The Value of Sonography in Diagnosis of Infantile Biliary Atresia

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ABSTRACT

Background: Biliary atresia is an aggressive disease of infancy. Early diagnosis of biliary atresia is critical to the recovery of bile drainage and long-term transplant-free survival.
Objectives: To assess the diagnostic value of various ultrasound findings related to infantile biliary atresia in association with surgery as the reference standard.
Methods: From January 2022 to March 2024 in the Pediatric Welfare Teaching Hospital, ultrasound findings were retrospectively evaluated for 48 infants with cholestatic jaundice, suspected to have biliary atresia being confirmed or excluded by surgical means, 11 infants were excluded due to missing data.
Results: Study group was composed of 21 boys and 16 girls, their age ranged from (20 days to 6 months) with mean of 2.42 ±1.14 months; biliary atresia confirmed surgically for 21 of 37 children. The triangular cord sign had a sensitivity, specificity, positive predictive value and negative predictive value, accuracy of 42.90%, 100%, 100%, 100% and 100% respectively. Common bile duct non-visualization had 95.20%, 100%, 100%, 94.10% and 97.3%. Gallbladder ghost triad were 95.20%, 100%, 100%, 94.10% and 97.3%. Finally, the overall combined assessment could discriminate biliary atresia with 95.20%, 100%, 100%, 94.10% and 97.3%.
Conclusion: Triangular cord sign, common bile duct non-visualization and gallbladder ghost triad were the most accurate predictors of biliary atresia on ultrasound and for more accurate diagnosis, combination of all findings should be considered.

Keywords: Biliary atresia, Infantile cholestasis, Triangular cord sign, Common bile duct non-visualization, Gall bladder ghost triad, Gall bladder contractility.

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Biliary Atresia (BA) is a severe obliterative progressive fibrosing cholangiopathy of infancy and the most common surgically treatable cause of cholestasis encountered during the newborn period. If not surgically corrected, secondary biliary cirrhosis invariably results[1].

Kasai classification[2] is used to describe the three main anatomical types of biliary atresia:

Type I: Obliteration of common bile duct (patent cystic and common hepatic duct).

Type IIa: Obliteration of common hepatic duct (patent cystic and common bile duct), sometimes with a cyst at hilum hence termed cystic biliary atresia.

Type IIb: Obliteration of common hepatic duct, cystic and common bile duct.

Type III: Obliteration of left and right main hepatic ducts at the level of porta hepatis (most common, 90% and has the worst prognosis), (Figure 1).

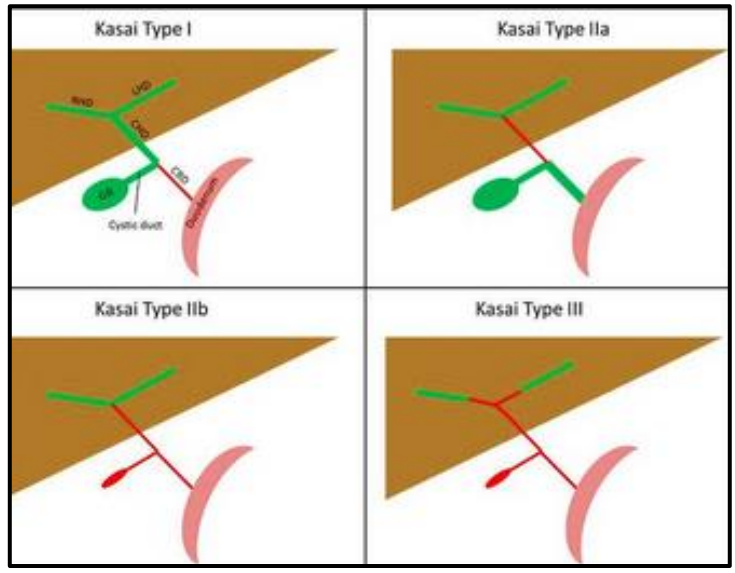

Figure 1: A diagrammatic representation of the Kasai classification for biliary atresia[2].

The etiology is still unclear, although there is evidence pointing to viral, toxic, and multiple genetic factors[3]. An in utero insult to the hepatobiliary system may result in a progressive sclerosis of the extrahepatic and intrahepatic bile ducts. In addition, certain drugs (e.g., carbamazepine) have been associated with biliary atresia. Fischler et al reported cytomegalovirus (CMV) infection in almost 25% of affected infants in one study based on immunoglobulin M (IgM) serology[4]. Interestingly, an even higher frequency of CMV infection has been found by Chang et al in cases of idiopathic neonatal hepatitis[5], lending support to the concept that both disorders are ends of the same pathological spectrum, originally described by Landing as infantile obstructive cholangiopathy[5].

