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Diagnostic Yield of Ultrasound in Infants with Cholestatic Jaundice

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ABSTRACT

Background: Cholestatic jaundice in infancy is an important clinical problem requiring rapid differentiation of biliary atresia from intrahepatic and other extrahepatic causes. Ultrasound is widely available, non-invasive, radiation-free and relatively inexpensive, making it particularly suitable for resource-limited settings. Objective: To determine the diagnostic yield and diagnostic performance of abdominal ultrasound in infants presenting with cholestatic jaundice, with particular emphasis on sonographic features suggestive of biliary atresia. Methods: This hospital-based diagnostic accuracy study included infants with conjugated hyperbilirubinemia who underwent standardized abdominal ultrasound. Gallbladder morphology, gallbladder visualization, triangular cord thickness, common bile duct visualization, hepatic artery caliber, liver and spleen morphology, portal venous anatomy and associated structural abnormalities were recorded. The final diagnosis was established using operative cholangiography, liver biopsy, magnetic resonance cholangiography, biochemical investigations and clinical follow-up, as appropriate. Results: Among the 180 infants included in the study, biliary atresia was established in 54 (30.0%). A composite ultrasound assessment identified 49 of 54 infants with biliary atresia and correctly classified 115 of 126 infants without biliary atresia, yielding a sensitivity of 90.7%, specificity of 91.3%, positive predictive value of 81.7%, and negative predictive value of 95.9% and overall accuracy of 91.1%. The triangular cord sign, abnormal gallbladder morphology and nonvisualization of the common bile duct were the most useful individual findings. Conclusion: Standardized ultrasound can provide a high diagnostic yield in infants with cholestatic jaundice and represents a practical first-line imaging investigation in resource-constrained settings such as Pakistan, although suspicious or equivocal examinations should be followed by definitive hepatobiliary evaluation.

Keywords: Cholestatic jaundice, Infants, Biliary atresia, Abdominal ultrasonography, Triangular cord sign, Gallbladder morphology, Diagnostic accuracy, Pediatric radiology, Neonatal cholestasis

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INTRODUCTION

Cholestatic jaundice in infancy is an important clinical condition requiring prompt evaluation because it may result from hepatobiliary, metabolic, infectious, genetic, or structural disorders, some of which require urgent medical or surgical treatment.[1] Neonatal cholestasis should always be considered pathological and investigated appropriately because early identification of the underlying cause can significantly influence clinical outcome.[2] Biliary atresia (BA) is particularly important because it is a progressive fibro-obliterative disorder of the extrahepatic biliary tree that can lead to hepatic fibrosis, cirrhosis, and liver failure if treatment is delayed.[4]

Early diagnosis of BA is essential because the success of Kasai hepatoportoenterostomy is strongly influenced by the age at which the procedure is performed.[3] Earlier surgical intervention is associated with improved bile drainage and better long-term survival with the native liver, emphasizing the importance of rapid diagnostic evaluation in infants with persistent conjugated hyperbilirubinemia.[4] However, distinguishing BA from neonatal hepatitis and other causes of intrahepatic cholestasis can be challenging because clinical and biochemical findings may overlap considerably.[5]

Abdominal ultrasonography is recommended as an important first-line imaging investigation in infants with cholestatic jaundice.[1] Ultrasound is non-invasive, does not involve ionizing radiation, is relatively inexpensive, and can provide information regarding the liver, gallbladder, extrahepatic biliary tract, portal venous system, spleen, and associated abdominal abnormalities.[6] These advantages are particularly relevant in low- and middle-income countries such as Pakistan, where advanced hepatobiliary imaging modalities may not be readily available in all healthcare facilities.[5]

Several sonographic findings have been evaluated for the diagnosis of BA, including the triangular cord sign, abnormal gallbladder morphology, gallbladder nonvisualization, nonvisualization of the common bile duct, and abnormal hepatic vascularity.[7] The triangular cord sign represents an echogenic fibrous remnant at the porta hepatis

and is considered one of the most useful sonographic findings associated with BA.[7] Objective measurement of triangular cord thickness has improved the standardization of this finding, with a thickness of approximately 3.5 mm or greater reported as highly suggestive of BA.[8]

