Ultrasound Features in the Diagnosis of

Biliary Atresia

By

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DISCLAIMER

I hereby certify that the work in this my own except for the quotations and summaries which have been duly acknowledged.

Date: 20th March 2017 ……...……

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ABSTRAK

Objektif: Untuk menilai peranan ultrasound (US) dalam diagnosis biliary atresia.

Metodologi:

Bayi yang berpuasa dengan hiperbilirubinemia terkonjugasi menjalani pemeriksaan US terperinci di Hospital Sultanah Bahiyah, Kedah. Pesakit telah dikumpulkan ke dalam biliary atresia (BA) dan bukan biliary atresia (tidak BA) berdasarkan hasil pembedahan dan mengikuti klinikal ke atasnya.

Ciri-ciri berikut telah dikaji: tri-angular cord sign, morfologi pundi hempedu, saiz hati, dan echotexure, saiz limpa, saiz arteri hepatik, nisbah saiz hepatik arteri dengan vena porta, kehadiran duktus hempedu, dan kehadiran aliran subcapsular pada warna Doppler. Kepekaan, kekhususan, nilai ramalan positif dan negatif telah dikira bagi setiap pembolehubah ultrasound. Kumpulan BA dan bukan BA telah dibandingkan dengan Fisher exact test dan unpaired t test untuk terus berubah-ubah.

Keputusan: Seramai 82 telah dimasukan di dalam kajian ini, 42 telah melalui pembedahan mengesahkan BA dan 40 bayi mempunyai sebab-sebab lain yang menyebabkan conjugated hiperbilirubinemia. Sembilan ciri-ciri ultrasound menunjukkan perbezaan yang signifikan antara BA dan kumpulan bukan BA. Dengan menggunakan semua ciri-ciri ultrasound, 82 bayi telah diklasifikasikan sebagai mempunyai atau tidak mempunyai BA, dan ketepatan keseluruhan adalah 98%

Kesimpulan: BA boleh didiagnosis dengan ultrasound dari sebab-sebab lain yang menyebabkan conjugated hyperbilirubinemia dalam 98% pesakit jika pelbagai ciri-ciri ultrasound dikaji dengan teliti. Setiap ciri-ciri ultrasound merupakan individu peramal yang bebas.

ABSTRACT

Objective: To assess the role of ultrasound (US) in the diagnosis of biliary atresia.

Methodology: Fasting infants with conjugated hyperbilirubinemia were subjected for US examination in Hospital Sultanah Bahiyah, Kedah. The patients were grouped into biliary atresia (BA) and non-biliary atresia (non-BA) based on the surgical findings and clinical follow up. The following features were recorded: tri-angular cord sign, gall bladder morphology, liver size, and echotexture, splenic size, hepatic artery size, hepatic artery to portal vein ratio, presence of a common bile duct, and presence of subcapsular flow on colour Doppler. Sensitivity, specificity, positive and negative predictive values were calculated for each US variable. BA and non-BA groups were compared by using the Fisher exact test for categorical variables and an unpaired t test for continues variable.

Results: A total of 82 infants were included in the study; 42 had surgically confirmed BA and 40 had other documented causes of neonatal jaundice. Nine US features showed a significant different between BA and non-BA group. Ultrasound able to correctly classified 82 infants into BA and non-BA group with 98% accuracy.

Conclusions: BA can be diagnosed with US from other cause of conjugated hyperbilirubinemia in 98% of patients if multiple US features are carefully evaluated. These ultrasound variables may serve as independent predictors of BA.

Chapter 1

Introduction

CHAPTER 1: INTRODUCTION

1.1 Introduction

Biliary Atresia (BA) or Idiopathic Neonatal Hepatitis (INH) is seen in 60-90% of persistent neonatal cholestasis. (Mittal *et al.*, 2011). These two diseases have similar clinical and biochemical findings. However, the pathogenesis, prognosis and approach to management of these two diseases differ substantially.

