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Epidemiology of Pediatric Acute Pancreatitis in Taiwan: A Nationwide Population-based Study

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ABSTRACT

Objective: Pediatric acute pancreatitis (AP) may be different from adult AP in various respects. This study focuses on the epidemiology and medical resource use of pediatric AP in Taiwan.

Methods: Patients aged 0 to 18 years with AP were identified from the Taiwan National Health Insurance Research Database based on the International Classification of Diseases, Ninth Revision code of AP 577.0. The medical resource use was measured by length of hospital stay and hospital charges.

Results: Between 2000 and 2013, a total of 2127 inpatient cases of pediatric AP were collected, which represented a hospitalization rate of 2.83 per 100,000 population. The incidence by age had 2 peaks, the first peak was at age 4 to 5 years old, and the second one started rising from 12 to 13 years old until adulthood. The incidence by year increased from 2.33 to 3.07 cases per 100,000 population during the study period. The average hospital stay is steady, but the medical cost is increasing. Girls have longer hospital stays, higher medical expenditures, more use of endoscopic retrograde cholangiopancreatography possibly due to more comorbidities with biliary tract diseases than boys ($P < 0.05$). The mortality in cases of AP is mostly associated with systemic diseases rather than AP itself.

Conclusions: The incidence of pediatric AP in Taiwan is in a rising trend. There are gender differences in length of hospital stay, medical costs, use of endoscopic retrograde cholangiopancreatography and comorbidities.

Key Words: acute pancreatitis, children, epidemiology, gender difference

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What Is Known

- Acute pancreatitis is relatively rare in pediatric group.
- Acute pancreatitis in children may differ from adult in many aspects, such as epidemiology, etiology, and medical resource use.

What Is New

- The incidence of acute pancreatitis by age had 2 peaks. The first peak was at age 4 to 5 years old, and the second one rose from teenagers until adulthood.
- Girls have longer hospital stays, higher medical expenditures, more use of endoscopic retrograde cholangiopancreatography and biliary tract diseases than boys.
- The mortality in cases of acute pancreatitis is mostly associated with systemic diseases rather than acute pancreatitis itself.

Acute pancreatitis (AP) refers to the reversible inflammation of the pancreas, starting from injury of acinar cells irrespective of the mechanism. It leads to pancreatic edema, acute inflammatory cell infiltrate, and varying degrees of pancreatic necrosis and hemorrhage (1–3). The diagnosis is made by the International Study Group of Pediatric Pancreatitis in search for a cure (INSPPIRE) group with at least 2 of the following: abdominal pain compatible with AP, serum amylase and/or lipase values over 3 times the upper limits of the normal range, and imaging findings consistent with AP (4). Its etiologies or risk factors include biliary tract diseases, medications, systemic diseases, traumatic events, metabolic disorders, and inborn errors of metabolism. Variable incidences are observed among different age groups related to the above etiologies. For example, inborn error is a major risk factor in children below 2 years old, while a biliary cause is predominant in children over 11 years (1). In our previous case series study, we found that more than one-third of the cases were due to trauma, followed by structural diseases and systemic diseases (5).

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In recent decades, medical resource use and disease burden have drawn attention in the care of patients with pancreatitis (6–10). Shorter lengths of hospital stay and increasing hospitalization charges have been observed in both child and adult AP studies (7,9). The mortality rate of pediatric AP decreased to less than 5%, which was lower than that for adults (5,11–13). Most mortality cases in children were due to underlying systemic diseases, and less than 6% have developed multi-organ dysfunction or pancreatic necrosis (1,12).

Although some large and population-based studies of adults or whole populations have been published (9,10,14), current publications of pediatric pancreatitis are limited and are mostly case series (5,13,15–17). Since the etiologies or associated risk factors are different between adults and children, it could be difficult to get reliable information from adult experiences. The aims of this study focus on the epidemiology of pediatric AP in Taiwan, pediatric AP patients' hospital stay lengths and medical resource use, and mortality and associated risk factors in pediatric pancreatitis.

METHODS

Data Source and Selection of Cases

This nationwide population-based study was conducted using the Taiwan National Health Insurance Research Database (NHIRD). The National Health Insurance program is a unique public health and medical insurance system that covered 99.9% of 23 million Taiwanese residents as of the end of 2013. The NHIRD is one of the largest and most comprehensive databases in the world and has been validated and used extensively for epidemiological studies in Taiwan (9,10,14,18). The NHIRD contains the demographic data of enrollees; service records and expenditure claims from outpatient, inpatient, and ambulatory care; and data associated with contracted pharmacies for reimbursement purposes. Information such as the date of admission, date of discharge, diagnostic codes (up to 5 diagnoses), and procedure codes (up to 5) for all hospital admissions were included. The disease diagnoses used in the NHIRD were coded according to the criteria of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). This study was reviewed and approved by the Institutional Review Board of the Ditmanson Medical Foundation Chia-Yi Christian Hospital, Taiwan.

