

Original Research Article

Effectiveness of Roux-en-Y hepaticojejunostomy in reversing the liver histological changes in patients presenting symptomatically and asymptotically with type I & IV choledochal cyst.

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 patients significant histological changes were seen pre-excisionally. Nineteen were reversible group and three had irreversible group. But in asymptomatic group all nine patients were reversible. Post excisionally there was significant regression in irreversible group both in symptomatic patients and asymptomatic patients. But post-excisionally irreversible group did not show reversibility 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 even after successful roux-en-Y hepaticojejunostomy who pre-excisional had irreversible changes.

Key Word: Choledochal Cyst, Liver Histology, Symptomatic vs. Asymptomatic, Reversibility, Hepaticojejunostomy.

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 choledochal 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 adults presented with symptoms. [1]. Asymptomatic patients present with nonspecific 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) [2]. 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 %. [3]. 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 gall bladder. 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 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 Okhuma'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

Liver shows extensive pathological changes in patients with choledochal cyst [4]. These changes correlate with not only clinical symptoms at presentation but also with response to surgery [4]. 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 [4]. 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 [5]. 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 [6]. Despite multiple studies, the aetio-pathogenesis of choledochal cyst has only been hypothesized [7]. 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.

OBJECTIVES:

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.

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

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.

Selection criteria:

Inclusion criteria:

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

Exclusion criteria:

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

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 were 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 distributed quantitative data which has been compared by unpaired test.

A 'p' value of <0.05 is considered statistically significant.

Ethical consideration:

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 be borne by the researcher. Patient party has been informed about the procedure and its complications. After counseling, patient party has given consent for this study. Informed written consent has been taken and identified respondents have been anonymous and confidentiality of the study was maintained in following manners:

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 6months after roux-en-Y hepaticojejunostomy. These liver histological changes were again categorized into reversible andirreversible changes for study purpose which was defined in operational definition. Results are depicted in the form of tableandchart infollowingpages

UNDER PEER REVIEW

RESULTS

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Age distribution of study population

The age distribution of the study population is depicted in figure 6 below. 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.

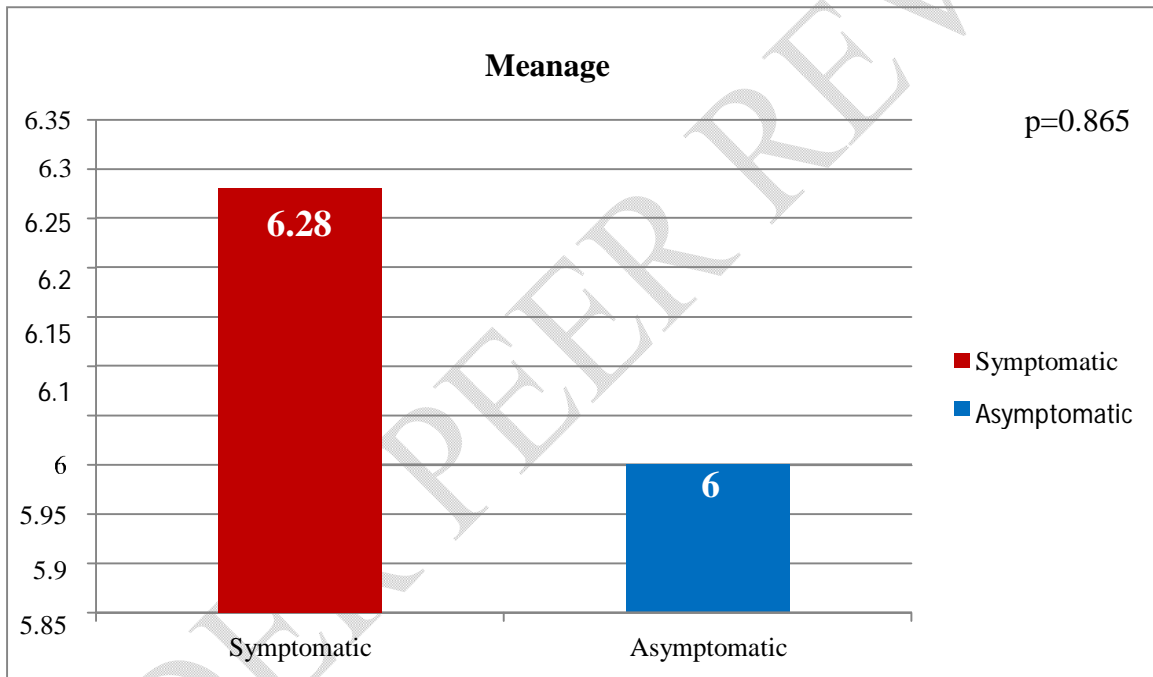


Figure 1: Age distribution of the study population

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.

