



# BILIARY ATRESIA; ACCURACY OF ULTRASOUND IN DIAGNOSING BILIARY ATRESIA TAKING HISTOPATHOLOGY AS GOLD STANDARD

1. MBBS, FCPS  
Assistant Professor  
Department of Diagnostic Radiology  
The Children's Hospital and  
Institute of Child Health, Lahore,  
Pakistan.
2. MBBS, FCPS  
Senior Registrar  
Department of Diagnostic Radiology  
Avicenna Medical College and  
Hospital, Lahore, Pakistan.
3. MBBS, FCPS  
Senior Registrar  
Department of Diagnostic Radiology  
Shalamar Hospital, Lahore,  
Pakistan.

#### Correspondence Address:

Dr. Ayesha Anjum,  
Assistant Professor  
Department of Diagnostic Radiology  
The Children's Hospital and  
Institute of Child Health, Lahore,  
Pakistan.  
anjumf@gmail.com

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## INTRODUCTION

Biliary atresia (BA) is the most frequent surgical cause of cholestasis in neonates, though the diagnosis is made by exclusion of various other non-surgical causes. The overall incidence of neonatal cholestasis has been reported as 1 in 2500 newborns.<sup>1</sup> Among children with neonatal biliary obstruction, approximately 34%-42% have been reported to have BA.<sup>2</sup> The actual frequency of biliary atresia is about 1 in 8000-18000 live births.<sup>3</sup>

Due to difference in etiopathogenesis, biliary atresia is classified into 2 forms, the acquired or perinatal form and the congenital or embryonic form. The congenital variety is the relatively less common variant (20%), and has syndromic association such as BASM (Biliary atresia, Splenic Malformation - abdominal heterotaxia, absent inferior vena cava, polysplenia, preduodenal

Aysha Anjum<sup>1</sup>, Saba Maqsood<sup>2</sup>, Eisha Tahir<sup>3</sup>

**ABSTRACT... Objectives:** To determine the accuracy of ultrasound in diagnosing biliary atresia taking histopathology as gold standard. **Design:** Cross Sectional Study. **Settings:** Department of Diagnostic Radiology and Gastroenterology at Children's Hospital and Institute of Child Health, Lahore. **Period:** Over 1 year from 13-01-2015 to 12-02-2016. **Material and Methods:** This study involved 210 infants aged between 2-6 weeks referred from outpatient department and emergency of gastroenterology department with suspicion of biliary atresia. Ultrasound of all these cases was carried out and biliary atresia was labeled on a positive triangular cord sign. Core needle biopsy sample was taken from the liver adjacent to the porta hepatis and histopathological examination was done. Results of histopathology were taken as gold standard and results of ultrasonography were judged accordingly as true positive or false positive. A written informed consent was taken from each patient. A predesigned proforma was used to record patient's demographic details along with ultrasound and histopathological diagnosis. **Results:** The mean age of the patients was  $4.31 \pm 1.22$  weeks. There were 109 (51.9%) male and 101 (48.1%) female patients with a male to female ratio of 1.1:1. Ultrasound was found 97.5% sensitive, 87.7% specific and 95.2% accurate with positive and negative predictive value of 96.31% and 91.5%, respectively. **Conclusion:** Ultrasound was found extremely sensitive tool for the diagnosis of biliary atresia. Its non-invasive nature and lack of radiation exposure further make it ideal for pre-operative diagnosis in suspected cases in future practice.

**Key words:** Biliary Atresia, Ultrasound, Triangular Cord Sign, Diagnostic Accuracy.

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portal vein, intestinal malrotation, aberrant hepatic artery), believed to be due to alteration in the gene that controls the development of biliary system. The more common acquired form (80%) is thought to be the sequel of viral infection followed by multifaceted collaboration between innate and adaptive immune reactions.<sup>4,5</sup>

The persistent passage of dark colored urine, clay colored stools and jaundice in a neonate around 2 wk. of age should warrant the comprehensive work up for biliary obstruction, particularly BA. Gross naked eye examination showing clay colored stool gives suspicion of BA. When the stools are normal, supplementary features like consistency and fecal fat can offer further information. Massive fat droplets on Sudan in stain with soil like consistency has high sensitivity but less specificity for biliary atresia.<sup>6</sup> In a child with jaundice, this exercise from clinical suspicion till confirmation

of the diagnosis of biliary atresia is a daunting assignment. The battery of currently available biochemical tests and imaging investigations help to reach the accurate diagnosis in judicious time frame. Ultrasonography has distinctive benefits of being less expensive, non-invasive, repeatable and freely available non-ionizing and bedside tool. Though, its use is limited by its operator dependent nature<sup>7</sup>, ultrasonography is used as the preliminary screening tool in the investigative work up of neonates with cholestatic jaundice. Imaging by ultrasonography has recognized various signs which can be used as diagnostic of biliary atresia. Visualization of a triangular cord sign (imagining of the fibrotic cord in the portal hilum) is hallmark of biliary atresia on ultrasonography with a positive predictive value of 73% - 95%.<sup>8,9</sup> A number of studies have evaluated the diagnostic performance of ultrasound in biliary atresia.<sup>9-22</sup> However, there was controversy in the existing literature while there was no such local published material which necessitated the present study.

