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ORIGINAL ARTICLE

CHOLEDOCAL DISEASE MANAGEMENT: TEN YEARS INSTITUTIONAL EXPERIENCE

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Abstract

Background: Choledocal cysts are congenital anomalies of the bile ducts. 60% of patients are diagnosed during first decade of life; about 20% go undiagnosed until adulthood.

Patients and Methods: seventy patients with CC disease had been managed between 2001 and 2011 at National Liver Institute, Menoufiya University, Egypt. Retrospective analysis of their records performed to evaluate types, frequency, presentation, management and outcome of choledocal disease.

Results: Pediatrics (< 2years) were 30 patients (43%), Pediatrics (> 2 years) were 16 patients (23%), & adults were 24 patient (34%). Type I was recorded in 55 cases (79%), type II in 3 cases (4%), type III in 2 cases (3%), type IV in 3 cases (4%) and type V in 7 cases (10%). Complete cyst excision with HJ had been performed in 82.5%, excision with primary closure of CBD in 4%, left hepatectomy in one case, right hepatectomy in 2 cases and non-operative management in 6 cases (8.5%). Postoperative bile leak occurred in 4%, biliary stricture in 7% with intrahepatic stones in 2.4%. The overall mortality was 8.5% and all were from the pediatric group.

Conclusion: Choledocal disease requires proper diagnosis and treatment to address associated symptoms, risk of malignancy, and disease progression. The presentation of CC varies between different age groups. MRCP is mandatory and could be sufficient in the diagnosis. The majority of cases of biliary cysts (type I and IVA) can be treated effectively with cyst resection and biliary reconstruction.

Keywords: Choledocal disease, Choledocal cyst, Caroli's disease, biliary cysts.

INTRODUCTION

Choledocal cysts (CC) are rare congenital anomalies of bile ducts with higher predominance in females than males. Asian population has the higher incidence than the western population. Japan, alone, reports two thirds of cases in Asian population. However, the reason is still unclear.[1]

In 1959, Alonso-Lej et al. classified CC into 3 types (type I-III). However, the most commonly used classification by surgeons is Modified Todani classification with the addition of type IV and V in 1977. Type I cyst is the dilation of entire extra-hepatic biliary tree without intra-hepatic duct dilation. Type I cyst is further subclassified into 3 types; type IA comprises marked dilation of the entire extra-hepatic biliary system, with sparing of intrahepatic one and the cystic duct arise from the dilated common bile duct (CBD), type IB is defined by focal, segmental dilation of the extrahepatic bile duct

while type IC is fusiform dilation of the entire extrahepatic biliary system. Type II cyst comprises discrete diverticulum of extra-hepatic with narrow stalk connection to CBD. Type III cyst, choledochocele, comprises the dilation of CBD confined to wall of duodenum which may bulge into duodenal lumen. Type IV cyst is subclassified into type IVA of complete intrahepatic and extrahepatic dilations, and type IVB of multiple dilations of extrahepatic tree only. Type V cyst, known as Caroli disease, is multiple saccular or cystic dilations of intrahepatic ducts.[2]

Many theories have been postulated explaining the pathogenesis of CC; however, the exact etiology is still unclear.[3] It is well known that CC is a premalignant condition in which the overall risk of malignancy has been reported to be 10-15% and increases with age. Types of malignancy vary as adenocarcinoma comprises 73%-84%, anaplastic carcinoma 10%, undifferentiated cancer 5%-7%, squamous cell carcinoma 5% while other carcinoma is 1.5 %.[4]

Only minority of cases presents with the classical triad of abdominal pain, jaundice and right upper quadrant mass. Eighty five percent of children often presents with at least two features of the triad compared with only 25% of adults. Patients may present with cholangitis, pancreatitis and biliary peritonitis, however asymptomatic presentation also occurs.[3]

Ultrasonography (US) is the best initial methods but less accurate in adults who have more secondary benign and malignant causes for bile duct dilation. Computed Tomography (CT) is used for differentiating large cystic lesion at portahepatis from other possible cysts. Magnetic resonance cholangiopancreatography (MRCP) is highly sensitive, safe and non-invasive tool for biliary pathology as it supervenes endoscopic retrograde cholangiopancreatography (ERCP).[3]

