

# Role of Hepatobiliary Scintigraphy and Ultrasonography in the Diagnosis of Biliary Atresia in Infant with Neonatal Jaundice – Experiences in NINMAS

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**Objective:** The purpose of this study was to determine whether gall bladder visualization can help to exclude the biliary atresia in hepatobiliary scintigraphic studies of infants with persistent jaundice.

**Methods:** This is a retrospective study carried out at the National Institute of Nuclear Medicine and Allied Sciences (NINMAS). Study subjects include infants with neo-natal jaundice who underwent Hepatobiliary scintigraphies for suspected biliary atresia and study period was 2 years. Food was withheld for 4 hours before the examination. Anterior images of liver and gall bladder were taken after i/v administration of 2 -3 mci 99m Tc labeled Brida (HIDA) at 5 min interval for 2 hours then at 4 hours and 24 hours. Non-visualization of bowel activity in HIDA scan in 24hours delayed images was considered as cases of diagnosis of biliary atresia.

**Results:** Thirty-six patients were included in this retrospective study. Patent biliary channels was seen by scintigraphies in 17(47%) patients and biliary atresia was seen in 19(52%) patients. By abdominal US non-visualization of gall bladder were found in 25(69%) cases and gall bladder visualized in 11(30%) cases. Eight (22%) of 36 patients had biopsy confirmed biliary atresia; all of these had positive scintigraphies and (60%) had positive sonographic findings. Among the 5 false-positive scintigraphies caused by hepatic dysfunction and 2 had normal sonography. Thirty-six patients had periscintigraphic sonography. There were 25/36 (61%) abnormal studies, which included cases with small gallbladder (n = 8) and non-visualized gallbladder (n = 17), but not periportal fibrosis.

**Conclusion:** Gall bladder was usually visible on Hepatobiliary scintigraphy of fasting patients with biliary patency. Both hepatobiliary scintigraphy and sonography are currently the standard imaging investigations for suspected biliary atresia. The

complementary role, in which scintigraphy and sonography are important, and recommend follow-up imaging reassessment before making definitive surgical decisions. This will serve to decrease the frequency of false-positive imaging diagnoses of biliary atresia, and hence, avoid unnecessary surgeries.

**Keywords:** Biliary atresia, HIDA scan, neonatal jaundice

## INTRODUCTION

Biliary atresia was initially thought to be a congenital malformation. The liver and biliary system develops from a bi-lobed endodermal bud. The cephalic bud gives rise to the right and left lobes of the liver. The caudal bud gives rise to biliary tract and the gallbladder. The biliary tract proper is formed after recanalization of the solid core by 12–14 weeks of intrauterine life (1). Bile secretion begins thereafter and flows into the small intestine. Most of the congenital abnormalities of the biliary tract are thought to be due to either failure of recanalization of the ducts (biliary atresia) or faulty recanalization with cystic dilatation of intrahepatic (Caroli's disease) and extrahepatic ducts (choledochal cyst). Subsequent research and clinical evidence did not support the hypothesis of congenital malformation. Now it is believed that biliary atresia is a progressive inflammatory pandoctular obliterative disease of the bile ducts starting in the antenatal period. The destructive inflammatory process might involve only the distal part of the extrahepatic bile duct causing obstruction and leaving the proximal ducts patent. The clinical presentation is that of infantile obstructive cholangiopathy, waxing and

waning icterus, pale colored stools and high colored urine from early neonatal period. It is estimated to affect 1 in 13,000 live births and is more commonly seen in Asian and Oriental neonates (2,3). Most cases of neonatal jaundice are due to Biliary Atresia (BA) or Neonatal hepatitis (4). The differentiation of BA from other causes of Persistent Neonatal Jaundice, holds the key to survival of neonates suffering from BA with a variety of 99mTc labeled iminodiacetic acid (IDA) agents and its analogues have been used in the past (1-3). Lately, 99mTechnetium trimethyl bromoiminodiacetic acid (TBIDA / Mebrofenin) has been shown to have better hepatic uptake and excretion (4)