The existence of the fetal form of BA, frequently associated with other GI and cardiac anomalies, suggests the possibility of a disorder in ontogenesis.

A worldwide prevalence ranging from 8-10 in 100,000 births with recognized male predilection[6].

Data regarding outcome from centers worldwide widely vary. The initial success rate of Kasai portoenterostomy (for achieving bile flow) is 60-80%. Clearly, the most critical determinant of outcome remains age at the time of operation[7].

Patients are significantly less likely to require early liver transplantation if the portoenterostomy is performed when they are younger than 10 weeks[8].

There is no pathognomonic physical finding for BA. Infants are typically full term and may manifest normal growth and weight gain during the first few weeks of life. However, the followings may be present[9]: Variable degrees of jaundice, dark urine, light clay-colored stools (acholic).

Surgical treatment by hepatoportoenterostomy or Kasai portoenterostomy[2], dissection into the porta hepatis with radical excision of all bile duct tissue up to the liver capsule, creation of a roux-en-Y anastomosis with a 35-40 cm retrocolic jejunal segment is the procedure of choice[2].

Percutaneous liver biopsy is widely regarded as the most valuable study for evaluating neonatal cholestasis. An adequate biopsy specimen can differentiate between obstructive and hepatocellular causes of cholestasis, with 90% sensitivity and specificity for biliary atresia[10].

Ultrasonography has been recommended as the preferred imaging tool for the initial detection of BA, it can exclude specific anomalies of the extrahepatic biliary system, particularly choledochal cysts[10].

- Triangular cord sign[11].
- Hepatic artery changes[11].
- Gallbladder ghost triad[12].
- Gallbladder contraction index decreased for the age (length to width ratio > 5.2)[12].

Figure 2: Ultrasound transverse scan at the porta, the common bile duct is not visualized. The portal vein and hepatic artery are identified. There is increased echogenicity along anterior wall of portal vein consistent with triangular cord sign[11].

Hepatobiliary scintiscanning (HIDA) using technetium-labeled iminodiacetic acid nuclear, is useful in evaluating infants with suspected biliary atresia. Unequivocal evidence of intestinal excretion of radiolabel confirms patency of the extrahepatic biliary system [10].

Magnetic Resonance Cholangiopancreatography (MRCP) permits the evaluation of the existence of an extrahepatic bile duct, but the need for sedation and the insufficient spatial resolution due to small body size limit it from being the preferred strategy[13].

Intraoperative cholangiography (IOC) definitively demonstrates anatomy and patency of the extrahepatic biliary tract. Perform IOC when liver biopsy findings suggest an obstructive etiology. The study is also indicated when biopsy results are equivocal or HIDA fails to demonstrate clear evidence of duodenal bile excretion[13].

The aim of the present study is to evaluate the various ultrasound findings and their accuracy both separately and combined for the diagnosis of biliary atresia in association with operative findings as the reference standard.

Methods

This retrospective study was conducted in the Pediatric Welfare Teaching Hospital, Medical City complex based on data collected during the period from January 2022 to March 2024.

Inclusion criteria: Every infant patient suspected of having BA. Examined in our center by US. Has surgical documentation that confirm or exclude BA.

Exclusion criteria: Parents refused interventions. Patients with missing files or surgical documentation.

All 37 patients (16 females and 21 males) were scanned by one expert pediatric radiologist. The patients were fasted for 4-6 hours before the examination and re-examined one hour post-prandial. They were not sedated.

- Triangular cord sign: echogenic fibrous tissue anterior to the portal vein, represents ductal remnant of extrahepatic bile duct[11].
- Hepatic artery changes[11]
  - Subcapsular hepatic arterial flow on Doppler
  - Right proximal hepatic artery diameter >1.5 mm
  - Hepatic artery to portal vein diameter ratio >0.45
- Gallbladder ghost triad[12]
  - Atretic gallbladder, length less than 19 mm in fasting.
  - Irregular or lobular contour.
  - Lack of smooth/complete echogenic mucosal lining with an indistinct wall [2].
- Gallbladder contraction index decreased for the age (length to width ratio >5.2) [13].