In patients with BA, early diagnosis (<35-45 days of life) and timing of the Kasai portoenterostomy improves survival and delays the need for liver transplantation. Kasai surgery is unlikely to be useful if performed after the patient is 3 months old. (Jonas MM, 2007). Delay in managing BA results in progression to liver cirrhosis and eventually end-stage liver failure. Ultrasound is useful in the diagnosis of BA because infants with BA typically have a certain degree of hepatic fibrosis or cirrhosis, which is usually complicated by portal hypertension, which can be observed on ultrasound as early as 8 weeks of life. (Howard *et al.*, 2002).

The reference standard for the diagnosis of BA is laparotomy with intra-operative cholangiography. However, making a prompt and accurate pre-operative diagnosis is difficult with the available diagnostic procedures including hepatic scintigraphy with technetium 99m-diisoprophyl imminodiacetic acid and magnetic resonance cholangiography. (Jaw *et al.*, 1999; Kim *et al.*, 2007) . Sonography is the most commonly used non-invasive radiologic investigation for pre-operative diagnosis of BA. In patients with neonatal hepatitis, correct diagnosis may avoid unnecessary invasive investigation and surgery. Various studies have evaluated the ultrasonographic features which may be useful to diagnose biliary atresia pre-operatively. *Humphrey et al* concluded that BA can be distinguished from other causes of conjugated

hyperbilirubinemia in 98% of infants if multiple US features are carefully evaluated. Those features include triangular cord (TC) sign, gall bladder (GB) length, GB contractibility, GB morphology, liver size, liver echotexture, hepatic artery size, portal vein size, portal vein colour Doppler waveform, common bile duct (CBD) visualization and subcapsular flow on colour Doppler, and signs of portal hypertension.

Osuoji et al defined the TC sign as a triangular or tubular echogenic structure anterior to the bifurcation of the portal vein. It is highly suggestive of biliary atresia when it is 3.5 – 4mm and above on a transverse or longitudinal scan, especially when the gall bladder is absent. Osuoji et al also observed that identification of the gall bladder is an integral part of excluding biliary atresia on ultrasound scans, apart from demonstrating the fibrous ductal remnant in the portal hepatis, i.e. the TC sign.(Osuoji R.I, 2013). Lee *et al*. concluded that the use of 4mm thickness as the criterion for TC Sign was statistically significant, with 80% sensitivity, 98% specificity and 94% positive and negative predictive values for the diagnosis of biliary atresia. Another study showed that TC sign had a sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of 23.3%, 97.1%, 77.8% and 74.4% respectively.(Lee *et al.*, 2003).

The gall bladder morphology is also an important ultrasound feature. Mittal et al observed that the sensitivity, specificity, PPV and NPV of an abnormal gallbladder were 83.3%, 82.6%, 67.6% and 91.9% respectively, while for that of poor gall bladder contractility were 87%, 72.5%, 51.3% and 94.3% respectively. A negative triangular cord sign with normal gall bladder morphology had an NPV of 91.9% for excluding extra-hepatic BA. (Mittal *et al.*, 2011). Li SY *et al.* concluded that an abnormal gallbladder, poor gallbladder contraction, the degree of hepatomegaly and echotexture of liver have significant diagnostic importance. (Li *et al.*, 2008)

Kim *et al* prospectively evaluated the accuracy of hepatic artery diameter and ratio of the hepatic artery diameter to the portal vein diameter for the diagnosis of BA. They concluded that enlargement of the hepatic artery diameter (>1.5mm at the level of proximal right hepatic artery) or a hepatic artery diameter to portal vein diameter ratio of more than 0.45 can be helpful in the US diagnosis of BA. A study of colour Doppler US findings in neonates and infants with BA found that the mean diameter of the hepatic artery in BA (2.1 ± 0.7 mm) was significantly larger than that of patients in the non-BA group (1.5 ± 0.4 mm) (P <0.001) or control subjects (1.5 ± 0.4 mm)(P=0.001). (Kim *et al.*, 2007).

