Section: Pediatric Surgery

Original Research Article

COMPARISON OF PRE-OPERATIVE EVALUATION WITH INTRA-OPERATIVE FINDINGS IN DIFFERENTIATING BILIARY ATRESIA FROM OTHER CAUSES OF INFANTILE CHOLESTATIC JAUNDICE

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Abstract

Background: Neonatal cholestasis is a group of hepatobiliary disorders occurring within the first three months of life. The common causes of neonatal cholestasis include biliary Artesia and non-biliary Artesia causes. Investigations such as liver biochemistry, ultrasonography, endoscopic Retrograde Cholangiogram (ERCP), magnetic Cholangio- Pancreaticogram (MCRP), and HIDA scan are the investigations that have been used for diagnosis. The aim of the present study is to compare the preoperative investigation findings with the per-operative findings in Pediatric surgical cases with Biliary Atresia. **Materials and Methods:** 25 infants with Cholestatic jaundice with clinical and investigational suspicion of biliary Artesia are included in the study. Liver function Test, Ultrasound of the abdomen in fasting state, Hepatobiliary Scintigraphy (HIDA Scan), Intra-operative Cholangiography and Liver biopsy. **Result:** Most of the infants presented with surgical jaundice after 30th Day of Life. Baby girls are mostly affected in the ratio (3:2) compared to Baby boys. Majority of these babies 21/25 presented with clay-colored stools. The average of total bilirubin of the patients with biliary Artesia was 12.1gm%. HIDA scan diagnosed statistically significant number of biliary Artesia cases. Intra-Operative Cholangiogram has 100% diagnostic accuracy. **Conclusion:** Neonates presented with Clay coloured stools, Jaundice with elevated GGT in Liver Function Test should be referred for Paediatric surgical consultation. This will facilitate early intervention with Kasai Porto-Enterostomy and prevents progression of disease to Liver Cell Failure.

INTRODUCTION

Neonatal cholestasis defined as persistence of direct bilirubin at > 20% of total serum bilirubin for more than 14days.[1]The incidence of cholestasis in infancy is variable; biliary Artesia occurs in 1 in 10,000 – 15,000 infants, whereas intrahepatic bile duct Artesia appears to be much less common (one in 50000 – 75000 live births).[2]

Biliary Atresia constitutes 30% of the Neonatal Cholestatic Jaundice cases. Cholestatic Jaundice is mainly due to Biliary and Non-Biliary causes. The most common surgical cause for conjugated hyperbilirubinemia is Biliary Artesia. Biliary Artesia is a neonatal condition in which there is Artesia of the extra hepatic biliary tree with variable extension to intrahepatic bile ducts. The only effective treatment for patients with biliary Artesia is surgical drainage of the bile,[4] or liver transplantation.[4]Biliary Artesia is the most frequent indication for paediatric liver transplantation. Hence early diagnosis and surgical intervention is the key factor in the outcome as well as survival of the infant.[5]

Investigations such as liver biochemistry, ultrasonography, and HIDA scan are the investigations that have been used for diagnosis but may not yield accurate results. Operative Cholangiography remains the gold standard investigation for demonstrating biliary duct patency and to rule out Biliary Atresia. The percutaneous liver biopsy found to have a 90-95% diagnostic accuracy for biliary atresia, but sometimes it may not be indicative of biliary Artesia. In the present

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study, we compared the preoperative investigation modalities with the per-operative findings and liver biopsy in infantile Cholestatic jaundice. Premedication with Phenobarbital increases the accuracy of Scintigraphy evaluation for biliary atresia. Liver biopsy: When the clinical picture is unclear and less invasive tests have failed to confirm or exclude a diagnosis of Biliary Atresia with adequate certainty, Cholangiogram with wedge liver biopsy is planned. A wedge biopsy from the the liver taken, and the specimen of the transacted portal plate sent for Histo Pathological analysis. Histo Pathological findings play a central role in the diagnosis of Biliary Artesia and provide an essential assessment of the structures present at the fibrous biliary remnant. The other biopsy findings in Biliary Artesia often include bile ductular proliferation, bile stasis, periportal inflammation, identification of giant cells, and varying degrees of fibrosis. These findings in the biopsy are typically seen in Biliary Artesia and can be used to differentiate it from other causes of infantile Cholestatic jaundice.[6]

Aims & Objectives: To compare Diagnostic accuracy between Pre-operative investigations modalities with that of per-operative findings and liver biopsy in infants with Cholestatic jaundice.

