

## Frank Intrabiliary Rupture of the Hepatic Hydatid Cyst Associated predictive Factors

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### ABSTRACT

**Aim:** to highlight the prediction of frank intrabiliary rupture (IBR) of liver hydatid disease **Design:** a prospective study of patients with hepatic hydatid cyst (HHC) presented between May 2013, and January 2015, in the Gastroenterology and Hepatology teaching Hospital. **Setting:** a tertiary care of Gastroenterology and Hepatology teaching Hospital. **Patients:** The clinical findings in 143 patients with a HHC were reviewed. Of the 143 patients, 32 (22%) had a cyst-biliary communication: 18 out of 32 (56.2%) had an occult rupture, and 14 out of 32 (43.7%) had a frank rupture. **Results:** Frank IBR was associated with significantly older age (median, 52 vs. 45 years), more in male patients (55.5%), longer duration of symptoms (53.8%), cysts larger than 10 cm (60%) and higher incidence of solitary (62.5% vs. 37.5%), left lobar (66.6%). **Conclusion:** Patients with large (=10 cm), multivesicular, solitary, left lobar Hydatid Cyst as well as those with prolonged history are at increased risk of frank IBR and should be offered early therapeutic intervention.

**Key words:** Hepatic Hydatid Cyst (HHC), Intrabiliary Rupture (IBR)

### Introduction:

Hydatid disease is endemic in most countries of the Middle East including Iraq<sup>1</sup>. Although, it is uncommon in Western countries, recent reports indicate an increase in incidence that is perhaps related to an increase in worldwide travel and immigration to non-endemic areas<sup>2</sup>. The liver is the commonest organ affected as it becomes involved in 45-75% of patients<sup>3</sup>. Hepatic hydatid cysts (HHC) are liable to serious complications such as infection, and leak or rupture into the biliary tree, the peritoneal cavity, pleural space, lung, and abdominal viscera. The onset of complications in Hepatic Hydatid disease marks a significant increase in operative morbidity compared with uncomplicated cysts [e.g. 55% vs. 25% in one study<sup>2,3,4</sup>]. Frank intrabiliary rupture (IBR) complicates 3- 17% of patients with hepatic hydatid disease<sup>5</sup>, and is characterized by the development of a cyst-biliary fistula that allows the escape of cyst contents such as daughter cysts into the biliary tree with subsequent onset of obstructive jaundice, infection of the HHC and cholangitis<sup>4,5,6</sup>. Frank IBR is recognized preoperatively from the presentation with obstructive jaundice and biliary dilatation with or without concomitant sepsis, and at the time of surgery as the cyst contents are invariably bile stained or infected, a cyst-biliary fistula may be detected, and the common bile duct is often dilated. This complication escalates the magnitude of

surgery, as cystectomy ought to be combined with a bile duct exploration with dilatation or division of the sphincter. It is not surprising therefore that frank IBR is associated with higher perioperative morbidity (6-54%)<sup>7,8</sup> and mortality (2.5-10%)<sup>8</sup>. Compared to patients with uncomplicated hydatid liver disease [morbidity, 2.5-14%<sup>9</sup>; mortality, <1%<sup>9</sup>]. Even the onset of occult IBR, which is recognized at the time of surgery as a minimal ooze of bile from the ectocyst after removal of the HHC or just bile stained of hydatid cystic content, may be associated with an increase in operative morbidity<sup>10</sup>, and postoperative hospital stay<sup>10</sup>, compared with surgery for uncomplicated HHC. There are several classifications of the communication between the cyst and the biliary tree. The most accepted divides communication according to their size: smaller communication is called simple communication (1037% of patients with liver hydatid cyst), which is a small communication between the cyst wall and small biliary radicals; some authors subdivided these breaks into honest (bile within the cyst), insidious (after opening no bile in the cyst)<sup>9,10,11</sup>, or frank IBR (317% of patients with liver hydatid cyst). Frank intrabiliary rupture is an open wide communication between the cyst and the bile duct allowing the contents of the cyst to drain directly into the bile duct and could cause obstructive

