International Journal of Pediatrics and Adolescent Medicine 5 (2018) 13–17

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Contents lists available at ScienceDirect

International Journal of Pediatrics and Adolescent Medicine

journal homepage: http://www.elsevier.com/locate/ijpam

Original article

Etiology and clinical characteristics of pediatric acute pancreatitis in Saudi Arabia: a 20-year experience from a single tertiary center

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ARTICLE INFO

Article history:
Received 1 November 2017
Received in revised form
29 December 2017
Accepted 2 January 2018
Available online 24 February 2018

Keywords:
Pediatric
Pancreatitis
Gastroenterology
Saudi Arabia
Isoniazid
Choledochal cyst

ABSTRACT

Background: Cases of acute pancreatitis (AP) have increased among pediatric populations worldwide; however, the natural course of this condition in Saudi Arabia was unknown.
Aim: To report the characteristics as well as outcomes of pediatric AP.
Patients and methods: A retrospective chart review study was conducted to include acute pancreatitis in patients ≤ 19 years. The period was from 1994 until 2015. Demographic, clinical, laboratory, imaging and outcome data were collected and analyzed.
Results: 50 patients (n = 26; 52% males vs. n = 24; 48% females) were included. The mean age at diagnosis was 11.6 years. The mean length of hospital stay was 10.5 days. 9 (18%) patients had a recurrence of AP and 4 (8%) had complications. Idiopathic AP was the most frequent etiology (n = 21; 42%), followed by cholelithiasis (n = 11; 22%). 2 patients (4%) had drug-induced AP, where one was taking isoniazid and the other had taken a large amount of erythromycin, amoxicillin and ibuprofen. 2 choledochal cysts complicated by AP (4%). Pancreaticobiliary diseases, as a complete entity, accounted for 34% (*n* = 17). Clinically, abdominal pain (n = 47; 94%) and vomiting (n = 38; 76%) were most commonly encountered. KUB was non-diagnostic in all patients. No patient died during their admission.
Conclusion: Although still relatively uncommon in Saudi Arabia, there are on average 2–3 cases of pediatric AP diagnosed annually in our institution. Idiopathic AP was the most common cause. Isoniazid and choledochal cysts are rare causes of AP and were reported in the study.

1. Introduction

Inflammation of the pancreas (pancreatitis) occurs as a result of the spillage and autodigestion of the pancreatic parenchyma by the digestive enzymes. Acute pancreatitis (AP) is characterized by the presence of inflammatory cells and results in reversible structural and functional changes over a short duration. In contrast, chronic pancreatitis causes irreversible changes that ultimately result in fibrosis and loss of exocrine and/or endocrine function [1].

According to the International Study Group of Pediatric Pancreatitis: in Search for a Cure (INSPPIRE), two of three criteria must be fulfilled to diagnose AP in the pediatric population; namely, abdominal pain, serum amylase or lipase levels that are three times the upper normal limit and radiological findings diagnostic of AP [2,3].

AP is a rare disorder among individuals aged younger than 20 years, the number of pediatric AP cases recorded worldwide has increased dramatically over the past few years [4]. A 10-year American study estimated that the incidence of primary AP among children had increased from 6350 cases to 9561 cases between 2000 and 2009, representing a 51% increase [5]. A retrospective chart review conducted in the United States of America

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Peer review under responsibility of King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia.

https://doi.org/10.1016/j.ijpam.2018.01.001

(USA) found that the incidence of first pediatric AP admission increased from 2.3 per 100,000 children in 1993 to 13.2 per 100,000 children in 2004 [6]. The authors concluded that the observed rise might reflect increased testing for AP among the pediatric population.

To date, no national or regional studies have been conducted in Saudi Arabia to assess pediatric AP. Therefore, the aim of the current study was to describe the etiology, clinical characteristics of this disease among Saudi children and increase clinical awareness pediatric AP.

2. Methods

A 20-year retrospective chart review study was conducted at King Abdullah Specialized Children Hospital and King Abdulaziz Medical City, National Guard Health Affairs, Riyadh, Saudi Arabia. Institutional Review Board (IRB) was obtained from the King Abdullah International Medical Research Center (KAIMRC), National Guard Health Affairs, Riyadh, Saudi Arabia, with a reference number of RC16/110/R.

