Original Research Article

EffectivenessofRoux-en-Yhepaticojejunostomyinreversingtheliverhistologicalchangesinpatientspresentingsymptomatically and asymptomaticallywithtypeI&IVcholedochal cyst.

ABSTRACT

Purpose: *Choledochal cyst, a cystic dilatation of biliary tree, is a congenital abnormality of unknown etiology. Excision ofcyst&biliaryreconstructionisthemainstayoftreatment.Mostpatients(80%)withcholedochalcystaredetectedafterclinicalmanifestations.Majorityissymptomaticpatientandothersareasymptomatic.Symptomaticpatientshaveconsequentialimpactonliverhistology and function.Thesechangesofliverhistologymaybereversibleorirreversibledependinginthedegreeandlengthofinsult.Thisstudyattempttoidentifywhethersymptomaticpatientsshowmoreirreversiblechangesthanasymptomaticcholedochalcystpatients.Thus,theaimofthisstudywastodeterminethereversibilityandirreversibilityoftheliverhistologicalchangesinpatientspresentingsymptomaticallyandasymptomatically.* ***Methods:*** *Itisaprospectiveanalyticstudy.Studyperiodwasfrom 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 asymptomatically.* ***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 reversible 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 whopre-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 orbothextraandintrahepaticbiliarychannel.Therearefivetypesofcholedochalcyst.TypesIandIVcystsaremorecommoninfemalethaninmalepatients,andfemaleto malerationgesfrom(3to4:1)that contributes to the belief thatcholedochal cyst is sex linked. The etiology of choledochal cyst remains unknown but is commonly accepted to be congenitalinnature.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,andanabdominalmass.80%ofpatientsarepresentbeforeageof10years.Childrenusuallyhavesignsand symptoms,but adults are asymptomatic. 82% of children present with two or more symptoms, on the other hand only 23% of adultpresented with symptoms. [1]. Asymptomatic patients present with non-specificabdominalpain(suchaslowerabdominalpain,gastroenteritis)withoutfeaturesofcholangitis.Thistypeofpatientcanbe identified by USG which show no features of obstruction. As infants, children and adults present with different signsandsymptoms,thepatientscanbedividedintotwogroups:aninfantgroup(lessthan1-year-old),andaclassicalpediatricoradultgroup (older than 1 year) [2]**.** Diagnosis is confirmed by imaging. Ultrasonography(USG)isinitialimaging methodof choice.Magneticresonancecholangiopancreatoghaphy(MRCP)studyisnowconsideredthe gold standard for diagnosis of

choledocal cyst. MRCP is highly accurate in detection and classification of the cysts. Theoverall detection rate is very high 96-100 %. [3]. Treatment of choledochal cyst is surgical excision. It dependson type of cyst. Excision ofcholedochal cyst and roux en Y hepaticojejunostomy is the most classic and widely acceptedmethod. If left untreated, they can cause morbidity and mortality from recurrent cholangitis, pancreatitis, sepsis, and biliarystoneformation,developmentofbiliarycirrhosis,cholangiocarcinomaandcarcinomaofgallbladder.Comprehensivetreatmentinvolvesmedicalmanagementofcomplications;surgeryandlongtermfollowup.Asitisadiseaseofcommonbileductaswellastheliver,solessimportancegivenonliverhistologyforcholedochalcystpatientbuttherearevariouspathologicalchangesoccurinliver.Table1 &table2showGradesofHepatocellular damage &portal fibrosisrespectively-Table1GradesofHepatocellulardamage.

