

# Different clinical presentations of choledochal cyst among infants and older children

## A 10-year retrospective study

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### Abstract

Choledochal cyst is a rare and often benign congenital cystic dilation throughout the biliary tree. Due to the benign nature of choledochal cyst among early-diagnosed patients, the clinical assumption and diagnosis seem to be of utmost significance. Therefore, we sought to assess different clinical manifestations of choledochal cyst and relevant laboratory findings in infants and older children.

Retrospectively, medical records of all patients with the diagnosis of choledochal cyst between 2005 and 2015 were reviewed. Demographic data, initial clinical presentation, positive findings on physical examination, history of any remarkable behavior such as persistent and unexplained crying and poor feeding, and diagnostic imaging modalities were listed. In addition, laboratory values for total and direct bilirubin, alkaline phosphatase, alanine transaminase, aspartate transaminase, prothrombin time, and partial thromboplastin time (PTT) were recorded for each patient. Patients were divided into 2 groups; younger than 1-year-old (infants), and 1 year to 18 years old (older children). Demographic data, clinical data, and laboratory values were compared between the infants and older children.

Thirty-two patients with a diagnosis of choledochal cyst were included in the study: 9 patients (28.12%) were infants and 23 patients (71.87%) were older children. Abdominal pain was the most common presenting symptom (62.5%), followed by nausea/vomiting (59.4%) and jaundice (28.1%). None of the patients presented with the classic triad of abdominal pain, jaundice, and right upper quadrant mass. Seventeen older children (73.91%) presented with nausea and vomiting, while 2 subjects (22.22%) in the infantile group presented with this feature ( $P = .01$ ). Similarly, abdominal pain was found in 20 older children (86.95%); however, none of the infants presented with abdominal pain at diagnosis ( $P < .001$ ). By contrast, the abdominal mass was more detected in infants than the older children (33.33% vs. 0%,  $P = .01$ ). In terms of laboratory values, the median PTT was 44 and 36 s in infants and older children, respectively ( $P = .04$ ).

Infants were more likely to present with abdominal mass and older children were more likely to have nausea, vomiting, and abdominal pain. Furthermore, infants had more prolonged PTT than older children, implying a potential bleeding tendency.

**Abbreviations:** ALP = alkaline phosphatase, ALT = alanine transaminase, AST = aspartate transaminase, CBD = common biliary duct, PT = prothrombin time, PTT = partial thromboplastin time.

**Keywords:** children, choledochal cyst, infant, symptoms

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## 1. Introduction

Choledochal cyst is a rare and often benign congenital cystic dilation throughout the biliary tree.<sup>[1]</sup> The incidence of choledochal cyst has been estimated to be 1 in 100,000 to 1 in 150,000 individuals in Western countries with an even higher incidence in some Asian countries (e.g., 1 in 13,000 in Japan). Some authors speculate that different mechanisms contribute to the formation of the disease. However, the exact etiology still remains unclear.<sup>[1,2]</sup> The most widely used classification of choledochal cyst is based on the site of cystic changes in the biliary tree. Type 1 (most common type) is characterized by a cystic or fusiform dilatation of common biliary duct (CBD). Type 2 is associated with a true CBD diverticulum. Type 3 presents as an intraduodenal choledochoceles. Type 4 consists of 2 other subtypes; type 4A is characterized by multiple intra- and extrahepatic cysts, whereas type 4B is quite rare and it is associated with multiple extrahepatic cysts. Type 5, also known as Caroli disease, is associated with single or multiple intrahepatic cysts in combination with simultaneous extrahepatic diseases.<sup>[3]</sup>

Choledochal cysts are considered benign disorders. However, sometimes their varying clinical presentations among different age groups and delay in diagnosis lead to severe late complications such as malignant transformations, cholangitis, pancreatitis, and cholelithiasis. The classic triad of jaundice, abdominal pain, and abdominal right upper quadrant mass in a female neonate is found only in minority of patients.<sup>14,51</sup> Due to the benign nature of choledochal cyst among early-diagnosed patients, the clinical assumption and diagnosis seem to be of utmost significance. Therefore, we sought to assess different clinical manifestations of choledochal cyst and relevant laboratory findings in infants and older children.

## 2. Methods

The study was approved by the Medical Ethics Committee of Tabriz University of Medical Sciences. Retrospectively, medical records of all patients with the diagnosis of choledochal cyst between 2005 and 2015 in the university-affiliated Tabriz Children's Hospital were reviewed. Demographic data including age, gender, and date of admission were collected. In addition, initial clinical presentation, positive findings on physical examination, history of any remarkable behavior such as persistent and unexplained crying and poor feeding, and diagnostic imaging modalities were listed. In addition, laboratory values for total and direct bilirubin, alkaline phosphatase (ALP), alanine transaminase (ALT), aspartate transaminase (AST), prothrombin time (PT), and partial thromboplastin time (PTT) were recorded for each patient. Patients were divided into 2 groups; younger than 1-year-old (infants), and 1 year to 18 years old (older children). Demographic data, clinical data, and laboratory values were compared between the infants and older children.