Medical records were reviewed to identify all pediatric patients (age ≤19 years) who were diagnosed with primary AP between 1994 and 2015. Patients with missing data were excluded from the analysis. We defined age groups as the following; pre-schooler (0–5 years), schooler (6–11 years) and adolescent (12–19 years).

Demographic, clinical and outcome data were evaluated to establish shared features among patients with primary AP in our population. Imaging techniques, including kidney–ureter–bladder (KUB) plain film, ultrasonography (US) and computed tomography (CT), were also evaluated.

3. Statistical analysis

Statistical analysis was performed using JMP version 12 (SAS Institute, Cary, NC, USA). Continuous and categorical variables are given as the mean ± standard deviation (SD) and as the number and percentage, respectively. The Student's *t*-test was used to assess the differences in means. Differences in categorical variables were analyzed with the chi-squared test. Analysis of variance (ANOVA) was used to assess continuous variables. A test with *P* value of less than .05 was statistically significant.

4. Results

A total of 50 patients ($n = 26$; 52% males vs. $n = 24$; 48% females) were included. The mean age at diagnosis was 11.6 years. Patients were diagnosed with primary AP during the present study at a rate of two to three cases per year. (Baseline demographics are presented in Table 1).

Idiopathic AP was the most frequent etiology ($n = 21$; 42%), followed by gallstones ($n = 11$; 22%) (Summary of etiologies is shown in Table 2). 2 (4%) had drug-induced AP, where one was taking isoniazid while the other had ingested a large amount of pain killers and antibiotics (erythromycin, amoxicillin and ibuprofen). 2 patients had choledochal cysts complicated by AP ($n = 2$; 4%). Congenital and non-congenital pancreaticobiliary diseases, as a complete entity, accounted for 34% ($n = 17$).

The co-morbid conditions of patients with gallstone induce AP were: morbid obesity, i.e. BMI>40 ($n = 2$; 18%), chronic recurrent cholecystitis ($n = 1$; 9%), Haemophilia A ($n = 1$; 9%), Sickle Cell Anaemia ($n = 1$; 9%), Chronic Kidney Disease complicated by Disseminated Intravascular Coagulation ($n = 1$; 9%), Epilepsy Syndrome manged by Levetiracetam ($n = 1$; 9%). The rest of the patient with gasllstones ($n = 4$; 36%) were medically free.

Most of the patients ($n = 47$; 94%) had abdominal pain, with vomiting ($n = 28$; 76%) and nausea ($n = 10$; 20%). Amylase levels were high in 96% (n = 48) of the patients and normal in 2% (n = 1). The mean amylase level was 1168 U/L, the median was 861 U/L and the standard deviation was 1009 U/L. Lipase were less tested ($n = 5$; 10%). Lipase mean level was 538 U/L.

Table 1
Baseline demographics.

	Male	Female	Total
Mean of Age, *yr*	11.8	11.4	11.6
Male/Female	26 (52)	24 (48)	50 (100)
Nationality, *n (%)*			
Saudi	26 (52)	24 (48)	50 (100)
Non-Saudi	0	0	0
Clinical Presentation, *n (%)*			
1. Abdominal Pain	24 (92.3)	23 (95.8)	47 (94)
2. Vomiting	20 (76.9)	18 (75)	38 (76)
3. Nausea	5 (20.8)	5 (21.7)	10 (20)
4. Anorexia	2 (8.3)	3 (13)	5 (9.2)
5. Fever	4 (16.6)	0	4 (8)
Blood Pressure, *mean*	115/66	113/68	114/68
Heart Rate, *mean*	106.3	106.3	106
Respiratory Rate, *mean*	26.8	21.3	24
O_2 Saturation, *mean*	97.6	97.9	98
Temperature (C°), *mean*	36.9	36.9	37
Length of Admission, *days*	11.2	9.7	10.5
Recurrences, *n (%)*	6 (23)	3 (12.5)	9 (18)

All patients underwent KUB had non-significant findings ($n = 21$; 42%). 37% of US were non-yielding ($n = 14$). Enlarged and bulky pancreas was commonly detected ($n = 11$; 46%). CT was the superior imaging modality as it showed pancreatic changes suggestive of AP 84% ($n = 16$). 6 patients (12) had endoscopic retrograde cholangiopancreatography (ERCP). One patient (16.6%) underwent ERCP for removal of common bile duct (CBD) stone, while another was diagnosed with choledochal cyst involving the CBD. (See Radiographic Findings of Pediatric Acute Pancreatitis in Table 3).