Demographic information were obtained and documented: Age and gender.

Statistical analyses have done by using Statistical Package for Social Sciences for windows version 26 (IBM Corp., Armonk, N.Y., USA). Descriptive statistics presented, Fisher exact test, quality assessment of diagnostic Accuracy tools.

Results

The study sample included 37 infants (16 females and 21 males), (Figure 3). Their age ranged from 20 days to 6 months at the time of abdominal US with a mean of 2.42 ±1.14 month and a median age of two months, (Table 1).

Only 21 (56.76%) infants confirmed surgically to have BA. The sex distribution of these confirmed cases was nearly equal 10 (47.62%) females and 11 (52.38%) males. All of them presented with cholesteric jaundice, 18 (85.7%) infants with isolated biliary atresia and only three (14.3%) infants with embryonic biliary atresia, two of them were associated with situs inversus, other one had situs inversus and polysplenia.

Table 1: Age distribution of BA patients.

Age in months		Frequency	Percentage %
	1	2	5.4
	2	26	70.3
	3	5	13.5
	4	1	2.7
	5	1	2.7
	6	2	5.4
	Total	37	100.0

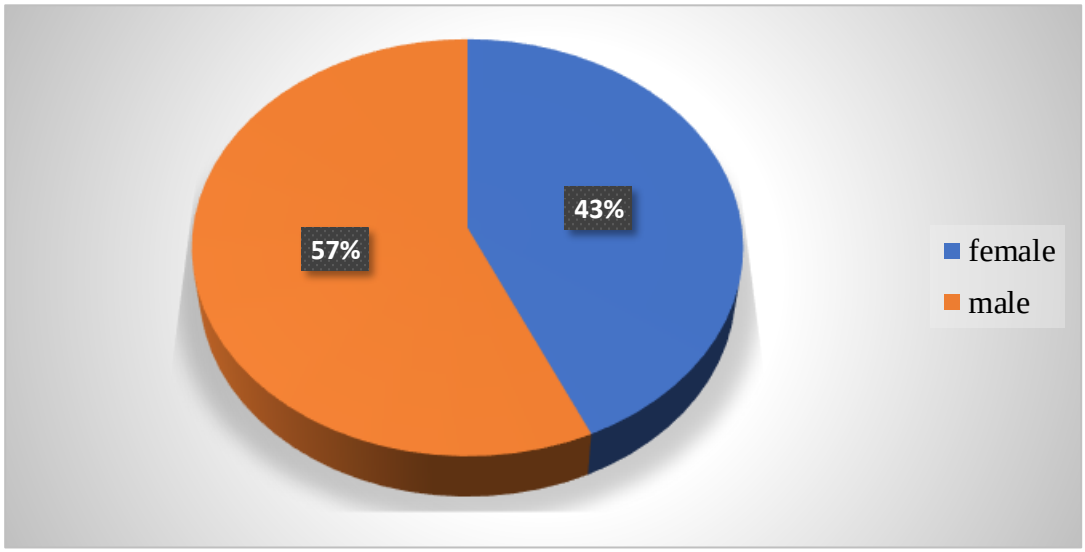

Figure 3: Sex distribution for BA patients.

On ultrasound image analysis, the triangular cord sign had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 42.90%, 100%, 100% and 100% respectively with accuracy of 100% (Table 2), (P <0.001, Fisher exact test).

CBD non-visualization had a sensitivity, specificity, PPV and NPV of 95.20%, 100%, 100% and 94.10% respectively with accuracy of 97.3%, (P < 0.001, Fisher exact test), (Table 2).

Hepatic artery to portal vein ratio were 61.90%, 100%, 100% and 66.00% respectively with accuracy of 78.3% (Table 2), (P<0.001, Fisher exact test). Which is slightly more accuracy than that of hepatic artery diameter with sensitivity, specificity, PPV and NPV of 57.10%, 100%, 100% and 64.00% respectively with accuracy of 75.7%, (P < 0.001, Fisher exact test), (Table 2).

Table 2: Diagnostic accuracy of sonographic parameters.

	TCS	CBD-non	HAD	HA/PVD	GB- triad	GBC index
Sensitivity	42.90%	95.20%	57.10%	61.90%	85.70%	33.30%
Specifity	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
PPV	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%
NPV	100.00%	94.10%	64.00%	66.70%	84.20%	72.70%
ACC	100%	97.3	75.7	78.3	91.9	79.3

Figure 4: A 72-day-old male patient presented with cholestasis, US scan showed abnormal GB, dilated HA & positive TCS, in keeping with BA.

