



Effectiveness of Roux-en-Y Hepaticojejunostomy in Reversing the Liver Histological Changes in Patients Presenting Symptomatically and Asymptomatically with Type I & IV Choledochal Cyst

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Purpose: Choledochal cyst, a cystic dilatation of biliary tree, is a congenital abnormality of unknown etiology. Excision of cyst & biliary reconstruction is the mainstay of treatment. Most patients (80%) with choledochal cyst are detected after clinical manifestations. Majority is symptomatic patient and others are asymptomatic. Symptomatic patients have consequential impact on liver histology and function. These changes of liver histology may be reversible or irreversible depending in the degree and length of insult. This study attempt to identify whether symptomatic patients show more irreversible changes than asymptomatic choledochal cyst patients. Thus, the aim of this study was to determine the reversibility and irreversibility of the liver histological changes in patients presenting symptomatically and asymptotically.

Methods: It is a prospective analytic study. Study period was from January 2017 to August 2018, done in Pediatric Surgery department of BSMMU & DMCH. This included 31 patients with choledochal cyst. They are divided in symptomatic patient and asymptomatic patient. Excision of the cyst with roux-en-Y hepaticojejunostomy and intra-operative liver biopsy was taken and liver biopsy was repeated after six months of surgery. Both the liver biopsies were compared & observe histologically in terms of reversibility and irreversibility in patients presenting symptomatically and asymptotically.

Results: Thirty-one patients were included. Among them symptomatic patients were 22 and asymptomatic patients were 09. In both group pathological changes were observed in all the patients pre-excisionally and post-excisionally. In symptomatic patient significant histological changes were seen pre-excisionally. Nineteen were reversible group and threehad irreversible group. But in asymptomatic group all nine patients were reversible. Postexcisionally there was significant regression in reversible group both in symptomatic patients and asymptomatic patients. But post-excisionally irreversible group did not showreversibility even after successful roux-en-Y hepaticojejunostomy.

Conclusions: Liver histology shows various degree of changes in all choledochal cyst patients whether symptomatic or asymptomatic. Symptomatic patient demonstrates more irreversible changes than asymptomatic patients. Majority of the pathological changes of the liver in early stage are reversible after roux-en-Y hepaticojejunostomy. There is no short term liver architectural improvement of the patients with choledochal cyst evenafter successful roux-en-Y hepaticojejunostomy who pre-excisional had irreversible changes.

Keywords: *Choledochal cyst; liver histology; symptomatic vs. asymptomatic; reversibility; hepaticojejunostomy.*

1. INTRODUCTION

Choledochal cyst is a developmental defect of biliary tree, it may involve either extrahepatic (mainly CBD) or intra hepatic or both extra and intra hepatic biliary channel. There are five types of choledochal cyst. Types I and IV cysts are more common in female than in male patients, and female to male ratio ranges from (3 to 4:1) that contributes to the belief that

choledochal cyst is sex linked. The etiology of choledochal cyst remains unknown but is commonly accepted to be congenital in nature. There are two leading hypotheses which explain some but not all features-(1) Distal stenosis, (2) Pancreatic reflux. It is an important cause of surgical jaundice in infants and children. The classical triad for choledocal cysts is abdominal pain, jaundice, and an abdominal mass. 80% of patients are present before age of 10 years.

Children usually have signs and symptoms, but adults are asymptomatic. 82% of children present with two or more symptoms, on the other hand only 23% of adult presented with symptoms. (Lipsett et al. 1994). Asymptomatic patients present with non-specific abdominal pain (such as lower abdominal pain, gastroenteritis) without features of cholangitis. This type of patient can be identified by USG which show no features of obstruction. As infants, children and adults present with different signs and symptoms, the patients can be divided into two groups: an infant group (less than 1-year-old), and a classical pediatric or adult group (older than 1 year) (Mishra et al. 2007). Diagnosis is confirmed by imaging. Ultrasonography (USG) is initial imaging method of choice. Magnetic resonance cholangiopancreatography (MRCP) study is now considered the gold standard for diagnosis of choledochal cyst. MRCP is highly accurate in detection and classification of the cysts. The overall detection rate is very high 96-100 %. (Yoon 2011). Treatment of choledochal cyst is surgical excision. It depends on type of cyst. Excision of choledochal cyst and roux en Y hepaticojejunostomy is the most classic and widely accepted method. If left untreated, they can cause morbidity and mortality from recurrent cholangitis, pancreatitis, sepsis, and biliary stone formation, development of biliary cirrhosis, cholangiocarcinoma and carcinoma of gallbladder. Comprehensive treatment involves medical management of complications; surgery and long term follow up. As it is a disease of common bile duct as well as the liver, so less importance given on liver histology for choledochal cyst patient but there are various pathological changes occur in liver. Table 1 & Table 2 show Grades of Hepatocellular damage & portal fibrosis respectively- Table 1 Grades of Hepatocellular damage.