Other important ultrasonographic features are visibility of the common bile duct and presence of hepatic subscapular flow on colour Doppler US. A non-visualized CBD has sensitivity, specificity, PPV and NPV of 93.3%, 47.8%, 43.8% and 94.3% respectively for the diagnosis of BA (Ref). The presence of hepatic subcapsular flow is also useful for differentiating between BA and other causes of neonatal jaundice, with a sensitivity and specificity of 100% and 86% respectively. (Lee *et al.*, 2009).

Although a TC sign and an abnormal gall bladder are widely accepted as the diagnostic criteria for BA, there is no single feature that is pathognomonic. Thus, it is important to study other associated US features when the triangular cord sign is negative or the gall bladder is normal. Identification of these ultrasonographic features which may predict BA may help clinicians to make an accurate and early diagnosis of BA.

Chapter 2

Objectives

CHAPTER 2: OBJECTIVES OF THE STUDY

2.1 General objectives

2.1.1 To assess the role of the ultrasound in the diagnosis of biliary atresia.

2.2 Specific objectives

2.2.1 To evaluate ultrasound parameters in neonates or infants with biliary atresia and non-biliary atresia.

2.2.2 To identify predictors for biliary atresia.

Chapter 3

Manuscript

3.1 Title Page

Ultrasound Features in the Diagnosis of Biliary Atresia

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Author roles:

SKS designed, carried out the study and wrote the manuscript. NFSNM and JH co-designed the study. NFSNM performed/ validated the US examination in all the patients that recruited for the study.

3.2 Abstract

Objective: To assess the role of ultrasound in the diagnosis of biliary atresia.

Methodology: There were eighty-two fasting infants with conjugated hyperbilirubinemia underwent detailed US examination in Hospital Sultanah Bahiyah, Kedah. The following features were recorded: tri-angular cord sign, gall bladder morphology, presence of a common bile duct, liver size, and echotexure, splenic size and vascular anatomy. Sensitivity, specificity and positive and negative predictive values were calculated for each US variable. Biliary Atresia (BA) and non-Biliary Atresia (non-BA) groups were compared by means of the Fisher exact test for categorical variables and an unpaired t test for continues variable.

Results: A total of eighty infants were included in the study; forty-two had surgically confirmed BA and forty had other documented causes of neonatal jaundice. Eight US features showed a significant different between BA and non-BA group ($p < .001$). By means of all these US features, 82 of 84 infants were correctly classified as having or not having BA, and the overall accuracy of 98%

Conclusions: BA can be diagnosed with US from other cause of conjugated hyperbilirubinemia in 98% of patients if multiple US features are carefully evaluated. These ultrasound variables may serve as independent predictors of BA.

3.3 Introduction

Biliary Atresia (BA) or Idiopathic Neonatal Hepatitis (INH) is seen in 60-90% of persistent neonatal cholestasis (Mittal *et al.*, 2011). These two diseases have similar clinical and biochemical findings. However, the pathogenesis, prognosis and approach to management of these two diseases differs substantially.

The importance of early diagnosis and surgical treatment of BA cannot be over-emphasized. In patients with BA, early diagnosis (<35-45 days of life) and timing of the Kasai portoenterostomy improves survival and delays the need for liver transplantation. If the surgery is performed after the age of 3 months, it is unlikely to provide any clinical benefit, as liver cirrhosis may already have developed (Jonas MM, 2007). Ultrasound (US) is useful as a non-invasive method to diagnose BA. These infants typically have a certain degree of hepatic fibrosis or cirrhosis, which is usually complicated by portal hypertension, which can be observed on ultrasound as early as 8 weeks of life.

Various studies have evaluated the ultrasonographic features which may be used to diagnose biliary atresia pre-operatively. These features include triangular cord (TC) sign, gall bladder (GB) length, GB contractibility, GB morphology, liver size, liver echotexture, hepatic artery size, portal vein size, portal vein colour Doppler waveform, common bile duct (CBD) visualization and subcapsular flow on colour Doppler, and signs of portal hypertension.

