Clinical characteristics of acute pancreatitis in children: a single-center experience in Western China

Rui Zhong
Southwest Medical University
Shali Tan
Southwest Medical University
Yan Peng
Southwest Medical University
Huan Xu
Southwest Medical University
Xin Jiang
Southwest Medical University
Yongfeng Yan
Southwest Medical University
Xiaowei Tang (solitude5834@hotmail.com)
Affiliated Hospital of Southwest Medical University

Research article

Keywords: acute pancreatitis, acute recurrent pancreatitis, child, etiology

Posted Date: August 6th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-48831/v1

Version of Record: A version of this preprint was published on March 9th, 2021. See the published version at https://doi.org/10.1186/s12876-021-01706-8.

Abstract

Background: The diagnosis of pediatric pancreatitis has been increasing over the last 20 years. We aimed to compare the clinical characteristics for pediatric acute pancreatitis (AP) with adult AP, and investigate the risk factor for acute recurrent pancreatitis (ARP) in children.

Method: From June 2013 to June 2019, a total of 130 pediatric patients with AP at the inpatient database were enrolled. Univariate analysis and multivariate Cox regression analysis were performed to identify the risk factors for ARP in children.

Result: Major etiologic factors in 130 patients were biliary (31.5%), idiopathic (28.5%), trauma (16.2%). There was a significant difference in the constituent ratio of etiology between pediatric patients and adult patients ($p<0.001$). Compared with the adult patients, the pediatric patients had significantly lower severity ($p=0.012$) and occurrence rate of pancreatic necrosis ($p=0.02$). During the follow-up time (34.2±20.8 months), 19 children (14.6%) developed into ARP. Multivariate Cox regression analysis showed that female ($p=0.025$; OR=3.632; 95%confidence interval(CI) 1.179-11.188), hyperlipidemia ($p=0.022$; OR=3.480; 95%CI 1.201-10.085), pancreatic necrosis ($p=0.001$; OR=8.815; 95%CI 2.446-31.774) were the independent risk factors of ARP. The risk of recurrence was significantly different in each etiology group. Hyperlipidemic AP had the highest risk of recurrence over time, while viral and drug-induced AP had the lowest risk of recurrence ($p=0.035$).

Conclusion: Biliary and idiopathic disease were the major etiologies of AP in children. Compared to adults, children tend to have milder disease conditions and a better prognosis. Female, hyperlipidemia, and first AP attack with pancreatic necrosis were associated with the increased risk of ARP.

Background

Acute pancreatitis (AP) is an inflammatory reaction that causes the digestion, edema, bleeding, and necrosis of pancreatic tissue after activation of various trypsin enzymes in pancreatic tissue, caused by a variety of etiologies [1]. Clinically, it is characterized by acute epigastric pain, vomiting, and elevated pancreatic amylase. It has been reported that the incidence of AP in children has increased in the past 20 years [2, 3]. At present, AP is more common in children over five years old, with an incidence of 3/100 000, but its severity is similar in children of all ages [3, 4]. The overall case fatality rate is less than 5% [2, 5]. Compared with adults, there are significant differences in the incidence, etiology, clinical manifestation, and prognosis of AP in children [6]. Therefore, the purpose of this study was to analyze the demographic characteristics, etiology, clinical manifestations, and prognosis of AP, compare to adult AP, and to investigate the risk factors for acute recurrent pancreatitis (ARP) in children in southwest China.

Methods

Patients

We collected data retrospectively on 130 children with AP from June 2013 to June 2019 at the inpatient database. The diagnostic criteria for pediatric AP were in accordance with the guidelines of the International Pediatric Pancreatitis Study Group, the European Pancreatic Club, and the Hungarian Pancreatic Group [2, 7, 8]. Pediatric AP can be recognized in patients less than 18 years old, when two of the following three criteria are fulfilled: (1) abdominal pain compatible with AP, (2) serum amylase and/or lipase values ≥ 3 times the upper limits of normal, (3) imaging findings consistent with AP. The clinical classification of AP includes: mild acute pancreatitis (MAP), characterized by the absence of organ failure and local or systemic complications; moderately-severe acute pancreatitis (MSAP), characterized by transient organ failure (< 48 h), or accompanied by local or systemic complications; severe acute pancreatitis (SAP), characterized by persistent organ failure (> 48 h). In addition, acute recurrent pancreatitis (ARP) is characterized by: (1) at least two distinct episodes of AP, irrespective of the specific time interval between AP episodes, with complete normalization of serum pancreatic enzyme levels before the subsequent episode of AP is diagnosed, along with complete resolution of pain symptoms, (2) there was absence of changes of chronic pancreatitis on noninvasive imaging [8]. We enrolled 130 adult patients with AP from the medical record database as the control group using the random number table method. The criteria for adult AP were in accordance with the Atlanta International consensus 2012 [9].