The mean length of stay (LOS) was 10.5 days (2–62), median 6. The pre-schooler group had a mean LOS of 12 days, whereas the schooler and adolescent groups had a mean LOS of 15 and 8.1 days, respectively. Patients who were admitted to the pediatric Intensive Care Unit (PICU) had a mean LOS in the unit of 2.7 (1–7), median 2. The pre-schooler group had a mean LOS of 5.5 days, and the schooler and adolescent groups had a mean LOS of 2.75 and 2 days, respectively. Patients who presented with abdominal pain and fever had significantly longer PICU stay ($P = .0007$, $P = .0211$, respectively).

18% ($n = 9$) experienced recurrence of AP. 8% ($n = 4$) had complications; 2 (33.3%) acute respiratory distress syndrome, 1 (16.6%) septic shock, 1 (16.6%) hypocalcemia, 1 (16.6%) pseudocyst and 1 (16.6%) pancreatic necrosis. No patients died due to AP.

5. Discussion

The present study aimed to define a baseline for pediatric AP in Riyadh, Saudi Arabia, by describing the etiological factors, clinical presentation, relevant laboratory tests and imaging findings among all cases of primary disease identified at our institute. Pediatric AP was diagnosed at a rate of approximately two to three cases per year in the present study.

The etiology of AP among children is variable. A US-based study published in 1999 found that 25% of pediatric AP cases are of unknown etiology, with 13%–33% of cases attributed to blunt trauma, making it the most common cause of pancreatitis among both adults and children [7]. However, a study published in 2013 claimed that pediatric AP due to trauma is less common than previously

Table 2
Summary of etiologies.

Etiology, *n (%)*	Male	Female	0-5 *yr*	6-12 *yr*	12-19 *yr*	Total
Idiopathic	10 (47.6)	11 (52.3)	2 (9.5)	6 (28.5)	13 (61.9)	21 (42)
Gallstone	6 (54.5)	5 (45.5)	0	2 (18.1)	9 (81.9)	11 (22)
Pancreatic Divisum	1 (33.3)	2 (66.6)	1 (33.3)	0	2 (66.6)	3 (6)
DKA[a]	1 (50)	1 (50)	0	1 (50)	1 (50)	2 (4)
Drug-Induced	1 (50)	1 (50)	0	1 (50)	1 (50)	2 (4)
Familial Hyperlipidaemia	1 (50)	1 (50)	1 (50)	1 (50)	0	2 (4)
Post ERCP[b]	2 (100)	0	0	0	2 (100)	2 (4)
Choledochal Cyst	1 (50)	1 (50)	1 (50)	1 (50)	0	2 (4)
Familial Hypertriglyceridemia	1 (100)	0	0	1 (100)	0	1 (2)
Herbs	0	1 (100)	0	0	1 (100)	1 (2)
CBD[c] sludge	0	1 (100)	0	0	1 (100)	1 (2)
Trauma	1 (100)	0	1 (100)	0	0	1 (2)
Viral Infection	1 (100)	0	0	0	1 (100)	1 (2)

[a] *DKA;* Diabetic Ketoacidosis.
[b] *ERCP*; Endoscopic Retrograde Cholangiopancreatography.
[c] *CBD*; Common Bile Duct.