Table 1 outlines the Grades of Hepatocellular damage, which includes features such as cholestasis, hepatocellular damage, parenchymal inflammation, bile duct proliferation, bile duct inflammation, and central venous distension. Each feature is graded from 1+ to 3+ based on the severity of the observed characteristics. Table 2 presents Ohkuma's classification of portal fibrosis, which ranges from Grade 0 (no fibrosis) to Grade 4 (liver cirrhosis with reconstruction of hepatic lobules). The grades reflect the degree of fibrosis in the portal-portal (P-P) areas, from mild fibrosis

(Grade 1) to severe expansive fibrosis with bridging (Grade3).

Liver shows extensive pathological changes in patients with choledochal cyst (Nanbirajan et al. 2000). These changes correlate with not only clinical symptoms at presentation but also with response to surgery (Howell et al. 1983). Typical liver changes in these patients include bile duct proliferation, cholestasis, bile plugs in biliary ducts, inflammatory cell infiltration, giant cell formation, portal fibrosis and finally cirrhosis in severe cases (Nanbirajan et al. 2000). It is an established fact that similar pathological changes occurring in the liver in case of extra hepatic biliary atresia are permanent. However, what changes occur in liver after roux en Y hepaticojejunostomy and how were the changes of liver histology between symptomatic and asymptomatic patients. The appropriate time of surgery and the requirement of surgery in these patients have been debated (Howell et al. 1983). The demonstration of pathological changes in the liver even in early, asymptomatic stages of the disease and its subsequent regression with treatment can provide a clear argument in favour of surgery (Sugandhi et al. 2014).

Despite multiple studies, the aetio-pathogenesis of choledochal cyst has only been hypothesized (O'Neill 1992). This study was also carried out with the expectation that histological changes in the liver and their behavior after surgery may help in understanding the pathophysiology of the disease and explain the varied symptoms, recovery patterns and complications in patients with choledochal cyst. Thus, the aim of this study was to determine the reversibility and irreversibility of the liver histological changes in symptomatic and asymptomatic choledochal cyst patients.

1.1 Objectives

1.1.1 General objective

To study-

- The difference between histopathological changes of liver in patients with symptomatic and asymptomatic type I and IV choledochal cysts.
- The effect of surgical drainage on liver histology 6 months after roux-en-Y hepaticojejunostomy in the same.

Table 1. Grades of Hepatocellular damage

Factors	Features	Grading
Cholestasis	Canalicular	1+
	Hepatocytes	2+
	Centrilobular	3+
Hepatocellular damage	Ballooning	1+
	Feathery degeneration	2+
	Necrosis	3+
Parenchymal inflammation	Mild	1+
	Moderate	2+
	Severe	3+
Bile duct proliferation	Mild	1+
	Moderate	2+
	Severe	3+
Bile duct inflammation	Mild	1+
	Moderate	2+
	Severe	3+
Central venous distension	Mild	1+
	Moderate	2+
	Severe	3+

Table 2. Ohkuma's classification

Factors	Grades	Features
Portal fibrosis:	Grade 0	No fibrosis
Okhuma's area classification	Grade 1	Mild fibrosis confined to portal
	Grade 2	Moderate fibrosis in portal-portal area (P- P) bridging fibrosis
	Grade 3	Severe expansive fibrosis with widened (P-P) bridging fibrosis
	Grade 4	Liver cirrhosis with reconstruction of hepatic lobules

1.1.2 Specific objective

- To identify the degree of histological changes of liver in symptomatic and asymptomatic type I and IV choledochal cyst patients before and 6 months after roux-en-Y hepaticojejunostomy.
- To compare the pre-excision and post-excision histopathological changes of liver in the same to identify reversibility of changes

2. MATERIALS AND METHODS

Study Design: This is a prospective analytic study.