Table1GradesofHepatocellulardamage

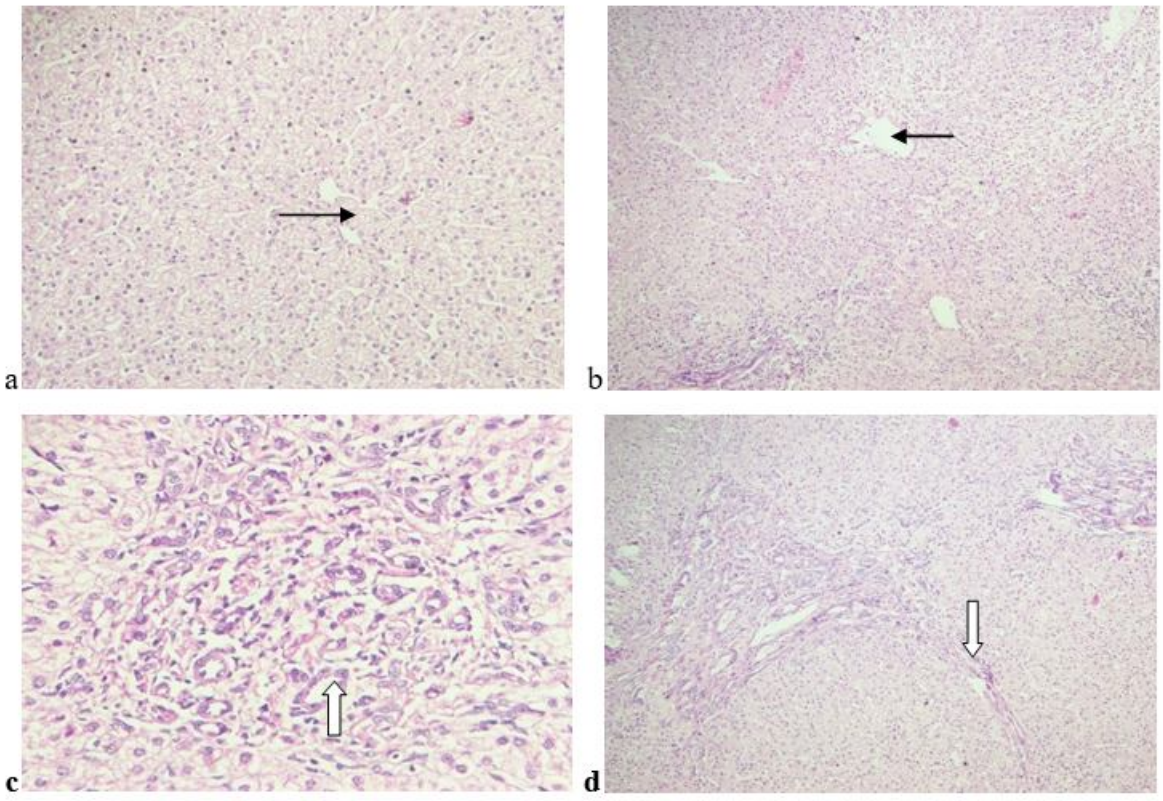
Factors	**Features**	**Grading**
Cholestasis	Canalicular	1+
	Hepatocytes	2+
	Centrilobular	3+
Hepatocellulardamage	Ballooning	1+
	Feathery degeneration	2+
	Necrosis	3+
Parenchymalinflammation	Mild	1+
	Moderate	2+
	Severe	3+
Bileductproliferation	Mild	1+
	Moderate	2+
	Severe	3+
Bileductinflammation	Mild	1+
	Moderate	2+
	Severe	3+
Centralvenousdistension	Mild	1+
	Moderate	2+
	Severe	3+

Table2Ohkuma'sclassification:

Factors	Grades	Features
Portalfibrosis:	Grade0	Nofibrosis
Okhuma'sareaclassification	Grade1	Mildfibrosisconfinedtoportal
	Grade2	Moderatefibrosisinportal–portalarea(P-P)bridging fibrosis
	Grade3	Severeexpansive fibrosiswith widened(P–P)bridging fibrosis
	Grade4	Livercirrhosiswithreconstructionofhepaticlobules

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 (Grade 3).

Liver shows extensive pathological changes in patients with choledochalcyst [4]. These changescorrelatewithnotonlyclinicalsymptomsatpresentationbutalsowithresponsetosurgery[4].Typicalliver changes in these patients include bile duct proliferation, cholestasis, bile plugs in biliary ducts, inflammatory cellinfiltration, giant cell formation, portal fibrosis and finally cirrhosis in severe cases [4]. It is anestablished 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 histologybetween symptomatic and asymptomatic patients. The appropriate time of surgery and the requirement of surgery in thesepatients have been debated [5]. The demonstration of pathological changes in theliverevenineарly,asymptomaticstagesofthediseaseandits subsequentregressionwithtreatmentcanprovideaclearargumentin favour of surgery [6]. Despite multiple studies, the aetio-pathogenesis of choledochal cyst has onlybeen hypothesized [7]. This study was also carried out with the expectation that histological changes in theliver and their behavior after surgery may help in understanding the pathophysiology of the disease and explain the variedsymptoms,recovery patterns andcomplications in patientswith choledochal cyst.Thus, theaim of this study was to determinethereversibilityandirreversibilityoftheliverhistologicalchangesinsymptomaticandasymptomaticcholedochalcystpatients.



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

OBJECTIVES:

Generalobjective:

Tostudy-

- thedifferencebetweenhistopathologicalchangesofliverinpatientswith symptomaticand asymptomatic typeIandIVcholedochalcysts.
- theeffectofsurgicaldrainageonliverhistology6monthsafterroux-en-Yhepaticojejunostomyinthe same.