The type of CC defines the management. Treatment of types I and IV includes cyst excision and hepatico-enterostomy whether by hepatico-duodenostomy or Roux-en-Y hepatico-jejunostomy (RYHJ), however, the latter has higher success rate. Early complications include pancreatic leak, anastomotic leak and bowel obstructions while late complications include cholangitis, biliary calculi, pancreatitis, liver failure and cancer. Type II is treated by simple excision and primary closure. Recently, endoscopic sphincterotomy is accepted to be sufficient treatment for type III but patient should be under endoscopic surveillance since malignancy has been reported in choledochoceles.[3]

In type V, Caroli's disease, when the intrahepatic duct dilation is localized and without congenital hepatic fibrosis, segmental hepatectomy can be done. Percutaneous or endoscopic drainage and stent are used for palliative treatment. For diffuse disease with life-threatening complications, liver transplantation should be considered. In a review of 110 cases of liver transplantation for Caroli's disease or syndrome, a 5-year patient and graft survival was observed to be 86% and 71%, respectively.[1,3]

The aim of this study is to evaluate frequency, mode of presentation, approach for management, and outcome of different types CC, along 10 years duration, at a tertiary referral and expertise centre of HBP surgery.

MATERIAL AND METHODS

This retrospective study was held from the period of 2001 to 2011 at National Liver Institute, including all patients (70 patients) diagnosed as having CC.

The following data were collected from patient files:

- Personal data; age, sex, then these patients were classified into adults and pediatrics. Pediatrics were defined as being less than 18 years and were further categorized; less or more than 2years.
- Presenting symptoms: either the classical triad (of abdominal pain, jaundice and mass in right upper quadrant), jaundice alone, recurrent abdominal pain or by cholangitis (pain, fever with or without jaundice).
- Pre-operative classification: according to modified Todani classification based on imaging studies.
- Imaging study: US, MRCP, or CT scan.
- Laboratory investigations; total leucocytic count, serum albumin, bilirubin (total and direct), alkaline phosphatase, gamma-glutamyl transferase, Carcinogenic Embryonic Antigen (CEA) and Carbohydrate Antigen 19-9 (CA19.9).
- Endoscopic or radiological intervention performed for any patient.
- Operative data; intraoperative findings, surgical procedure, operative time, data of re-exploration (if any), and operative management of any complications.
- Post-operative data; drain output (nature and amount) and presence of postoperative complications and its management.
- Follow up visits were recorded and as well as survival and mortalities.

Statistical Analysis: Data were collected and SPSS (Statistical Package for Social Science) program were used for statistical analysis. Descriptive statistics: Quantitative data were shown as mean, SD, and range. Qualitative data were expressed as frequency and percent. P-value was considered statistically significant when it was less than 0.05.

RESULTS

Seventy patients were included in this study. Forty six patients (66%) were from pediatric group (24 patient are <2years and 22 are >2years) with female predominance in total patients (64%) (Table1).

Table 1. Gender distribution among pediatrics and adults.

	Pediatric	Adult	Total
Male	21	4	25 (36%)
Female	25	20	45 (64%)
Total	46 (66%)	24 (34%)	

According to Todani's classification, 79% of the patients had type I, (4%) type II, (3%) type III, (4%) type IV and (10%) type V (Table 2).

Table 2. Types of CC in pediatrics and adults.

	Pediatric(n=46)	Adult(n=24)	Total
Type I	40	15	55 (79%)
Type II	1	2	3 (4%)
Type III	1	1	2 (3%)
Type IV	1	2	3 (4%)
Type V	3	4	7 (10%)

As regards the presenting manifestations in our patients according to the age groups: jaundice alone represented the most common presentation among the pediatric group; in 32 patients (69.6%), other manifestations included recurrent attacks of cholangitis, right upper quadrant (RUQ) pain and the classical triad of abdominal pain, jaundice and palpable mass. on the other hand, among the adult group, cholangitis represented the most common presenting symptom; in 14 patients (58.3%), followed by RUQ pain in 10 patients (41.7%). None of the adults presented with the classical triad or jaundice alone (Table 3).