Data Collection

In order to analysis of the clinical characteristics of AP in children of different ages, patients were divided into two groups: a low age cohort (2–9 years old) and a high age cohort (10–17 years old). Basic information on these patients was collected, including age, sex, etiologies, clinical symptoms, laboratory indexes (blood amylase, lipase, triglyceride (TG), C-reactive protein (CRP), blood glucose, serum calcium), complications, and treatment outcome. We compared the characteristics between the recurrence and the non-recurrence group, and analyzed the risk factors associated with ARP in children. We also compared the clinical characteristics between children with AP and adults with AP. 130 children had telephone follow-up for at least 3 months.

Statistical analysis

The data were analyzed using SPSS software version 25.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were described by mean ± standard deviation or median (range) and classified variables by percentages. Comparison of non-normally distributed data and hierarchical data groups used the Mann–Whitney U test. The chi-squared test and Fisher's exact probability test were employed to complete the univariate analysis. The chi-squared test for trend was used for unidirectional ordered classification, and Goodman–Kruskal gamma analysis was used for variables with bidirectional ordered classification. Factors with $p < 0.05$ were entered into a multivariate Cox regression analysis to determine adjusted odds ratios (Ors). A Cox proportional hazards model was used to analyze etiology groups and time to ARP for the whole sample. $P < 0.05$ was considered statistically significant for analyses.

Results

Baseline characteristics

Major etiologic factors in 130 patients were biliary (31.5%)(including 29 cases of bile duct stones, 8 cases of congenital biliary dilatation. 4 cases of biliary tapeworm), idiopathic (28.5%), trauma (16.2%), viral infection (10%), hyperlipidemia (9.3%)(TG > 11.30 mmol/L in 12 children), and drug-induced (4.6%) (including 5 children were taking dexamethasone and 1 child with leukemia was receiving chemotherapy with Cytarabine). There was a significant difference in the etiological constituent ratio between children and adults ($p < 0.001$): cases in children were mainly biliary and idiopathic, and those in adults were mainly hyperlipidemic and biliary. The severity of AP in the children was milder than that in the adult group ($p = 0.012$), and the rate of pancreatic necrosis in the children was lower than that in the adult group ($p = 0.02$). (Table 1)

Table 1
Clinical characteristics of acute pancreatitis in children and adults.

Variables	Pediatric (n = 130)	Adult (n = 130)	P-value
Onset to admission time (days)	1.7 (0.9 ~ 4)	1 (0.3 ~ 3)	0.075[a]
Age, years	11.2 ± 4.2	46.2 ± 13.7	< 0.001[a]
Sex, Male, n%	72 (55.4%)	84 (64.6%)	0.129[b]
Etiology, n%			< 0.001[c]
Biliary	41 (31.5%)	43 (33.1%)	0.791[b]
Idiopathic	37 (28.5%)	6 (4.6%)	< 0.001[b]
Trauma	21 (16.2%)	0 (0%)	< 0.001[b]
Hyperlipidemic	12 (9.2%)	44 (33.8%)	< 0.001[b]
Viral infection	13 (10%)	0 (0%)	< 0.001[b]
Drug-induced	6 (4.6%)	0 (0%)	0.029[c]
Alcoholic	0 (0%)	12 (9.2%)	< 0.001[b]
Multiple etiologies*	0 (0%)	20 (15.4%)	< 0.001[b]
Other**	0 (0%)	5 (3.9%)	0.060[c]
Severity, n%			
MAP	96 (73.8%)	78 (60%)	
MASP	30 (23.1%)	41 (31.5%)	0.012[a]
SAP	4(3.1%)	11 (8.5%)	
Blood amylase(U/L)	534.8 (226.4 ~ 1131.1)	314.5 (198.9 ~ 768.3)	0.018[a]
Blood lipase(U/L)	361.2 (167.5 ~ 1055.2)	257.1 (110.5 ~ 777.0)	0.061[a]

[a] Mann-Whitney U test. [b] Chi-square test. [c] Fisher's exact test.

