excluded in our study.

RESULTS AND DISCUSSION

Epidemiologic aspects

The more comprehensive understanding of the clinical aspects and the growing level of suspicion of AP cases (resulting in growing requests for amylase and lipase biochemical tests), in addition to the progressive increase in making use of drugs that might induce AP as a negative effect, have actually caused a progressive boost in the number of medical diagnosis of the disease over the last few years (Park *et al*., 2009). Another possible description for the growing incidence of AP is the boost in cases of children with systemic diseases that affect the pancreas secondarily. It is claimed that, due to this fact, the referral of patients to tertiary and school medical facilities, where the majority of the scientific research studies are carried out, adds to a greater identification of the cases of AP (Morinville *et al*., 2010). Fagenholz *et al*. (2007) studied retrospectively the medical records of the disease in the United States and discovered that, in the basic population, the variety of AP cases has doubled from 1998 to 2002, from 101,000 cases to 202,000 brand-new cases every year in the country, according to records of the nationwide medical facility discharge survey. Between 1988 and 2003, 645 cases were diagnosed in adolescents and children, with an occurrence of 0.1 new cases per 1,000 occupants. The authors do not make considerations relating to the findings in the pediatric population and point out that the study was limited to a research study based upon diagnosis through the code of International Classification of Diseases (ICD), with no requirements to define cases of pancreatitis. Nydegger *et al*. (2007) assessed, also retrospectively, the medical diagnosis of AP in children at an Australian medical facility from 1993 to 2002. During this duration, 279 cases of the disease were detected, with mean age of 10 years, and 74.9% of cases had actually an associated etiology (mainly trauma, metabolic and systemic drugs and diseases). The authors compared the incidence rate in the first five years of the studied period with the last 5 years, and discovered an increase of approximately 7 new cases each year from 1998 to 2002 when compared to the period from 1993 to 1997. Another pertinent epidemiological study examined the incidence of AP at the Children's Hospital of Pittsburgh, through a retrospective study of Morinville *et al*. (2010) Between 1993 and 2004, 1,021 patients were released with a medical diagnosis of AP, with 731 brand-new cases, with a boost in new cases per year from 28 in 1993 to 141 in 2004. The occurrence computed in this work has increased over the same duration, from 2.4 to 13.2 new cases per 100,000 children (Morinville *et al*., 2010).

Complications and prognosis of acute pancreatitis in children

The issues observed in children with AP can be immediate or late. Immediate issues may consist of hypovolemic and septic shock connected with dysfunction of multiple organs and systems. Renal dysfunction and cavity effusions, such as ascites and pleural effusion, as well as acute breathing distress syndrome, might also complicate the patient's condition (MekitarianFilho *et al*., 2012; Pastor *et al*., 2003). The most typical late issues include pancreatic necrosis and formation of pseudocysts. Pseudocysts, when badly symptomatic and without any proof of issues (such as infection and bleeding), might be handled without surgical intervention. Death of children with AP might reach 11%, and greater rates are