As regards the presentation according to each type of CC (shown in table 4); The main presentation of type I CC in pediatric group was jaundice alone; which was recorded in 30 (75 %) out of 40 patients, followed by the classical triad, while in adult group RUQ pain was the most frequent presentation; that was recorded in 11 (73.3%) out of 15 patient, followed by cholangitis. All patients with type III presented with RUQ pain, while all patients with type IV presented with cholangitis. The majority of type V patients presented with cholangitis; in 6 (85.7%) out of the 7 patients.

Table 3. Various presentations of both groups.

	Pediatric(n=46)	Adult(n=24)	Total(n=70)
Cholangitis	4 (8.7%)	14 (58.3%)	18 (25.7%)
RUQ pain	5 (10.9%)	10 (41.7%)	15 (21.4%)
Jaundice	32 (69.6%)	-----	32 (45.7%)
Classical triad	5 (10.9%)	-----	5 (7.1%)

Table 4. Various presentation in relation to types of CC.

Type	No	Pediatric (n=46)		Adult (n=24)	
Type I	55	Jaundice	30 cases	RUQ pain	11cases
		Classical triad	5 cases	Cholangitis	4 cases
		RUQ pain	4 case		
		Cholangitis	1 cases		
Type II	3	Jaundice	1 case	RUQ pain	2 cases
Type III	2	RUQ pain	1 case	RUQ pain	1 case
Type IV	3	Cholangitis	1 case	Cholangitis	2 cases
Type V	7	Cholangitis	2 cases	Cholangitis	4 cases
		Jaundice	1 case		

The diagnosis of Choledocal cyst was reached by abdominal ultrasound and MRCP in all patients. MRCP is performed for all cases (figures 1, 2, 3, and 4). The diagnosis was reached by MRCP in 68 patients. The remaining 2 patients were one patient Type II CC and the other one had Type III CC. The diagnosis of them was reached during exploration and by using of intraoperative cholangiogram in the patient with type II CC, and by ERCP in the type III case. The sensitivity of MRCP in detecting type I was 100%, with overall sensitivity 97.1%. Ten patients (14.3%) needed abdominal CT scan to confirm the diagnosis and to verify the extension of types IV & V (Fig. 5).

Five patients (7.1%) underwent endoscopic retrograde cholangiopancreatography (ERCP); which was for therapeutic purpose in the 2 patients with type III CC, while in the other 3 patients, it was performed for

management of sever attaches of cholangitis for urgent drainage (with stent insertion).

The way of management was tailored according to the type of Choledocal cyst. In all patients of type I, surgical management was done in the form of complete cyst excision and RYHJ. The 3 patients of type II were managed surgically by cyst excision and primary closure of CBD in transverse V manner. The two patients with type III underwent ERCP with sphincterotomy and stent insertion. In cases of type IV the 3 patients were managed surgically by excision of the whole extra-hepatic biliary system with high RYHJ. (figures 6, 7, 8).The management of type V cases was variable; surgical management was done in 3 cases in whom the disease was confined to one hepatic lobe and lobectomy was done in these patients (left lobectomy in one patient and right lobectomy in 2 patients). The other 4 cases of type V had diffuse bilobar cysts which were complicated by liver abscesses due to 2ry infection and were managed by US guided drainage using pigtail catheters.

The early outcome of type I cases was uneventful in 52 patients (94.5%) and only 3 (5.4%) patients had early post-operative biliary leak (BL). The diagnosis of BL became obvious by the 5th postoperative day. The amount of drain output ranged 100-350 ml/day. Operative drain achieved good control of BL without residual abdominal collection in 2 cases, while US guided drainage of bilious abdominal collection was needed in one patient. Conservative management by close observation was successful with spontaneous cessation of minor leak in two patients, while, the 3rd case was explored wherein re-anastomosis was done with good successful outcome.

Four cases (7.3%) out of the 55 patient in type I had late onset biliary stricture. These cases presented from 2 to 7 years after management. The presenting symptoms were jaundice, recurrent epigastric pain or cholangitis. The diagnosed was confirmed by MRCP. The four patients were managed surgically by redo RYHJ (Fig. 9). Intrahepatic stones were discovered in 2 cases with long standing BS (Fig. 10).