MATERIALS AND METHODS

Infants recruited from outpatient clinic and inpatient department of Paediatrics and Paediatric Surgery, King George Hospital, Visakhapatnam.25 infants with Cholestatic jaundice with clinical and investigational suspicion of Biliary Atresia are included in the study. Cross-sectional Study carried out from October 2017 to January 2020.

Inclusion Criteria

All infants with Biliary Atresia and those with Cholestatic jaundice who underwent evaluation for Biliary Atresia with Cholangiography.

Exclusion Criteria

Infants with Cholestatic Jaundice, undergoing only percutaneous liver biopsy without open surgery. Infants investigated with LFT, USG Abdomen, HIDA Scan who do not require surgical intervention.

All patients primed with Ursodeoxycholic acid and Phenobarbitone for a minimum of five days before the scan—the hepatic uptake as well the presence or absence of dye in the intestine after 24hours was noted[7]. If there is no excretion of dye into the intestine beyond 24 hours, a presumptive diagnosis of Biliary Atresia is made. The Histo Pathological report reviewed to look for bile duct proliferation, bile plugs, periportal inflammatory infiltrates, identification of giant cells and fibrosis[8]. The Intra-operative, Cholangiogram findings and biopsy compared with the various preoperative diagnostic modalities to evaluate their efficacy[9]. A Chi-square test and t-test used to compare the variables between the Biliary Atresia and Non-biliary Atresia patients. For both, Accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) calculated for selected tests.[10]

RESULTS

A total of 25 patients with Cholestatic jaundice included in the study, of which 20 cases were Biliary Atresia 2 were Inspissated Bile Syndrome, and 3 were Choledochal cysts.

The comparison of Liver enzyme levels between Biliary Atresia infants and other jaundiced infants was statistically not significant.

Visible common bile duct, abnormal liver architecture was significant with a p-value <0.0001. The common bile duct was visible in all the non-biliary atresia patients and none of the biliary atresia patients and the abnormal liver architecture was seen in biliary atresia patients only.

The Intra-operative Cholangiogram had an accuracy of 100%, a sensitivity of 100%, the specificity of 100%, a positive predictive value of 100% and a negative predictive value of 100% for differentiating biliary atresia and non-biliary atresia. The difference is statistically significant, P-value < 0.00001.

When the biopsy findings of the biliary atresia and non-biliary atresia compared, it was found that bile duct proliferation, bile plug, giant cells, periportal inflammatory, infiltrate, and fibrosis seen in all 20 patients of biliary atresia. However, all these were absent in non-biliary atresia cases.

Females outnumbered males with a female/male ratio of 15/10= 1.5. Only 2 patients presented in the neonatal period, but fortunately, most of the patients 16/25 (64%) presented within the golden period, i.e., 1-2 months, whereas 7 patients presented after2months.

The average direct bilirubin of the patients with biliary atresia was 6.295, and that with non-biliary atresia was 6.04. The difference was not significant (p-value 0.39), the average of total bilirubin of the patients with biliary atresia was 12.1, and those with non-biliary atresia was11.1, and the differences were not significant (p-value0.35). The average AST of the patients with biliary atresia was 120.2 I.U, and that with non-biliary atresia was121.6.The difference is not significant (p-value 0.47). The average ALT of the patients with biliary atresia was 138.4 and those with non-biliary atresia was139.6.The difference was not significant (p-value0.48). For differentiating biliary atresia and non-biliary atresia contracted gallbladder on USG had an accuracy of 68%,as sensitivity of 70%,a specificity of 40%,the positive predictive value was 63.63%,and a negative predictive value of 33.33 % and the difference was not significant (p=0.1838).Others like visible CBD, abnormal liver architecture were significant, with a P-value of <0.00001. For differentiating biliary atresia and non-biliary atresia HIDA scan had an accuracy of 88%, a sensitivity of 100%, a specificity of 40%, the positive predictive value is 86.95%,the negative