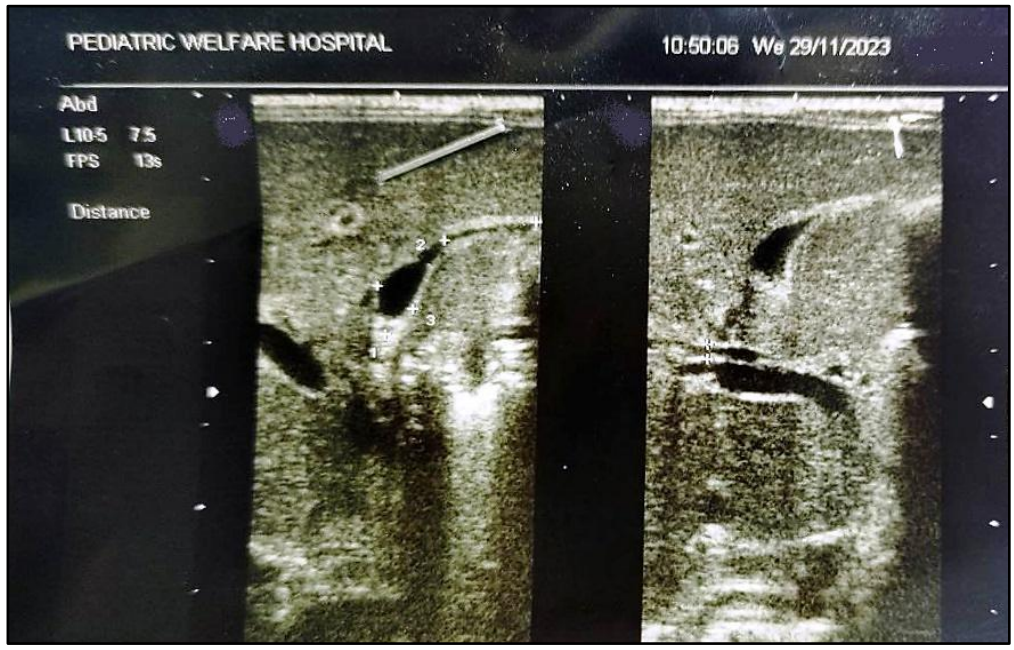

Figure 5: A 96-day-old male patient presented with cholestasis, US scan shows normal GB, HA and negative TCS.

Discussion

The etiology of biliary atresia is still unknown, unless the surgical operation is performed within early life, cirrhosis will be evident with poor survival rate and high co-morbidities; therefore, accurate and early diagnosis is crucial for early management. However, distinguishing biliary atresia from other infantile cholestatic causes such as neonatal hepatitis or other causes is difficult. HIDA was used for this purpose, but it has poor reliability at very high conjugated bilirubin levels. In many researches HIDA specificity was as low as 70.4%[14,15]. Several studies found that the

specificity and accuracy of ultrasound were better than that for HIDA[16].

Although MRCP permits the evaluation of the existence of an extrahepatic bile duct, but its availability, cost, sedation need, artifacts and insufficient spatial resolution due to small body size, limit it from being the preferred strategy[13].

Validation of sonography revealed its high discrimination ability, which was better it offers the advantages of being simple, quick, affordable, radiation-free, non-invasive and real time imaging modality, that made it the imaging of choice for the initial detection of BA, it can also detect any associated anomalies, exclude specific anomalies of the extrahepatic biliary system, particularly choledochal cysts[14].

Previously sonography focused on the assessment of atretic gallbladder and loss of its contraction or both in fasting infants to distinguish biliary atresia from neonatal hepatitis, which thought to be suggestive of BA[17]. However, these findings might be seen in other conditions. Furthermore, in the present work and previous reports also indicate that some patients with BA have a normal gallbladder [12,17].

In the present study, gallbladder contraction alone was not a satisfactory diagnostic tool with low sensitivity (33.3%) where it observed in only half of patients with biliary atresia, it has the drawback of equivocal results and it is operator dependent. Gallbladder morphology has high overall diagnostic accuracy (91.9%).

The sonographic finding of the triangular cord sign although it has high specificity and diagnostic accuracy (100%), but of low sensitivity (42.9%), it was observed in less than half of patients with biliary atresia in this study, though many researches conclude that TCS was more evident at follow up US and was not ‘‘missed’’ at earlier exams[18]. The CBD non-visualization has high overall diagnostic accuracy.