Categorical variables were reported as count and proportion; continuous variables were reported as median and interquartile

range. Statistical comparisons were made using Fisher exact test for proportions and the Mann-Whitney test for continuous variables, as determined prior to analysis. A  $P < .05$  was considered statistically significant. Statistical analysis was performed using SPSS for windows (v 19.0, Chicago, IL).

## 3. Results

Thirty-two patients with a diagnosis of choledochal cyst were included in the study: 9 patients (28.12%) were infants, and 23 patients (71.87%) were older children. The diagnosis of choledochal cyst was established in both infants and older children with a combination of ultrasonography (25 patients), computerized tomography (15 patients), and cholangiography (11 patients). We found type 1 and 4 cysts in 23 (71.87%) and 6 patients (18.75%), respectively. However, cyst type was not determined in the remaining patients (9.37%). Abdominal pain was the most common presenting symptom (20 patients [62.5%]), followed by nausea/vomiting (19 [59.4%]) and jaundice (9 [28.1%]). None of the patients presented with the classic triad of abdominal pain, jaundice, and right upper quadrant mass.

Seventeen older children (73.91%) presented with nausea and vomiting, while 2 subjects (22.22%) in the infantile group presented with this feature ( $P = .01$ , Table 1). Similarly, abdominal pain was found in 20 older children (86.95%); however, none of the infants presented with abdominal pain at diagnosis ( $P < .001$ , Table 1). By contrast, the abdominal mass was more detected in infants than the older children (33.33% vs. 0%,  $P = .01$ , Table 1). There were no significant differences in abdominal distension, jaundice, clay-colored stool, and dark urine between the infants and older children ( $P > .05$ , Table 1). Furthermore, 5 older children had 2 of the classic triad symptoms (21.73%), while none of the infants had 2 of the 3 symptoms ( $P = .28$ ).

**Table 1**

**Demographic data, clinical features, and laboratory findings for infants and older children with choledochal cyst.**

Variables	Infants (n=9)	Older children (n=23)	Odds ratio (95% CI)	P
Female, n (%)	5 (55.55)	20 (86.95)	5.33 (0.89–31.91)	.07
Median age at diagnosis, d (IQR)	65 (24.5–224.5)	1218 (841–2552)	—	<.001*
Cyst type, n (%)				
Type I	6 (66.66)	17 (73.91)	—	—
Type IV	1 (11.11)	5 (21.73)		
Undetermined	2 (22.22)	1 (4.34)		
Clinical features				
Nausea/vomiting, n (%)	2 (22.22)	17 (73.91)	9.91 (1.59–61.59)	.01*
Abdominal pain, n (%)	0 (0)	20 (86.95)	NA	<.001*
Abdominal mass, n (%)	3 (33.33)	0 (0)	NA	.01*
Abdominal distension, n (%)	1 (11.11)	0 (0)	NA	.28
Jaundice, n (%)	3 (33.33)	6 (26.08)	0.7 (0.13–3.74)	.68
Achollic stool, n (%)	2 (22.22)	2 (8.69)	0.33 (0.03–2.82)	.55
Dark urine, n (%)	1 (11.11)	2 (8.69)	0.76 (0.06–9.61)	1.00
Laboratory findings				
Median total bilirubin, mg/dL (IQR)	10.5 (0.8–12.4)	1.3 (0.87–2.3)	—	.11
Median direct bilirubin, mg/dL (IQR)	4.6 (0.3–4.9)	0.3 (0.2–0.82)	—	.07
Median alkaline phosphatase, IU/L (IQR)	769.5 (584.75–2422.25)	612 (479–829)	—	.26
Median alanine transaminase, IU/L (IQR)	43 (26.25–100.75)	157 (35–246)	—	.92
Median aspartate transaminase, IU/L (IQR)	62 (46–513)	92 (48–204)	—	.08
Median prothrombin time, s (IQR)	12.5 (11.62–14.75)	12.25 (12–13.12)	—	.94
Median partial thromboplastin time, s (IQR)	44 (34–47)	36 (29.75–39)	—	.04*

CI = confidence interval, IQR = interquartile range.

\* Statistically significant ( $P < .05$ ).

In terms of laboratory values, the median PTT was 44 and 36 s in infants and older children, respectively ( $P=.04$ , Table 1). Other laboratory parameters including total and direct bilirubin, ALP, AST, ALT, and PT did not significantly differ between infants and older children ( $P>.05$ , Table 1).