Table 3
Main radiographic findings of pediatric acute pancreatitis.[a]

Radiological findings, *n* (%)	US[b] (# Pt = 38)	CT[c] (# Pt = 19)
Normal	14 (22.5)	3 (8.1)
Enlarged, bulky pancreas	11 (17.7)	8 (21.6)
Acute peripancreatic fluid collections	1 (1.6)	9 (24.3)
Gallstone	9 (14.5)	–
Peritoneal fluid	6 (9.6)	3 (8.1)
Dilated CBD[d]	4 (6.4)	–
Dilated intrahepatic duct	3 (4.8)	–
Dilated gallbladder	3 (4.8)	–
Necrotic pancreatitis	–	2 (5.4)
pseudocyst	1 (1.6)	2 (5.4)
Dilated pancreatic duct	–	2 (5.4)
Choledochal cyst	–	1 (2.7)
Budd-Chiari Syndrome	1 (1.6)	–
Choledocholithiasis	1 (1.6)	–

[a] 2 patients had ERCP and 1 patient had MRCP.
[b] US; Ultrasound.
[c] CT; Computed Topography.
[d] CBD; Common Bile Duct.

believed [8]. A long list of causes includes biliary tract disease, systemic diseases, autoimmune disorders, anatomic anomalies, drugs and genetic and hereditary diseases [8].

Geographic, racial, demographic and nutritional variations have recognizable effects on the course and etiology of pediatric AP [9]. One study found that congenital dilatation of the common bile duct was the most frequent cause of pediatric AP among Japanese, Chinese and other Asian children, whereas trauma was more common among Western children [10]. Most cases of AP identified in our present study were either idiopathic or had occurred because of gallstones. Unlike western findings, trauma ($n = 1$; 2%) was not the most commonly encountered etiology [7]. Suzuki et al. stated that biliary diseases, including gallstones, was much more common in eastern Asian Population [10]. Even though it is not the number one cause in our analysis, gallstones were associated with 22% of pediatric AP. However, our analysis showed that idiopathic AP and pancreaticobiliary disorders accounted for 42% and 34%, respectively. Though idiopathic causes were more common, pancreaticobiliary diseases contributed to a huge bulk of the AP cases. In terms of racial differences, Majbar et al. reported that United Kingdom children of Pakistani origin have a seven-fold increased risk of developing AP compared to white children [11]. This could have not been assessed by us, as all patients were Arabs/Saudis.

The diagnosis of idiopathic AP is not quite reassuring, as some genetic and/or congenital anomalies could be the reason. Physicians should reasonably exhaust resources to exclude all possible causes of AP before labelling it as idiopathic. Our review does not show any genetic causes, despite the fact some patients had multiple recurrences. Childhood AP trend is increasing. This should alert healthcare providers, i.e pediatricians, to fully work-up patients before making such diagnosis. However, Ballinger et al. stated that 1 in 31 patients with first attack of idiopathic AP suffers from another one in median of 36 moths [12]. This suggests that looking for other underlying cause of AP after only the 1st attack is not cost-effective, as most of them will not have another. This is quite similar to our study where 9 out 50 had subsequent attacks. In conclusion, there is no clear guidelines to when to work up a patient for other underlying causes and when not. This study demonstrated this lack of clear pathway to assist in patients' diagnosis.

Furthermore, we believe that it is highly unlikely that some of the common causes mentioned in the literature were missed, i.e. trauma, due to the fact that the study was conducted in a tertiary trauma center, where AP post motor vehicle accident or handle-bar injury was unlikely to be missed. In addition, some other form of trauma, such as child abuse, is hard to diagnose especially in our culture.

On the other hand, one 5.5-year-old male presented with AP as result isoniazid (INH) ingestion. INH is relatively safe tuberculosis chemoprophylaxis and INH-induced AP is uncommon, however, there have been case reports of INH-induced AP around the world in both children and adults [13–15]. INH-induced hepatitis (21/100,000) is well recognized since the early 1970s, however, INH-induced AP is less common and not well described in the literature [15]. Badalov and colleagues had built a classification drug-induced AP [16]. Their system had 4 classes, in which isoniazid had been classified into Class I. They defined Class I as “include medications in which at least 1 case report described a recurrence of acute pancreatitis with a rechallenge with the drug”. To our knowledge, this is the first time INH-induced AP has been reported in Saudi Arabia.