Specificobjective:

- Toidentifythedegreeofhistologicalchangesofliverinsymptomaticandasymptomatictype IandIVcholedochalcystpatients before and 6monthsafter roux-en-Y hepaticojejunostomy.
- Tocomparethepre-excisionandpost-excisionhistopathologicalchangesofliverin thesametoidentifyreversibilityofchanges

MATERIALSANDMETHODS

Study design: This is a prospective analytic study. **Study place:** Department of Paediatric Surgery, BangabandhuSheikhMujibMedicalUniversity Hospital&DhakaMedical CollegeHospital,Dhaka,Bangladesh.
Study period: January 2017 to August 2018. **Study population:** Children with type I & type IV choledochal cystadmittedinpediatricsurgery department ofBSMMU&DMCH.**Studyvariables:**Degreeofcholestasis,hepatocellular damage, parenchymal inflammation, bile duct proliferation, bile duct inflammation, central venousdistentionand portalfibrosis.**Samplingtechnique:**Purposivesamplingtechnique.

Selectioncriteria:

Inclusioncriteria:

- TypeI& IV choledochalcystpresentingwithorwithoutsymptoms.

Exclusioncriteria:

- Lossofpatient
- Patientswhorefusetoparticipate
- Patientswithknownliverdisease
- Patients being unfit for operationPatientsdevelopingcomplicationofdrainage

DataCollectionandANALYSIS:

Thestudysubjectshavebeenselectedonthebasisofselectioncriteriafromthepatientsadmittedin theDepartmentofPediatricSurgery, BSMMU & DMC Hospital. Some patients with acute cholangitis was admitted, we treat them conservatively withantibiotics and advised them to come after two months. Some patients came with history of acute cholangitis within last twomonths,wehaveexcludedthem. Thedemographicinformation,relevanthistory,examinationfindingsandinvestigationreportsand 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,SPSSwindowssoftware,version24Fornormallydistributivequantitativedatawhichhasbeencomparedbyunpairedtest. A‘p’value of<0.05isconsidered statisticallysignificant.

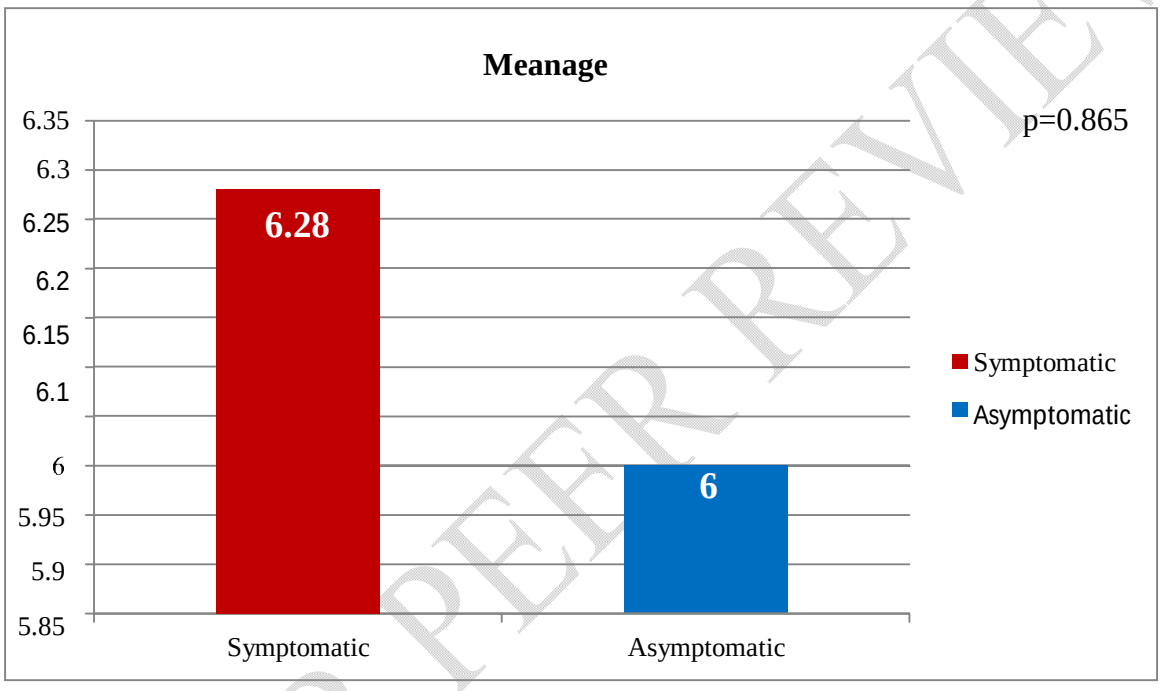
Ethicalconsideration:
During surgery & 6 months after surgery liver biopsy was taken which was done for research purpose. For this they will notreceiveanyfinancialsupportandallcostwillbearresearcher.Patientpartyhasinformedaboutprocedureanditscomplication.After counseling patients party has given consent for this study. Informed written consent has been taken and identify ofrespondents hasbeenanonymousand confidentialityofthestudy wasmaintained infollowing 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 cystand 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.