We used the diagnostic codes of the ICD-9 to identify patients with primary diagnosis of AP (ICD-9-CM Code 577.0), and patients who were 18 years old or less at the time of admission were included. We only included the inpatient cases and their first hospitalization record in the analysis. Those for whom information on sex or age was missing were excluded. The mortality cases and the associated risk factors were analyzed according to the diagnostic codes (up to 5) of each case and were classified into different disease category. For example, ''cholelithiasis'' (ICD-9-CM code:574) was classified into biliary tract disease risk factor while ''Injury to gastrointestinal tract'' (ICD-9-CM code:863) was classified into traumatic risk factor. In addition to providing clinical diagnosis, clinical history of receiving total parenteral nutrition (ICD-9-CM codes: V49.89 and 99.15), abdominal ultrasound (ICD-9-CM code: 88.74, 88.76, and 88.79), abdominal computed tomography examinations (ICD-9-CM code: 793.6, V15.89 and 88.38) or endoscopic retrograde cholangiopancreatography (ICD-9-CM code: V45.89, 51.10, 51.11, 52.13, 52.92, 52.14) were included. Medical resource usage refers to the length of hospital stay and hospital charge. The hospital charge comprised of all the cost of blood work and imaging examinations, procedures, medications, nursing treatment, and ward fee. The examinations and procedures done during hospitalization included abdominal sonogram, abdominal computed tomography, endoscopic retrograde cholangiopancreatography, and others. The costs were converted from Taiwan dollars to US dollars using a currency exchange rate of 30:1.

Statistical Analysis

Statistical analysis was performed with SPSS for Windows version 21.0 (IBM Corp, Armonk, NY). Continuous data were presented as the means (± standard deviation, SD) or medians (interquartile range, IQR). Categorical data were presented as numbers and percentages. Descriptive statistics about the distribution of age, gender, LOS, and hospital charges were evaluated by Student's *t* test for continuous variables and expressed as the mean ± standard deviation (SD). Categorical variables were analyzed using contingency (cross-tabulation) tables and the chi-square test or Fisher's exact test when appropriate. Trends in the prevalence of AP patients were analyzed by Cochrane-Armitage trend tests. $P < 0.05$ was considered to indicate statistical significance.

RESULTS

Characteristics of the Study Population

Between 2000 and 2013, there were 2127 patients admitted to hospitals due to AP, representing a hospitalization rate of 2.83 per 100,000 population. The distributions of selected characteristics between the 1061 girls (49.88%) and 1066 boys (50.11%) are summarized in Table 1. Age was slightly higher in the boys ($P = 0.003$). Significant differences between girls and boys were found in average LOS, medical costs, receiving endoscopic retrograde cholangiopancreatography (ERCP) procedures, and association with gallstone/biliary tract diseases ($P < 0.05$).

Incidence of Acute Pancreatitis by Age

The incidence of AP reached a peak at age 4 to 5 years in preschool children, and it became stationary in elementary school children (age 7–12 years). After that, the incidence of AP increased steadily with age, up to above 4.0 for girls and 5.0 for boys per 100,000 population. Both genders presented similar trends (Fig. 1).

Incidence of Acute Pancreatitis by Year

From 2000 to 2013, the incidence of AP showed a significant increase from 2.33 to 3.07 cases per 100,000 population, with an annual increase of 0.05 cases per 100,000 population. Both genders presented similar trends (see Fig. A, Supplemental Digital Content, *http://links.lww.com/MPG/B503*).

Length of Stay and Medical Expenditure of Hospitalization by Year

Girls had longer length of stay (LOS) than boys (7 days vs 6 days, $P < 0.05$). We found that the annual LOS presented a steady rising trend from 2000 to 2007. After reaching a plateau in 2007, the LOS started to decline in both boys and girls (see Fig. B, Supplemental Digital Content, *http://links.lww.com/MPG/B503*). There was, however, a slight rebound in boys in the year 2012–2013. Figure C of the Supplemental Digital Content (*http://links.lww.com/MPG/B503*) shows the medical expenditures of AP patients during the period 2000–2013. We have observed an increasing and steady trend of expenditure (P for trend <0.05) with an increase of US$ 24.58 per year. Girls had a higher medical expenditure than boys. This implies that girls may have more severe clinical courses and longer LOS than boys.