## MATERIAL AND METHODS

It was a descriptive cross-sectional survey conducted at Department of Diagnostic Radiology and Gastroenterology Children's Hospital and Institute of Child Health, Lahore over 1 year from 13-01-2015 to 12-02-2016. Sample size of 210 cases was calculated with 95% confidence level and 6% margin of error with an expected percentage of positive predictive value of ultrasound as 73% in the diagnosis of biliary atresia.<sup>18</sup> Infants of both genders aged between 2-6 weeks referred from outpatient department and emergency of gastroenterology department with persistence jaundice, dark urine, enlarged spleen, floating stools, foul-smelling stools, pale or clay-colored stools and slow or no weight gain with suspicion of Biliary Atresia were included after written informed consent. Patients with neonatal hepatitis (jaundice appearing before 2 weeks of age and normal alkaline phosphatase levels) were excluded. Ultrasound of all these cases was carried out in supine and then right or left decubitus positions with linear probe of at least 7–15 MHz. The frequency was kept as high as possible. The ultrasound was carried

out in the longitudinal, transverse and oblique planes, systematically, including scans through the intercostal and subcostal routes and biliary atresia was labeled on a positive triangular cord sign. Core needle biopsy sample was taken from the liver adjacent to the porta hepatis and histopathological examination was done. Results of histopathology were taken as gold standard and results of ultrasonography were judged accordingly as true positive or false positive. A written informed consent was taken from each patient. A predesigned proforma was used to record patient's demographic details along with ultrasound and histopathological diagnosis. Numerical variables like age has been presented as mean±sd while categorical variables like gender and ultrasound and histopathological diagnosis of biliary atresia have been presented as frequency and percentage. A 2x2 contingency table has been generated to determine the diagnostic performance of ultrasound taking histopathology as gold standard.

## RESULTS

The age of the patients ranged from 2 weeks to 6 weeks with a mean of  $4.31 \pm 1.22$  weeks. Majority (n=113, 53.8%) of the patients were aged between 5-6 weeks followed by 46.2% patients aged between 2-4 weeks. There were 109 (51.9%) male and 101 (48.1%) female patients with a male to female ratio of 1.1:1 as shown in Table-I. Ultrasound diagnosed biliary atresia in 163 cases while biliary atresia was confirmed in 161 cases on histopathology as shown in Table-II.

Characteristics	Participants n=210
Age (weeks)	4.31 ± 1.22
2-4 weeks	97 (46.2%)
5-6 weeks	113 (53.8%)
<b>Gender</b>	
Male	109 (51.9%)
Female	101 (48.1%)

**Table-I. Demographic Characteristics**

When cross tabulated diagnosis of biliary atresia on ultrasound and histopathology, there were 157 true positive, 6 false positive, 4 false negative and 43 true negative cases. It yielded sensitivity,

specificity and accuracy of 97.5%, 87.7% and 95.2% respectively for ultrasound with positive and negative predictive value of 96.31% and 91.5% respectively as shown in Table-III.

	Frequency (n)	Percent (%)
Ultrasound	163	77.62
histopathology	161	76.67

**Table-II. Frequency of biliary atresia on ultrasound and histopathology**

Ultrasound Diagnosis	Histopathological Diagnosis		Total
	Biliary Atresia	No	
Biliary Atresia	157	6	163
No	4	43	47
Total	161	49	210

**Table-III. 2x2 contingency table between ultrasound and histopathological diagnosis**

Statistic	Formula	Value
Sensitivity	$\frac{a}{a + b}$	97.50%
Specificity	$\frac{d}{c + d}$	87.70%
Accuracy	$\frac{a + d}{a + b + c + d}$	95.20%
Disease prevalence	$\frac{a + b}{a + b + c + d}$	76.67%
Positive Predictive Value	$\frac{a}{a + c}$	96.31%
Negative Predictive Value	$\frac{d}{b + d}$	91.50%

**DISCUSSION**

Biliary atresia is a heterogenous condition with diverse clinical outcome mainly depending upon the timing of surgery. Firm compliance of procedures in biochemical and imaging investigations leads to smooth progress from diagnosis to management.<sup>1</sup> Due to the inconstant nature of the diagnostic investigations and their coinciding predisposition, it is wiser to depend on a recipe of examinations with clinical correlation to the condition, to reach an early and assertive conclusion in an individual case of cholestatic jaundice.<sup>5</sup> Majority of these investigations do not give a clear cut distinction between BA and other non-surgical causes of neonatal biliary obstruction by themselves.<sup>4,5</sup> Therefore, it has directed to a tactic of mix and match of tools to correctly identify a child with biliary atresia from a group of other causes.<sup>5</sup>

Ultrasonography has distinctive benefits of being less expensive, non-invasive, repeatable and freely available non-ionizing and bedside tool. Though, its use is limited by its operator dependent nature<sup>7</sup>, Ultrasonography is used as the preliminary screening tool in the diagnostic work up of neonates with cholestatic jaundice. The utility of ultrasonography, as an initial diagnostic modality has been established in several studies.<sup>9-22</sup> However, there was controversy in the existing literature while there was no such local published material which necessitated the present study.