Table 2. Major identified studies of AP in children in the last 4 decades

Authors	Age range, y	Location	Patients, n	Most common etiologies			Mortality, %	Recurrence, %
				1st	2nd	3rd		
Park *et al*. (2005)	0–20	USA	215	Biliary	Medication	Idiopathic	1.9	Overall, 15.3 (infants, 7.1)
Kandula and Lowe (2008)	<3	USA	87	Systemic	Biliary	Infectious	8	10
Nydegger *et al*. (2007)	0.2–15.9	Australia	279	Trauma	Idiopathic	Systemic	11.1	—
Sanchez-Ramirez *et al.* (2007)	—	Mexico	36	Idiopathic	Biliary	Systemic	0	34.5
Chen *et al*. (2006)	—	Taiwan	75	Idiopathic	Systemic	Biliary	5.3	21.3
Stringer *et al*. (2005)	4.0–16.0	UK	33	Biliary	Idiopathic	Medication	—	24.2
Werlin *et al*. (2003)	0–18	USA	180	Systemic	Biliary	Medications/idiopathic	6.1	12.2
DeBanto *et al*. (2002)	0.1–16	USA	301	Idiopathic	Trauma	Biliary	—	—
Pezzilli *et al*. (2002)	2.0–17.0	Italy	30	Idiopathic	Infectious	Trauma	2	28
Tiao *et al*. (2002)	2.0–18.0	Taiwan	61	Trauma	Idiopathic	Systemic	1.6	14.8
Lopez (2002)	—	USA	NA	Systemic	Trauma	Idiopathic	—	—
Weizman and Durie(1988)	1–18.5	Canada	61	Systemic	Idiopathic	Trauma	21.3	—
Yeung *et al*. (1996)	2–18	Taiwan	43	Trauma	Systemic	Biliary	23	—
Haddock *et al*. (1994)	1–16	UK	49	—	—	—	—	—
Ziegler *et al*. (1988)	0.1–18	USA	49	—	—	—	—	—
Synn *et al*. (1987)	2–18	USA	48	—	—	—	—	—
Buntain *et al*. (1978)	2–18	USA	30	—	—	—	26.7	—
Jordan and Ament (1977)	0–21	USA	54	—	—	—	—	—

AP = acute pancreatitis; CECT = contrast-enhanced computed tomography; ULN = upper limit of normal; u/s = ultrasound.
*Included only studies that had 30 or more children.

probably found in children with underlying diseases (Werlin *et al*., 2003; Park *et al*., 2009).

Acute biliary pancreatitis as a complications of AP

Intense biliary pancreatitis Similarly to what occurs in adults, diseases of the biliary system, whether represented by biliary gallstones, biliary sludge or anatomical anomalies of the pancreas and its ductal system (such as sphincter of Oddi dysfunctions or pancreas divisum), are important causes of AP, representing 10 to 30% of cases; (Park *et al*., 2009; Bai*et al*., 2011) nevertheless, in retrospective accomplice studies, the occurrence of biliary AP might be higher, rising to 50% (Chang *et al*., 2011). The biliary sludge (excess of bile salts in the gallbladder) can represent approximately 30% of the cases of biliary obstruction in children, unlike grownups, whose blockage is nearly just due to the biliary lithiasis or tumors with compressive attributes. Nevertheless, the casual relation between the presence of the biliary sludge and the event of AP is not completely identified, exactly what makes some authors choose not to consist of such condition as an etiology of AP in children (Kandula and Lowe, 2008). Besides, except for some cases of reoccurring AP, cholecystectomy is not regularly indicated for patients with AP and diagnosed biliary sludge, instead of patients with cholelithiasis and AP, whose surgical treatment needs to be performed ideally in the first 2 weeks after resolution of the acute condition (van Geenen *et al*., 2009).We have identified more than 30 studies which have been discussing children with acute pancreatitis in the past 40 years, some of these studies are demonstrated in orders of year of publication in (Table 2). The majority of these studies are from the United States, but many others originate from other regions of the world. Many studies had just 1 dozen to 50 patients, but 4 research studies in particular, from Pittsburgh, New Haven, Wisconsin, and Australia, made up 87 to 280 patients each (Kandula and Lowe, 2008) These studies differ in numerous key areas: the proportion of children belonging to various pediatric age groups, intensity of disease, diagnostic addition requirements, and etiologic category. Regardless of these limitations, numerous essential patterns associating with discussion, management, and result emerge. Listed below we highlight these typical themes in children with acute pancreatitis from the literature.

Conclusion

The incidence of intense pancreatitis in children has actually been increasing for the past 2 years, most likely as a result of multifactorial causes. AP is a disease of great significance in children, due to its tough medical diagnosis and severity of symptoms and associated complications; besides, it has a significantly higher occurrence because of a growing suspicion and better knowledge of its clinical qualities. The main causes of AP in children are biliary disease and medication, however as much as 1/3 of patients might not have a defined etiology at diagnosis. Issues of severe pancreatitis in children are sterilized and infected collections, fistulas, and vascular complications. The most common issue in pediatric pancreatitis is the development of pseudocysts, which was reported to occur in 13% of patients in the analysis of studies in the literature by Benifla and Weizman (2003).

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