Gallbladder morphology is another important sonographic parameter in the evaluation of suspected BA. A small, irregular, elongated, or poorly defined gallbladder is more frequently associated with BA than with other causes of neonatal cholestasis.[9] Studies have demonstrated that combining gallbladder morphology with the triangular cord sign can improve diagnostic performance compared with using either feature alone. [10, 11]

Despite the diagnostic value of ultrasound, individual sonographic findings have variable sensitivity and specificity, and diagnostic performance may be influenced by operator expertise, equipment quality, patient age, and examination technique.[12] A systematic review and meta-analysis demonstrated that the triangular cord sign has high specificity but variable sensitivity, supporting its use as part of a multi parametric ultrasound assessment rather than as an isolated diagnostic criterion.[12] Studies using decision-making models have further demonstrated that combining gallbladder morphology with triangular cord thickness can improve the discrimination of biliary atresia from other causes of neonatal cholestasis.[13] Importantly, a normal or equivocal ultrasound examination does not completely exclude biliary atresia, and infants with persistent conjugated hyperbilirubinemia may require further definitive evaluation.[6]

In resource-limited settings, standardized ultrasound assessment can provide a practical and relatively low-cost approach for early identification of infants at high risk of BA.[5] Establishing the diagnostic yield of ultrasound may facilitate timely referral for pediatric surgical assessment and reduce delays in definitive diagnosis. Therefore, the present study was conducted to determine the diagnostic yield and diagnostic accuracy of abdominal ultrasound in infants with cholestatic jaundice, with particular emphasis on sonographic features suggestive of biliary atresia.

In resource-limited settings such as Pakistan, standardized abdominal ultrasound offers a practical, affordable, and readily available method for the early assessment of infants with cholestatic jaundice. Timely identification of sonographic features suggestive of biliary atresia can facilitate early referral for definitive evaluation and surgical management. Therefore, this study was conducted to assess the diagnostic yield and accuracy of abdominal ultrasound in infants with cholestatic jaundice, with particular emphasis on sonographic findings associated with biliary atresia.

MATERIALS AND METHODS

This hospital-based diagnostic-accuracy study was conducted in the Department of Radiology of a tertiary-care teaching hospital in Pakistan over 12 months, from January 2025 to December 2025. Consecutive infants with persistent jaundice and conjugated hyperbilirubinemia were enrolled. The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Research Ethics Committee. Written informed consent was obtained from the parents or legal guardians of all participants.

The sample size was determined based on the expected prevalence of biliary atresia among cholestatic infants and the required precision for estimating ultrasound sensitivity. A total of 180 infants were enrolled using consecutive sampling to minimize selection bias and ensure adequate representation of infants with biliary atresia.

Infants aged 1 day to 6 months with clinically suspected cholestatic jaundice were eligible. Cholestasis was defined according to established pediatric recommendations based on elevated direct or conjugated bilirubin in the presence of persistent jaundice.[1,2] Infants were included if they underwent abdominal ultrasound and had sufficient clinical, laboratory, operative, histopathological, or follow-up information to establish a final diagnosis. Infants with predominantly unconjugated hyperbilirubinemia, physiological jaundice, incomplete medical records, previously diagnosed chronic liver disease, or technically inadequate ultrasound examinations were excluded.

All ultrasound examinations were performed using a conventional ultrasound machine equipped with high-frequency linear and low-frequency curvilinear transducers. Infants were examined after an age-appropriate period of fasting when clinically feasible. Examinations were performed by a radiologist experienced in pediatric abdominal imaging using a standardized protocol.

The liver was assessed for size, echotexture, surface contour, focal lesions, and features of fibrosis or portal hypertension. The gallbladder was evaluated for visualization, size, shape, wall thickness, wall regularity, and contractility when feasible. An abnormal gallbladder was defined by nonvisualization, marked reduction in size, irregular shape, or an indistinct or irregular wall. The common hepatic duct and common bile duct were assessed in longitudinal and transverse planes, and their visualization or nonvisualization was recorded. The triangular cord region at the porta hepatis was systematically evaluated, and the thickness of the echogenic anterior wall of the right portal vein was measured where technically feasible. A triangular cord thickness ≥3.5 mm was considered suggestive of biliary atresia.

Color Doppler examination was performed to assess the hepatic artery, portal vein, and hepatic subcapsular flow. Hepatic arterial caliber, abnormal peripheral hepatic flow, and portal venous abnormalities were recorded. The spleen was assessed for size, morphology, and the presence of polysplenia or asplenia. Associated abnormalities, including choledochal cyst, gallstones, biliary sludge, ascites, situs abnormalities, and vascular anomalies, were also documented.