MAP: Mild acute pancreatitis MASP: Moderately-severe acute pancreatitis

SAP: Severe acute pancreatitis

*At least two etiologies of biliary, hyperlipidemic, alcoholic

**Two patients of pregnancy, two patients of surgery, one patient of tumor

Variables	Pediatric (n = 130)	Adult (n = 130)	P-value
C-reactive protein (mg/L)	18 (3.4 ~ 74.4)	18.4 (5.7 ~ 99)	0.144[a]
Pancreas necrosis, n%	5 (3.8%)	15 (11.5%)	0.020[b]
Pancreatic pseudocyst, n%	14 (10.8%)	10 (7.7%)	0.391[b]
ICU admission, n%	4 (3.1%)	11 (8.5%)	0.063[b]
Cholecystectomy, n%	8 (6.2%)	14 (10.8%)	0.181[b]
Hospital stay (days)	11 (7.8 ~ 19)	10 (6 ~ 15)	0.058[a]
Death, n%	0 (0%)	1 (0.7%)	1.000[c]
[a] Mann-Whitney U test. [b] Chi-square test. [c] Fisher's exact test.			
MAP: Mild acute pancreatitis MASP: Moderately-severe acute pancreatitis			
SAP: Severe acute pancreatitis			
*At least two etiologies of biliary, hyperlipidemic, alcoholic			
**Two patients of pregnancy, two patients of surgery, one patient of tumor			

Clinical characteristics based on age

AP was more likely to occur in older age groups of children. However, the severity of the disease was independent of the increase in age, and there was no significant difference in etiology, sex and the constituent ratio of complications among different age groups. Viral infectious pancreatitis was more likely to occur in young children (p = 0.03). (Table 2)

Table 2
Patient demographics and hospital characteristics by age groups.

Variables	Aged 2 ~ 9 (n = 43)	Aged 10 ~ 17 (n = 87)	P-value
Etiology, n%			
Biliary	10 (24.4%)	31 (75.6%)	0.153[b]
Idiopathic	15 (40.5%)	22 (59.5%)	0.254[b]
Trauma	9 (42.9%)	12 (57.1%)	0.298[b]
Hyperlipidemic	1 (8.3%)	11 (91.7%)	0.103[c]
Viral infection	8 (61.5%)	5 (38.5)	0.030[c]
Drug-induced	0 (0%)	6 (100%)	0.177[c]
Sex, n%			
Male	21 (29.2%)	51 (70.8%)	0.291[b]
Female	22 (37.9%)	36 (62.1%)	
Severity, n%			
MAP	34 (35.4%)	62 (64.6%)	
MSAP	9 (30%)	21 (70%)	0.260[d]
SAP	0 (0%)	4 (100%)	
Complication, n%			
Yes	9 (26.5%)	25 (73.5%)	0.341[b]
No	34 (35.4%)	62 (64.6%)	
[b] Chi-square test. [c] Fisher's exact test. [d] Goodman-Kruskal Gamma analysis			
MAP: Mild acute pancreatitis MASP: Moderately-severe acute pancreatitis			
SAP: Severe acute pancreatitis			

Treatment

130 patients were mainly treated with conservative medicine and clinical outcomes were good, of which 123 patients were cured and discharged, 7 patients were improved or discharged for further treatment, 8 patients were treated with cholecystectomy, 14 patients had pancreatic pseudocysts, 10 patients of which healed after medical treatment, 4 patients underwent pseudocyst drainage, none died.

Risk factors for ARP

Of the 130 children with AP, 19 (14.6%) progressed to ARP during the study period. The median interval from AP to ARP was seven months (interquartile range (IQR): 3–14), and the median age at development of ARP was 12 years (IQR: 8–14). The recurrence rate increased with an increase in disease severity ($p = 0.034$). Female sex ($p = 0.001$), hyperlipidemia ($p = 0.016$), and the presence of pancreatic necrosis during the first AP attack ($p = 0.022$) were significantly correlated with ARP. (Table 3)

Table 3
Characteristics of patients in Recurrence and Non-recurrence groups.