Another case of drug-induced acute pancreatitis (DIAP) was shown in our analysis. A 17-year-old female who had ingested multiple medication, including erythromycin, amoxicillin and ibuprofen. These medications have been reported in the global literature as an etiology of AP [17–19]. There is an obvious shortage in the local literature of DIAP, where clinicians and researchers of our nation should aid in filling this gap.

The association between choledochal cysts and acute pancreatitis is well-established [20,21]. Acute pancreatitis tends to reoccur in the presence of any type of choledochal cysts. Saluja and

Table 4
Pediatric acute pancreatitis characteristics from different studies [11,28–37].

Study	Country	Year	# Cases	#1 Etiology	#1 Presentation
Berny et al. [32]	Switzerland	1996	21	Systemic (38%)	Abdominal Pain (83%)
Suzuki et al. [29]	Japan	2008	135	Pancreaticobiliary Anomalies (54.5%)	–
Park et al. [33]	USA	2009	271	Biliary (32.6%)	Abdominal Pain (88%)
Nydegger et al. [30]	Australia	2007	279	Trauma (36.3%)	–
DeBanto et al. [28]	USA	2002	301	Idiopathic (34%)	–
Werlin et al. [31]	USA	2002	180	Systemic & Trauma (14% per each)	Abdominal Pain (68%)
Yeung et al. [34]	Taiwan	1996	43	Trauma (37%)	Abdominal Pain (95%)
Lautz et al. [35]	USA	2011	211	Idiopathic (31.3%)	–
Poddar et al. [36]	India	2017	320	Idiopathic (52.5%)	–
Majbar et al. [11]	UK	2016	94	Idiopathic (37%)	–
Minen et al. [37]	Italy	2012	34	Medications (28%)	–

colleagues had reported 6 cases of chronic pancreatitis in the presence of choledochal cysts. Interestingly, pancreatitis occurrence, weather acute or chronic, with choledochal cysts are less likely to be reported in the Middle East, North Africa, North America and/or Europe. Most of the reports of this pheromone has been described in eastern and central Asia, such as China, Japan and India [20–23]. In Saudi Arabia, Crankson et al. reported a case of choledochal cyst in 10-month-old boy, however, the patient was surgically manged without developing pancreatitis [24]. Another case report form Saudi Arabia has been described by Al Saleem et al., however, pancreatitis occurrence was not described [25]. To our knowledge, this is the first time where choledochal cysts and acute pancreatitis have reported in Saudi Arabia.

Most patients included in the current analysis complained of abdominal pain at presentation, with or without vomiting/nausea. One of the INSPIRE criteria for AP diagnosis was almost always fulfilled by our patients, where abdominal pain was, by far, the most common symptom ($n = 47$; 96%).

Pediatric AP has a better prognosis than AP diagnosed among adults [26]. Compared to pediatric patients without AP, US children with AP have longer LOS (median 4 days vs. 2 days), higher financial costs ($22,663 vs. $11,364) and a higher mortality rate (7.6 per 100,000 individuals vs. 2.7 per 100,000 individuals) [5]. Pediatric AP has decreased LOS, increased costs and decreased mortality rates. Our study shows AP LOS had a mean of 10.5 days and median of 6 days.

A US-based study found that both AP patients with pseudocysts and those who were malnourished had longer LOS than other patients [27]. Furthermore, African American children had a greater need for pediatric intensive care unit (PICU) admission than white children (18% vs. 7%, respectively white) [27]. In the current series, there were statistically significant differences in patients who presented with abdominal pain and fever and length of PICU admission ($P = .0007$, $P = .0211$, respectively).

No clear guideline or protocol is currently available for working-up a patient with suspicion of pediatric AP, nor when to admit. Ultrasonography detected abnormal findings in approximately 50% of the patients included in the present study, with an enlarged pancreas the most frequent finding. US findings were confirmed using CT. KUB was of no use in diagnosing children with AP. Summary of pediatric AP characteristics from different studies is shown in Table 4.

The limitation is that it is a retrospective study in a one center, hence the small number of cases. We recommend multicenter study to fully assess the characteristics of AP in children. Another limitation is the lack of proper documentation in patients' charts, especially the older ones. This is most apparent in this study where viral cause of AP was not documented in the file. The main strength of the present study was it is the first report from our nation to shed the light on pediatric AP. Also, our paper report one of the rarest causes of AP, i.e., INH-induced AP and choledochal cysts, both locally and globally.