In a study by Osuoji R.I, the TC sign was defined as a triangular or tubular echogenic structure anterior to the bifurcation of the portal vein, which is the fibrotic biliary tree. It is highly suggestive of biliary atresia when it is 3.5 – 4mm and above on a transverse or longitudinal scan, especially when the gall bladder is absent(Osuoji R.I, 2013). If triangular cord sign is negative and the gall bladder morphology normal, extra-hepatic BA is unlikely (Mittal *et al.*, 2011). Other studies postulated that enlargement of the hepatic artery diameter (>1.5mm at the level of proximal right hepatic artery) or a hepatic artery diameter to portal vein diameter ratio of more than 0.45 is suggestive of BA.

Kim et al prospectively evaluated the accuracy of hepatic artery diameter and ratio of the hepatic artery diameter to the portal vein diameter for the diagnosis of BA. According to the study, enlargement of the hepatic artery diameter (>1.5mm at the level of proximal right hepatic artery) or a hepatic artery diameter to portal vein diameter ratio of more than 0.45 can be helpful in the US diagnosis of BA (Kim *et al.*, 2007).

Although a TC sign and an abnormal gall bladder are widely accepted as the gold standard diagnostic criteria for BA, there is no single feature that is pathognomonic. Our study thus aims to identify the ultrasonographic features which may predict BA, to facilitate an accurate and early diagnosis of BA. Apart from identifying the ultrasonographic features to predict BA, this study was conducted to collect the local data of the diagnosis biliary atresia as the studies in this field are limited locally.

3.4 Materials & Method

This study was conducted at Hospital Sultanah Bahiyah, Alor Setar, Kedah. The study participants were all term neonates or infants with persistent conjugated hyperbilirubinemia referred to the Paediatric Surgical Team with suspected biliary atresia. All of the patients required an abdominal ultrasound study as part of the work up for persistent conjugated hyperbilirubinemia. The patients were subsequently followed up for clinical evidence of biliary atresia. Biliary atresia was confirmed by intra-operative cholangiogram or hepatoportoenterostomy. We divided the sample into two groups: Biliary Atresia (BA) and Non- Biliary Atresia Group (non-BA) groups. Retrospective data collection of the patients who underwent ultrasound from Jan 2013 to June 2016. The study was approved by Ministry of Health Research and Ethics Committee (MREC) and Jawatankuasa Etika Penyelidikan (Manusia) of USM (JEPeM), Universiti Sains Malaysia. The data collection was originally planned to be conducted between May 2015 and Feb 2016, but due to delay in obtaining the ethical approval, we were compelled to delay initiation of data collection. As a result, data collection was started in April 2016 and completed August 2016.

US Imaging/ Techniques

After a minimal 4 hours of fasting, all the neonates or infants underwent a detailed abdominal US examination performed by a radiologist with 10 years' experience in paediatric ultrasound). Sonography examinations were performed on a SSA-370A Power Vision 6000, Toshiba ultrasound system using PLT-1204AT linear transducer probe which has frequency range 7-14MHz and PVT-674BT Convex transducer probe which has 6MHz. All the neonates or infants were not sedated during the US examination. Numerous sonographic parameters were assessed;