Variables	Recurrence group n = 19	Non-recurrence group n = 111	P-value
Age, years	11.2 ± 4.2	11.3 ± 4.2	0.926[a]
Sex, n%			
Male	4 (5.6%)	68 (94.4%)	0.001[b]
Female	15 (25.9%)	43 (74.1%)	
Etiology n%			
Biliary	5 (12.2%)	36 (87.8%)	0.804[b]
Idiopathic	6 (16.2%)	31 (83.8%)	0.745[b]
Trauma	3 (14.3%)	18 (85.7%)	0.963[b]
Hyperlipidemic	5 (41.7%)	7 (58.3%)	0.016[c]
Viral infection	0 (0%)	13 (100%)	0.116[b]
Drug-induced	0 (0%)	6 (100%)	0.299[b]
Severity n%			
MAP	11 (11.5%)	85 (88.5%)	
MASP	6 (20%)	24 (80%)	0.034[e]
SAP	2 (50%)	2 (50%)	
Complication n%			
Pancreas necrosis	3 (60%)	2 (40%)	0.022[c]
Pancreatic pseudocyst	2 (14.3%)	12 (85.7%)	1.000[c]
[a] Mann-Whitney U test. [b] Chi-square test. [c] Fisher's exact test. [e] Trend Chi-squared test			
MAP: Mild acute pancreatitis MASP: Moderately-severe acute pancreatitis			
SAP: Severe acute pancreatitis			

Multivariate Cox regression analysis showed that female sex (p = 0.025; OR = 3.632; 95%CI 1.179–11.188), hyperlipidemia (p = 0.022; OR = 3.480; 95%CI 1.201–10.085), and pancreatic necrosis (p = 0.001;

OR = 8.815; 95%CI 2.446–31.774) were the independent factors influencing ARP. (Table 4)

Table 4
Univariate and Multivariate Cox regression analysis of factors associated with ARP in children.

Variable	Univariate analysis		Multivariate analysis	
	OR(95%CI)	P-value	OR(95%CI)	P-value
Sex, Female	4.626 (1.535–13.941)	0.007	3.632 (1.179–11.188)	0.025
hyperlipidemic	4.505(1.619–12.537)	0.004	3.480 (1.201–10.085)	0.022
Pancreas necrosis	8.288 (2.380-28.865)	0.001	8.815 (2.446–31.774)	0.001

We were also interested in studying the etiology or risk factors associated with the first AP occurrence and their effect on progression to ARP over time for the whole sample. We compared patients with biliary, idiopathic, traumatic, hyperlipidemic, viral, and drug-induced AP. We found that hyperlipidemic AP had the highest risk of recurrence over time, while viral and drug-induced AP had the lowest risk of recurrence (p = 0.035). (Fig. 1)

Discussion

It has been reported [10–12] that the incidence of AP in children has shown an upward trend in recent years. The incidence rate in children in the United Kingdom was about 0.78/100 000 [13], while in the United States, this figure was 3–13/100 000 [3]. In this study, the clinical characteristics of AP in children in southwest China were analyzed and summarized. As far as we know, this is the first report in English on the clinical features of AP in children from China.

The etiology of AP in children is significantly different from that in adults. In previous studies, Poddar et al. [14] studied 320 children with AP from India and found that trauma (21%) and biliary tract disease (10%) were the most common causes of AP in children. Park et al. [15] found that the biliary tract (36.2%) and drugs (25.6%) were the leading causes of AP in 215 children in the United States. In another study of 115 children in the United States [16], idiopathic (31%) and drug associated (23%) were the main causes. We found that biliary (31.5%), idiopathic (28.5%) and traumatic (16.2%) were the main causes, which was consistent with most studies. In adults, biliary obstruction leading to AP is almost always due to a stone or tumor; however, in children, 30% of cases are caused by biliary silt rather than complete calculus [3, 6]. No study has reported on this difference. In addition, metabolic problems such as hyperlipidemia in children were significantly rarer than in adults. Only 2–7% of children with AP have metabolic causative factors [10, 11]. In this study, 12 cases (9.2%) were caused by hyperlipidemia. In the control group of adults, high fat levels accounted for 33.8%, and the difference was significant. The most exciting finding in our study was that viral infectious pancreatitis was more common in young children and the rate was