Age distributionof studypopulation

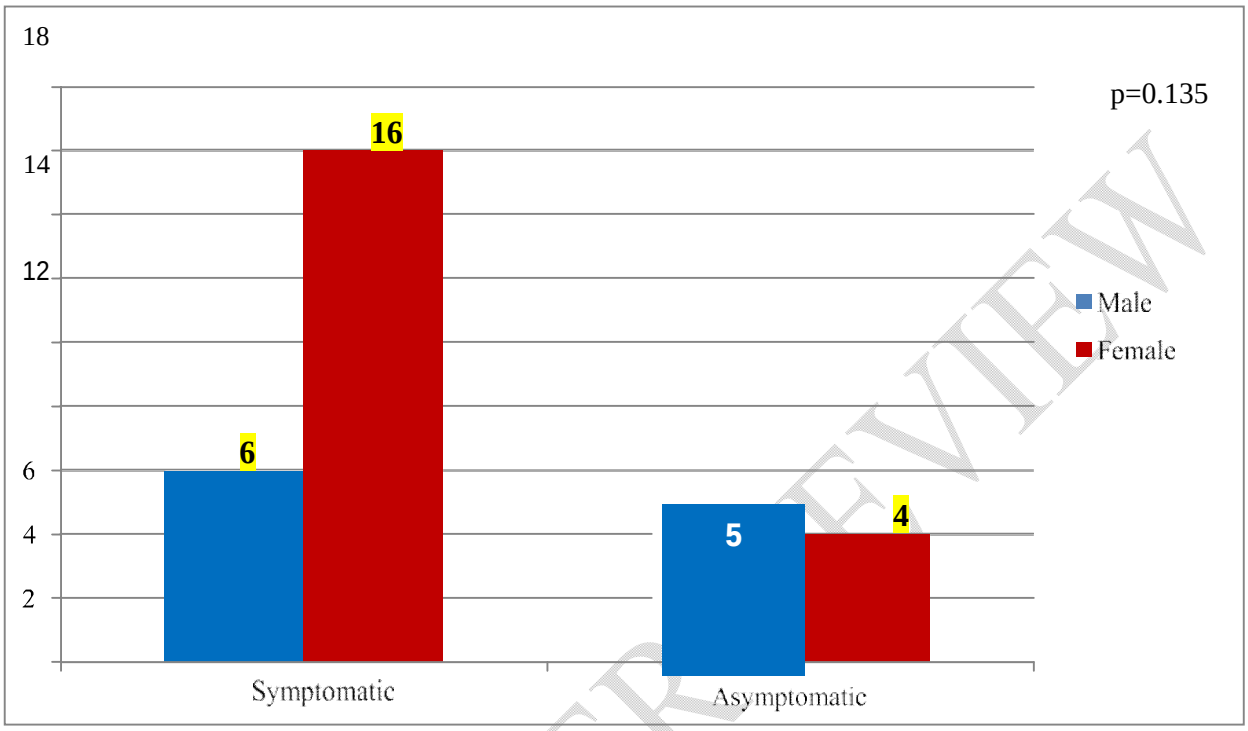
The age distribution of the study population is depicted in figure 6 below. The mean age distribution in bothsymptomatic and asymptomatic patient was near equal 6.28 and 6.00 respectively and there was no significant agedistribution (p = 0.865) betweensymptomaticand asymptomaticCDCpatients.



FigureII:Agedistribution ofthestudypopulation

Genderdistributionamongstudypopulation

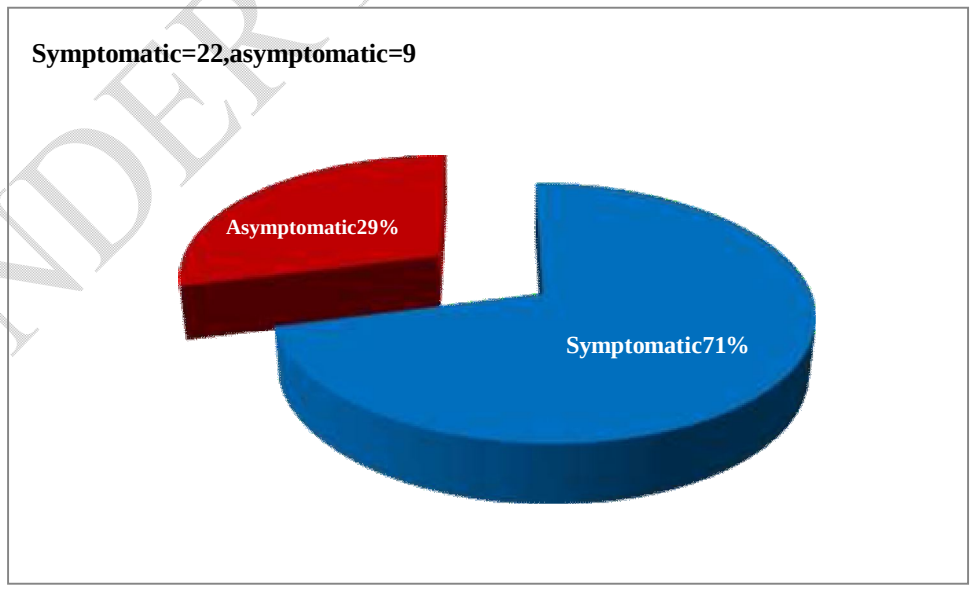
Female predominance was seen in symptomatic CDC patient but not in asymptomatic patient. And there was nosignificantsex distributionamongbothgroupsofpatients.



