

Research Article

Evaluation of diagnostic efficacy of hepatobiliary scintigraphy as a diagnostic procedure in pediatric practice with special reference to cholestatic jaundice

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ABSTRACT

Background: The objective was to assess the diagnostic efficacy of hepatobiliary scintigraphy (Tc^{99m} mebrofenin) in case of cholestatic jaundice in pediatric practice.

Method: Study conducted on 45 cases from 0-6 yrs. of age. Out of 45 pt 20 pt excluded from study Hepatobiliary Scintigraphy (Tc^{99m} Mebrofenin) was performed in 25 cases. Injection of Tc^{99m} mebrofenin (1-2 mCi) IV was given to each subject. Dynamic hepatic scan was done upto initial 1 hour study and additional delayed images were taken at 4 & 24 hrs only in case of non-visualization of tracer in the intestine after initial 1 hr. study.

Results: In this study hepatobiliary scintigraphy was 100% sensitive, 93.73% specific, 80% positive predictive values, 100% negative predictive value, 6.23% false positive result and virtually no false negative result for biliary atresia.

Conclusion: It is concluded that Tc^{99m} mebrofenin hepatobiliary scintigraphy has proven to be reliable noninvasive imaging modality in evaluating cholestatic jaundice in pediatric practice as it carries a high sensitive & specific value, good positive & no negative predictive value, few false positive & virtually no false negative results.

Keywords: Hepatobiliary Scintigraphy, Cholestatic jaundice, Mebrofenin Tc^{99m}

INTRODUCTION

Hepatobiliary disorders are commonly encountered in pediatric practice with diverse etiology and varied clinical presentation of various disorders, related with hepatobiliary system, Jaundice especially Cholestatic jaundice remains a common manifestation of hepatobiliary disorder, more during infancy. It always signifies primary defect in the hepatocellular phase of bile excretion or in canalicular or ductal function or loss of patency of these structures. The multifactorial etiology of cholestatic jaundice possesses a great diagnostic dilemma as it includes infection, metabolic and

anatomical defects of hepatobiliary system. In young infants it is always urgent and usually very difficult to make a specific diagnosis. Urgency required because of the need of therapeutic intervention before liver damage is irreversible. Diagnostic difficulties arise from the relative inadequacies of existing techniques for clinical evaluation.

Investigations such as USG, percutaneous needle liver biopsy, endoscopic retrograde cholangiopancreatography (ERCP) etc. contribute to a large extent in exploring these disorders. However, hepatobiliary scintigraphy has proven outstanding noninvasive technique in evaluation

of cholestatic jaundice in infancy. In Radionuclide scintigraphy a biological compound labelled with suitable radioisotope is administered to the patient. It rapidly localizes in the organ of interest. The gamma camera enables the sequential visualization and follow up of radio pharmaceuticals injection. The IDA Agent like HIDA, PIPIDA, EHIDA and mebrofenin are selectively taken by hepatocytes excreted into duodenum via hepatobiliary system.^{1,5,6} Mebrefenin has shown the most ideal biochemical characteristic both in vivo and vitro studies especially in high level of serum bilirubin.⁴

METHODS

Total five patient similar age group without cholestatic jaundice were included in study to know normal physiological excretion, hepatic uptake of Tc 99m. In hepatobiliary system. In study group total 40 patient were selected. Out of forty patient 20 patient were excluded on the basis of exclusion criteria.

Exclusion Criteria in study:

1. Those patient who had not given written consent for procedure.
2. Hemodynamically unstable patient
3. GCS below -8 or (unconscious patient, Encephalopathy)
4. Patient with INR > 3.5.

In our study 7 patient not given consent & two were in encephalopathy, 8 patient were critically ill with unstable vital & two patient were with INR > 3.5. All were excluded from the study. Hepatobiliary scintigraphy not performed on these patients.