Study Place: Department of Paediatric Surgery, Bangabandhu Sheikh Mujib Medical University Hospital & Dhaka Medical College Hospital, Dhaka, Bangladesh.

Study Period: January 2017 to August 2018.

Study Population: Children with type I & type IV choledochal cyst admitted in pediatric surgery department of BSMMU & DMCH.

Study Variables: Degree of cholestasis, hepatocellular damage, parenchymal inflammation, bile duct proliferation, bile duct inflammation, central venous distention and portal fibrosis.

Sampling Technique: Purposive sampling technique.

2.1 Selection Criteria

2.1.1 Inclusion criteria

- Type I & IV choledochal cyst presenting with or without symptoms.

2.1.2 Exclusion criteria

- Loss of patient
- Patients who refuse to participate
- Patients with known liver disease
- Patients being unfit for operation Patients developing complication of drainage

2.3 Data Collection and Analysis

The study subjects have been selected on the basis of selection criteria from the patients admitted in the Department of Pediatric Surgery, BSMMU & DMC Hospital. Some patients with acute cholangitis was admitted, we treat them conservatively with antibiotics and advised them to come after two months. Some patients came with history of acute cholangitis within last two months, we have excluded them. The demographic information, relevant history, examination findings and investigation reports and follow up of all the study subjects has been recorded in the data collection sheet. Any complications during the procedure & hospital admission, if required have been recorded. After compiling, the data has been presented in the form of tables, figures and graphs as necessary. Statistical analysis of the results has been done by using computer based statistical software, SPSS windows software, version 24 For normally distributive quantitative data which has been compared by unpaired test. A 'p' value of <0.05 is considered statistically significant.

3. RESULTS

In this study total thirty-one patients with choledochal cyst were enrolled to observe the histological changes of liver (Pre- excision and post excision). Among them twenty-two were symptomatic patients and nine were asymptomatic patients. Excision of cyst and roux-en-Y hepaticojejunostomy with intra-operative liver biopsy was done. Liver biopsy was repeated 6 months after roux-en-Y hepaticojejunostomy. These liver histological changes were again categorized into reversible and irreversible changes for study purpose which was defined in operational definition. Results are depicted in the form of table and chart in following pages.

3.1 Age Distribution of Study Population

The age distribution of the study population is depicted in Fig. 6. The mean age distribution in both symptomatic and asymptomatic patient was near equal 6.28 and 6.00 respectively and there was no significant age distribution ($p = 0.865$) between symptomatic and asymptomatic CDC patients.

3.2 Gender Distribution among Study Population

Female predominance was seen in symptomatic CDC patient but not in asymptomatic patient. And there was no significant sex distribution among both groups of patients.

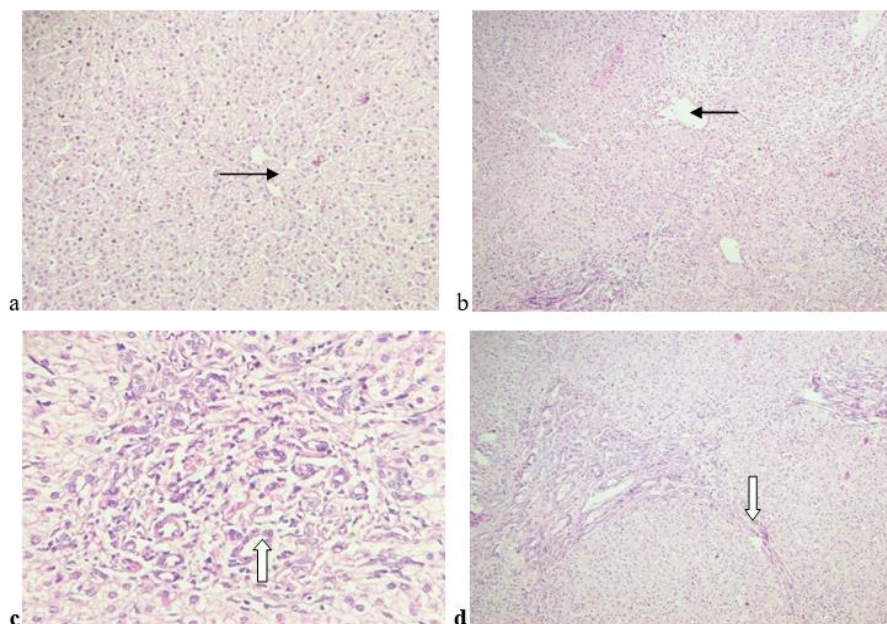


Fig. 1. Histopathological changes in the pre-operative liver biopsies: a hepatocellular damage, b central venous distension, c bile duct inflammation, d portal fibrosis