FigureIII:Sexdistributionofthestudypopulation

Symptomaticdistributionofthestudypopulation (N=31)

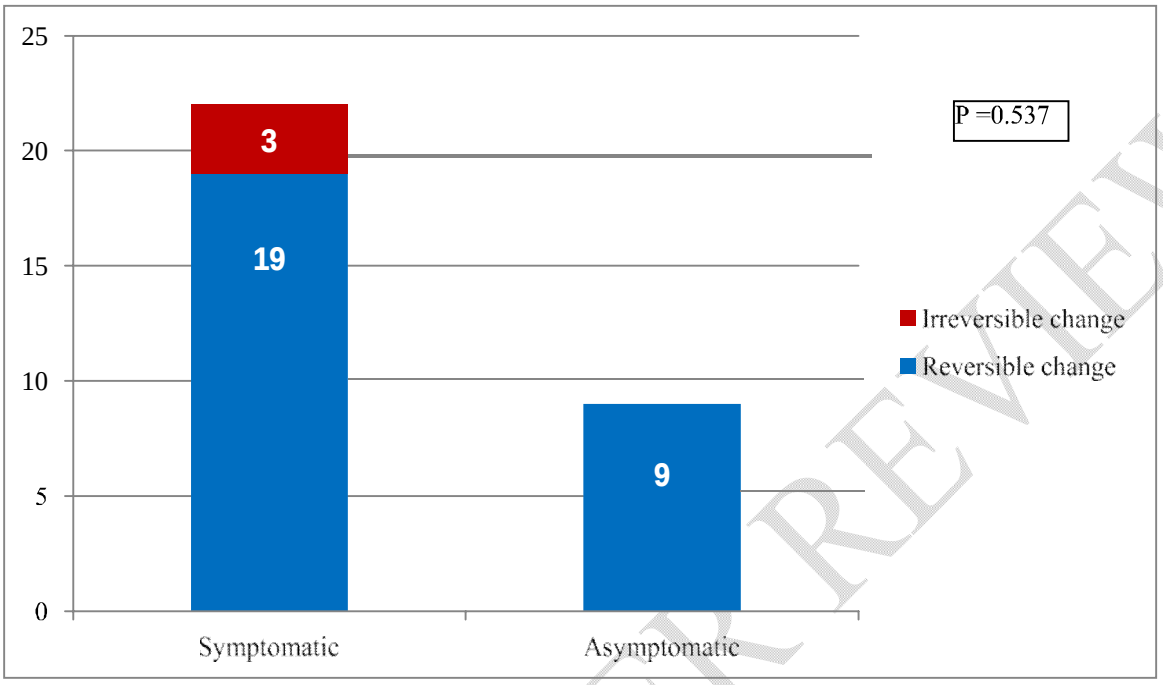
Distributionofstudypopulationaccordingtopresenceofsymptomisshowninfigure8.Morethan2/3rd(71%)patients were symptomaticandrestsofthem(29%) were asymptomatic.



FigureIV:Distributionofstudypopulationaccordingtosymptom

Histopathological changes of liver in symptomatic and asymptomatic choledochal cyst patients (Pre-excision) (N=31)