- ***Triangular cord sign***: It is an echogenic triangular or tubular shape anterior to the bifurcation of portal vein on longitudinal or transverse scanning was considered a positive triangular cord sign. A triangular cord thickness of 4mm or greater was considered a positive triangular cord sign (Lee *et al.*, 2003).
- ***Gallbladder morphology:*** The gallbladder was examined with MHz high frequency linear transducer. When the gallbladder was seen, its length was measured along the long axis from outer wall to outer wall. The walls were assessed to identify any irregularities of the mucosa and contours. The gallbladder was considered abnormal if it was less than 19mm long, or if there was lack of smooth and complete echogenic mucosal lining with an indistinct wall or an irregular or lobular contour (Tan Kendrick *et al.*, 2003). The gallbladder was also evaluated at the end of the examination after the child had been fed for 15 to 20 minutes to see whether gall bladder contraction had occurred.
- ***Liver Size and Echotexture:*** Liver size was assessed by measuring liver length. The liver was measured on a longitudinal scan in the mid-clavicular or mid-axillary line. It is based on the reference range that of the liver size we classified the child into normal size or hepatomegaly (Rocha *et al.*, 2009). The echotexture of the liver was recorded subjectively as homogenous (normal) or heterogeneous (abnormal).
- ***Presence or Absence of Common Bile Duct at Portal Hepatis:*** If the common bile duct (CBD) was visualized, its diameter was measured.
- ***Hepatic Artery Size:*** The right hepatic artery was measured at the level of right proximal hepatic artery running parallel to the right portal vein. For consistency, the measurement was obtained at the level of the proximal portion of the right portal vein just proximal to the division of the anterior and posterior branches; this area was chosen because the

anatomical locations of the hepatic artery and portal vein are more constant in the right lobe of the liver (Berland *et al.*, 1982). A right hepatic artery greater than 1.5mm was considered enlarged (Kim *et al.*, 2007).

- ***Portal Vein*:** The portal vein was measured at the level just proximal to the division of the right portal vein into the anterior and posterior branches by placing electronic cursors from inner wall to inner wall. A ratio of greater than 0.45 for the diameter of the right hepatic artery and diameter of the right portal vein was considered significant (Kim *et al.*, 2007).
- ***Spleen:*** The spleen was measured along its long axis from the upper pole to the lower pole. The patients were divided into normal and splenomegaly group according to the reference range (Megremis *et al.*, 2004).
- ***Subcapsular flow of liver:*** Transverse scanning performed with the linear transducer; the colour box was positioned on the anterior surface around the falciform ligament. The colour box measured 1 cm in height and 3–4 cm in width. We considered hepatic sub capsular flow to be present when vascular structures continued to the liver capsular surface on colour Doppler US images (Lee *et al.*, 2009).

Statistical Analysis

Two-sample *t* test was used to compare age and total bilirubin and direct bilirubin levels and age, between the patients with BA and non-BA. Pearson Chi-Square test was used to compare the distribution of gender and ethnicity among patients with BA and those with non-BA. The sensitivity, specificity, positive and negative predictive values were calculated using 2 x 2 table for the TC signs, gall bladder morphology, liver size, liver echotexture, spleen size, and present of abnormality of common bile duct on US images and the hepatic subcapsular flow, hepatic artery size, hepatic artery to portal vein ratio abnormality on Colour Doppler US images. Finally, simple logistic regression analysis was used to determine whether the presence of the TC sign, GB length, GB morphology, diameter of portal vein and hepatic artery, liver size, liver echogenicity, spleen size and presence of hepatic sub capsular flow are useful in predicting the presence of absence of BA.

3.5 Results

Demographic data

A total of 82 subjects were recruited into the present study, which comprised 42 subjects with BA and 40 subjects without BA, as shown in Table 1. All the patients with BA had undergone surgery. There was no significant difference in gender and race distribution between the two study groups. Similarly, there was no significant difference in mean birth weight between the two study groups. However, mean age and age at the onset of jaundice were significantly higher in the BA group than the non-BA group.

Blood parameters

Blood analysis showed no significant differences in mean values of total bilirubin, indirect bilirubin, total protein, albumin, and globulin between the two study groups. Interestingly, the mean values of direct bilirubin, alkaline phosphatase, and alanine transaminase were significantly higher in BA subjects than non-BA subjects, as shown in Table 2.

Ultrasound features

In the analysis of ultrasound findings, the Table 3 shows that significantly more patients in the BA group had abnormal ultrasound parameters studied (triangular cord sign, gall bladder morphology, liver size, hepatic artery size, hepatic artery to portal vein ratio abnormality, spleen size, common bile duct, and subcapsular flow on colour Doppler) than those in the non-BA group. Besides that, higher mean values of liver length, hepatic artery size, portal vein size and hepatic artery to portal vein ratio were found in the BA group.