Hepatic artery diameter has good specificity (100%) but with low sensitivity (57.1%), observed in 12 of patients with biliary atresia, hepatic artery to portal vein diameter ratio has same specificity (100%), but higher sensitivity (61.9%), observed in 13 of patients with biliary atresia, both parameters necessitate high skills and practice making them not practical for in non-specialized centers.

The Fisher exact test resulted in a p-value of 0.001 for all of sonographic finding evaluated, which indicates that there is statistical significance ($P < 0.01$) with the outcome of BA.

Diagnostic accuracy values were in concordance with the results reported by Mittal V and other previous studies [19].

The triangular cord sign had a sensitivity 23.3%, specificity of 97.1%, positive predictive value (PPV), and negative predictive value (NPV), and accuracy found to be 77.8%, 74.4%, and 74.7%, respectively.

While in this study had a sensitivity 42.9%, specificity 100%, PPV, NPV, and accuracy were found to be 100%, 100% and 100%, respectively, in early stages TCS may not have completely formed, making its evaluation unclear; thus, the positive rate of the TC sign varies greatly in different age groups[11]. Li et al and Mittal V[19,20] proposed several possible reasons for the absence of the TCS as follows: Either there is no changes established at the porta hepatis or the triangular cord is too small to be identified on sonography. In our study, false-negative reported TCS are likely to be the same.

CBD non-visualization had a sensitivity, specificity, PPV and NPV of 93.3%, 47.8%, 43.8%, and 94.3% respectively, same for Tan Kendrick AP[12], Azuma T study results was (83%, 71%, 90%, 56% and accuracy of 80%)[21].

Present study had a sensitivity, specificity, PPV and NPV of 95.2%, 100%, 100% and 94.1% respectively with accuracy of 97.3%.

In both studies, the non-visualized gallbladder on sonography was always associated with BA. Noted that CBD non-

visualization was much more sensitive than TCS.

The sensitivity, specificity, PPV, and NPV of the gallbladder ghost triad were 83.3%, 82.6%, 67.6%, and 91.9%, by Kanegawa K, sensitivity was 72%, and specificity was 69% and diagnostic accuracy was 71% [22].

Of present study, they were 95.2%, 100%, 100% and 94.1% respectively with accuracy of 97.3%.

For Hepatic artery to portal vein ratio were 76.7%, 46.4%, 38.3%, and 82.1%, for Kim WS study (sensitivity, 76%; specificity, 79%; accuracy, 78%)[23]. Ours were, 61.9%, 100%, 100% and 66% respectively with accuracy of 78.3%.

Furthermore, in present study, the diagnostic value of other US findings were compared to each other and noted that hepatic artery diameter almost had the same accuracy (75.7%) as hepatic artery to portal vein ratio with sensitivity, specificity, PPV and NPV of 57.1%, 100%, 100% and 64% respectively.

GB contractility yield an accuracy of 79.3%, sensitivity, specificity, PPV and NPV of 33.3%, 100%, 100% and 72.7% respectively, by Kanegawa K. it has diagnostic accuracy of 77%, sensitivity was 85%, and specificity was 73%[22].

Overall combined assessment could discriminate BA with sensitivity, specificity, PPV, and NPV of 95.2%, 100%, 100% and 94.1% respectively with accuracy of 97.3%. These results were in concordance with work of Jiang LP sensitivity, specificity, and accuracy were 91.3%, 92.9%, and 92.2%, respectively[24]. The same was for Nemati M 94%, 92%, 94%, 97% and accuracy of 86%[25].

In conclusion; Depending on evaluation of various sonographic features (triangular cord sign, CBD non-visualization, gallbladder ghost triad and hepatic artery changes); ultrasonography has high diagnostic accuracy, which makes it possible substitute to invasive procedures in most of the cases. It can exclude other causes of cholestasis with high values of sensitivity and specificity.

We recommend a combined evaluation of all sonographic features to improve the diagnostic accuracy.

The gallbladder morphology (the gallbladder ghost triad) suggested to be evaluated at first as it is the most practical one and then triangular cord sign with CBD non-visualization subsequently followed by hepatic artery changes.

In doubtful cases with almost normal gallbladder morphology, post-prandial GB contractility assessment will be of great value in reaching for the definite diagnosis.

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