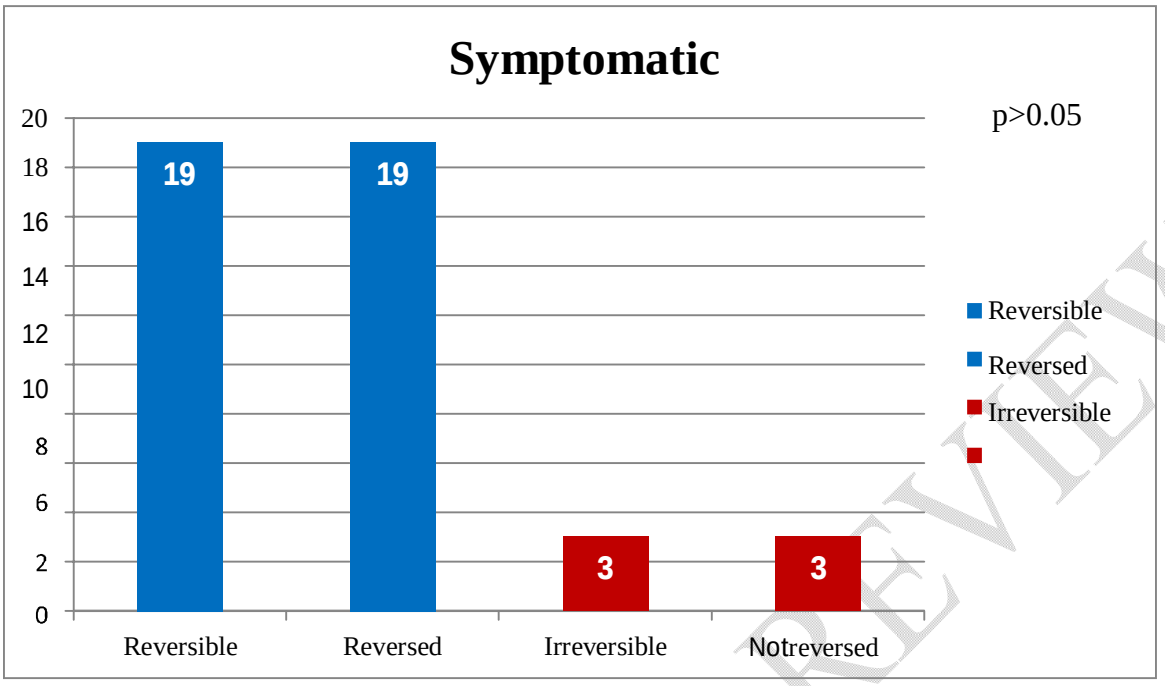
Bardiagramshowingpre-excisionallymost of thesymptomaticpatient wasshownreversiblechangesandresthadirreversiblechanges, whereas,allofthe asymptomaticpatientsfoundreversiblechanges.



FigureV: Histopathologicalchanges ofliverinsymptomatic and asymptomatic choledochalcystpatients(Pre-excision).

Reversibilityofhistopathologicalchangesofliverinsymptomaticcholedochalcystpatients(Pre-excisionandpost-excision)(N=22)

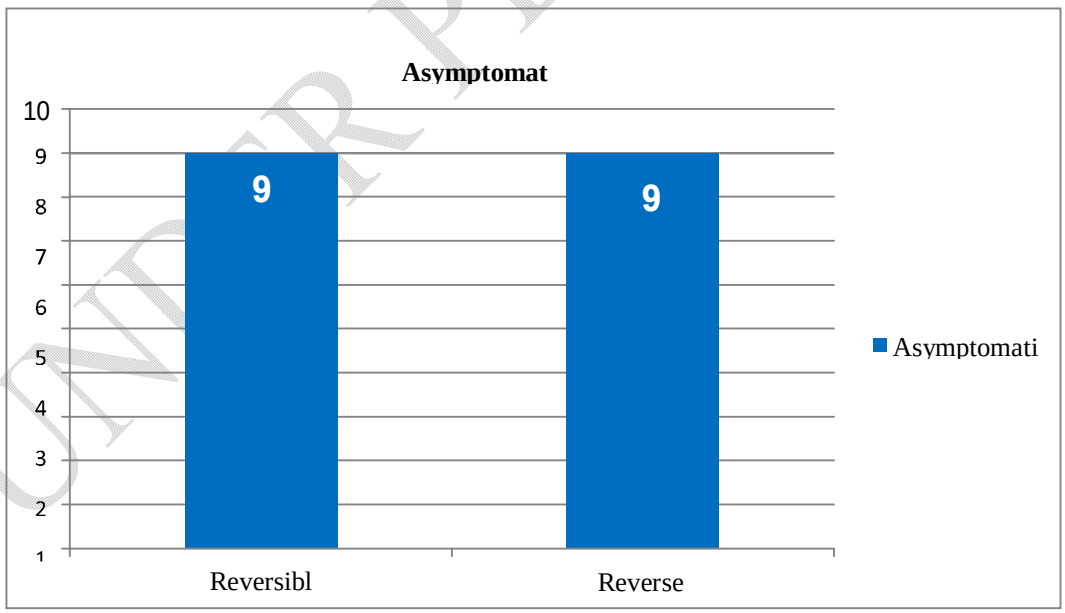
Figure VI showing histopathological changes of liver in symptomatic choledochal cyst patients (Pre-excision andpostexcision).Hereitwasfoundthatfollowingrouxloopsurgeryfortype Iand IVcholedochalcyst,therewasnoshorttermliver architecturalimprovement ofthesymptomaticpatientswhowerepre-excisionallyirreversible.