Final diagnosis of each case with cholestatic jaundice of more than 14 days was established by detailed history, clinical evaluation and investigations especially percutaneous liver biopsy & USG. An informed consent was taken from parent of all patients included in the study. Every Patient was subjected to a full history taking stressing on evaluation and progression of hepatobiliary symptoms, like the appearance of jaundice, colour of urine and stool, pruritus, vomiting, fever. All subjects were thoroughly investigated including total & direct serum bilirubin, Alkaline phosphatase and gammaglutyrase transpeptidase, Aspartate transaminase, Alanine transaminase, prothrombin time, serum albumin, urine for bile salt & bile pigment. Prescan diagnosis as based on overall clinical evaluation & investigations. All the cases were subjected to hepatobiliary scintigraphy with Tc^{99m} mebrofenin after a written consent from the parent. Oral feeds were withheld for 2 hrs. prior to scan & 1 hr. after the scan.

Triclofos Sodium (10-20 mg/kg) orally was given for sedation in case of irritable & uncooperative subjects. Emergency resuscitation kit was kept ready to deal with any unexpected reaction. The IV canula was placed and

urinary bladder emptied in older children & wet diapers were changed in the younger ones to avoid urinary contamination.

Gamma Camera equipped with low energy all purpose leap collimeter was positioned over supine patient covering upper abdomen including liver, spleen, heart & small intestine. Injection of 1-2 mCi Tc^{99m} mebrofenin was given intravenously in a bolus form and gamma camera was started immediately.

The computer started reading the counts from that moment as well as acquiring the pictures on a fixed pattern set in protocol digital images, at 1 frame/n per minute for 60 minutes. At the end of sixty minutes right lateral and posterior images were taken for 2 minutes each. Additional Anterior images were also taken at 4 hrs. and 24 hrs. later in case of nonvisualization of tracer in the intestine.

Standard protocol for dynamic Hbs.

Phase	No. of frame/Image	Total Time (minutes)
I	60	60
II Rt. Lateral	1	2
III Posterior	1	2

Each standard hepatic dynamic scan took 64 minutes. Phenobarbital in dose of 5mg/kg/day per oral for 5 days was given to those patients who were unable to show any radioactivity in gut after 24hrs. of imaging and a repeat scan was performed in a similar way as the previous one.

RESULTS

The mean age of study and control group was 2.5 yrs. \pm 2.5 SD and 2.2 yrs \pm 1.7 SD respectively mean age of total population was 2.25 yrs. \pm 2.2 SD.

The most consistent clinical finding were icterus and yellow coloration of urine with clay colored stool (100%). Other symptoms like vomiting (45%), Hepatomegaly (65%) Splenomegaly (35%), Pruritus (45%) & bleeding diathesis in (10%) was present in study group. Mean total and direct serum bilirubin in study group were 8.90 mg% \pm 2.20 SD and 5.60 mg% \pm 2.20 SD respectively while 0.90 mg% \pm 0.14 SD and 0.23 mg% \pm 0.05 SD respectively in control group.

A statistical significant difference was observed in the liver enzyme assay between the study and control group with mean value of SGPT 100.30 IU/L. \pm 35.30 SD, SGOT 133.30 IU/L \pm 16.10 SD and Alk, phosphatase 173.16 KA \pm 69.43 SD INR 1.5 \pm SSD, in study group. USG & percutaneous liver biopsy also done over all assessment including clinical presentation, USG & liver biopsy, study group (n=20) was grouped into biliary atresia group, acute hepatitis & fulminant hepatitis group.

Table 1: Hepatobiliary scintigraphy in various clinicopathological conditions.