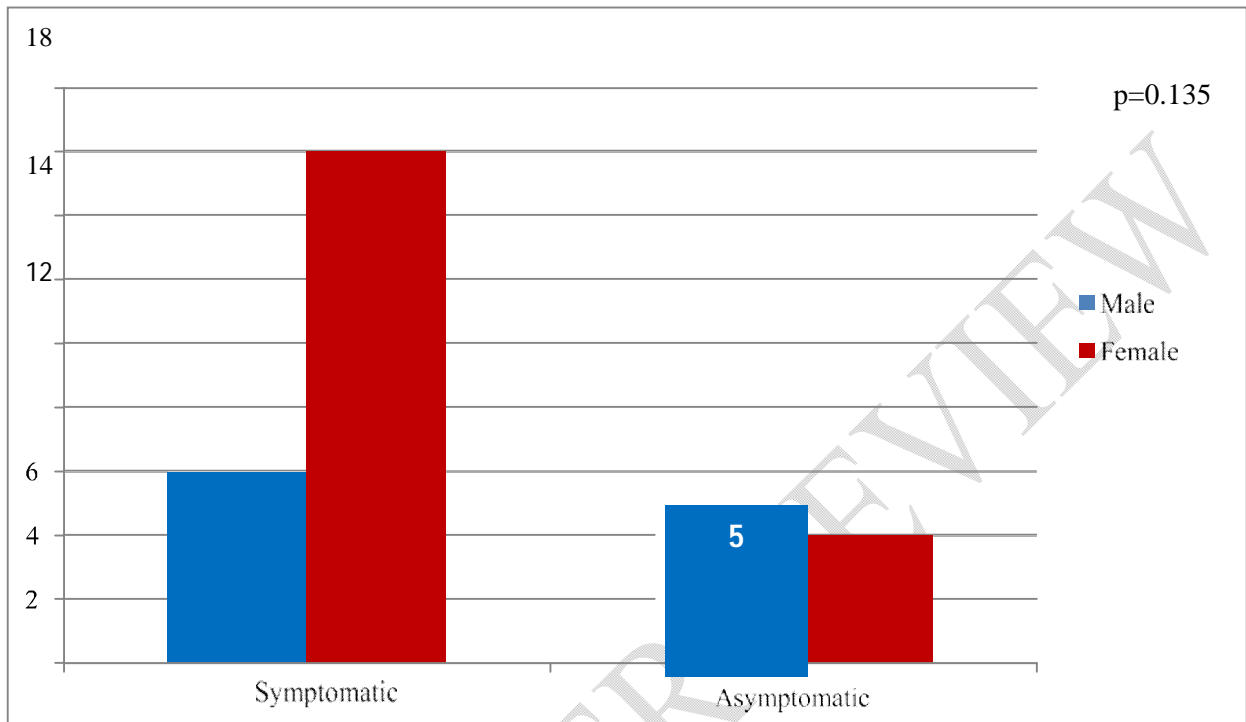


Figure II: Sex distribution of the study population

Symptomatic distribution of the study population (N=31)

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

were

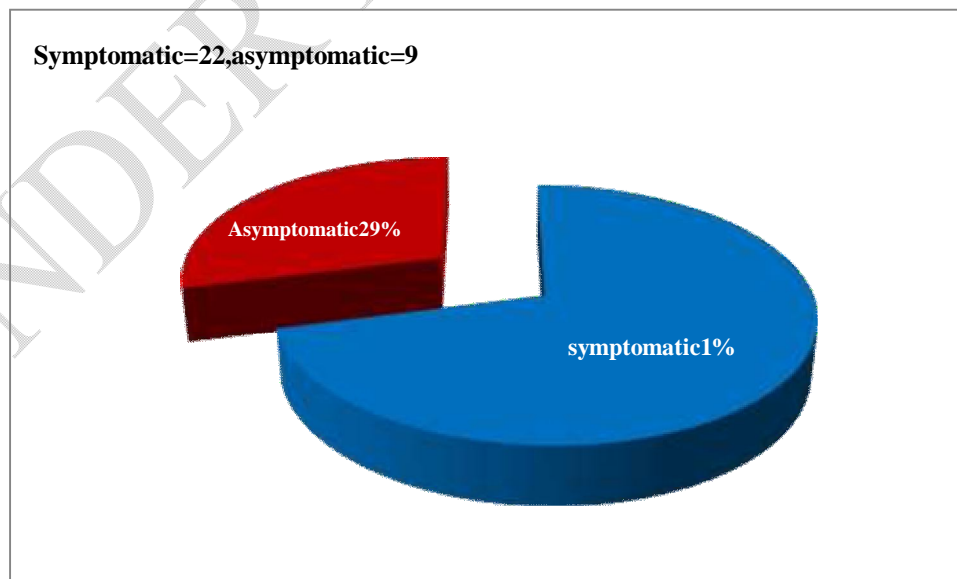


Figure III: Distribution of study population according to symptom

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.