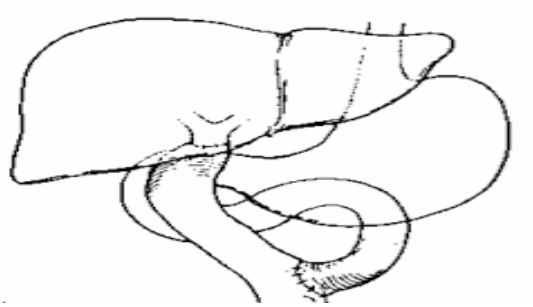
FigureVI:Histopathologicalchangesofliverinsymptomaticcholedochalcystpatients(Pre-excisionandpost-excision).

Reversibilityofhistopathologicalchangesofliverinasymptomaticcholedochalcystpatients(Pre-excisionandpost-excision)(N=09)

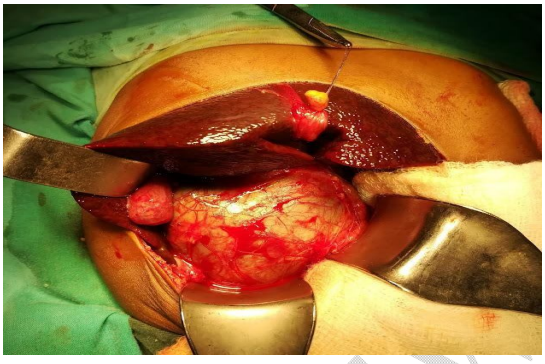
In this study all of the asymptomatic patients were shown reversible changes pre- excisionally and post excisionally there wassignificantshorttermliverarchitecturalimprovementofthepatients.



FigureVII:Histopathologicalchangesofliverinasymptomaticcholedochalcystpatients(Pre-excisionandpost-excision).



FigureVIII:schematicdrawingofRouxenYhepaticojejunostomy



FigureIX:Choledochalcyst

DISCUSSION

Choledochal cyst is a congenital anomaly of the biliary tree of unknown etiology, characterized by single cystic orfusiform dilatations usually of the extrahepatic duct in isolation or multiple dilatations of usually the intrahepaticduct system or different parts of both extrahepatic and intrahepatic biliary tree. It is potentially a serious disease ofthe biliary tree and may affect the liver in the infants and the children or in the adults particularly if there is actualobstruction or obstructive complications. For the classic type of extrahepatic choledochal cyst, excision of the cystand roux-en-Y hepaticojejunostomyis the common surgical method of treatment. If the surgical treatment is notdoneearly,itcancauseseriousmorbidityandmortalityfromcomplicationslikerecurrentcholangitis,pancreatitis,sepsis,biliarystoneformation, development of biliary[8].Choledochalcystspersehavenosymptomsotherthanalargecystpresentingasanasymptomaticabdominallump.However, most patients (80%) with choledochal cysts are detected after clinical manifestations. These clinicalsymptoms and signs are usually due to complications like obstruction, cholangitis, associated pancreatitis andsepsis, stone formation and others. These usually manifest in the infants and the children, but mayremainasymptomatic and present in the adulthood. Some asymptomatic one are diagnosed incidentally. It is likely that,patientswhopresentsymptomaticallymayhavediscernibleconsequentialimpactintheliverhistologyandfunction.These changes in liver histology may be reversible or irreversible depending in the degree and length of time thatthe liver is exposed to complications due to in symptomatic choledochal cyst. It is likely that greater the symptomsand signs in choledochal cyst patients, the more severe is the degree of liver histological changes that are lessreversible occur.In the study, it was considered that those patients who developed early histological changes in the liver with portalfibrosis(Ohkuma'sgrade1&2)onlywerereversible.On theotherhand,thosewhohaveadvancedchangesgreaterthan grade 2 were considered irreversible. Earlier, H. Toshimichi and colleague in Japan (2006) observed therelationship between the degree of liver fibrosis and its impact on the post-operative clinical course in 43 patientswithcholedochalcysts.Theyfoundthatirrespectiveofthedegreeofliverfibrosisandfunctionalstatusoftheliverat pre-operative period, all the patients with choledochal cysts had improved clinically one month after roux-en-Yhepaticojejunostomy. The laboratory parameters (S-Bil, S-AST, S-GGTP, S-Bile acid, S- amylase) that they hadstudiedasmarkersofimprovementcamewithinnormallimit.Buttheydidnothaveanyevidenceofmorphologicalimprovement of the liver such as observed by post-operative liver biopsy examination. However, in two patientswho had to undergo re-laparotomy for some other reasons later on, liver biopsy was done. It was found that bothhaving 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 choledochalcystthatcouldbegradeduptoOhkuma'sgrade2,wasalsolikelytodisappearinthepost-operativeclinicalcourseresultingintheclinicalimprovement.In the present analytical study, attempt was made to identify whether symptomatic patients show more irreversiblechanges than asymptomatic patients and if the post- excision roux-en-Y hepaticojejunostomy helps in reversingthese liver histological changes that are defined as irreversible. Thus, the aim of this study was to determine