Prescan (HBS) Diagnosis	No. of cases	Imaging at 5 mts.		Imaging at 1hrs.		Imaging at 4hrs.		Imaging at 24hrs	
		Hepatic uptake		Intestine		Intestine		Intestine	
		Normal N. (%)	Reduced N. (%)	Vis. N. (%)	Non. vis. N. (%)	Vis. N. (%)	Non. vis. N. (%)	Vis. N. (%)	Non.vis. N. (%)
Physiological control	5	5 (100%)	–	5(100%)	0	–	–	–	–
Biliary atresia	4	4 (100%)	–	0	4(100%)	0	4(100%)	0	4(100%)
Acute hepatitis	11	7 (63.63%)	4 (36.37%)	7(63.63)	4(36.37%)	2(18.18%)	1(9.09%)	1(9.09%)	0
Fulminant hepatitis	5	2 (40%)	3 (60%)	1(20%)	4(80%)	2(40%)	2(40%)	2(40%)	1(20%)
Total	25	18 (72%)	7 (28%)	8(30%)	12(48%)	4(16%)	7(28%)	3(12%)	5(20%)

Vis = Visualization
Non vis = Non visualization

HBS in various clinicopathological conditions. All physiological controls had normal hepatic uptake at 5 minutes of imaging and 100% cases visualized intestine within 1 hr. & on dynamic scanning of Gall bladder & CBD visualizing within 12 minutes. Intestine visualized within 25 minutes. Activity/time curve is showing activity of liver & heart. Liver uptake reaches at peak within 5 minutes after that liver activity decreases gradually & no detectable activity after 1 hr. study. As the liver uptake increases, cardiac activity goes down gradually.

All cases of biliary atresia had not visualized intestine at 4, 24 hrs. of imaging. And all 4(100%) had normal hepatic uptake at 5 minutes in this group. Activity/Time Curve of biliary atresia group indicating good hepatic uptake & no decline in radio activity of liver that means hepatobiliary tract is not patent. In acute hepatitis group 63.63% case had normal hepatic uptake and 36.37% reduced uptake at 5 minutes imaging, 7(63.36%) case of acute hepatitis visualized intestine with in 1 hour & 10(90.91%) patients had visualized intestine, but 9.09% not visualized at 4 hrs. imaging and 11(100%) subjects of this group had visualized intestine after 24 hr. of imaging.

Eighty percent (4) cases of fulminant hepatitis had reduced hepatic uptake & 1(20%) cases had normal uptake at 5 minutes. Eighty percent (4) cases of this group not visualizes traces in intestine at one hour study. Sixty percent cases had not visualized intestine but 40% cases visualized intestine at 4 hr. of imaging & 80% cases had visualized intestine and 20% cases not visualized intestine at 24 hr. imaging in fulminant hepatitis group.

Figure 1st is showing hepatobiliary scintigraphic images in a physiological control after the dynamic scan. The figure shows 32 minute frames (1 frames/minute), 10 and 12 minute images are showing gall bladder and CBD activity respectively and intestine is visualizing at 23 minutes.

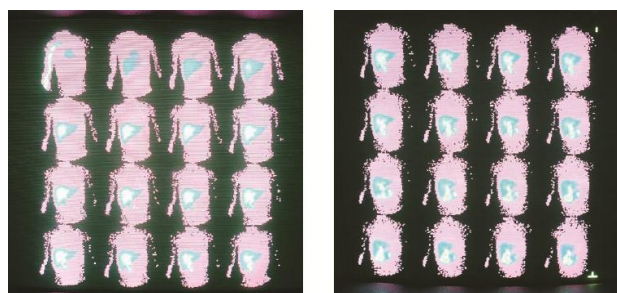


Figure 1: Dynamic HBS scan in a physiological subject.

Activity/time curve (figure 2) is showing activity of liver (line 1) and heart (line 2). Liver uptake reaches at peak within 5 minutes after that liver activity decreases gradually and no detectable activity after 1 hour study. As the liver uptake increases cardiac activity goes down gradually.