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jaundice, cholangitis, cyst infection, or anaphylaxis<sup>10,11</sup>. There are other classifications of the communication between the cyst and the biliary tree; Lewall et al. distinguished three clinical forms of communications: contained rupture, communicating, and frank intrabiliary rupture<sup>11,12</sup>. Cysto-biliary communications have also been classified depending on the location in tangential (side to side) or terminal (end to side), or according to the caliber of the affected BD: small or large caliber (sectorial, right or left duct) and by size (smaller or larger than 5 mm)<sup>11,12</sup>. The walls of the liver hydatid cyst with frank intrabiliary rupture are usually fibrotic or calcified<sup>13,14</sup>. El Malk et al. identified (univariate analysis) that a fibrotic or calcified pericystic wall, preoperative jaundice, cyst Gharbi type IV and recurrent disease were predictors of communication between the cyst and the biliary tree<sup>15,16</sup>. Other predictors described are male sex, older age group, high preoperative ALP, GGT, and bilirubin or the presence of nausea and vomiting<sup>16,17,18</sup>. The presence of a frank IBR usually causes the death of the parasite due to the destruction of the germinative layer in contact with bile, but may produce a superimposed infection of the cystic cavity by secondary infection<sup>18</sup>. Atli et al. recommended preoperative ERCP in the liver hydatid cyst Gharbi type IV and diameter greater than 10.5 cm<sup>19,20</sup>. ERCP with sphincterotomy allows the evacuation of the biliary tract, treats cholangitis and biliary obstruction if present, and allows a scheduled intervention<sup>20,21</sup>. In some elderly patients with significant comorbidities, ERCP can also be used as the sole treatment of frank intrabiliary rupture associating oral albendazole<sup>21,22</sup>. In a variable percentage (0-30%) of patients who underwent ERCP for suspected frank intrabiliary rupture (jaundice, dilated bile duct, and liver hydatid cyst); no frank intra-biliary rupture is identified, only bile duct compression by the cyst, but after ERCP, cholangitis and jaundice usually resolve<sup>22,23</sup>.

#### Aim Of The Study:

The aim of this study is to highlight patient-related factors and HHC characteristics that may independently predict the development of frank IBR.

#### Patients And Methods:

A prospective study of 143 patients who were presented to the Gastroenterology and Hepatology Teaching Hospital, from October 2013 to February 2015 with liver hydatid cysts. A Special Form was used that were included the detailed history, examination, laboratory tests, imaging, interventions and outcome for each patient were reported. All patients were evaluated by clinical assessment, hematological and biochemical profile. Then the diagnostic work up was directed for establishing the site, size, number,

biliary communication and intra-biliary rupture of liver hydatid cysts. These works up include abdominal ultrasound for all patients. CT of the liver, MRI of the upper abdomen and MRCP for some patients. Detailed operative findings including the number, site, content (univesicular or multivesicular), and the presence of frank Intrabiliary rupture as well as the presence of occult IBR was described. Patients who had frank IBR were compared with those with occult IBR with regard to the patient demographics (age and sex distribution), duration of symptoms, cyst characteristics (size, site, content and cyst multiplicity). Data was analyzed; Results were expressed in numbers (percent).

#### Results:

During the period from October 2013 to February 2015, Frank IBR was detected either Intraoperatively or via ERCP in 32 patients (22.3%). Female patients were 23 (71.8%) while male patients were 9 (28%), female to male ratio 2.1: 1. (Table 1) The highest age distribution were between 50-60 yrs. (Fig. 1) The most common symptom was pain on the right-upper quadrant in 11 patients (92.8%). Jaundice was seen in 13 patients (92.8%) and fever in 11 patients (78.5%). (Table 2) Blood tests were labeled with and without frank intrabiliary rupture as shown in (Table 3) Ultrasonography was done for all patients with hydatid liver disease, out of 14 patients with frank intrabiliary rupture, ultrasonography was sensitive to 11 (78.5%), while preoperative diagnosis of frank intrabiliary rupture was 8 out of 11 patients (72.7%) had CT scan imaging test. The magnetic resonance cholangiography (MRCP) done for 12 patients, 10 of them (83.3%) was diagnosed as having frank intrabiliary rupture. (Table 4)

The presence of frank IBR among cysts of 10cm or more in diameter was higher than that of smaller cysts (6 of 10 patients, 60% vs. 8 of 22 patients, 36.3%). Although HHC with frank IBR were more frequently located in the right lobe of the liver (n=17, 53.1%) than in the left lobe (n=6, 18.75%) or bilaterally (n=9, 28.1%), the incidence of frank IBR was significantly higher amongst left lobe cysts (4 out of 6 patients, 66.6%) than right lobe cysts (7 out of 17 patients, 41.1%) or bilobar cysts (3 out of 9 patients, 33.3%). Multivesicular cysts were significantly more likely to be complicated with frank IBR compared with univesicular cysts (8 of 14 patients, 57.1% vs. 6 of 18 patients, 33.3%) and so were solitary cysts compared with multiple cysts (5 of 8 patients, 62.5% vs. 9 of 24 patients, 37.5%). (Table 5)