#### 4. Discussion

The current study revealed that nausea, vomiting, and abdominal pain were the most common presenting symptoms in older children (1–18 years of age at presentation), while abdominal mass was predominant in infants (<1 year of age at presentation). Our finding on nausea and vomiting (as signs of the biliary tract irritation) is in contrast to that of the study by Hung et al<sup>[6]</sup> disclosing no difference in vomiting between the infants and classical pediatric group (1–18 years of age at presentation). In addition, Lipsett et al<sup>[7]</sup> and Edil et al<sup>[8]</sup> found that nausea and vomiting were similar between the children (<16 years old) and adults.

In the present study, we also found that abdominal pain was more common among older children than infants. Similar to our study, Hung et al<sup>[6]</sup> and Fumino et al<sup>[9]</sup> failed to find any abdominal pain in infants, while children had significantly more pain at presentation. Likewise, Tsai et al described a statistically different proportion of abdominal pain presentation between infants and older children (3.8% vs. 50%).<sup>[10]</sup> In addition, majority of the previous studies reported that adults, compared with children, were more likely to present with abdominal pain.<sup>[7,8,10–13]</sup> By contrast, a recent multicenter study by Ouaisi et al<sup>[14]</sup> observed similar proportions of abdominal pain presentation in children and adults. Furthermore, our study demonstrated that the proportion of patients presented with right upper quadrant mass was greater in infants compared with the older children. Consistently, Tsai et al<sup>[10]</sup> concluded that infants more commonly had abdominal mass in comparison with the children and adults. However, other 2 studies carried out in the setting of infants versus older children with choledochal cyst did not find any significant difference with regard to abdominal mass.<sup>[6,9]</sup>

The classic triad of abdominal pain, jaundice, and right upper quadrant mass has been reported in 0% to 22% of the patients.<sup>[5–8,10,11,13,15,16]</sup> In the present study, none of the patients showed the classic triad. Although Tsai et al reported the classic triad in 8/107 (7.47% of their total study population), they noted no difference in proportions of the classic triad among their study groups (infants, children, and adults).<sup>[10]</sup> Nevertheless, an earlier study by Shah et al<sup>[5]</sup> concluded that children were more likely to present with the classic triad. Among 42 children and adults with choledochal cyst, Lipsett et al<sup>[7]</sup> showed that 2 of the 3 classic symptoms were more commonly seen in children; however, our analysis did not result in similar significant difference. Lack of the classic triad in patients with choledochal cyst has been attributed to having access to and seeking medical care at the onset of symptoms.<sup>[13]</sup>

The present study yielded no evidence to suggest a difference between the infants and older children in terms of abdominal distension, jaundice, clay-colored stool, and dark urine. By contrast, the majority of previous investigations of choledochal cyst in infants and children revealed that jaundice was more commonly seen in infants.<sup>[6,9–11]</sup> In addition, our observation about the clay-colored stool is in contrast to that previously reported by Hung et al<sup>[6]</sup>: infants displayed acholic stool more commonly than the children.

Indeed, a few previous reports have indicated changing pattern of laboratory values in the setting of infants and older children. Notably, reports are indicative of bleeding tendency (prolonged PT and PTT) with manifestations such as intracranial hemorrhage, subcutaneous bleeding, bloody stools, or hematuria in infants compared with older children.<sup>[9,17–20]</sup> This rare finding is consistent with our study, in which we observed prolonged PTT in infants than older children. In addition, Tsai et al<sup>[10]</sup> showed that compared with children, infants had higher total and direct bilirubin levels, and lower liver function markers (ALP, AST, and ALT). Our study failed to detect any difference in these laboratory values between infants and older children.

This study had certain limitations. First, relatively small number of patients in our study could be increased by a multi-institutional design or a longer study period. The latter, however, might be challenging due to the less advanced imaging and detection modalities. Second, the study population only included type 1 and 4 cysts, while types of the remaining cysts were undetermined. Third, the present study did not consider operative and postoperative information for determining potential predictive factors for postoperative outcomes and complications. Fourth, we did not include laboratory values for biliary amylase, lipase, and gamma-glutamyl transpeptidase. However, one notable strength of the present study is the evaluation of different clinical presentations in the setting of infants and older children. Our observations on the symptoms and laboratory findings of choledochal cyst in infants could be useful in early diagnosis of the disease and minimizing late complications.

In conclusion, there is a changing pattern of choledochal cyst presentation between infancy and older childhood. Infants were more likely to present with abdominal mass and older children were more likely to have nausea, vomiting, and abdominal pain. Furthermore, infants had more prolonged PTT than older children, implying a potential bleeding tendency.

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