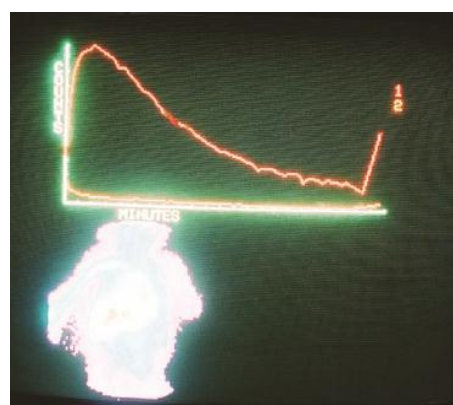


Figure 2

Figure 4 shows imaging at 24 hrs in a case Biliary atresia this shows good hepatic uptake but no traces of Tc⁹⁹ in intestine even after 24 hrs. of HBS imaging.

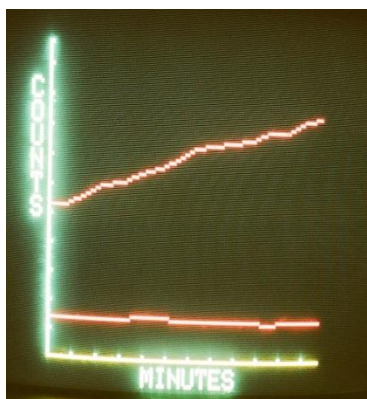


Figure 3: Activity Vs time curve (Biliary atresia).

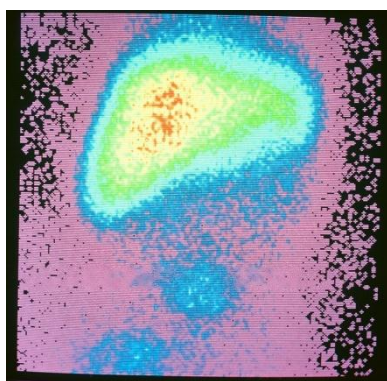


Figure 4: HBS imaging at 24 hrs (biliary atresia).

Activity/time curve of biliary atresia case has shown in figure 3 and this curve is indicating good hepatic uptake and no decline in radioactivity of liver that means hepatobiliary tract is not patent.

Table 2: Efficacy of hepatobiliary scintigraphy in biliary atresia.

Result	Diagnosis				Total
	Biliary atresia		Other than biliary atresia		
	No.	No.	No.	No.	
Positive	(a) True positive	4	(b) False positive	1	a+b=5
	(c) False negative	0	(d) True negative	15	
Negative					15
Total	a+c	4	b+d	16	20

1. Sensitivity 100
2. Specificity 93.15%
3. Predictive value of a positive test 80%
4. Predictive value of a negative test 100%
5. Percentage of false negative 0%
6. Percentage of false positive 6.25%

Our Study Showed diagnostic efficacy of HBS in cases of biliary atresia Sensitivity 100% specificity 93.75% predictive values of Positive test 80%. Predictive values of negative test 100%. Percentage of false negative 0% & percentage of false positive cases 6.25% respectively.

DISCUSSION

USG evaluation of Cholestatic jaundice cases in this study showed positive finding in 75% of cases. The results were comparable with Picozzi (1985)⁷ who reported 78% cases with positive USG scan. BB scott (1980)⁹ reported an overall USG accuracy of 68% in his study while 80.2% and 83% sensitivity for USG was noted by Ming Wei Lai et al (1994)¹⁴ and Haim, S.B. et al (1995)⁴ respectively.

Percutaneous liver biopsy was performed in 14 out of 20 cases of cholestatic jaundice showed distorted liver morphology in 100% of cases. An accuracy of 96% liver biopsy was reportedly Ming Wei Lai et al 1994,¹⁴ Leonard et al (1980)⁵ was established diagnosis in 11 of 13 cases with accuracy 85% by liver biopsy.

