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ARTICLE

THE CLINICAL ASSESSMENT OF BILIARY ATRESIA PATIENTS REFERRING TO PEDIATRIC WARDS OF HOSPITALS AFFILIATED TO SHIRAZ UNIVERSITY OF MEDICAL SCIENCES FROM MARCH 2007 TO MARCH 2013

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ABSTRACT

Background: *Biliary atresia (BA) is the terminal stage of multiple inflammatory and fibro proliferative mechanisms which may have no certain causes. Fast diagnosis is a key in improving the outcome of the disease. So it is necessary to evaluate the main clinical signs of BA.* ***Methods and Materials:*** *It was a retrospective cross sectional study conducted between March 2007 and March 2013. Medical records of all confirmed patients in this time section were obtained and then analyzed. Main clinical sings and indications of each patient were extracted from their records in specific forms. Forms were sent to a biostatistician for further statistical analyses.* ***Results:*** *73 cases met our inclusion criteria .Jaundice was the chief complain of 98.6% of the cases. 28.8% of the patients had a positive family history. 32.9% of patients had hepatomegaly. 35.6% had splenomegaly and 21.9 % patients had both.Dark urine was observed in 58.9% of patients. Pale stool was recorded for 68.5% of patients. 50.6%of patients had both dark urine and pale stool.* ***Conclusion:*** *fast diagnosis of BA is possible with a combination of different diagnostic methods. It may be really beneficial if we educate the parents on how to tell if there is something wrong from the color of the newborn's urine and stool.*

KEY WORDS
Biliary atresia, hepatic disease, cholestasis, bile duct, gall bladder, liver

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INTRODUCTION

Biliary atresia (BA) is a congenital or acquired hepatic disease which is mostly seen in neonatal phase of life.

In this rare disease, common hepatic duct is either obstructed or absent. It is also called "extra hepatic ductopenia" or "progressive obliterative cholangiopathy ".[1]BA causes a persistent jaundice which won't respond to the casual treatment methods and surgical procedure is the only choice .In children, BA is the most common indication for liver transplantation.[2]BA is yet an idiopathic disease with no certain causes .Different types of BA have been observed. Most of the time BA present without any other malformations and anomalies. This type is called perinatal BA. [3]In prenatal BA, Jaundice is not present since birth and it will start to develop within the first two months of life. [4] The other types of BA are associated with other anomalies and malformations which may include asplenia , polysplenia, malrotation , situs inversus and etc.[5] Ones affected with these kinds of BA have a poorer prognosis. [6]

It is not a common problem as its occurrence rate in the United States is 1/10,000 to 1/15,000 cases in live births .[7]

Different mechanisms have been under observation and it is believed that some of these mechanisms may contribute in the onset of BA. Viral etiology is still a hypothesis and no specific viruses have been found to have a connection with BA. Yet some viruses showed the potential to cause BA[8]Genetic factors may play an important role in this disease . Some alleles may make the carrying person more susceptible to developing BA. [9] Immunologic and toxic etiologies are still under investigations as hypotheses .[10]

The prognosis of BA is very complex and variable in different patients and it largely depends on the liver transplantation and the respond of patients body to the transplanted organ .–[11] without transplantation the outcomes are fairly poor. Only 55% of the patients may survive after 5 years without the surgery. –[12]

First and the most important sign of the disease is jaundice which is mostly detected in the sclera. The jaundice is likely to happen from birth to 8th week. After this period the onset of jaundice is really unlikely. Acholic and pale stool is another sign of BA, but most of the time it will remain unnoticed. Bilirubin will be secreted to the urine and it will make the urine look dark and make the diaper look yellow. This is also very likely to stay unnoticed by the parents.

Fast diagnosis is very important in BA because the success rate of interventions and surgeries largely drops when the patient get older. [13] Alagille Syndrome or alpha-1-antitrypsin deficiency are two diseases that have similar signs as BA and this make fast diagnosis a challenge. Abdominal Ultra sound is the first line tool to investigate the anatomy of liver and bile duct. It is beneficial to exclude other anatomical problems associated with the similar symptoms and signs as BA. In children with BA the gall bladder is either absent or in a mal shape. The absence of common bile duct can be detected too. [14] Hepatobiliary scintigraphy is the next tool for diagnosing BA. Liver biopsy is done on every infants who are under

investigation for BA .After all these procedures, liver biopsy will confirm the BA and the urge of surgical intervention.

After that the infant will be taken to the operation room and after the pre-cutaneous Cholangiogram the surgeon will decide whether to do the KASAI procedure or not. KASAI procedure and liver transplantation are two main surgical treatments of BA.

As time plays an important role we should study the clinical features of BA in the infants so that we can achieve a faster diagnosis process. We designed this study to record and evaluate clinical signs of infants with biliary atresia in Shiraz,Iran in order to find a fast and sharp diagnosis method .

MATERIALS AND METHODS

It was a retrospective cross sectional study conducted between March 2007 and March 2013. After the legal and ethical approval of the local health authorities, all the patients that was diagnosed as BA patient in pediatrics ward of hospitals affiliated to Shiraz University of medical sciences was entered in our sample. At the end 72 confirmed BA patients were remained in the study. The patients were aged 1 week to 12 yrs. The BA was confirmed by ultrasound investigation and liver biopsy. Only the hospitalized patients were included in the study and all the outpatient cases were excluded. Patients with the lack of required information in their medical sheet were excluded too. Based on the previous studies and the consultation of a biostatistician a minimum of 70 patients were required for the study to achieve a power of 80. All the cases had a medical sheet which was recorded in the medical records library of Shiraz university of Medical sciences. We first examined their medical records and all their clinical signs and findings were transferred to another form which was designed for the study. Patients' age, birth weight, family history and chief complaint was extracted and written down in the first part of the form. Then it was checked if the patient had pale stool and dark urine. Then the anatomical abnormalities of the patients were checked. [Hepatomegaly, splenomegaly, situation of gall bladder and the condition of intra and extra hepatic bile duct].