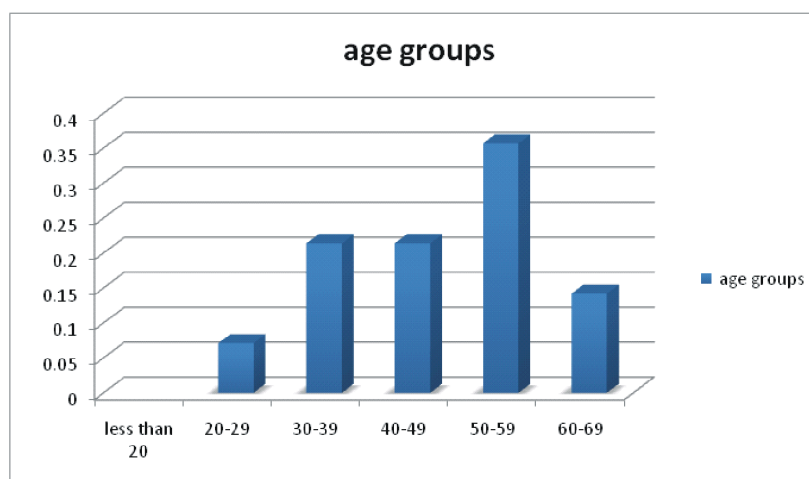
Endoscopic retrograde cholangiography with ES was performed in 4 of the 14 patients with a frank communication: the cyst was completely drained in 1 patient, while the other patients, after passing hydatid material into the common bile duct (CBD),

underwent an operation and bile leakage was sutured without CBD exploration. Cholecystectomy, choledochotomy, evacuation and lavage of the CBD, and endocystectomy were performed in the remaining patients.

Closure of the CBD with T-tube drainage was carried out in 4 patients. External drainage with or without omentoplasty was performed for the management of the cyst cavities. All patient's operative procedures with liver hydatid cyst are reported in Tables 6.

**Table 1. Distribution of patients according to their gender**

Gender	No.	Frank rupture (%)	Occult rupture (%)
Female	23(71.8%)	9(39.1%)	14(60.8)
Male	9(28.1%)	5(55.5%)	4(44.4%)
Total	32	14(43.7%)	18(56.2%)



**Fig. 1: Age distribution of the patients with frank intrabiliary rupture**

**Table 2. The dominant symptoms of patient with frank hydatid intrabiliary rupture**

Symptoms	No. (14)	%
Symptomless	-	0%
RUQ pain	13	92.8%
Fever	11	78.5%
Jaundice	13	92.8%
Pruritus	13	92.8%
Vomiting	10	71.4%
Weight loss	9	64.2%

Nearly all patients had more than one symptom

**Table 3. Laboratory results of patients with and without frank intrabiliary rupture**

Investigations	Patients with frank rupture (no.14)	Patients without frank rupture
T.S.B (mg/dl)	3.9±2.5	1.5±1
W.B.C count * 10 <sup>9</sup> /L	12±6	6±2
SGOT	85±50	30±15
ALK.PH u/l	270±120	110±45

**Table 4. Organ imaging, intervention and detection of frank intrabiliary rupture**

Imaging study	No. Of patients (14)	Frank Intrabiliary rupture diagnosis
Ultrasonography	14	11(78.5%)
CT Scan	11	8(72.7%)
MRI and MRCP	12	10(83.3%)

**Table 5 Comparison of characteristic in patients with and without frank cysto- biliary communication.**

		Patients no.32	Frank rupture 14(%)	Occult rupture 18(%)
<b>Age (year)</b>	Mean =50	18	7(38.8%)	11(61.1%)
	>50	14	7(50%)	7(50%)
<b>Gender</b>	Female	23	10(43.4%)	13(56.5%)
	Male	9	4(44.4%)	5(55.5%)
<b>Number of cyst</b>	Single	8	5(62.5%)	3(37.5%)
	Multiple	24	9(37.5%)	15(62.5%)
<b>Size of cyst (cm)</b>	<10	22	8(36.3%)	14(63.6%)
	>10	10	6(60%)	4(40%)
<b>Localization of cyst</b>	Right Lobe	17	7(41.1%)	10(58.8%)
	Left Lobe	6	4(66.6%)	2(33.3%)
	Bilobar	9	3(33.3%)	6(66.6%)
<b>Type of cyst</b>	Unilocular	18	6(33.3%)	12(66.6%)
	Multilocular	14	8(57.1%)	6(42.8%)
<b>Duration of symptoms</b>	≤6 months	19	7(36.8%)	12(63.1%)
	>6 months	13	7(53.8%)	6(46.1%)