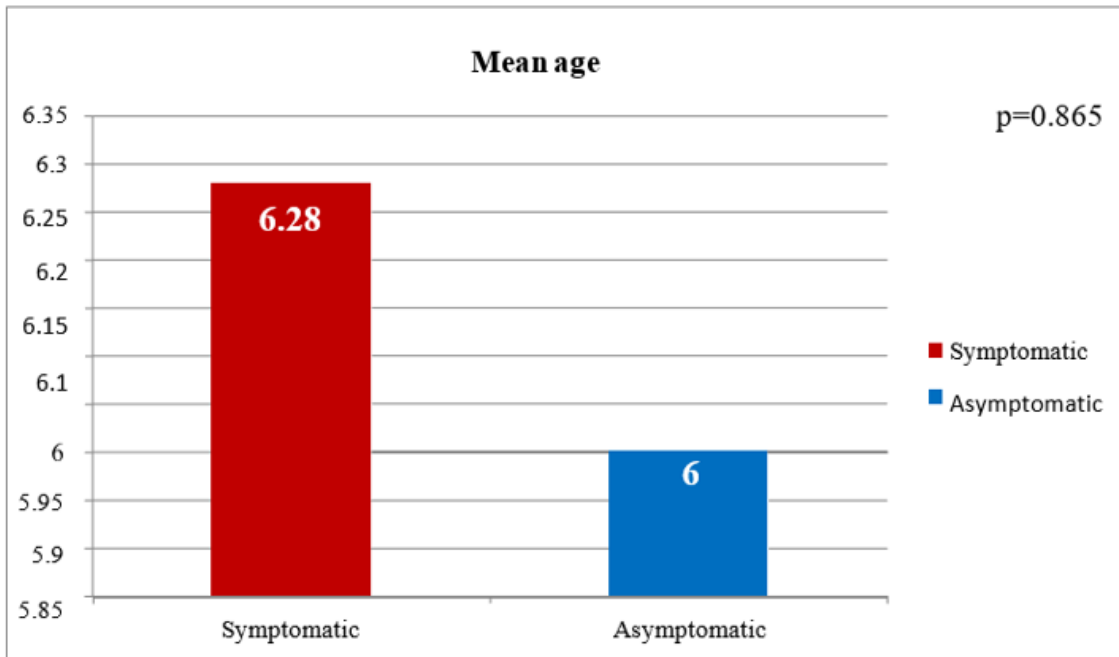


Fig. 2. Age distribution of the study population

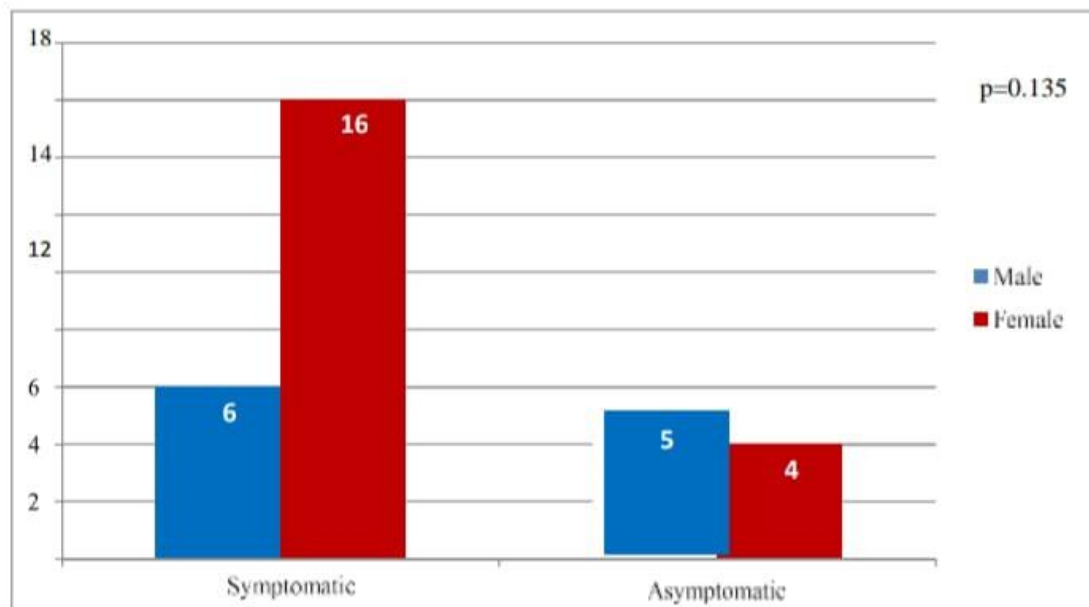


Fig. 3. Sex distribution of the study population

3.3 Symptomatic Distribution of the Study Population (N=31)

Distribution of study population according to presence of symptom is shown in Fig. 8. More than 2/3rd (71%) patients were symptomatic and rests of them (29%) were asymptomatic.

3.4 Histopathological Changes of Liver in Symptomatic and Asymptomatic Choledochal Cyst Patients (Pre-Excision) (N=31)

Bar diagram showing pre-excisionally most of the symptomatic patient was shown reversible changes and rest had irreversible changes,

whereas, all of the asymptomatic patients found reversible changes

symptomatic patients who were pre-excisionally irreversible.

3.5 Reversibility of Histopathological Changes of Liver in Symptomatic Choledochal Cyst Patients (Pre-Excision and Post-Excision) (N=22)

3.6 Reversibility of Histopathological Changes of Liver in Asymptomatic Choledochal Cyst Patients (Pre-Excision and Post-Excision) (N=09)

Fig. 6. showing histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision and post excision). Here it was found that following roux loop surgery for type 1 and 4 choledochal cyst, there was no short term liver architectural improvement of the

In this study all of the asymptomatic patients were shown reversible changes pre- excisionally and post excisionally there was significant short term liver architectural improvement of the patients.