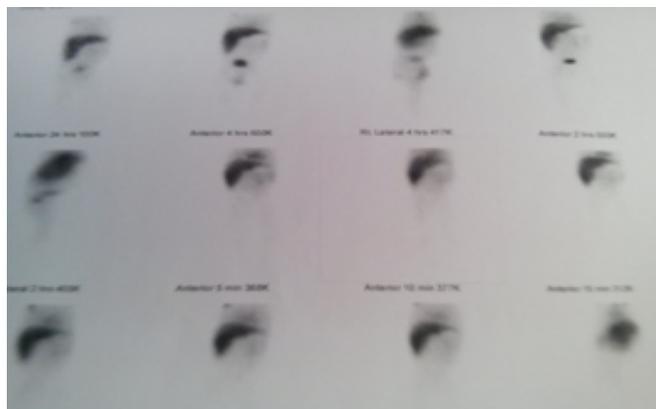
**MATERIAL AND METHODS**

From January 2013 to December 2014, 36 infants (Age ranged from 41 days to 6 months, mean age, 36 days , 26 male and 10 female) with prolonged conjugated cholestatic jaundice in the National Institute of Nuclear Medicine and Allied Sciences (NINMAS) were retrospectively studied. Their medical records were reviewed with regard to liver function test results (total bilirubin, direct bilirubin, alkaline phosphatase), ultrasonography (US) of hepatobiliary systems, hepatobiliary scintigraphy and liver biopsy results. Each patient was given an intravenous injection of 2-3 mci 99m Tc-Mebrofenin. Imaging was carried out on a single Head Gamma Camera using a high-resolution collimator with the patient in supine position. Serial anterior static images were acquired at 5 min, 15 min, 30 min, 45 min and hourly for 2 hours. If no radiotracer was detected in the bowel till 4 hours, a delayed scan was taken at 24 hr. All scans were reviewed and considered positive for Biliary Atresia (Figure 1) if the scans showed good liver uptake with no intestinal activity till 24 hr (5) or reduced background activity.

**RESULTS**

Thirty six cases were included in this retrospective study. Clinical and demographic data and

differences are summarized in Table 1. Total bilirubin, direct bilirubin and alkaline phosphatase were significantly higher in infants with BA as compared to those in other group (Table 2).



**Figure1. HIDA scan of Biliary Atresia**

Study result revealed delayed images after 24 hours, the excretion of the bile was absent in 19 (52%)cases out of 36 infants suggest infants with BA (Table 3).

**Table 1: Clinical manifestations of BA and Non- BA cases at the time of the presentations**

Clinical manifestation	Biliary atresia (BA) cases (n=19)	Non- Biliary atresia cases (n=17)
Age at study (mean days)	45 (age range 30-60 days)	35.8 (age range 20-45 days)
Female /Male	10/09	12/05
Hepatosplenomegaly	09	0

**Table 2: Laboratory differences between BA and other cause of cholestasis jaundice**

	BA cases (n= 19)	Non- BA cases (n=17)	P value
Total bilirubin (mean ± SD, mg/dl)	9 ± 0.77	8.5 ± 0.45	0.004
Direct bilirubin (mean ± SD, mg/dl)	4 ± 0.33	3.5 ± 0.23	0.001
Alkaline Phosphatase (mean ± SD, mg/dl)	789 ± 16	781 ± 16	0.06

Patent biliary tree was seen by scintigraphies in 17(47%) cases. Abdominal US revealed non-visualization of gall bladder in 25(69%) cases and visualization of gall bladder in 11(30%) cases. Liver biopsy was done among 08 (22%) infants to confirm the diagnosis of BA and all of those had positive scintigraphies and with (37%) had positive

sonographic findings. Peri-scintigraphic sonography had performed in thirty-six patients.