Prescan (HBS) diagnosis through the clinical, biochemical USG and liver biopsy reported biliary atresia in 4 cases (20%), hepatitis in 11 cases (55%) and fulminant hepatitis in 5 cases (25%) the similar result showing Silverberg et al¹⁰ 1973 & S.B. Haim et al 1995.⁴ In our study overall 72% subject showed normal hepatic uptake and reduced uptake in 28% cases and intestinal visualization was present in 80% cases at 24 hrs. of imaging. Similar results were shown by K. Zeman et al 1984¹² William, S. Pivak et al¹¹ Seven Cases (63.63%) of acute hepatitis had normal hepatic uptake and rest cases 36.37% had reduced uptake.

Our data indicate hepatobiliary imaging with Tc^{99m} mebrofinin can be used to diagnose biliary atresia non invasively with high degree of sensitivity and specificity. The most useful criteria was the absence of intestinal radioactivity through 24 hrs.

In acute hepatitis 90.9% cases were visualized intestine at 4 hrs. and all cases (100%) were visualized intestine at 24 hrs. of imaging. Eighty percent cases of fulminant hepatitis had reduced hepatic uptake and 20% had normal uptake at 5 min. & Sixty Percent cases had not visualized intestine but 40% cases had visualized intestine at 4 hrs. of imaging while 80% cases had visualized intestine and 20% cases not visualized intestine at 24 hrs./ imaging in this group.

William Spivak (1985)¹¹ found reduced hepatic uptake in 37% cases but contrast to present study S.B Haim et al 1995⁴ showed good hepatic uptake in all cases of hepatitis. This discrepancy may be due to that mean age of our cases in much higher than Simona Ben Haim et al

1995⁴ study. Mossoud et al 1981⁶ study had shown 71.3% Cases of hepatitis had not visualized intestine at 24 hrs. of HBS scanning in contrast to 20% in our study. This difference in result may be due to our study population is small & Mossoud et al used different IDA agent for their study.

Ninety four percent cases of non biliary atresia had shown intestinal activity at 24 hr. of imaging and similar interpretation of 93% intestinal visualization were observed by S. Benhaim et al 1995.⁴

Leonard et al 1982⁵ described the hepatic activity/time curve in normal subject can be characterized by prompt uptake and rapid elimination, patient with neonatal hepatitis show poor hepatic uptake with persistent cardiac activity while with biliary atresia show prompt hepatic uptake but prolonged retention of radio trace in the liver. The curve of activity/time in our study resemble Leonard et al curve.

Superiority of mebrofenin as an imaging agent had been proven by A.D. Nunn et al.²

Hepatobiliary scintigraphy proved 100% Sensitive, 93.73% Specific, 80% Positive and 100% Negative predictive value for biliary atresia in present study. Comparative result of HBS were also given by Gelhald et al (1983)³ 100% sensitive 93.2% specific, Picozzi et al 1985⁷ 100% sensitive and 92% specific and William Spivak et al 1985¹¹ (100% sensitive and 92% specific) Philip Rosenthal et al 1989⁸ reported 100% sensitive, 93% specific, 83% Positive predictive value and 93% negative predictive value in their study Massoud et al 1981⁶ showed in 5 out of 11 cases of hepatitis with non visualization of intestine after phenobarbitone therapy were visualized intestine at 24 hrs. imaging. In contrast to S. B en Haim et al 1995⁴ suggested phenobarbital induction may not be required in Tc^{99m} mebrofenin scintigraphy.