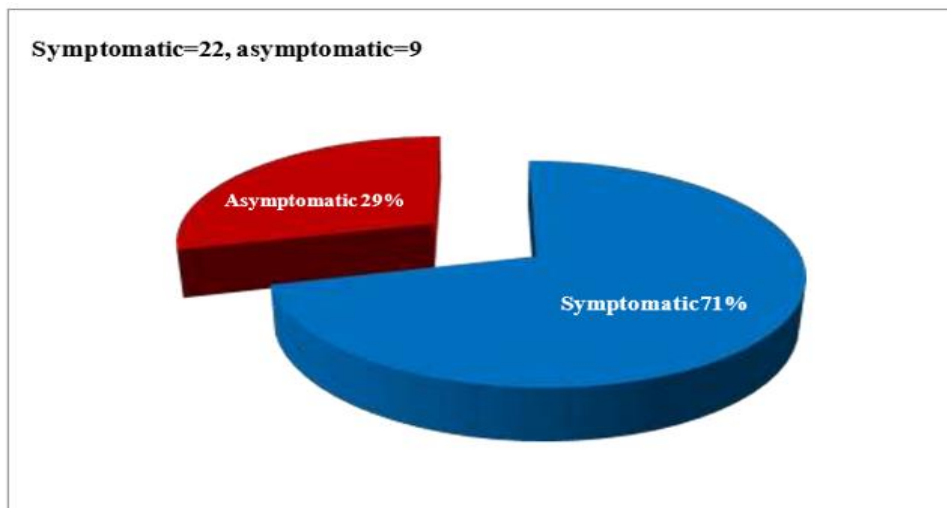


Fig. 4. Distribution of study population according to symptom

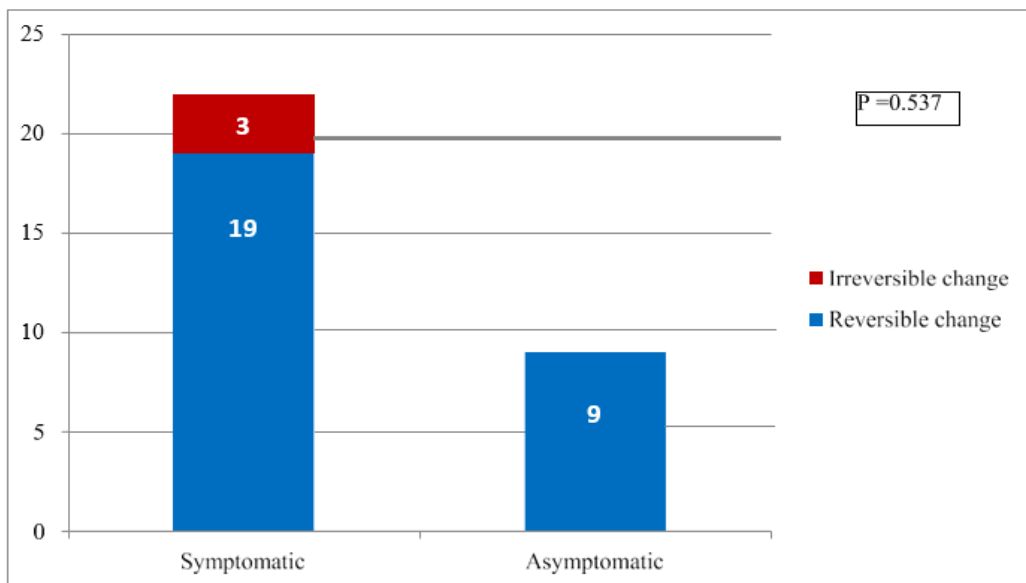


Fig. 5. Histopathological changes of liver in symptomatic and asymptomatic choledochal cyst patients (Pre-excision)

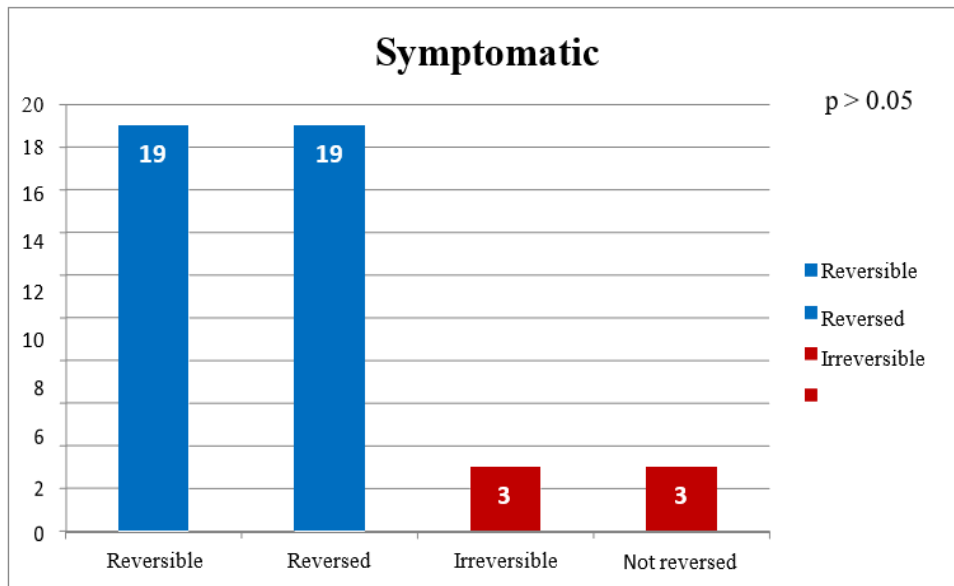


Fig. 6. Histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision and post-excision)