There were 25/36 (61%) abnormal studies, which included cases with small gallbladder (n = 8) and non-visualized gallbladder (n=17), but not periportal fibrosis.

**Table 3: US, Scintigraphic findings and Liver biopsy results**

Abdominal Ultrasonography		HIDA scan		Liver Biopsy
Visualization of GB	Non-Visualization of GB	Bowel activity Present	Absence of bowel activity after 24 hours	
(11/36,30%)	(25/36,70%)	Patent (17/36, 47%)	BA (19, 53%)	08(22%)

## DISCUSSION

Though the causes of persistent conjugated hyperbilirubinemia in infants are many, BA and neonatal hepatitis (secondary to CMV, HAV, HBV, Rubella and Toxoplasma infection) account for 70-80% (5). It usually presents by 1-2 months of age with persistent direct hyperbilirubinemia and icterus. Both sexes are affected equally. No single test has proven 100% reliable in diagnosing BA (6, 7). <sup>99m</sup>Tc trimethyl bromo iminodiacetic acids is considered best for Hepato-biliary Scintigraphy because of its 98% hepatic extraction and urinary excretion of 1.5% (8). In neonates extraction of Mebrofenin by the liver is prompt and uniform distribution is reached within 5 minutes. Gall bladder is seen as early as ten minutes and Bowel activity is by 30-40 minutes. The presence of tracer within the small bowel excludes BA (6). Most reviews report sensitivity of hepato-biliary scintigraphy for the diagnosis of BA between 97-100% and the specificity from 33-91% (3, 6). The present study as being retrospective is not structured to yield comparable data. In a larger prospective study, Cox et al (8) reported that one third of the patients with patent biliary tracts had no detectable tracer excretion at 24 hrs, falsely indicating biliary atresia. To summarize, prompt and accurate diagnosis of BA is of utmost

importance in neonates as the success of surgical procedure is inversely related to age.

## CONCLUSION

Hepatobiliary scintigraphy and sonography are currently the standard imaging investigations for suspected biliary atresia. Mebrofen in hepatobiliary scintigraphy is a simple, cost-effective, minimum invasive with a very low radiation hazards and accurate diagnostic tool for suspected Biliary Atresia. This will serve to decrease the frequency of false-positive imaging diagnoses of biliary atresia, and hence, avoid unnecessary surgeries.

## REFERENCES

- Balistreri WF. Neonatal Cholestasis. *J Pediatrics* 1985; 106: 171-84.
- Nadel HR. Hepatobiliary Scintigraphy in children. *Semin Nucl Med* 1996;26:25-42.
- Majd M, Reba RC, Altman RP. Hepato-biliary scintigraphy with <sup>99m</sup>Tc-PIPIDA in evaluation of neonatal jaundice. *Paediatrics* 1981; 67:142-5.
- Hitch BC, Leonard JC, Psyher TJ. Differentiation of Cholestatic Jaundice in infants. Utility of Diethyl IDA. *Am J Surgery* 1981; 142:671-7.
- Krishnamurthy GT, Turner FF. Pharmacokinetics and clinical application of Technetium <sup>99m</sup> labeled Hepatobiliary agents. *Semin Nucl Med* 1990; 20:130-49.
- Gerhold JP, Klingensmith WC, Kuni CC et al. Diagnosis of biliary atresia with radionuclide Hepato-biliary imaging. *Radiology* 1983; 146:499-504.
- Howman – Giles R. Hepatobiliary scintigraphy in infancy. *J Nucl Med* 1998; 39:311-9.
- Cox KL, Stadalnik RC, McGahan JP, Sanders K, Cannon RA and Ruebner BH. Hepatobiliary scintigraphy with Technetium – <sup>99m</sup> Disofenin in the evaluation of neonatal Cholestasis. *Journal of Paediatric Gastroenterology and Nutrition* 1987; 6: 885.