significantly different from that in adults. We consider that is was related to the incomplete development of the immune system in young children. The mechanism of AP related to virus infection is not clear at present, although some research has shown that the virus directly invades pancreatic cells [3]. In recent years, with the extensive use of drugs, drug-induced pancreatitis has shown a significant increasing trend, although, overall, it is still constitutes less than 10% of cases [17].

Our study showed that the severity of AP in children was similar in all age groups, which is consistent with a previous report [3], but the disease was less severe than in adults. Possible reasons are: (1) Children were admitted to the hospital earlier than adults because of reduced tolerance, in order to get treatment as soon as possible; (2) In terms of etiological composition, hyperlipidemia and alcoholic pancreatitis account for few cases in children, and some studies have shown that hyperlipidemia and alcohol can easily lead to SAP [18]; (3) In terms of complications, pancreatic necrosis is positively correlated with the severity and prognosis of the disease. Necrotizing pancreatitis is rare in children. According to the literature [19], necrotizing pancreatitis occurs in less than 1% of children with AP. Among the five large sample pediatric cases reported in the United States [20], only 3 of 1014 children with AP had pancreatic necrosis, which was significantly less severe than that of adults. (4) Pediatric biliary AP often results from the formation of silt, so the rate of operation is less than in adults, and there are fewer complications due to biliary diseases.

For AP with specific causes, such as bile duct stones, anatomical abnormalities, bile duct dilatation, etc., it has been suggested that surgery should be performed as soon as possible after the condition is controlled and stable, to prevent recurrence [11, 21]. In the literature [22], the mortality rate of pediatric AP is less than 5%, which is significantly lower than that of adult AP, possibly because: (1) Alcoholic pancreatitis is rare in pediatric cases, and alcoholic pancreatitis is a known cause of high mortality, with a mortality rate as high as 30.6% [23]. (2) With age, adults may lose some critical protective mechanism, which children retain [6]. (3) Adult cases may be associated with severe underlying diseases, while AP in children is rarely associated with multiple problems with organ function. (4) The severity of the disease in children is significantly lower than that in adults, which has also been confirmed in this study.

Some single-center studies have estimated that 10–35% of children with AP develop ARP [24, 25]. These studies showed that mutations of PRSS1, SPINK1, CFTR, and CTRC13 were firmly related to the progression of ARP. During the first attack of AP in children, age, male sex, pancreatic necrosis, and higher Body Mass Index (BMI) have been associated with the progression of ARP. Anatomic abnormalities of the biliary tract, hyperlipidemia, and genetic factors should be evaluated in cases of recurrence [11, 16, 26]. In our study, among the 19 children (14.6%) with ARP, includes a 2-year-old toddler with congenital bile duct dilatation. We found that female sex, hyperlipidemia, and primary AP with pancreatic necrosis were significantly correlated with ARP, and the severity of primary AP was positively correlated with ARP. The relationship between ARP and sex is controversial and perhaps related to the predominance of hyperlipidemia and biliary tract disease in women [27, 28].

Differences in our findings from those of from previous studies may have resulted from differences in race, region, and environment. Hyperlipidemia is an apparent cause of AP and ARP in adults [29], but there has been no analysis of a large sample of ARP cases in children. It has been reported in the literature that hypertriglyceridemia occurring secondary to AP may be related to various genetic mutations [30]. From this point of view, our findings coincide with previous research results.

The disadvantage of this study is that it was a single-center study in China. Thus, the findings of this study cannot be generalized. For the 19 patients with ARP, the etiology of recurrence needs to be examined by endoscopic retrograde cholangiopancreatography and genetic analysis, and there is a lack of corresponding genetic and clinical data in this study. In future, multi-center studies with a larger sample and more rational perspective are needed to analyze pediatric pancreatitis in order to facilitate better treatment.