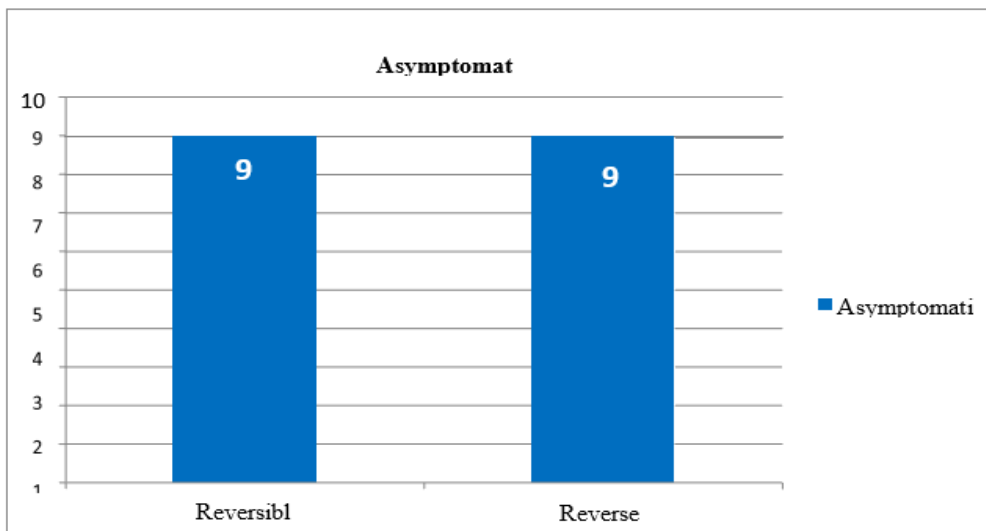


Fig. 7. Histopathological changes of liver in asymptomatic choledochal cyst patients (Pre-excision and post-excision)

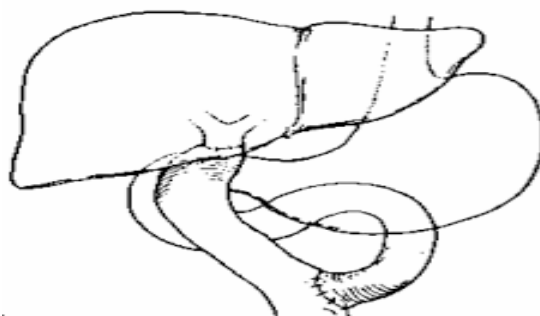


Fig. 8. Schematic drawing of Roux en Y hepaticojejunostomy



Fig. 9. Choledochal cyst

4. DISCUSSION

Choledochal cyst is a congenital anomaly of the biliary tree of unknown etiology, characterized by single cystic or fusiform dilatations usually of the extrahepatic duct in isolation or multiple dilatations of usually the intrahepatic duct system or different parts of both extrahepatic and intrahepatic biliary tree. It is potentially a serious disease of the biliary tree and may affect the liver in the infants and the children or in the adults particularly if there is actual obstruction or obstructive complications. For the classic type of extrahepatic choledochal cyst, excision of the cyst and roux-en-Y hepaticojejunostomy is the common surgical method of treatment. If the surgical treatment is not done early, it can cause serious morbidity and mortality from complications like recurrent cholangitis, pancreatitis, sepsis, biliary stone formation, development of biliary (Ono et al. 2010). Choledochal cysts per se have no symptoms other than a large cyst presenting as an asymptomatic abdominal lump. However, most patients (80%) with choledochal cysts are detected after clinical manifestations. These clinical symptoms and signs are usually due to complications like obstruction, cholangitis, associated pancreatitis and sepsis, stone formation and others. These usually manifest in the infants and the children, but may remain asymptomatic and present in the adulthood. Some asymptomatic one are diagnosed incidentally. It is likely that, patients who present symptomatically may have discernible consequential impact in the liver histology and function. These changes in liver histology may be reversible or irreversible depending in the degree and length of time that the liver is exposed to complications due to in symptomatic choledochal cyst. It is likely that greater the symptoms and signs in choledochal cyst

patients, the more severe is the degree of liver histological changes that are less reversible occur. In the study, it was considered that those patients who developed early histological changes in the liver with portal fibrosis (Ohkuma's grade 1 & 2) only were reversible. On the other hand, those who have advanced changes greater than grade 2 were considered irreversible. Earlier, H. Toshimichi and colleague in Japan (2006) observed the relationship between the degree of liver fibrosis and its impact on the post-operative clinical course in 43 patients with choledochal cysts. They found that irrespective of the degree of liver fibrosis and functional status of the liver at pre-operative period, all the patients with choledochal cysts had improved clinically one month after roux-en-Y hepaticojejunostomy. The laboratory parameters (S-Bil, S-AST, S-GGTP, S-Bile acid, S- amylase) that they had studied as markers of improvement came within normal limit. But they did not have any evidence of morphological improvement of the liver such as observed by post-operative liver biopsy examination. However, in two patients who had to undergo re-laparotomy for some other reasons later on, liver biopsy was done. It was found that both having grade 1 and 2 liver fibrosis on initial biopsies had no such features on their later biopsies. They, therefore, suggested that mild to moderate liver fibrosis that was present in almost half of all their children with choledochal cyst that could be graded up to Ohkuma's grade 2, was also likely to disappear in the post-operative clinical course resulting in the clinical improvement. In the present analytical study, attempt was made to identify whether symptomatic patients show more irreversible changes than asymptomatic patients and if the post- excision roux-en-Y hepaticojejunostomy helps in reversing these liver histological changes that are defined as irreversible. Thus,