TABLE 1. Characteristics of Acute Pancreatitis in Children Aged <18 Years, National Health Insurance Claims Database of Taiwan, 2000–2013

	Total (N = 2127)	Female (N = 1061)	Male (N = 1066)	*P*
Age, y	11.91 ± 5.38	11.55 ± 5.45	12.25 ± 5.29	0.003
Length of stay, days	6 (3–14)	7 (4–15)	6 (3–13)	<0.001
Medical cost (USD)	711 (322–2955)	857 (346–3683)	640 (300–2053)	<0.001
Level of hospital				
Medical center	954 (44.85)	499 (47.03)	455 (42.68)	0.127
Regional hospital	839 (39.45)	400 (37.70)	439 (41.18)	
District hospital	334 (15.70)	162 (15.27)	172 (16.14)	
Procedure				
Parental nutrition	51 (2.40)	30 (2.83)	21 (1.97)	0.196
Abdomen ultrasound	303 (14.25)	156 (14.70)	147 (13.79)	0.547
CT scan of abdomen	13 (0.61)	7 (0.66)	6 (0.56)	0.774
ERCP	79 (3.71)	55 (5.18)	24 (2.25)	< 0.001
Risk factors				
Biliary/anatomy disease	642 (29.57)	365 (33.12)	277 (25.91)	< 0.001
Metabolic	463 (21.77)	246 (23.19)	217 (20.36)	0.114
Trauma	120 (5.64)	50 (4.71)	70 (6.57)	0.064
Infection	694 (32.63)	344 (32.42)	350 (32.74)	0.840
Hematology/oncology	171 (8.04)	83 (7.82)	88 (8.26)	0.714
Systemic disease	741 (34.84)	373 (35.16)	368 (34.52)	0.759
In-hospital death	35 (1.65)	16 (1.51)	19 (1.78)	0.619

CT = computed tomography; ERCP = endoscopic retrograde cholangiopancreatography.