CONCLUSION

Tc^{99m} mebrofenin hepatobiliary scintigraphy has proven to be a reliable noninvasive imaging modality in evaluating cholestatic jaundice in pediatric practice as it carries a high sensitive and specific value, good positive and no negative predictive value, few false positive and virtually no false negative results. HBS Provide real time assessment of hepatocyte function and bile progression from liver to intestine and this is of great importance in study of jaundice specially in differentiating surgical jaundice from medical jaundice. The effectiveness of treatment for biliary atresia decreases significantly after ten weeks of age.¹³ Therefore It is essential that the diagnosis should be made as early as possible, Radionuclide hepatobiliary imaging with newer Tc^{99m} labelled hepatobiliary agent to offer an accurate and noninvasive means of differentiating biliary atresia from other cases of cholestasis.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Abramson, S.J., Salvador T., and R.L.T. 'The infant with possible biliary atresia, evaluation by USG & Nuclear Medicine' *Pediatr. Radio* (1982) 12: 1-5.
2. Nunn A.D., Loberg and conley R.A. 'A structure distribution relationship approach leading to the development of Tc^{99m} mebrofenin' *An improved cholescintigraphic Agent. J. Nucl. Med.* 1983; 24: 423-30.
3. Gerhald J.P., Klingensmith W.C., Kunni C.C., et al 'Diagnosis of biliary atresia with radioneuclide hepatobiliary imaging, *Radiology* 1983; 146, 499-504.
4. Benhaim S.B., Seabald JE, Kao SC, et al 'Utility of Tc^{99m} mebrofenin scintigraphy in the assessment of neonatal jaundice' *clin Nucl Med.* 1995; 20: 153-163.
5. Leonard C, Hitch V, Masion 'The use of diethyl IDA T99m clearance curves in the differentiation of biliary atresia from other forms of neonatal jaundice, *Radiology* 1982; 142:773-76.
6. Majid M, Reba R.C. and Altman R.P. 'Hepatobiliary scintigraphy with 99m Tc PIPIDA in the evaluation of neonatal jaundice' *pediatrics* 1981; 67: 140-145.
7. Picozzi R, Bossi M.C., et al 'Value of hepatobiliary scintigraphy and ultrasonography in the differential diagnosis of jaundice, *Nucl. Med. Communication* 1985; 6: 97-108.
8. Russenthal P, Miller J.H. and Sinatra F.R. 'Hepatobiliary scintigraphy and the string test in the evaluation of neonatal cholestasis' *J. Paed, Gastroent and Nutrit.* 1989; 8 : 298-96.
9. Scott B.B., Evans J.A. et al. 'The initial investigation of Jaundice in a district general hospital a study of ultrasonography and hepatobiliary scintigraphy' *Brit. J. Rad.* 1980; 53: 557-62.
10. Silverberg M., Rosenthal L, and freeman L.M. 'Rose Bengal excretion studies as on aid in the differential diagnosis of neonatal jaundice' *Seminar Nucl. Med.* 1973; 3 : 69-80.
11. Spivak W., Sarkar S. et. al. 'Diagnostic utility of hepatobiliary scintigraphy with Tc^{99m} DISIDA in neonatal cholestasis' *J. Pediatre.* 1985; 106 : 171-84.
12. Zeman R.K., C.Lee, Jaffe P.H. et al 'Hepatobiliary scintigraphy sonography in early biliary obstruction' *Radiology* 1984; 153 : 793-98.
13. Hitch D.C., Shikes R.H. Lilly J.R. 'Determination of survival after Kasai's operation for biliary atresia using actuarial analysis' *J. Pediatr Surg* 1980; 15: 1315.

14. Sokol R.J, Mack C, Norkewicz MR, Karrer F.M. 'Pathogenesis and outcome of biliary atresia current concept' *J Ped Gastroenterol Nutri.* 2003; 37: 4-21.
15. Matthai J, Pauls, 'Evaluation of cholestatic jaundice in young infants' *Indian Pediatr* 2001;38:893-8.
16. Gilmour SM, Herskop M, Reifen R, Gilday D, Rober is EA 'Out come Of hepatobiliary scanning in neonatal hepatitis syndrome' *J Nucl. Med.* 1997; 38: 1279-82.
17. Gupta D.K., Charles AR., Srinivas M, et al, Betamethasone plus phenobarbital prior to

hepatobiliary scintigraphy increase diagnostic accuracy in infant with jaundice. *Indian J Pediatr* 2001;68:1039-41.

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