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predictive value is 100%,and the difference between the two categories was significant, with a p-value of <0.00001. The intra operative findings of a contracted gall bladder had had an accuracy of 84% a sensitivity of 90%, the specificity of 60%, negative predictive value 60%, and a positive predictive value of 90% in differentiating biliary atresia and non-biliary atresia. However, the difference was not significant (P-value,0.101).The Intra operative Cholangiogram had an accuracy of 100%, a sensitivity of 100%, the specificity of 100%, the negative predictive value of 100% and a positive predictive value of 100%. The difference is statistically significant P-value<0.00001. In differentiating biliary atresia and non-biliary atresia biopsy findings like peri ductal proliferation, bile plugs, giant cells and periportal inflammatory infiltrates and fibrosis had an accuracy of 100%, a sensitivity of 100%, the specificity of 100%,the negative predictive value of 100% and a positive predictive value of 100%. The difference is statistically significant P-value<0.00001.In 2 patients with Inssipated bile syndrome, the biopsy confirmed the absence of biliary atresia as in 3 patients with choledochalcyst.The biopsy of the cyst excised was suggestive of Choledochal cyst the by ruling out the cystic variant of biliary atresia.

Table 1: Comparison of Liver enzymes

Average	Biliary Atresia	Other causes	P-value
Total bilirubin	12.1	11.1	p value 0.35
Direct Bilirubin	6.295	6.04	p value 0.39
AST	120.2	121.6	p value 0.47
ALT	138.4	139.6	p value 0.48
Alkaline Phosphatase	541.82	492	p value 0.25
GGT	447.5	446	p value0.48

Table 2: Comparison of Ultra Sonography findings

USG Abdomen	Biliary Atresia n (%)	Others n(%)	P-value
Gallbladder			
a)Normal	6 (30%)	3 (60%)	0.1838
b)Abnormal/contracted	14 (70%)	2(40%)	(not significant)
CBD visible	0	3 (60%)	<0.0001
Abnormal liver architecture	4 (20%)	0	<0.0001

Table 3: Comparison of HIDA Scan findings

	Biliary Atresia n (%)	Others n (%)	P Value
Absent HIDA excretion Into the intestine	20(100%)	3 (60%)	<0.00001
HIDA excretion Into the intestine	0	2 (40%)	<0.00001

Table 4: Comparison of operative findings

Intra operative findings	Biliary Atresia n(%)	Others n(%)
Distended gallbladder	2 (10%)	3 (60%)
Contracted/ atretic gallbladder	18 (90%)	2(40%)
Common bile duct visible	0	3(60 %)
Abnormal liver architecture	4 (20%)	0
Intra-operative cholangiogram		
a) Absent intrahepatic radicals	20(100%)	0
b)Patent EHBA	0	5 (100%)

Table 5: Biopsy findings

Biopsy findings	Biliary atresia n=20	Non-Biliary atresia n=5	P-value
Bile duct proliferations	20(100%)	0	<0.00001
Bile plugs	20(100%)	0	<0.00001
Peri portal inflammatory Infiltrates and fibrosis	20(100%)	0	<0.00001
Giant cells	20(100%)	0	<0.00001

DISCUSSION

Biliary atresia is an essential cause of neonatal cholestasis in developing countries like India, where though jaundice develops early, most of the children are referred late to the hospital.The only clinical feature which is suggestive of biliary atresia is an acholic stool, while other biochemical and clinical features lack specificity as other causes of neonatal cholestasis also show similar rends.Any patient with history and clinical picture suggestive Cholestatic jaundice and if the stool is clay-colored, with a liver function test indicative of a raised GGT we can directly go for an intra-operative Cholangiogram to rule out biliary atresia, the only surgical cause which needs treatment as early as possible to yield a better survival with an a native liver.It is paramount important to educate not only people but also the health care givers, especially the Paediatrician and the general practitioners in the periphery, that any jaundice beyond two weeks in any neonate could be

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biliary atresia and needs a detailed evaluation as the timely intervention is the key to success in such cases.

CONCLUSION

Infantile cholestasis is characterized by persistently raised conjugated bilirubin beyond the period of physiological jaundice, i.e.,>2 weeks. Neonate with Cholestatic jaundice, if there is a delay in getting investigation done, but clinical features highly indicative of cholestasis, they can directly subject to Mini-Laparotomy with liver biopsy, and intra operative Cholangiogram should be done without delay, as the prognosis of the patient is best if treated within two months of age. At the same time we can proceed with Kasai Porto Enterostomy if intra operative Cholangiogram is suggestive of atresia of extra hepatic biliary ducts.

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