### Discussion:

Hydatid disease is a major economic and public health problem in Iraq causing a great morbidity and mortality, which attributed in most of the cases to the cyst complications<sup>(1,2)</sup>. It is clinically relevant therefore to identify patients with HHC who are at risk of developing IBR.

The highest incidence of frank rupture occurred in the ages between 30-60 years which is similar to other study, Zeki A. Al-Fadagh et al. found that the highest incidence of liver hydatid cyst complications between ages 20-50 while Zuhair R Al-Bahrani et al. found that the age incidence ranges between 30-60. This is explained by the fact that these age groups are the most active worker groups and most of their meals are from unhealthy sources outside their home. Our study shows gender incidence of about 1:2 (M: F) and the complication will be more in female groups, this is because most of our patients comes from rural areas where females are farmers and used to deal with animals and they don't care to disinfect their contaminated food & vegetable, this gender difference is close to Jawed Akther et al. And Metin Ertemet al. Study; although we noticed in our study that frank rupture occurred more in males than females (44.4% vs. 43.4%) similar to study done by Pircoveanu M et al, this may be due to that male more get involved in harder and more tough physical action which render them more subjected to physical trauma.

The main presenting symptom was Upper abdominal pain reported in (92.8%) patients. In a series of 70 patients with liver hydatidosis reported by Little et al, 60% complained of right upper- quadrant abdominal pain or lower chest pain at some time in the illness. (92.8%) reported that they had been jaundiced at some time in the past or were jaundiced on admission to the hospital, mainly due to debris works as a stone thus causing symptoms such as jaundice, biliary colic, transaminasemia, and cholangitis. same finding reported in many studies<sup>(3,5,7)</sup>.

that found higher presenting sign and symptoms were jaundice & RUQ abdominal pain. 9(64.2%) patients presented with features of cholangitis, in which, 4 of them were labeled as emergencies and subjected to an emergency ERCP, 3 of them healed completely. In a study done by T.S. Papavramidis et al. mentioned that endoscopy plays a significant role in the nonsurgical management of intra- biliary rupture of the hydatid. In patients presented with obstructive jaundice or cholangitis, endoscopic sphincterotomy in combination with extraction of the cysts and membranes using a Dormia basket or a balloon catheter may result in final treatment.

<sup>(10)</sup>Accurate, non-invasive, repeatable organ imaging has added a new dimension to the diagnosis of hydatid disease. In our study was showing that US

study was done for all the patients who were referred to our hospital as a case of hydatid liver disease.

Ultrasound is particularly useful in the work- up of patients presenting with jaundice, as it is possible to differentiate daughter cysts from gallstones in many of these patients. In the hands of skilled, experienced staff, the precision of ultrasound diagnosis is high<sup>(11,13)</sup>.