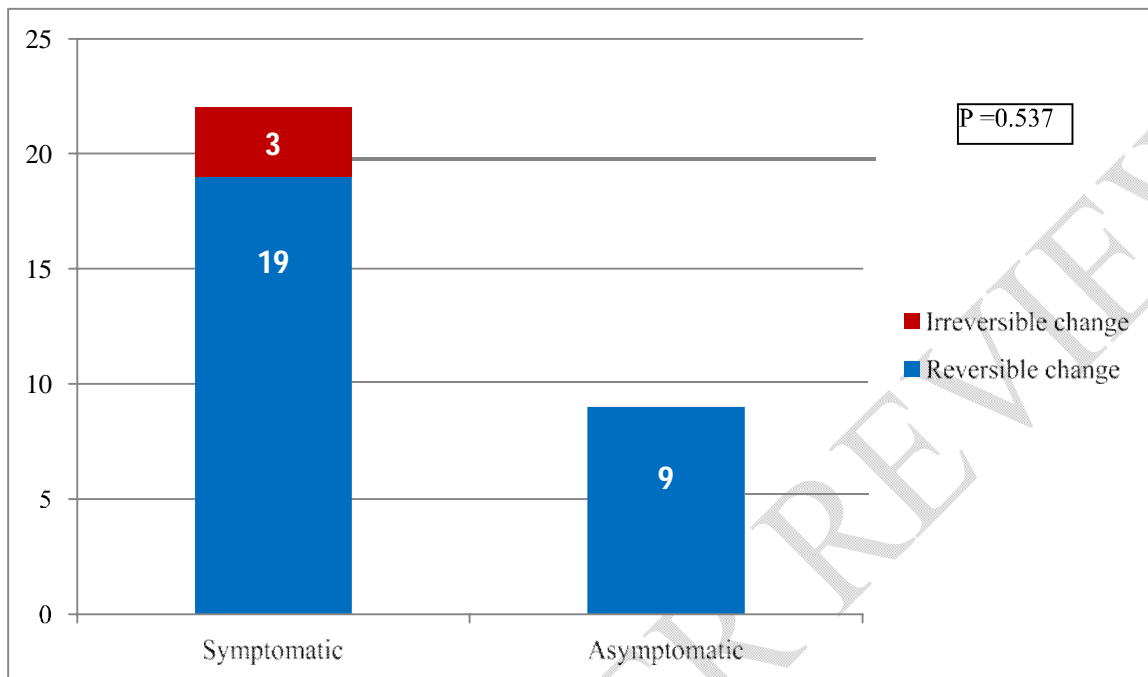


Figure IV: Histopathological changes of liver in symptomatic and asymptomatic choledochal cyst patients (Pre-excision).

Reversibility of histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision and post-excision) (N=22)

Figure 9 showing histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision and post-excision). Here it was found that following Roux-Y loop surgery for type I and IV choledochal cyst, there was no short-term liver architectural improvement of the symptomatic patients who were pre-excisionally irreversible.