Conclusion

Biliary disease and idiopathic cases were the leading causes of AP in children, and, when compared with adults, children tend to have milder disease and a better prognosis. The recurrence rate increased with an increase in disease severity. Female sex, hyperlipidemia, and a first AP attack involving pancreatic necrosis were associated with an increased risk of ARP. Genetic and anatomical factors need to be studied further in children with ARP.

Abbreviations

AP Acute Pancreatitis

ARP Acute Recurrent Pancreatitis

BMI Body Mass Index

CRP C-reactive Protein

IQR Interquartile Range

MAP Mild Acute Pancreatitis

MASP Moderately-severe Acute Pancreatitis

SAP Severe Acute Pancreatitis

TG Triglyceride

Declarations

Acknowledgements

We thank all the parents for consenting and participating in this study. We also thank the nurses and doctors for their participation in our study.

Authors' contributions

Study conception and design: Xiaowei Tang, Yan Peng. Drafting of manuscript: Rui Zhong and Shali Tan. Acquisition of data and critical revision: Huan Xu, Xin Jiang, Yongfeng Yan. Revision of manuscript, and final approval of manuscript: Xiaowei Tang.

Funding

This study is independent research funded by the following grants: Medical science and technology plan projects of Zhejiang Province (No. 2017196257), Youth Foundation of Southwest Medical University (No. 0903-00031099), Doctoral research start-up funding project of Affiliated Hospital of Southwest Medical University (No. 16229).

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Ethics approval and consent to participate

This study was approved by the Clinical trial Ethics Committee of the affiliated Hospital of Southwest Medical University (batch number: KY2019054). Date:2019/05/04

Consent to publish

Not Applicable

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Crockett SD, Wani S, Gardner TB, Falck-Ytter Y, Barkun AN, Crockett S, et al. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis. Gastroenterology. 2018;154(4):1096–101.
2. Abu-El-Haija M, Kumar S, Quiros JA, Balakrishnan K, Barth B, Bitton S, et al. Management of Acute Pancreatitis in the Pediatric Population: A Clinical Report From the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition Pancreas Committee. J Pediatr Gastroenterol Nutr. 2018;66(1):159–76.
3. Husain SZ, Srinath AI. What's unique about acute pancreatitis in children: risk factors, diagnosis and management. Nat Rev Gastroenterol Hepatol. 2018;14(6):366–72.

4. Chang YJ, Chao HC, Kong MS, Hsia SH, Lai MW, Yan DC. Acute pancreatitis in children. Acta Paediatr. 2011;100(5):740–4.
5. Abu-El-Haija M, El-Dika S, Hinton A, Conwell DL. Acute Pancreatitis Admission Trends: A National Estimate through the Kids' Inpatient Database. J Pediatr. 2018;194:147–51 e1.
6. Bai HX, Lowe ME, Husain SZ. What Have We Learned About Acute Pancreatitis in Children? J Pediatr Gastroenterol Nutr. 2011;52(3):262–70.
7. Parniczky A, Abu-El-Haija M, Husain S, Lowe M, Oracz G, Sahin-Toth M, et al. EPC/HPSG evidence-based guidelines for the management of pediatric pancreatitis. Pancreatology. 2018;18(2):146–60.
8. 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;55(3):261–5.
9. Gress TM, El-Omar EM. Revision of the Atlanta classification of acute pancreatitis: the editorial perspective. Gut. 2013;62(1):1.
10. Restrepo R, Hagerott HE, Kulkarni S, Yasrebi M, Lee EY. Acute Pancreatitis in Pediatric Patients: Demographics, Etiology, and Diagnostic Imaging. AJR Am J Roentgenol. 2016;206(3):632–44.
11. Grzybowska-Chlebowczyk U, Jasielska M, Flak-Wancerz A, Wiecek S, Gruszczynska K, Chlebowczyk W, et al. Acute pancreatitis in children. Prz Gastroenterol. 2018;13(1):69–75.
12. Pant C, Deshpande A, Sferra TJ, Gilroy R, Olyaee M. Emergency department visits for acute pancreatitis in children: results from the Nationwide Emergency Department Sample 2006–2011. J Investig Med. 2015;63(4):646–8.
13. Majbar AA, Cusick E, Johnson P, Lynn RM, Hunt LP, Shield JP. Incidence and Clinical Associations of Childhood Acute Pancreatitis. Pediatrics. 2016;138(3).
14. Poddar U, Yachha SK, Borkar V, Srivastava A, Kumar S. A Report of 320 Cases of Childhood Pancreatitis: Increasing Incidence, Etiologic Categorization, Dynamics, Severity Assessment, and Outcome. Pancreas. 2017;46(1):110–5.
15. Park A, Latif SU, Shah AU, Tian J, Werlin S, Hsiao A, et al. Changing referral trends of acute pancreatitis in children: A 12-year single-center analysis. J Pediatr Gastroenterol Nutr. 2009;49(3):316–22.
16. Sweeny KF, Lin TK, Nathan JD, Denson LA, Husain SZ, Hornung L, et al. Rapid Progression of Acute Pancreatitis to Acute Recurrent Pancreatitis in Children. J Pediatr Gastroenterol Nutr. 2019;68(1):104–9.
17. Ksiadzyna D. Drug-induced acute pancreatitis related to medications commonly used in gastroenterology. Eur J Intern Med. 2011;22(1):20–5.
18. Zhu Y, Pan X, Zeng H, He W, Xia L, Liu P, et al. A Study on the Etiology, Severity, and Mortality of 3260 Patients With Acute Pancreatitis According to the Revised Atlanta Classification in Jiangxi, China Over an 8-Year Period. Pancreas. 2017;46(4):504–9.
19. Raizner A, Phatak UP, Baker K, Patel MG, Husain SZ, Pashankar DS. Acute necrotizing pancreatitis in children. J Pediatr. 2013;162(4):788–92.