Simple logistic regression revealed significant associations between ultrasound abnormalities (i.e. triangular cord sign, gall bladder length abnormality, liver size abnormality, hepatic artery length spleen size abnormality) and BA group. Study subjects with ultrasound abnormalities were more likely to have BA, as shown in Table 4. These ultrasound variables may thus serve as independent predictors of BA, as no significant associations were found in multiple logistic regression. The following features were recorded: tri-angular cord sign, gall bladder morphology, presence of a common bile duct, liver size, and echotexture, splenic size and vascular anatomy. Sensitivity, specificity and positive and negative predictive values were calculated for each ultrasound variable, as shown in Table 5.

3.6 Discussion

Ultrasound assessment is useful in the pre-operative diagnosis of BA. This study identified the US features associated with BA. Most of the US features studied were significantly different between the BA and non-BA groups and the sensitivity and specificity of these features has been described in the literature.

The most significant ultrasonographic feature associated with BA was the TC sign. According to the criteria proposed by Lee *et al*. and L Lee *et al*. (use of 4mm thickness as the criterion for TC Sign), our study found that the TC sign had a sensitivity of 88%, specificity, 98%, positive predictive value of 97% and negative predictive value of 90% for the diagnosis of BA. (Lee *et al.*, 2003; Lee *et al.*, 2009) . However, Humphrey and Stringer *et al* and Kim *et al.* reported that the TC sign only had a sensitivity of 73% and 58% respectively(Humphrey and Stringer, 2007; Kim *et al.*, 2007). In our study, only one patient with neonatal hepatitis showed a significant TC sign; this was attributed to diffuse periportal echogenicity secondary to the hepatitis. Tan Kendrick *et al.* reported that fibrotic cord can be masked by diffuse the diffuse periportal echogenicity when there is nonspecific inflammation and cirrhotic. Hence, the TC sign is specific but not sensitive when there is widespread periportal inflammation or cirrhosis(Tan Kendrick *et al.*, 2003).

Gall bladder morphology is another significant criterion on US. Using a combination of the criteria for abnormal gallbladder length (<19mm), lack of echogenic mucosa lining, and irregular contour proposed by Tan Kendrick *et al.,* Humphrey and Stringer *et al*, and Li SX *et al.*, we found that an abnormal gallbladder has 81% sensitivity, 100% specificity, 100% positive and 85% negative predictive values for the diagnosis of BA. (Humphrey and Stringer, 2007; Li *et al.*, 2008; Tan Kendrick *et al.*, 2003).

In our study, the hepatic artery diameter was significantly larger in patients with BA, compared with non-BA patients (P<.001). This is in agreement with the results of Humphrey and Stringer *et al.* (Humphrey and Stringer, 2007). According to Kim *et al*'s criterion, an enlarged hepatic diameter (>1.5mm) showed a sensitivity of 66.7%, a specificity of 100%, a positive predictive value of 100% and a negative predictive value of 74.1% in the diagnosis of BA. The calculated ratio of the hepatic artery diameter to the portal vein diameter (>0.45) showed a sensitivity of 23.8%, a specificity of 100%, positive predictive value of 100% and negative predictive value of 55.6% (Kim *et al.*, 2007). These results suggest that enlargement of the hepatic artery enlargement is specific but not sensitive for BA. However, it has significant positive predictive value. This could be operator dependent, and measurement errors may occur if only one reading is performed. The aetiology of the enlargement of extra-hepatic artery in BA patients is unknown, but postulated to occur secondary to increase in arterial resistance. The combination of enlarged hepatic artery diameter with other US findings can be highly suggestive of BA. Thus, measurement of hepatic artery diameter is a useful US component in the diagnosis of BA.