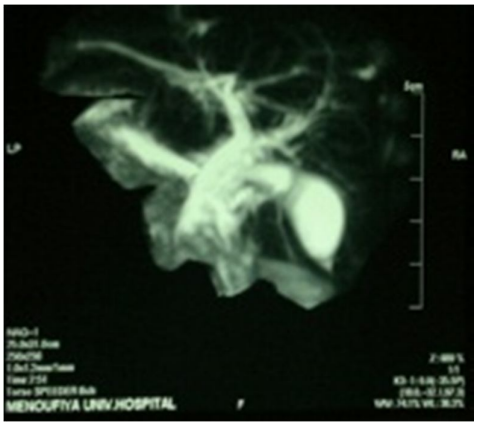


Fig 1. Type I CC.

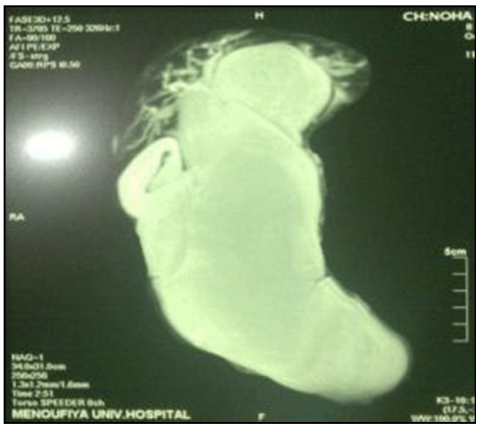


Fig 3. Type IV CC.

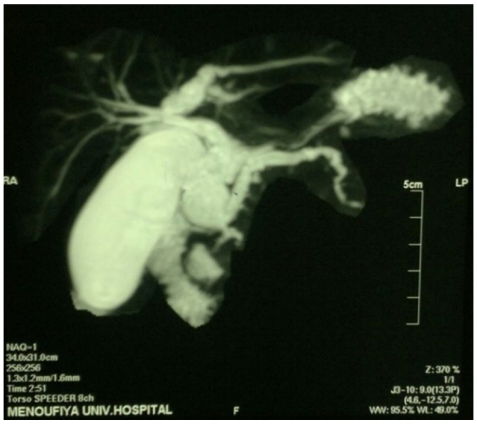


Fig 2. Type III CC.

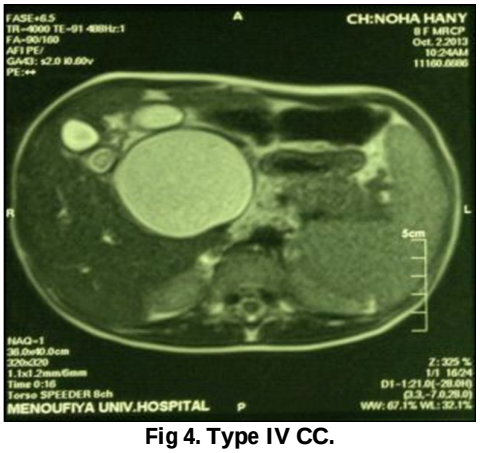


Fig 4. Type IV CC.

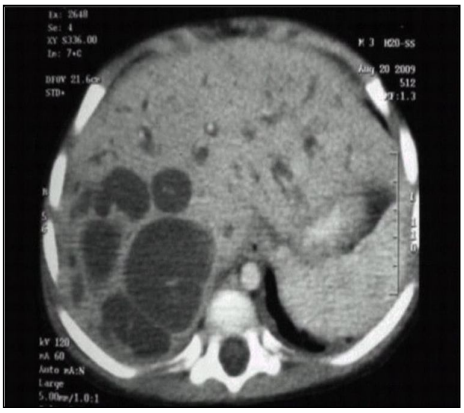


Fig 5. Type V CC.

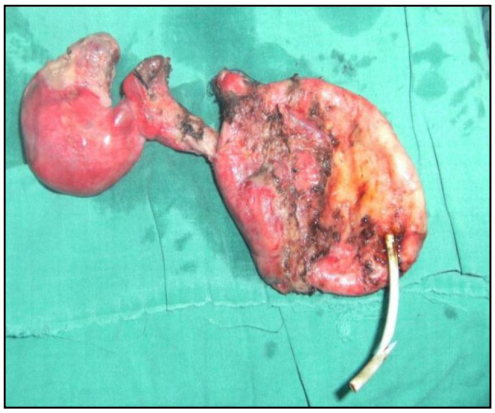


Fig 8. Excision of extra hepatic biliary system with CC with stent.