In our study, ultrasonography was proved diagnostic in all hydatid cystic diseases. In the study conducted by Balik et al. ultrasonography showed diagnostic accuracy of 97.7%, while Ajaz A Malik et al. mentioned in his study that ultrasound and CT scan define the extent of disease in uncomplicated cases but they are not always sensitive and specific in suspected biliary tract involvement and prefer the endoscopy as a diagnostic tool<sup>(13)</sup>. CT, however, probably yields the most information regarding the position and the extent of intra-abdominal hydatid disease. Daughter cysts are clearly seen and CT will demonstrate exogenous daughter cysts as well. This may be of the utmost importance in planning surgery. CT will also demonstrate cysts in other parts of the peritoneal cavity, and there are no problems caused by the bowel containing gas, as there may be with ultrasound. CT may also be able to provide an estimate of the density of the cyst contents, thus suggesting the vitality of the cyst. In our study, CT scan was done in 11 patients; eight of them (72.7%) were diagnosed with frank rupture. In the study conducted by Konstantinos Alexiou et al. CT scan showed diagnostic accuracy of 95%<sup>(14)</sup> in which he recommend that CT examination must be performed with slice thickness of maximum 3 - 5 mm. so as focal herniation of the cyst wall can be seen, which may be explained our results. Magnetic resonance imaging (MRI) provides good images of liver hydatidosis, but it is too complex and expensive for routine use. The real value of MRI is that it provides additional multiplanar images in demonstrating a characteristic intense rim, daughter cysts, detachment of the membranes, and dilated biliary tree containing hydatid material<sup>(15)</sup>. In our study, MRI of the liver and MRCP were done for 12 patients. The main indications for MRI and MRCP were cholangitis, jaundice, repeated vomiting and pruritus to excludes other causes. 10(83.3%) patients had frank intrabiliary rupture. In the study done by Von Siner et al., he mentioned that Ultrasound (US), computed tomography (CT) and magnetic resonance imaging (MRI) allowed recognition of ruptured hydatid cysts.<sup>(15)</sup> Despite the fact that it is supported that ultrasound and ERCP are enough for the preoperative diagnosis of intrabiliary rupture of hepatic echinococcal cyst<sup>(16,17)</sup>, the ERCP is not available in all hospitals and mainly used the repeatedly. In rare cases of complete evacuation, when characteristic findings of hydatid cyst are

absent or when there is no evidence of the previous existence of liver hydatid cyst, the diagnosis may be difficult. In such cases, MRI, MRCP, ERCP are employed. Although there is higher rate of right lobe involvement with hydatid disease mention in many literatures<sup>(15-17)</sup>, we found the risk of frank IBR greater amongst cysts located in the left lobe of the liver. AZ Al-Bahrani et al had the same out comes in his study, Small size left lobe, long coarse left hepatic bile duct and repeated trauma facilitate erosion of the cyst to the biliary ducts. It is possible that the smaller size of liver segments in the left lobe and the proximity of cysts in these segments to the hilum of the liver might explain the higher incidence of ruptured cysts in this lobe. Multivesicular cysts carry a significantly higher incidence of frank IBR. In our study, approximately 57% of cysts with frank IBR were multivesicular with increase in the incidence of frank IBR compared with univesicular cysts. Similar findings were reported by Bouzidi and Chehab<sup>(22)</sup> who in their report of 479 patients with HHC of whom 83 patients (17%) had frank IBR, some 72% of complicated cysts were multivesicular. Although there is no clear explanation for the higher tendency of multi-vesicular HHC to rupture into the biliary tree, the potential ease with which some of the hundreds of daughter cysts could escape into the biliary tree compared with shreds of a single lamellated membrane in univesicular cysts may play a role. It is important to predict whether the liver cysts communicate with the biliary tree in asymptomatic patients or not. Size of cyst, ALP, SGOT and bilirubin has been reported as risk factors for cysto-biliary communication in literature. Zuhair R Al-Bahrani et al. concluded that Patients with large (=10cm), multivesicular, solitary, left lobar or infected hepatic hydatid cyst as well as those with prolonged history are at increased risk of frank intrabiliary rupture, this study is nearly compatible with our study in which the higher percent of frank rupture were among those with these criteria as shown in table 6. In our study, the average Laboratory results in patients with frank rupture are higher than those without (Table 4), but some patients still present with normal or little bit elevation in one blood test or another. This maybe explained by either that there is spontaneous passage of cystic content and complete drainage or may be explained by the study done by Kemal Karakaya et al. who proved that a high intracystic pressure causing intermittent passage of cyst fluid and minor fragments into the biliary system. However, an apparent biliary obstruction does not occur. ALP, SGOT and bilirubin levels increase but patients stay asymptomatic, Reabsorption of the bile from the cyst cavity may be another mechanism for the increased bilirubin and ALP levels.