We found that presence of subcapsular flow on US has 100% positive predictive value for BA. This result is consistent with the findings by Seung-seob Kim *et al*, in which the subcapsular flow was positive for all of their patients with BA (Kim *et al.*, 2014). Another study by El-Guindi *et al*. 2013 reported that this sign has a sensitivity of 96.3% and specificity of 96.3%(El-Guindi *et al.*, 2013). In our study, we found that subcapsular flow had a specificity of 100% but a relatively low sensitivity of 54.6%. However, these results should be interpreted with caution as only approximately one-quarter of our patients had assessment of subcapsular flow (11 in the BA group, 11 in the non-BA group). Lee *et al.* observed that all BA patients who had subcapsular flow on Doppler study were also found to have subcapsular telangiectatic

vessels intra-operatively (Lee *et al.*, 2009). As subcapsular flow and enlarged hepatic artery size have high positive predictive values in the patients with BA, a colour Doppler study should be included in the routine US examination of prolonged neonatal jaundice patients.

In a recent study by Seung-seob Kim *et al* concluded that CBD can be either present or absent on US in the diagnosis of BA. When the CBD is present in the patients with BA, the other US features such as TC sig, GB length and GB morphology may have a false negative status(Kim *et al.*, 2014). Our result showed that visibility of CBD in BA patients has low sensitivity (7.1%) and specificity (72.5%) for BA.

Both hepatomegaly and enlarged spleen were found to be statistically significant features in infants with BA. The abnormal echotexture of the liver also observed in the patients of BA. However, these features are relatively non-specific, and other US features of BA should be sought (Humphrey and Stringer, 2007). The strengths of this study are that all US examinations were performed by a single operator, thus eliminating inter-observer bias. Secondly, we observed that no patient with BA was incorrectly classified into the non-BA group, which supports our assertion that US is useful to diagnose BA, thus avoiding the need for potential harmful and invasive investigations. However, our study is limited by its retrospective nature, and the few numbers of patients who had assessment of subcapsular flow.

Conclusion

Accurate diagnosis of BA in patient with conjugated hyperbilirubinemia is possible if multiple US features are cautiously analyszed. Future prospective ultrasonographic studies should explore the optimal combination of ultrasound features which can provide rapid, reliable diagnosis of this potentially life-threatening condition.

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3.8 Tables and figures

Table 1: Demographic data of study subjects according to groups

Demographic Data	Non-BA (n=40)	BA (n=42)	P value
Age, day (SD)	38(41)	78 (27)	<0.001*[a]
Gender, n (%)			
Male	16 (40)	16 (38)	0.860[b]
Female	24 (60)	26 (62)	
Race n (%)			0.061[b]
Malay	38 (95)	33 (79)	
Chinese	2 (5)	5 (12)	
Indian	-	4 (9.5)	
Onset of jaundice, day (SD)	8 (6)	25 (27)	<0.001*[a]
Birth weight	2.77 (0.61)	4.31 (8.82)	0.274[a]

Note: [a]Independent t-test; [b]Chi-square test for homogeneity; *statistically significant at p<0.05

Table 2: Blood profiling of study subjects according to groups

Blood Profile	Non-BA (n=40)	BA (n=42)	P value
Total bilirubin, μmol/L (SD)	191.85 (92.44)	189.76 (78.41)	0.912
Direct bilirubin, μmol/L (SD)	72.85 (46.27)	96.12 (41.28)	0.018*
Indirect bilirubin, μmol/L (SD)	119.35 (61.71)	93.57 (58.45)	0.056
Total protein, g/L (SD)	56.30 (8.52)	59.64 (10.84)	0.126
Albumin, g/L (SD)	35.20 (6.14)	36.98 (8.17)	0.271
Globulin, g/L (SD)	21.10 (3.97)	21.90 (5.71)	0.463
Alkaline phosphatase, U/L (SD)	399.63 (338.22)	691.12 (406.94)	0.001*
Alanine transaminase, U/L (SD)	90.00 (125.92)	192.95 (193.03)	0.006*

* $p<0.05$ is significant