20. Park AJ, Latif SU, Ahmad MU, Bultron G, Orabi AI, Bhandari V, et al. A comparison of presentation and management trends in acute pancreatitis between infants/toddlers and older children. J Pediatr Gastroenterol Nutr. 2010;51(2):167–70.
21. Alabdulkareem A, Almahmoud T, Al-Tahan H, Javad S, Al Hatlani M. Etiology and clinical characteristics of pediatric acute pancreatitis in Saudi Arabia: a 20-year experience from a single tertiary center. Int J Pediatr Adolesc Med. 2018;5(1):13–7.
22. Uc A, Husain SZ. Pancreatitis in Children. Gastroenterology. 2019;156(7):1969–78.
23. Karjula H, Saarela A, Ohtonen P, Ala-Kokko T, Mäkelä J, Liisanantti JH. Long-term Outcome and Causes of Death for Working-age Patients Hospitalized Due to Acute Pancreatitis With a Median Follow-up of 10 Years. Ann Surg. 2019;269(5):932–6.
24. Kumar S, Ooi CY, Werlin S, Abu-El-Haija M, Barth B, Bellin MD, et al. Risk Factors Associated With Pediatric Acute Recurrent and Chronic Pancreatitis. JAMA Pediatrics. 2016;170(6).
25. Pant C, Sferra TJ, Lee BR, Cocjin JT, Olyaee M. Acute Recurrent Pancreatitis in Children: A Study From the Pediatric Health Information System. J Pediatr Gastroenterol Nutr. 2016;62(3):450–2.
26. Abu-El-Haija M, Valencia CA, Hornung L, Youssef N, Thompson T, Barasa NW, et al. Genetic variants in acute, acute recurrent and chronic pancreatitis affect the progression of disease in children. Pancreatology. 2019;19(4):535.
27. Xu T, Liu J, Liu J, Zhu G, Han S. Relation between metabolic syndrome and body compositions among Chinese adolescents and adults from a large-scale population survey. BMC Public Health. 2017;17(1).
28. Sarrami M, Ridley W, Nightingale S, Wright T, Kumar R. Adolescent gallstones-need for early intervention in symptomatic idiopathic gallstones. Pediatr Surg Int. 2019;35(5):569–74.
29. Scherer J, Singh VP, Pitchumoni CS, Yadav D. Issues in hypertriglyceridemic pancreatitis: an update. J Clin Gastroenterol. 2014;48(3):195–203.
30. Jin JL, Sun D, Cao YX, Zhang HW, Guo YL, Wu NQ, et al. Intensive genetic analysis for Chinese patients with very high triglyceride levels: Relations of mutations to triglyceride levels and acute pancreatitis. EBioMedicine. 2018;38:171–7.