For diagnostic analysis, a composite ultrasound assessment was considered positive for biliary atresia when characteristic findings, particularly abnormal gallbladder morphology, a positive triangular cord sign, nonvisualization of the extrahepatic bile duct, or characteristic vascular abnormalities, were present. The composite approach was used because previous studies have demonstrated better diagnostic performance when multiple sonographic features are interpreted together rather than relying on a single finding.

The final diagnosis served as the reference standard. Biliary atresia was confirmed by intraoperative cholangiography and/or operative findings, with histopathology used as supportive evidence where available. Non-biliary-atresia diagnoses were established through liver biopsy, magnetic resonance cholangiography, biochemical and metabolic investigations, microbiological evaluation, clinical response to treatment, or follow-up, as appropriate. Infants with choledochal cyst, neonatal hepatitis, inspissated bile, metabolic cholestasis, and other established causes were classified in the non-biliary-atresia group.

The primary outcome was the diagnostic yield of ultrasound, defined as the proportion of examinations providing clinically useful findings contributing to etiological diagnosis or appropriate referral. Secondary outcomes included sensitivity, specificity, positive predictive value, negative predictive value, and overall diagnostic accuracy for biliary atresia. Continuous variables were expressed as mean ± standard deviation or median with interquartile range, while categorical variables were presented as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Continuous and categorical variables were compared using appropriate parametric or non-parametric tests and chi-square or Fisher's exact tests,

respectively. Diagnostic performance was assessed using sensitivity, specificity, predictive values, and receiver operating characteristic analysis. A p-value <0.05 was considered statistically significant. Data were analyzed using SPSS version 26.0.

Standardized ultrasound assessment protocol

Ultrasound parameter	Assessment	Suspicious finding
Liver	Size and echotexture	Hepatomegaly, coarse echotexture
Gallbladder	Visualization, size, shape and wall	Absent, small, or irregular gallbladder
Gallbladder wall	Regularity and thickness	Irregular or indistinct wall
Triangular cord	Porta hepatis echogenicity	≥3.5 mm
Common bile duct	Visualization	Nonvisualization
Hepatic artery	Color Doppler/diameter	Increased caliber
Hepatic subcapsular flow	Color Doppler	Abnormal peripheral flow
Portal vein	Course and caliber	Abnormal anatomy
Spleen	Number, size and morphology	Polysplenia/asplenia
Extrahepatic obstruction	Biliary tract survey	Choledochal cyst, sludge, calculus
Associated abnormalities	Complete abdominal survey	Heterotaxy, situs abnormalities, ascites

RESULTS

A total of 180 infants with cholestatic jaundice were included in the study. The mean age at presentation was 7.1 weeks, with most infants presenting between 4 and 10 weeks of age. Of the participants, 103 (57.2%) were male and 77 (42.8%) were female. Biliary atresia was diagnosed in 54 (30.0%) infants, while 126 (70.0%) had other causes of cholestasis, including neonatal hepatitis, inspissated bile, choledochal cyst, metabolic cholestasis, and other intrahepatic disorders.

The mean age at ultrasound examination was slightly lower among infants with biliary atresia than those without biliary atresia. Pale or acholic stools and hepatomegaly were more frequently observed in infants with biliary atresia. The demographic and clinical characteristics of the study population are presented in Table 2.

Demographic and clinical characteristics of the study population

Variable	Biliary atresia (n=54)	Non-BA (n=126)	Total (n=180)
Male sex, n (%)	32 (59.3)	71 (56.3)	103 (57.2)
Age at ultrasound, weeks, mean ± SD	7.0 ± 2.3	7.3 ± 3.1	7.2 ± 2.9
Age ≤8 weeks, n (%)	43 (79.6)	96 (76.2)	139 (77.2)
Acholic/pale stools, n (%)	45 (83.3)	43 (34.1)	88 (48.9)
Hepatomegaly, n (%)	39 (72.2)	68 (54.0)	107 (59.4)
Splenomegaly, n (%)	11 (20.4)	16 (12.7)	27 (15.0)
Direct bilirubin, mg/dL, mean ± SD	7.8 ± 3.0	6.5 ± 3.1	6.9 ± 3.2
GGT, U/L, median (IQR)	485 (310–690)	280 (165–495)	325 (190–560)

Abnormal gallbladder morphology was the most frequent ultrasound abnormality among infants with BA. It was identified in 48 (88.9%) infants with BA compared with 15 (11.9%) infants without BA. Gallbladder nonvisualization was observed in 31 (57.4%) infants with BA and 8 (6.3%) infants in the non-BA group.