thereversibilityandirreversibilityoftheliverhistologicalchangesinsymptomaticandasymptomaticcholedochalcystpatients.Totalthirty-onepatientswithtypeIandtypeIVcholedochalcystwereincludedinthisstudy.Theratioofsymptomatic to asymptomatic patient was 2:1. The mean age in both symptomatic and asymptomatic choledochalcystpatientswerenearlyequal(6.28,6.00).However,thesexdistributionsinbothsymptomaticandasymptomaticcholedochalcystpatientswerenotsimilar.Therewereoverwellbeinglymorefemalepatientsinsymptomaticgroup.Histopathological changes of varying severity were evident in the pre-excision liver biopsy in all patients withcholedochal cyst. Hepatocellular damage was the most widespread change noted in all patients in both groupsindicating that at leastsome degree of liver damage occurs irrespective of symptomatic status. All asymptomaticand great majority of symptomatic choledochal cyst patients demonstrated reversible histological changes in liverand these changes were reversed after 6 months of roux-en- Y hepaticojejunostomy in all. Conversely, the threesymptomaticpatientswhoshowedirreversibleliverhistologicalchangesdidnotundergoreversalafter6monthsofroux-en-Y hepaticojejunostomy. It is possible that gradedhistological changes occur in the liver of symptomaticcholedochal cyst patients depending on severity and length of the insult. Therefore, those patients who have earlyliver histological changes has the chance of reversibility to normal liver histology and those patients who presentwithadvance changeshavelittlescopeforregainingnormalliverhistologyevenaftersuccessfulroux-en-Yhepaticojejunostomy. Liver fibrosis is one of the major complications of choledochal cyst patients that may persistas a sequel. Obstructive cholangiopathy has been considered as the main cause of liver fibrosis in pediatriccholedochal cyst patients [9]. If the obstruction is removed early liver fibrosis may cease toprogress and be limited to a minimum. Yeong M L et al. (1982) [10] reported a case report on improvement of liverfibrosis after roux-en-Y hepaticojejunostomy in a choledochal cyst patient. It was postulated that the amount ofliverfibrosisdependsontherateofcollagensynthesiswhichwasstimulatedbyrefluxingchemicalinjurytobiliarychannel (common channel theory of choledochal cyst). Therefore, they suggested that if the fibro genic factor isremoved,thequantityoffibroustissueinthelivermaybedecreased.Evenincaselivercirrhosis,whichisgenerallyconsidered as irreversible phenomenon in adults and children, there are evidences of improvement after roux-en-Yhepaticojejunostomy in paediatric patients with choledochal cyst (Ishimaru T. et al. 2010, [11] Jackson CC 2002) [12]. Butin this study, those patients with irreversible liver histological changes had no reversal of liver histopathology sixmonths after roux-en-Y hepaticojejunostomy. Therefore, it can be suggested that following successful roux loopsurgeryfortypeIandIVcholedochalcysts,liverarchitecturalimprovementsinpatientswhohavepre-excisionallyirreversible changes is not to be expected at least in the short term. Longer follow-up may indicate the degree ofimprovement withtime.

CONCLUSION

Liverhistologyshowsvariousdegreeofchangesinallcholedochalcystpatientswhether symptomaticorasymptomatic. Symptomatic patient demonstrates more irreversible changes than asymptomatic patients. Majorityof the pathological changes of the liver in early stage are reversible after roux-en-Y hepaticojejunostomy. There isno short term liver architectural improvement of the patients with choledochal cyst evenafter successful roux-en-Yhepaticojejunostomywho pre-excisionallyhadirreversible changes.

LIMITATIONOFTHESTUDY:

- Samplesizeis small
- Followupperiodisshort
- Operativeprocedurewasnotdoneinsinglehand

STRENGTHOFTHESTUDY:

- Itisaprospectivetype of study,sochanceof data missingisminimal
- Histopathologicalreport wasdoneinsinglePathologist
- Liverbiopsyprocedure wasdonebysingleinterventionradiologist

Disclaimer (Artificial intelligence)

No generative AI technologies were used in writing or editing this manuscript.

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