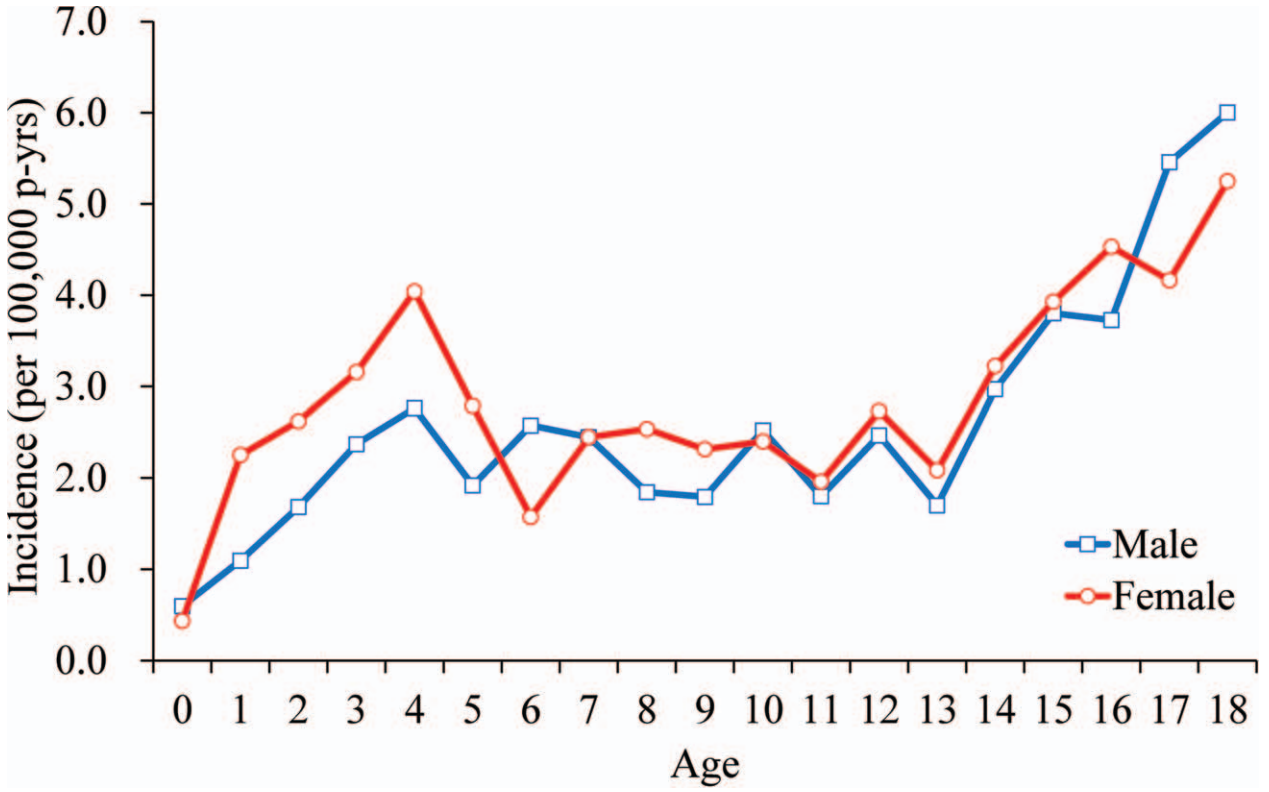

FIGURE 1. Incidence of acute pancreatitis (AP) in children and adolescents by age.

Differences Between Endoscopic Retrograde Cholangiopancreatography and Non-endoscopic Retrograde Cholangiopancreatography Procedure Groups and Factors Associated With In-hospital Mortality

Seventy-nine patients (3.85%) received the ERCP procedure during the study period. We observed that ERCP was more frequently performed in female patients with AP (69.62% vs 49.12%, $P < 0.001$), with a ratio of 2.29 (Table 2). Significant differences were also found in average LOS, hospital levels, and association with gallstone/biliary tract disease as risk factors between ERCP and non-ERCP groups ($P < 0.05$). We also noticed that average LOS, medical cost, hospital levels, and clinical history of parenteral nutrition administration were significant factors associated with in-hospital mortality (all $P < 0.001$, Table 3).

DISCUSSION

This study presents the epidemiology of pediatric pancreatitis in Taiwan and is the first nationwide population-based study in Asian children. The incidence by age had 2 peaks, with the first at age 4 to 5 years old and the second appearing in adolescents. The incidence of AP in Taiwanese children presents a rising trend. The medical cost of AP also increased by years, while the LOS remained stationary during the study period. Girls were noted to have longer LOS and higher medical cost of AP than boys.

During the 14 years of our study period, the incidence of pediatric AP increased from 2.33 to 3.07 cases per 100,000 population (Fig. a, Supplemental Digital Content, *http://links.lww.com/MPG/B503*), similar to the increasing trend noted in Western countries (7–9,19–22), ranging from 3.6 to 13.2 cases per 100,000 children (7,8,19–22). Of course, the increase of AP could be due to increased diagnostic awareness (19). Unfortunately, our dataset did not have the information of specific blood test and we were unable to assess the usage of lipase measurements over the study years. In addition, the advancement of endoscopic and imaging techniques may make the diagnosis of AP more feasible and prompt (23–25). Furthermore, the advance of genetic testing and molecular techniques may also help in revealing the etiology of the previous ''idiopathic'' cases (26,27). At the same time, the associated risk factors or comorbidities are also simultaneously increasing. For example, the prevalence of obesity and incidence of inflammatory bowel disease in Taiwan increased in the same period (28–31).

In addition, the incidence of pediatric AP in Taiwan had 2 peaks by age (Fig. 1). The incidence increased with age since birth, reached the first peak at age 4 to 5 years old and became stationary in elementary school children (age 7–12 years). Then, the incidence increased again in adolescents, which is similar to findings in other pediatric studies (7,8). We suggest that the first peak is due to some congenital causes that are gradually discovered after birth. In contrast, the second peak could be mainly attributed to acquired cases, such as gallstones and biliary diseases, which have been mentioned in several studies (1,7,8,12). Furthermore, the increasing prevalence of obesity in adolescence in recent years also results in the increasing risk of dyslipidemia or gallstone diseases (30,31), further contributing to the rising trend of AP.

The annual LOS presented a steady trend, but the medical cost of hospitalization increased gradually during the study period. These findings are different from previous studies in Western countries in which the LOS decreased during their study period (6,8). This could be explained by different cultural and national conditions between Asian and Western countries. For example, hospitalization fees are generally relatively higher in Western countries. Furthermore, younger children had longer hospital stays and higher medical costs, which was in line with a previous study (32). More difficulty in diagnosis and a longer transition to oral feeding in pediatric patients may result in the longer LOS.