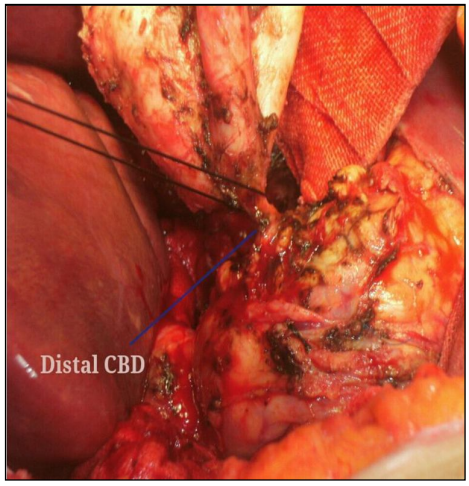


Fig 6. Complete Excision of extra-hepatic biliary system.

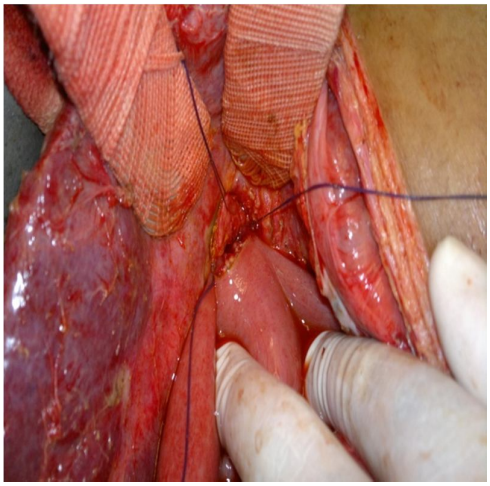


Fig 9. Redo of RYHJ.

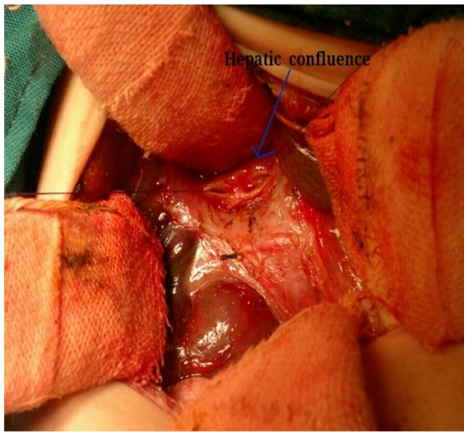
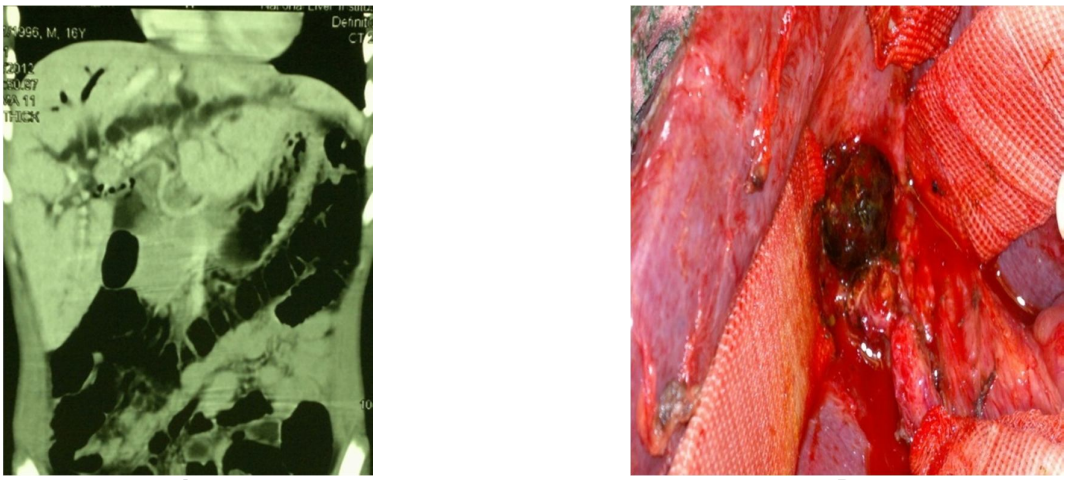


Fig 7. Hepatic confluence prior to RYHJ.