Authors	Country	Year	Sensitivity (%)	Specificity (%)	Accuracy (%)
Roquete et al. <sup>9</sup>	Brazil	91	49.0	100.0	72.5
Yang et al. <sup>10</sup>	China	2009	50.0	82.85	-
Ağın et al. <sup>11</sup>	Turkey	2016	67.6	65.0	66.0
Zhou et al. <sup>12</sup>	China	2015	76.9	84.8	82.2
Lee et al. <sup>13</sup>	Korea	2003	80.0	98.0	94.0
Kendrick et al. <sup>14</sup>	Singapore	2000	83.3	100.0	96.7
Park et al. <sup>15</sup>	Korea	1997	85.0	100.0	95.0
Tam et al. <sup>16</sup>	China	2013	86.0	45.0	53.0
Nemati et al. <sup>17</sup>	Iran	2009	86.0	97.0	94.0
Jiang et al. <sup>18</sup>	China	2013	91.3	92.9	92.2
Kanegawa et al. <sup>19</sup>	Japan	2003	93.0	96.0	95.0
Osuoji et al. <sup>20</sup>	Nigeria	2013	93.2	85.7	90.3
Visrutaratna et al. <sup>21</sup>	Thailand	2003	95.7	73.9	84.8
Kotb et al. <sup>22</sup>	Egypt	2001	100	100	100
Present Sudy	Pakistani	2015	97.5	87.7	95.2

**Table-IV. Review of existing literature on the diagnostic performance of ultrasound in biliary atresia**

In the presents study, the mean age of the patients was  $4.31 \pm 1.22$  weeks. There was slight male predominance with male to female ratio of 1.1:1. Biliary atresia was confirmed in 76.67% cases. Ultrasound was found 97.5% sensitive, 87.7% specific and 95.2% accurate with positive and negative predictive value of 96.31% and 91.5%, respectively. Jiang et al. (2013) in a similar study involving Chinese infants with mean age of  $2.91 \pm 1.08$  months reported the prevalence of biliary atresia to be 31.37% and the sensitivity, specificity and accuracy of ultrasound to be 91.3%, 92.9% and 92.2% respectively similar to the present study. In Japanese infants with biliary atresia, Kanegawa et al. (2003) reported similar sensitivity of 93.0%, specificity of 96.0% and accuracy of 95.0% for ultrasound. Similar results have also been reported by Osuji et al. (2013) in Nigeria who reported similar sensitivity (93.2%), specificity (85.7%) and accuracy (90.3%) of ultrasound in diagnosing biliary atresia while Kotb et al. (2001) reported the sensitivity, specificity and accuracy of ultrasound to be 100% in Egypt. Visrutaratna et al. (2003) reported the prevalence of biliary atresia to be 50.0% in Thailand and observed the sensitivity, specificity and accuracy of ultrasound to be 95.7%, 73.9% and 84.8% respectively. Zhou et al. (2015) studied Chinese infants with mean age of  $68.4 \pm 20.4$  days and male to female ratio of 1.5:1. They reported the prevalence of biliary atresia to be 47.25% with 76.9% sensitivity, 84.8% specificity and 82.2% accuracy of ultrasound with PPV and NPV of 71.4% and 88.2% respectively. Nemati et al. (2009) in a similar study in Iran reported the mean age of  $56.1 \pm 17.8$  days with equal gender distribution (m:f, 1:1). They reported the prevalence of biliary atresia to be 49.0% with ultrasound being 86.0% sensitive, 97.0% specific and 94.0% accurate.

The present study is first of its kind in local population and has found that a considerable proportion of infants with cholestasis suffer biliary atresia so biliary atresia should be at the top of list among differentials while evaluating such an infant in future practice. We also found ultrasound extremely sensitive and accurate in the non-invasive pre-operative diagnosis of such cases

which favor its preferred use during evaluation of such infants.

There is a strong limitation to the present study and that is we didn't compare the diagnostic accuracy of ultrasound with other existing non-invasive tools like MRCP. Such a study will further help in the selection of more appropriate diagnostic modality in future practice and is highly recommended in future research.

## CONCLUSION

Ultrasound was found extremely sensitive tool for the diagnosis of biliary atresia. Its non-invasive nature and lack of radiation exposure further make it ideal for pre-operative diagnosis in suspected cases in future practice.



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### AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Aysha Anjum	1st Author	
2	Saba Maqsood	2nd Author	
3	Eisha Tahir	3rd Author	