6. Conclusion

Although still relatively uncommon in Saudi Arabia, approximately 2–3 cases of pediatric AP were diagnosed annually at our institution. Idiopathic AP and pancreaticobiliary disorders accounted for 42% and 34%, respectively. Isoniazid-induced AP and choledochal cysts are rare causes, even though, they were reported in the study.

Conflicts of interest

None.

References

[1] Bai HX, Lowe ME, Husain SZ. What have we learned about acute pancreatitis in children? J Pediatr Gastroenterol Nutr 2011;52(3):262–70.
[2] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis –2012: revision of the Atlanta classification and definitions by international consensus. Gut 2012;62(1):102–11.
[3] Morinville VD, Husain SZ, Bai H, Barth B, Alhosh R, Durie PR, et al. Definitions of pediatric pancreatitis and survey of present clinical practices. J Pediatr Gastroenterol Nutr 2012 Sep;55(3):261–5.
[4] Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144(6):1252–61.
[5] Pant C, Deshpande A, Olyaee M, Anderson MP, Bitar A, Steele MI, et al. Epidemiology of acute pancreatitis in hospitalized children in the United States from 2000–2009. PLoS One 2014 May 7;9(5), e95552.
[6] Morinville VD, Barmada MM, Lowe ME. Increasing incidence of acute pancreatitis at an American pediatric tertiary care center: is greater awareness among physicians responsible? Pancreas 2010 Jan;39(1):5–8.
[7] Uretsky G, Goldschmiedt M, James K. Childhood pancreatitis. Am Fam Physician 1999 May 1;59(9):2507–12.
[8] Srinath AI, Lowe ME. Pediatric pancreatitis. Pediatr Rev 2013;34(2):79–90.
[9] Suzuki M, Sai JK, Shimizu T. Acute pancreatitis in children and adolescents. World J Gastrointest Pathophysiol 2014;5(4):416–26.
[10] Tomomasa T, Tabata M, Miyashita M, Itoh K, Kuroume T. Acute pancreatits in Japanese and westren children: etiologic comparisons. J Pediatr Gastroenterol Nutr 1994;19(1):109–10.
[11] Majbar AA, Cusick E, Johnson P, Lynn RM, Hunt LP, Shield JP. Incidence and clinical associations of childhood acute pancreatitis. Pediatrics 2016 Sep;138(3).
[12] Ballinger AB, Barnes E, Alstead EM, Fairclough PD. Is intervention necessary after a first episode of acute idiopathic pancreatitis? Gut 1996;38:293.
[13] Saleem AF, Arbab S, Naz FQ. Isoniazid induced acute pancreatitis in a young girl. J Coll Phys Surg Pakistan 2015 Apr;25(4):299–300.
[14] Izzedine H, Launay-Vacher V, Storme T, Deray G. Acute pancreatitis induced by isoniazid. Am J Gastroenterol 2001 Nov;96(11):3208–9.
[15] Jin CF, Sable R. Isoniazid-induced acute hepatitis and acute pancreatitis in a patient during chemoprophylaxis. J Clin Gastroenterol 2002 Jul;35(1):100–1.
[16] Badalov N, Baradarian R, Iswara K, Li J, Steinberg W, Tenner S. Drug-induced acute pancreatitis: an evidence-based review. Clin Gastroenterol Hepatol 2007 Jun;5(6):648–61.
[17] Moslim MA, Sodeman TC, Nawras AT. A case of suggested ibuprofen- induced acute pancreatitis. Am J Therapeut 2016 Nov/Dec;23(6):e1918–21.
[18] Tenenbein MS, Tenenbein M. Acute pancreatitis due to erythromycin overdose. Pediatr Emerg Care 2005 Oct;21(10):675–6.