The triangular cord sign was present in 46 (85.2%) infants with BA compared with 5 (4.0%) infants without BA. Nonvisualization of the common bile duct was observed in 47 (87.0%) infants with BA and 14 (11.1%) infants without BA. Enlargement of the hepatic artery was identified in 37 (68.5%) infants with BA compared with 16 (12.7%) in the non-BA group. Abnormal hepatic subcapsular vascular flow was observed in 25 (46.3%) infants with BA and 4 (3.2%) infants without BA.

Splenic abnormalities were uncommon but were more frequently observed among infants with BA. Splenic or heterotaxy-related abnormalities were identified in 4 (7.4%) infants with BA compared with 1 (0.8%) infant in the non-BA group. Choledochal cysts were identified in 8 (6.3%) infants without BA, while biliary sludge was observed in 18 (14.3%) non-BA infants and 2 (3.7%) infants with BA.

Ultrasound findings according to final diagnosis

Ultrasound finding	BA (n=54), n (%)	Non-BA (n=126), n (%)
Abnormal gallbladder morphology	48 (88.9)	15 (11.9)
Gallbladder not visualized	31 (57.4)	8 (6.3)
Triangular cord sign ≥3.5 mm	46 (85.2)	5 (4.0)
CBD not visualized	47 (87.0)	14 (11.1)
Enlarged hepatic artery	37 (68.5)	16 (12.7)
Abnormal subcapsular flow	25 (46.3)	4 (3.2)
Hepatomegaly	39 (72.2)	68 (54.0)
Splenomegaly	11 (20.4)	16 (12.7)
Splenic/heterotaxy abnormality	4 (7.4)	1 (0.8)
Choledochal cyst	0 (0)	8 (6.3)
Biliary sludge	2 (3.7)	18 (14.3)

The triangular cord sign demonstrated high discriminatory ability, with a sensitivity of 85.2% and specificity of 96.0%. Abnormal gallbladder morphology demonstrated a sensitivity of 88.9% and specificity of 88.1%. Gallbladder nonvisualization showed lower sensitivity but high specificity. Nonvisualization of the common bile duct demonstrated high sensitivity but comparatively lower specificity.

A composite ultrasound assessment incorporating gallbladder morphology, triangular cord thickness, and extrahepatic bile duct visualization identified 49 of 54 infants with BA as ultrasound-positive. Eleven of 126 infants without BA were also classified as ultrasound-positive. Therefore, there were 49 true-positive, 11 false-positive, 5 false-negative, and 115 true-negative examinations.

Diagnostic performance of ultrasound for biliary atresia

Diagnostic measure	Results
Sensitivity	90.7%
Specificity	91.3%
Positive predictive value	81.7%
Negative predictive value	95.8%
Positive likelihood ratio	10.43
Negative likelihood ratio	0.10
Overall accuracy	91.1%

The overall diagnostic yield of ultrasound was 88.3%. Ultrasound provided a specific structural diagnosis in infants with choledochal cyst, biliary sludge, and other extrahepatic abnormalities, while characteristic sonographic features allowed a high proportion of infants with BA to be identified for further evaluation.

Five infants with confirmed BA had ultrasound examinations that did not meet the composite criteria for a positive examination. Three had relatively well-visualized gallbladders with subtle wall abnormalities, while two had triangular cord measurements below the predefined threshold. Among the 126 infants without BA, 115 were correctly classified as negative by the composite assessment, while 11 were categorized as suspicious for BA but were subsequently diagnosed with other causes of cholestasis.