After that the forms were sent to a biostatistician for the analyses. SPSS V 15 were used as the statistics program. Independent T-test were used and p value under 0.05 was defined as significantly meaningful .

RESULTS

At the end, after all the evaluations and exclusions, 73 cases were included in the results. Of these 73 cases, 72 was referred to hospital with the chief complaint of jaundice and 1 with cirrhosis. Patients were aged one week to 12 yrs. with the mean age of 2.50±3.31. 21 (28.1%) of patients had a family history of BA. Mean weight was 5.86 ± 3.31 kg . Thirty out of 72 (43.66%) were diagnosed at the age of 2 months and earlier. The time interval between onset of signs and symptoms and diagnosis is as follows: 1) Less than 1 month: 37 patients (51.38%), 2) 1 to 3 months: 19 patients (26.38%), 3) 3 to 6 months: 4 patients (5%), 4) 6 to 12 months: 8 patients (11.11%), and after 12 months: 4 patients (5%).

Regarding physical examination abnormalities ,24(32.9%) patients had hepatomegaly. 26(35.6%) had splenomegaly and 16 (21.9) patients had both. 19 (26%)patients had BA in intrahepatic bile duct while 7(9.5 %) patients had dilated intrahepatic bile duct , 7 out of these 8 patients had obstructed extrahepatic bile duct which may cause the intrahepatic duct to dilate . Extrahepatic bile duct was obstructed in 48 (65.7%) patients .Gall bladder was absent in 24 (32.9%) patients.

Dark urine was observed in 43 (58.9%) patients. Pale stool was recorded for 50(68.5%) patients. 37(50.6%) patients had both dark urine and pale stool.

DICUSSION AND CONCLUSION

Although diagnosis of BA isn't a hard thing to do, doing it fast is still a big challenge. Because most of the clinical signs and symptoms of BA is also present in other hepatic diseases. Scientists are really keen to screening tests for BA because early diagnosis is really important. Mushtaq *et al* designed a study to find if it is possible to create an easy and fast screening method. They used dry blood spots on the universal Guthrie screening card to evaluate the concentration of bile salts in the blood. Though they find a slight concentration difference between the affected infants and normal ones , they thought that the difference isn't sufficient enough to accept this test as a certain screening method .[15]

Our results showed that most of the families took in the infants because of jaundice . More than half of diagnoses were made at the time when newborns were older than 2 months. BA is associated with a persistent jaundice. Most Iranian parents assume the jaundice to be normal at the beginning. As they see no signs of recovery they will bring the infant to the hospital. This is not a good news. No one noticed the changes in the infants' urine color or the pale stool. This demonstrates the urge to train the families and parents after child birth .It can be really beneficial if we train the parents about normal urine and stool. Hsiao *et al* started a national wide project to create an easy and simple screening method for BA which could be done by the parents. A card was given to the parents with a child health booklet. In the card they showed the parents how to tell if the stool color is right and how to know if there is something wrong about the color. By using this method they found that the sensitivity of detecting BA before two months of age

was 72.5% in 2004, which was significantly improved to 97.1% in 2005.They concluded that using such methods may enhance early detection of the disease, and as a result the outcomes will be better. [16] Similar studies are suggested in Iran.

Table 1: Main clinical signs and symptoms of the patients diagnosed with BA.

Chief complain	Percent
Jaundice	98.60%
Cirrhosis	1.40%
Family history	
Positive	28.80%
Negative	71.20%
Dark urine	
Positive	58.90%
Negative	41.10%
Pale stool	
Positive	68.50%
Negative	31.50%
Hepatomegaly	
Present	32.90%
Absent	67.10%
Splenomegaly	
Present	35.60%
Absent	64.40%
Gall bladder	
normal	38.40%
absent	32.90%
dilated	2.70%
contracted	26%
Liver transplantation	
received	28.80%
not received	71.20%

71.20% of the patients in our study didn't have any family history of BA. In current literature there aren't enough supporting data to directly link BA with the genetics, as the twins doesn't share the phenotype and it is usually just seen in one of them. Silveira *et al* evaluated the possibility of familial inheritance of BA and concluded that there aren't any direct link between BA and genetics, but genetics may indirectly make an infant more susceptible than another.[17]

Using the ultrasound to evaluate the anatomic situation of liver and gall bladder have been a first line diagnostic tool for BA. Regarding our data splenomegaly and hepatomegaly can't be a good sign of BA, as most of the patients were negative regarding these two issues. Splenomegaly is usually detected if the presentation is late and it is a signof portal hypertension.Nowadays, clinicians use the triangular cord sign in ultra sound evaluation to diagnose BA. This sign shows a fibrotic mass at porta hepatis. One of the weak points of our study is that we didn't have data about whether the clinicians used this sing for diagnosis or no. Takamizawa*et al* reviewed the medical data of 85 infants who were diagnosed with BA. They concluded that with emphasising on the triangular cord sign and gallbladder length and gallbladder contractility we can diagnose BA with a great certainty level. [18] By using these and combining them with laboratory tests and Hepatobiliary scintigraphy will make a fast diagnosis possible and may indirectly enhance the prognosis of this complex problem . Yet more research is needed regarding this issue.

CONFLICT OF INTEREST
None

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None

FINANCIAL DISCLOSURE
None

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