[19] Yap I, Gwee KA, Wee A. Augmentin-induced cholestatic jaundice—a case report. Singap Med J 1993 Oct;34(5):464–5.
[20] Saluja SS, Mishra PK, Nayeem M, Nag HH. Choledochal cyst with chronic pancreatitis: presentation and management. JOP 2010 Nov 9;11(6):601–3.
[21] Zhao L, Li Z, Ma H, Zhang X, Mou X, Zhang D, Lin W, Niu A. Congenital choledochal cyst with pancreatitis. Chin Med J (Engl) 1999 Jul;112(7):637–40.
[22] Okada A, Higaki J, Nakamura T, Fukui Y, Kamata S. Pancreatitis associated with choledochal cyst and other anomalies in childhood. Br J Surg 1995 June;82:829–32.
[23] Yamaguchi M. Congenital choledochal cyst. Analysis of 1,433 patients in the Japanese literature. Am J Surg 1980 Nov;140(5):653–7.
[24] Crankson S, Ahmed S. Choledochal cyst: case report and review of literature. Ann Saudi Med 1991 Sep; 1991;11(5):585–8.
[25] Al-Salem AH. Choledochal cyst. Saudi Med J 2004 Jan;25(1):99–102.
[26] Uc A. Death in pediatric intensive care unit: not for children with acute pancreatitis. J Pediatr Gastroenterol Nutr 2015 Jul;61(1):1–2.
[27] Goday Praveen S, Wakeham, Martin Kuhn, Evelyn M, et al. Acute pancreatitis in the pediatric intensive care unit. J Pediatr Gastroenterol Nutr 2015;61(1):108–12.
[28] DeBanto JR, Goday PS, Pedroso MR, Iftikhar R, Fazel A, Nayyar S, Conwell DL, Demeo MT, Burton FR, Whitcomb DC, et al. Acute pancreatitis in children. Am J Gastroenterol 2002;97:1726–31.
[29] Suzuki M, Fujii T, Takahiro K, Ohtsuka Y, Nagata S, Shimizu T. Scoring system for the severity of acute pancreatitis in children. Pancreas 2008;37:222–3.
[30] Nydegger A, Heine RG, Ranuh R, Gegati-Levy R, Crameri J, Oliver MR. Changing incidence of acute pancreatitis: 10-year experience at the royal children's hospital, Melbourne. J Gastroenterol Hepatol 2007 Aug;22(8):1313–6. Epub 2007 Apr 19.
[31] Werlin SL, Kugathasan S, Frautschy BC. Pancreatitis in children. J Pediatr Gastroenterol Nutr 2003;37:591–5.
[32] Berney T, Belli D, Bugmann P, Beghetti M, Morel P, LeCoultre C. Influence of severe underlying pathology and hypovolemic shock on the development of acute pancreatitis in children. J Pediatr Surg 1996 Sep;31(9):1256–61.
[33] Park A, Latif SU, Shah AU, Tian J, Werlin S, Hsiao A, Pashankar D, Bhandari V, Nagar A, Husain SZ. Changing referral trends of acute pancreatitis in children: a 12-year single-center analysis. J Pediatr Gastroenterol Nutr 2009 Sep;49(3):316–22. https://doi.org/10.1097/MPG.0b013e31818d7db3.
[34] Yeung CY, Lee HC, Huang FY, Ho MY, Kao HA, Liang DC, Hsu CH, Hung HY, Chang PY, Sheu JC. Pancreatitis in children—experience with 43 cases. Eur J Pediatr 1996 Jun;155(6):458–63.
[35] Lautz TB, Chin AC, Radhakrishnan J. Acute pancreatitis in children: spectrum of disease and predictors of severity. J Pediatr Surg 2011 Jun;46(6):1144–9. https://doi.org/10.1016/j.jpedsurg.2011.03.044.
[36] Poddar U, Yachna SK, Borcar V, et al. A report of 320 cases of childhood pancreatitis: increasing incidence, etiologic categorization, dynamics, severity assessment, and outcome. Pancreas 2017;46:110–5.
[37] Minen F, De Cunto A, Martelossi S, Ventura A. Acute and recurrent pancreatitis in children: exploring etiological factors. Scand J Gastroenterol 2012 Dec;47(12):1501–4. https://doi.org/10.3109/00365521.2012.729084.