Overall, the findings demonstrated that the combination of multiple sonographic parameters provided better diagnostic discrimination than reliance on an individual ultrasound finding. The multi parametric ultrasound assessment therefore facilitated early identification of infants with suspected BA and helped distinguish them from infants with other causes of cholestatic jaundice

DISCUSSION

The present study demonstrated that abdominal ultrasound had a high diagnostic yield in infants presenting with cholestatic jaundice. The composite ultrasound assessment showed a sensitivity of 90.7%, specificity of 91.3%, and overall diagnostic accuracy of 91.1% for biliary atresia (BA). These findings supported the role of ultrasound as an effective first-line imaging modality for differentiating BA from other causes of infantile cholestasis, particularly in settings where advanced hepatobiliary imaging facilities were limited.[14]

The high diagnostic performance observed in this study was clinically important because BA is a progressive disorder in which delayed diagnosis can result in advanced hepatic fibrosis and poorer outcomes following surgical treatment.[15] Therefore, the principal clinical value of ultrasound was its ability to rapidly identify infants with sonographic features suggestive of BA and facilitate timely referral for further hepatobiliary assessment and surgical management.[15]

Abnormal gallbladder morphology was the most frequently observed sonographic abnormality among infants with BA in our study, being present in 88.9% of affected infants. This finding was consistent with previous observations that gallbladder abnormalities were strongly associated with BA.[16] However, gallbladder visualization alone was not sufficient to exclude BA because a pseudo-gallbladder appearance could occur in affected infants.[16] Careful assessment of gallbladder size, shape, wall definition and contour was therefore important for accurate interpretation.

The triangular cord sign was also an important finding in our study and was identified in 85.2% of infants with confirmed BA. This finding was consistent with the pathological changes occurring at the porta hepatis in BA.[17] Previous studies demonstrated that objective assessment of the triangular cord improved the diagnostic utility and reproducibility of this sonographic
sign.[17] In our study, the triangular cord sign was particularly useful when interpreted together with gallbladder abnormalities and other biliary tract findings.

Color Doppler assessment provided additional diagnostic information. Enlargement of the hepatic artery was observed more frequently in infants with BA, while abnormal hepatic subcapsular flow was also associated with the disease. Similar vascular changes have previously been reported in infants with BA and were attributed to increased hepatic arterial flow associated with chronic biliary obstruction. [18] Although these findings were not sufficiently specific to establish the diagnosis independently, they provided useful supportive information when conventional ultrasound findings were equivocal.

The composite ultrasound assessment identified 49 of 54 infants with BA, compared with the diagnostic performance observed for individual sonographic parameters. This finding emphasized the importance of using a multi parametric approach rather than relying on a single sonographic sign. [19] A systematic review and meta-analysis reported that individual ultrasound findings demonstrated variable sensitivity and specificity, while combinations of characteristic sonographic features provided better overall diagnostic performance.[19] Our findings therefore supported the use of a structured ultrasound assessment incorporating gallbladder morphology, triangular cord appearance and extrahepatic biliary tract visualization.

The diagnostic performance observed in our study was also comparable with findings reported from other developing-country settings. Arsena et al. reported useful diagnostic accuracy of ultrasound among cholestatic infants with BA, demonstrating the potential applicability of conventional ultrasound in settings where access to advanced imaging may be limited.[20] These findings were particularly relevant to Pakistan, where ultrasound is relatively inexpensive and widely available compared with magnetic resonance cholangiography and other specialized hepatobiliary investigations.

Ultrasound elastography has also been investigated as an additional imaging technique for differentiating BA from other causes of neonatal cholestasis. A meta-analysis demonstrated promising diagnostic performance of ultrasound elastography, suggesting that assessment of liver stiffness may provide additional information in selected patients.[21] However,

elastography
requires appropriate equipment and technical expertise and was not routinely available in the study setting. Conventional grayscale and Doppler ultrasound therefore remained the most practical imaging approach for routine evaluation.

The findings emphasized the value of standardized ultrasound reporting, including gallbladder morphology, triangular cord thickness, bile duct visualization, and vascular abnormalities, to improve diagnostic consistency and multidisciplinary communication. [14] This was particularly useful in a tertiary-care setting with limited access to advanced imaging.

The study was limited by the operator-dependent nature of ultrasound and variations in equipment, radiologist expertise, and patient factors.[19] False-positive and false-negative findings occurred; therefore, a negative or equivocal ultrasound could not completely exclude biliary atresia.[14]

Overall, standardized abdominal ultrasound demonstrated a high diagnostic yield for cholestatic jaundice, particularly in identifying features suggestive of biliary atresia. A multiparametric approach improved diagnostic discrimination, making ultrasound a practical, affordable first-line investigation for early diagnosis and referral in resource-limited settings such as Pakistan.

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