A B

Fig 10. A) Saggital CT view of intra-hepatic stones in 15 years old child post-RYHJ. B) Intra-operative view of the stones.

Complete recovery occurred in one patient of type II cases while the other one had biliary stricture 2 years later and was managed by redo RYHJ. There is no available follow up data about post management outcome for the patients with type III.

Table 5. Treatment and outcome of the cases according to the type of CC.

Types	No	Type of management		Outcome (management)	
Type I	55	Cyst excision and RYHJ	55 cases	BL (treated conservatively in 2, and reanaestemosis in 1)BS (redo RYHJ)	3 cases 4 cases
Type II	3	Cyst excision and 1ry repair of CBD	3 case	Successful outcome BS (RYHJ)	2 cases 1 case
Type III	2	Endoscopic sphincterotomy	2 cases	No available data	
Type IV	3	Complete excision of extrahepatic biliary system and high RYHJ	3 cases	Successful outcome Died from septicemia	1 case 2 case
Type V	7	left hepatectomy right hepatectomy percutaneous drainage of abscesses	1 case 2 cases 4 cases	Successful outcome Successful outcome all died from infection and liver failure	1 case 2 cases 4 cases

There was successful outcome in one case of type IV and the 3 cases of type V who managed by liver resection. Two patients with type IV died due to septicemia after recurrent cholangitis and multiple liver abscesses as well as the 4 patients with bilobar cysts of type V died from infection and liver failure.

DISCUSSION

Biggest series of CC is reported in Asian people however, this study encounters large series outside Asian population as it was done in a referral centre. Previous large series was analyzed in Vancouver, British Colombia reporting 70 patients from all age groups between 1971 and 2003, however, the authors concluded it was secondary to the large Asian population in this

area.[5] In the current study, a number of 70 patients had been reported in a single centre experience along 10 years, owing to that it is a referral tertiary centre expertise in HBP surgery, also, our results revealed female preponderance (64%) which is supported by the literature.[6] However, the reason for this preponderance remains unclear.

According to Todani classification, 5 types of CC were described; the majority of cases in our study were type I followed by type V. However, previous study reported that the most common are type I and type III.[2]

Among pediatrics in this study, jaundice was observed in 32 patients (69.6%), however, the classical triad was found in 5 patients (10.9%) of pediatrics and none of adults presented with this triad. Reported literature supports our results as this triad is present in <20% of patients and was mainly found in pediatrics.[7,9-11]

Choledocal cysts become usually symptomatic due to associated complications of ascending cholangitis and pancreatitis.[7] Complications result from stasis of bile, stone formation, recurrent superinfection and inflammation. Ductal stricture and dilated cysts caused by chronic inflammation lead to proximal bile stasis with subsequent stone and sludge formation in addition to infected bile. Those factors cause ascending cholangitis and more obstruction with resultant classical symptoms of episodic pain, obstructive jaundice and fever.[8] Attacks of cholangitis had been recorded in overall 18 (25.7%) patients in our study, this included 14 adult (58.3%) and only 4 (8.7%) of the pediatric group. In the other hand jaundice-only represented the dominant symptom in pediatric group in 32 (69.6%) patient. Cholangitis signifying biliary infection and jaundice indicating biliary obstruction are considered as an evidence of complicated disease that mandate urgent management.

MRCP is non-invasive modality in delineating anatomy of biliary system and its sensitivity for diagnosis has been reported to be as high as 90-100%.[12] Pre-operative modalities in diagnosis of CC in our study depended mainly on US and MRCP. Ultrasound is considered as the first imaging modality generally used for the biliary system, however, MRCP is mandatory in all suspicions cases. The sensitivity of MRCP in detecting type I was 100%, with overall sensitivity 97.1%.