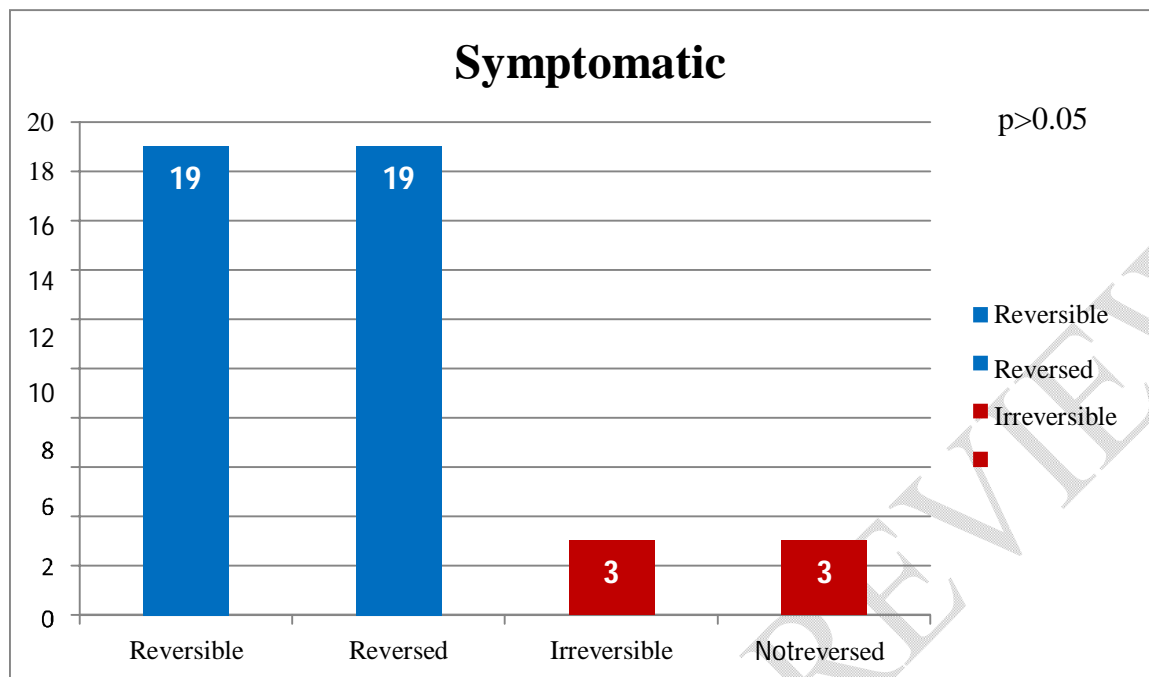


Figure V: Histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision and post-excision).

Reversibility of histopathological changes of liver in asymptomatic choledochal cyst patients (Pre-excision and post-excision) (N=09)

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.

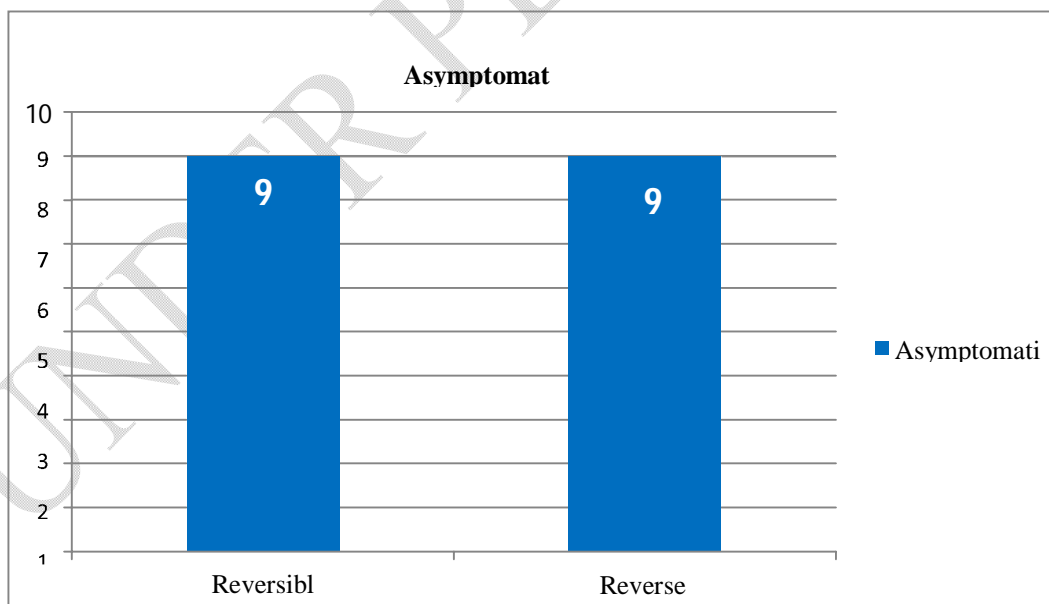


Figure Vi: Histopathological changes of liver in asymptomatic choledochal cyst patients (Pre-excision and post-excision).

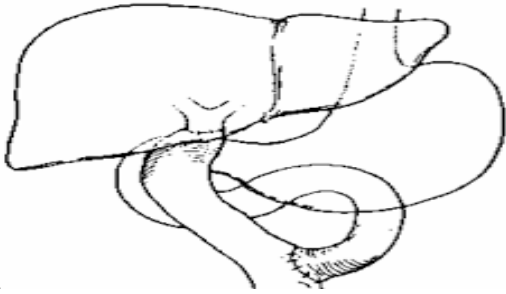


Figure VII: schematic drawing of Roux-Y hepaticojejunostomy



Figure VIII: Choledochal cyst

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 [8]. 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 ones 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 on 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 overall being slightly 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 advanced 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 [9]. If the obstruction is removed early liver fibrosis may cease to progress and be limited to a minimum. Yeong M L et al. (1982) [10] 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 fibrogenic factor is removed, the quantity of fibrous tissue in the liver may be decreased. Even in case of 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, [11] Jackson CC 2002) [12]. 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-en-Y hepaticojejunostomy, 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.

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.

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 the chance of data missing is minimal
- Histopathological report was done in single pathologist
- Liver biopsy procedure was done by single interventional radiologist

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