In our study, frank rupture noticed to be higher as the cyst get larger in size, those with cyst larger than 10 cm had 60% frank rupture vs. 36.3% frank rupture with cyst smaller than 10 cm, these results similar to the study conducted by Yalin et al. who showed that intracystic pressure increases along with the diameter of a hydatid cyst and leads to a spontaneous intrabiliary rupture.<sup>(16)</sup> The role of local factors of hepatic hydatid cyst in predicting the risk of frank IBR has not been adequately explored in the medical literatures. In a multivariate analysis that involved 116 patients with hepatic hydatid cyst of whom 9 had frank IBR, Atli et al.<sup>(11)</sup> identified a cyst diameter of more than 10.5cm, type IV cysts on ultrasound (peripheral or diffuse distribution of coarse echoes in a complex and heterogeneous mass) and a history of obstructive jaundice as independent predictors of frank IBR. Atli et al.<sup>(11)</sup> however did not evaluate the potential impact of other cyst characteristics such as vesicularity, number and anatomical location on the risk of frank IBR. In our experience, the risk of frank IBR of cysts of 10cm or larger was greater than that of smaller cysts. This risk appeared to be particularly related to cysts situated centrally or near the hilum of the liver, as these were probably more likely to cause pressure necrosis of the wall of adjacent major branches of bile ducts. On the other hand, cysts placed peripherally or near the surface of the liver and there-fore away from sizeable branches of bile ducts were likely to attain larger sizes with minimal risk of frank IBR. In the report by Tacyildiz et al.<sup>(18)</sup>, the mean size of HHC with frank IBR was 12.6 (range, 6-20) cm. ERCP has been proved a useful diagnostic tool, and endoscopic sphincterotomy is currently the treatment of choice for hepatic hydatid disease open to the biliary tree as mentioned in many studies<sup>(10,17)</sup>. The indications for its use include the preoperative presence of daughter vesicles or hydatid debris into the biliary tree, in our study, 4 patients undergone ERCP as a therapeutic procedure with sphincterotomy as they were presented with cholangitis, jaundice and/or vomiting. Correct indications for endoscopic papillotomy are of paramount importance in managing complicated cysts. Papillotomy should be performed for the pre- and postsurgical removal of fragmented intrabiliary hydatid membranes and in the management of postoperative external biliary fistulae. Preoperative endoscopic papillotomy facilitates flushing of the bile ducts but renders intraoperative cholangiography even less informative<sup>(20,21,22)</sup>. The conventional surgical management of ruptured hydatid disease includes surgery for eradication of the cyst; exploration, clearance, and T-tube insertion into the common bile duct (CBD); or transduodenal sphincteroplasty.<sup>(20-24)</sup>

In our study most of patients treated surgically by endocystectomy with drainage or omentoplasty. The most effective procedures following the evacuation of hydatid material from the biliary tree remain controversial. Alper et al argued that wide choledochoduodenostomy decreases morbidity and mortality.

The groups of Lygidakis, Paksoy, and Kornaros preferred T-tube drainage and performed choledochoduodenostomy in less than 10% of cases. According to our study, T-tube drainage and / or choledochoduodenostomy both applied according to surgeon preference. During the operation, the cyst cavity may be filled with saline and air injected from the cystic duct to locate opening of the biliary channel into the cyst cavity.<sup>(7)</sup>

Another method is to pack the cyst with gauze soaked in hypertonic saline and wait for bile stains to appear. We generally prefer this method in our patients. Following the evacuation, the cyst cavity should be drained with closed-suction drains preferably if a bile leak is present.<sup>(19,20)</sup> However, bile may not be present in the cavity despite cysto-biliary communication.

Because biliary system pressure is 1520 cm H<sub>2</sub>O but intracystic pressure is 3080 cm H<sub>2</sub>O and, flow is normally toward the biliary system in these cases.<sup>(21,22)</sup> If cysto-biliary communication remains undetected or unrepaired, the pressure gradient is reversed. The operative approach is to clean the mother cyst of hydatid membranes and to explore and clear the CBD if preoperative clearance was not done. Biliary communications with the cyst are identified and meticulously sutured<sup>(14)</sup>. A supraduodenal choledochostomy is made and bile duct cleared by all membranes and debris with the help of choledochoscope. The choledochostomy is closed over a T-tube. If CBD is grossly dilated or clearance is not complete or there is a major cyst biliary communication, a drainage procedure such as choledochoduodenostomy is performed<sup>(14)</sup>. Omentoplasty is an alternative procedure done in patients with small biliary communication<sup>(14)</sup>. Here a flap of omentum is brought to rest within the pericyst cavity with the assumption that omentum will seal small biliary leaks and obliterate the cavity. Omentoplasty also protects against infection by promoting reabsorption of serosal fluid and by inducing macrophage migration in septic foci.

### Conclusion:

- In endemic areas, Intra biliary rupture of hydatid cysts should be suspected in every case with RUQ pain, jaundice and/or cholangitis
- The highest age group presented with hydatid cysts between 50-60 years about 76%.

- The incidence of biliary communication and intrabiliary rupture more in left lobe, larger size, solitary, multivesicular and long history hydatid cysts

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