the aim of this study was to determine the reversibility and irreversibility of the liver histological changes in symptomatic and asymptomatic choledochal cyst patients. Total thirty-one patients with type I and type IV choledochal cyst were included in this study. The ratio of symptomatic to asymptomatic patient was 2:1. The mean age in both symptomatic and asymptomatic choledochal cyst patients were nearly equal (6.28, 6.00). However, the sex distributions in both symptomatic and asymptomatic choledochal cyst patients were not similar. There were overwellbeingly more female patients in symptomatic group. Histopathological changes of varying severity were evident in the pre-excision liver biopsy in all patients with choledochal cyst. Hepatocellular damage was the most widespread change noted in all patients in both groups indicating that at least some degree of liver damage occurs irrespective of symptomatic status. All asymptomatic and great majority of symptomatic choledochal cyst patients demonstrated reversible histological changes in liver and these changes were reversed after 6 months of roux-en-Y hepaticojejunostomy in all. Conversely, the three symptomatic patients who showed irreversible liver histological changes did not undergo reversal after 6 months of roux-en-Y hepaticojejunostomy. It is possible that graded histological changes occur in the liver of symptomatic choledochal cyst patients depending on severity and length of the insult. Therefore, those patients who have early liver histological changes has the chance of reversibility to normal liver histology and those patients who present with advance changes have little scope for regaining normal liver histology even after successful roux-en-Y hepaticojejunostomy. Liver fibrosis is one of the major complications of choledochal cyst patients that may persist as a sequel. Obstructive cholangiopathy has been considered as the main cause of liver fibrosis in pediatric choledochal cyst patients (Fujishiro et al. 2011). If the obstruction is removed early liver fibrosis may cease to progress and be limited to a minimum. (Yeong M L et al. (1982). reported a case report on improvement of liver fibrosis after roux-en-Y hepaticojejunostomy in a choledochal cyst patient. It was postulated that the amount of liver fibrosis depends on the rate of collagen synthesis which was stimulated by refluxing chemical injury to biliary channel (common channel theory of choledochal cyst). Therefore, they suggested that if the fibro genic factor is removed, the quantity of fibrous tissue in the liver

may be decreased. Even in case liver cirrhosis, which is generally considered as irreversible phenomenon in adults and children, there are evidences of improvement after roux-en-Y hepaticojejunostomy in paediatric patients with choledochal cyst (Ishimaru T. et al. 2010, Jackson CC 2002). But in this study, those patients with irreversible liver histological changes had no reversal of liver histopathology six months after roux-en-Y hepaticojejunostomy. Therefore, it can be suggested that following successful roux loop surgery for type I and IV choledochal cysts, liver architectural improvements in patients who have pre-excisionally irreversible changes is not to be expected at least in the short term. Longer follow-up may indicate the degree of improvement with time.

5. CONCLUSION

Liver histology shows various degree of changes in all choledochal cyst patients whether symptomatic or asymptomatic. Symptomatic patient demonstrates more irreversible changes than asymptomatic patients. Majority of the pathological changes of the liver in early stage are reversible after roux-en-Y hepaticojejunostomy. There is no short term liver architectural improvement of the patients with choledochal cyst even after successful roux-en-Y hepaticojejunostomy who pre-excisionally had irreversible changes.

6. LIMITATION OF THE STUDY

- Sample size is small
- Follow up period is short
- Operative procedure was not done in single hand

STRENGTH OF THE STUDY

- It is a prospective type of study, so chance of data missing is minimal
- Histopathological report was done in single Pathologist
- Liver biopsy procedure was done by single intervention radiologist

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

During surgery & 6 months after surgery liver biopsy was taken which was done for research purpose. For this they will not receive any financial support and all cost will bear researcher. Patient party has informed about procedure and its complication. After counseling patients party has given consent for this study. Informed written consent has been taken and identify of respondents has been anonymous and confidentiality of the study was maintained in following manners:

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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