Figures

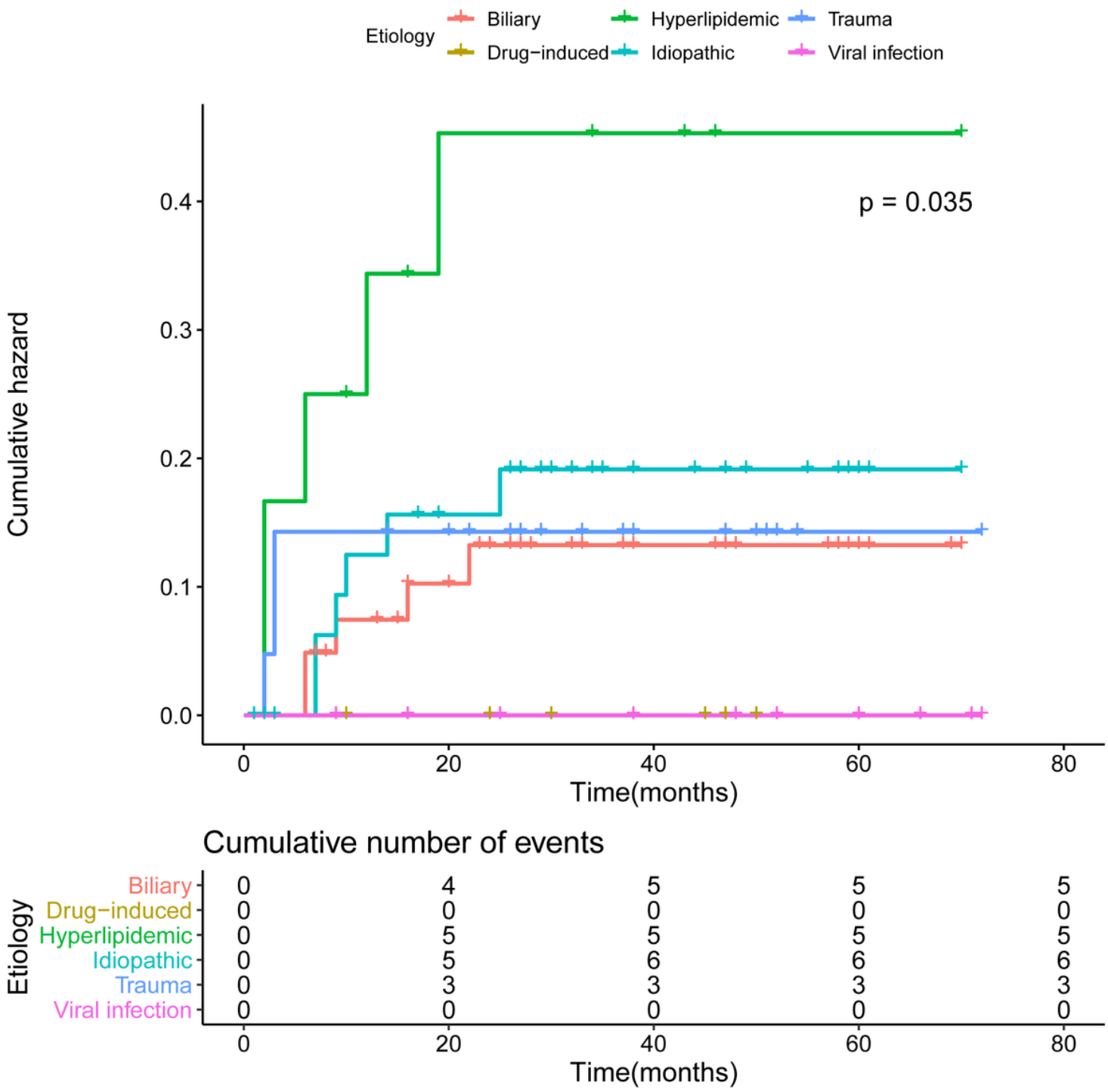

Figure 1

Risk of acute recurrent pancreatitis (ARP) by etiology.