Although female predominance was observed in previous studies (5,7), the incidence of AP was not different between the 2

TABLE 2. Children With Endoscopic Retrograde Cholangiopancreatography

	Non-ERCP (N = 2048)	ERCP (N = 79)	*P*
Sex			
Female	1006 (49.12)	55 (69.62)	<0.001
Male	1042 (50.88)	24 (30.38)	
Age, y	11.92 ± 5.34	11.47 ± 6.17	0.463
Length of stay, days	6 (3–14)	12 (8–18)	<0.001
Medical cost (USD)	674 (315–2601)	3585 (1892–5277)	
Level of hospital			
Medical center	896 (43.75)	58 (73.42)	<0.001
Regional hospital	819 (39.99)	20 (25.32)	
District hospital	333 (16.26)	1 (1.27)	
Procedure			
Parental nutrition	47 (2.29)	4 (5.06)	0.118
Abdomen ultrasound	295 (14.40)	8 (10.13)	0.286
CT scan of abdomen	13 (0.63)	0 (0.00)	1.000
Risk factors			
Biliary/anatomy disease	572 (27.93)	70 (88.61)	<0.001
Systemic disease	728 (35.55)	13 (16.46)	<0.001
Hematology/oncology	166 (8.11)	5 (6.33)	0.569
Trauma	117 (7.91)	3 (3.80)	0.759
Metabolic	460 (22.45)	3 (3.80)	<0.001
Infection	692 (33.79)	2 (2.53)	<0.001
In-hospital death	34 (1.66)	1 (1.27)	1.0000

CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography.

TABLE 3. In-hospital Mortality

	Survival (N = 2092)	In-hospital Death (N = 35)	*P*
Sex			
Female	1045 (49.95)	16 (45.71)	0.619
Male	1047 (50.05)	19 (54.29)	
Age, y	11.90 ± 5.37	12.23 ± 5.60	0.712
Length of stay, days	6 (3–14)	23 (5–43)	<0.001
Medical cost (USD)	693 (318–2734)	16058 (5759–30089)	<0.001
Hospital level			
Medical center	923 (44.12)	31 (88.57)	<0.001
Regional hospital	836 (39.96)	3 (8.57)	
District hospital	333 (15.92)	1 (2.86)	
Procedure			
Parental nutrition	46 (2.20)	5 (14.29)	<0.0001
Abdomen ultrasound	300 (14.34)	3 (8.57)	0.333
CT scan of abdomen	13 (0.62)	0 (0.00)	1.000
ERCP	78 (3.73)	1 (2.86)	1.000
Risk factors			
Systemic disease	710 (33.94)	31 (88.57)	<0.001
Infection	682 (32.60)	12 (34.29)	0.833
Hematology/oncology	163 (7.79)	8 (22.86)	<0.001
Biliary/anatomy disease	637 (30.45)	5 (14.29)	0.039
Metabolic	460 (21.99)	3 (8.57)	0.123
Trauma	119 (5.69)	1 (2.86)	0.520

CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography.

genders in our study. We, however, found that girls had longer LOS and higher medical cost than boys. Menarche, pregnancy, obesity, and the use of oral contraceptives are common risk factors of cholelithiasis (33), which could make girls more susceptible to gallstone disease. That is why there is a significantly higher proportion of girls receiving ERCP procedures (Table 2). Underlying conditions and the performance of ERCP procedures both lead to the longer hospital stay and higher medical cost in girls. A recent study stated that the children with choledocholithiasis underwent ERCP before cholecystectomy may have longer LOS if not having available ERCP proceduralists (34). Similar situation was also noted in Taiwan, and it further supports our argument. In this study, we found that in-hospital mortality rate of AP ranged from 0.35% to 4.2% in the last 14 years (Table 3), without a significant trend or gender difference. The most common risk factor or comorbidity was systemic disease, which was consistent with previous studies (5,11–13).

There are some limitations in our study. First, this is a retrospective secondary data analysis study, and all data were from the Taiwan National Health Insurance Research Database. The AP in this study was defined by the International Classification of Diseases, Ninth Revision codes rather than by clinical, laboratory and radiological findings. There may be some bias due to coding error or inconsistent diagnosis of AP by the institutions and clinicians. Second, unlike other studies using single institute data, the lack of pharmacy data and chart review of our study made it difficult to clarify the true etiology of each case. In addition, as we only focused on the first episode of AP cases, without their following information, we are unable to tell whether the ''risk factors'' were pre-existing conditions or something that developed at the onset of the pancreatitis. Similar limitations have been described in other database research (8). Therefore, our study favors using the term ''risk factor'' or ''comorbidity'' rather than ''etiology'' in the analysis.

CONCLUSIONS

This study presents the epidemiology of pediatric pancreatitis in Taiwan and is the first nationwide population-based study in Asian children. The incidence of pediatric AP in Taiwan is rising. The average hospital stay is steady, but the medical cost of AP has been increasing during the past decade. There is a gender difference in that girls have longer hospital stays and higher medical expenditures than boys. The mortality in cases of AP is mostly associated with systemic diseases rather than AP itself. Further studies are needed to better clarify the etiologies and associated risk factors of AP in children.

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