Although ERCP and percutaneous transhepatic cholangio-pancreatography (PTC) were previously used for cases of CC, their use is falling due to many reasons. Those include invasiveness and subsequent complications such as cholangitis and pancreatitis. [1] In the current study, ERCP was indicated in cases of type III for therapeutic purposes, with inability to assess its outcome due to lack of post ERCP follow up data. In cases who underwent ERCP prior to operation for drainage purpose; surgical dissection were more difficult probably due to associated sever pericholedochitis, which could be explained by ERCP and stent insertion.

In 1924, Mcwhorter first described cyst excision and RYHJ that was initially abandoned due to its complications, but it becomes now the surgery of choice.[13,14] It excises both the damaged and presumably premalignant cyst tissue. Again, if any cyst tissue is left in situ, the risk of malignancy in remained part is as high as 50% and occurs 15 years earlier than primary malignancy.[15] Therefore, the cyst should be excised completely from hepatic hilum to pancreatic duct.[16] As regards the operative procedure performed for our patients, all cases with type I and type IV underwent cyst(s) excision and RYHJ and high RYHJ in type IV.

Early complications of cyst excision and RYHJ include anastomotic leak, pancreatic leak with injury to pancreatic duct, bowel obstruction due to intussusceptions, bowel kinking due to manipulation or adhesions. Late complications include peptic ulcer disease, cholangitis, biliary calculi, pancreatitis, liver failure and cancer.[2,17] Our study revealed early post-operative bile leak in 3 patients (4.2%) 2 of whom were treated conservatively and only one case needed re-operation. and 4 patients (5.7%) had late biliary stricture with intra-hepatic stones in 2 cases, and the all 4 cases underwent redo of RYHJ.

Type II and III CC have exceedingly low risk of malignancy thus complete excision is not necessary. However, simple excision of Type II is sufficient and choledochocele often need endoscopic sphincterotomy to allow free drainage of bile and stones.[18,19] In this study, patients with Type II CC underwent excision of the cyst and primary closure of common bile duct in transverse V manner. Of those, one had biliary stricture which was managed by RYHJ. Type III patients has ERCP with sphincterotomy but no available data was present later.

Surgical approach in type IVA is still debatable, usually due to presence of intra hepatic pathology. Some authors suggest that the excision of extrahepatic biliary system and high RYHJ (as mentioned before) is accepted irrespective of the changes. In case of extensive intra hepatic dilation accompanied by complications as cholangitis, lithiasis, or biliary cirrhosis, other modalities should be considered. Those include hepatic resection in unilobar cysts and liver transplantation in bilobar disease.[3] In our study, only one patient was managed successfully while the other 2 patients died from septicemia.

Treatment of Type V (Caroli's disease) remains difficult. Type V, when localized, can be treated by hepatic lobectomy while diffuse disease needs liver transplantation.[1,20,21] Our study included one patient with type V underwent left hepatectomy, 2 patients; right hepatectomy with successful outcome, while 4 patients had bilobar cysts and were managed non

operatively by percutaneous drainage of intra-hepatic abscesses but they all died due to repeated infection and liver failure. In these 4 patients; liver transplantation (LT) was considered as rescue management. Unfortunately, two of them died before the start of our LT program and LT was not performed for the other 2 cases due to unavailability of suitable donors.

Causes of mortality in cases of CC are usually present in type IV and type V due to recurrent infection, recurrent attacks of cholangitis, septicemia, biliary cirrhosis and liver failure.(1) This match with the our results which reported mortality in 6 patients (8.5%), two patients with type IV, underwent RYHJ, died from multiple liver abscesses and subsequent septicemia, and 4 patients with Caroli's disease who had recurrent infection and liver failure.

In conclusion the presentation of CC varies between different age groups; with jaundice predominate in pediatric and cholangitis in adults. MRCP is mandatory and could be sufficient in the diagnosis; however, the role of ERCP is limited only to the management of type 3 CC. The majority of cases of biliary cysts (type I and IV) can be treated effectively with cyst excision and biliary reconstruction with low incidence of morbidity. While operative therapy decreases the risk of subsequent cancer, patients continue to require long-term surveillance for recurrent cholangitis, intrahepatic stones, postoperative biliary strictures, and malignancy. Highest risk of mortality occurs in type IV and V if neglected.

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