https://menj.journals.ekb.eg
Print ISSN: 2735-3974
Online ISSN: 2735-3982
DOI:10.21608/menj.2025.416883

MNJ
Menoufia Nursing Journal
Faculty of Nursing
Menoufia University

Clinical Practice Update:

Biliary Atresia

Doaa Mahmoud Hamid El khouly[1], Maha Ibrahim Khalifa[2], Yahya Ahmed Mortada Fayed[3], Hanaa Mabrouk Ahmed[4]

[1]Nursing Specialist at National Liver Institute, Menoufia University
[2]Professor of Pediatric Nursing, Faculty of Nursing, Menoufia University
[3]Lecturer of HPB Surgery, National Liver Institute, Menoufia University
[4]Assist. Professor of Pediatric Nursing, Faculty of Nursing, Menoufia University

Abstract: Biliary atresia (BA) is a rare inflammatory sclerosing obstructive cholangiopathy that initiates in infancy as complete choledochal blockage and progresses to the involvement of intrahepatic biliary epithelium. Children with BA are usually presented with jaundice. A greenish-yellow color is observed; acholic stool and dark urine usually accompany jaundice. Biliary atresia may be suspected prenatally, when a cystic structure is observed in the portahepatis. Biliary atresia is usually diagnosed by performing liver enzymes, direct& indirect bilirubin. Levels of (GGT) and (Alk-p), are higher than hepatocellular enzymes, such as (ALT) and (AST). Special attention should be paid to GGT as well as liver biopsy.

***Key words**: - Biliary atresia- jaundice*

Introduction:

Biliary atresia is an obstructive cholangiopathy of unknown etiology involving both the intrahepatic and extrahepatic bile ducts. It presents in the neonatal period with persistent jaundice, clay-colored stools, and hepatomegaly. It is fatal if left untreated with a reported survival of less than ten percent at three years of age (Siddiqui & Ahmad, 2023).

Review of literature

The exact cause of BA is unknown. A number of factors may induce or cause the final common pathology of biliary inflammation, luminal obliteration and fibrosis.

1) Viral Exposure

There are hepatotropic cholangiopathic viruses (e.g. Reovirus type 2, cytomegalovirus, and rotavirus) which can possibly cause biliary damage during the perinatal period. Such viruses are a common source of gastrointestinal symptoms during infancy. Cytomegalovirus is much more prevalent in Asia and South Africa and is a possible reason for the increased overall prevalence in those regions. It may not be direct viral damage that causes the problem more an immune-mediated injury in a normally developed bile duct. However, given the prevalence of such viruses in the community, biliary atresia is a rare disease (Hannah & Mark, 2023).

Regarding the role of viral infection and immunologic factors in the etiology of BA, three agents have been

consistently associated with BA; CMV, reovirus, and rotavirus (Szavay et al., 2022).

2) Congenital Embryopathy

Infants with biliary atresia splenic malformation (BASM) have a parallel range of anomalies, which could only have arisen at key points in organ development within the embryonic phase of development (up to the eighth week of gestation). Thus, there are certainly genes where there is obvious overlap between biliary and visceral development, but proof of linkage is lacking in clinical practice. Recently, an American study identified mutations in the PKD1L1 gene, possibly linked to cilial abnormalities, in about 10% of their cohort. There is also some evidence that such infants have been exposed to an abnormal intrauterine environment during the first trimester (e.g. maternal diabetes).There is a remarkable similarity between the normal biliary appearance of the fetal porta hepatis at 12 weeks' gestation and what is seen pathologically in biliary atresia (Szavay et al., 2022).

3) Immune Causes

The immune response has received the most attention in human based studies of BA pathogenesis. The infiltration of CD4+ and CD8+ T lymphocytes and macrophages has been consistently observed in the periductal space or along the duct epithelium in conjunction with increased expression of cytokines and receptors commonly seen when these cells are activated (Kahn, 2024).

Two studies were carried out; comprehensive molecular and cellular surveys of liver biopsies and found a proinflammatory gene expression signature, with increased activation of interferon-γ (IFN-γ), osteopontin, tumor necrosis factor-α (TNF-α) and other inflammatory mediators (Mack et al., 2024).

4) Genetic Causes

It was reported that, infants with BA had high levels of intrahepatic expression of pro-inflammatory genes, particularly IFN-γ (Bezerra et al., 2022).

Pathogenesis: -

It is increasingly evident that the genetic and epigenetic predispositions combined with the environmental factors to which the mother is exposed are potential triggers for biliary atresia. There is also an indication that a progressive thickening of the arterial middle layer occurs in this disease, suggestive of vascular remodeling and disappearance of the interlobular bile ducts. It is suggested that the hypoxia/ischemia process can affect portal structures in biliary atresia and is associated with both the extent of biliary proliferation and the thickening of the medial layer (Quelhas et al., 2023).

The Japanese Association of Pediatric Surgeons classification is the most widely used, and it groups BA into three main variants as determined by both the anatomical level and degree of biliary obstruction (Ibrahim et al, 1997):

- **Type I**: about 5 percent of children have luminal patency down to the common bile duct (often associated

with a proximal cystic element). It is considered surgically correctable.

- **Type II**: about 2 percent of cases and has patency to the level of the common hepatic duct. It is considered surgically correctable. It can be subdivided into;
  1) Subtype in which the cystic and common ducts are patent (atresia of common hepatic duct with cystic dilations of the proximal intrahepatic ducts)
  2) Subtype in which the cystic and common ducts are obliterated (atresia of the gallbladder, cystic duct, and common hepatic ducts).
- **Type III**: more than 90% of cases and the most proximal part of the extra hepatic biliary tract within the portahepatis are entirely solid. Nonetheless, even in type III cases, residual but microscopic biliary ductules (of varying size and number) retain continuity with the intrahepatic biliary system (obliteration of the entire intrahepatic and extrahepatic biliary trees). It is considered surgically non correctable (Blumgart et al., 2016).

Children with BA are usually presented with jaundice. A greenish-yellow color is observed in conjugated hyperbilirubinemia and is unlikely to occur after 8 weeks. Acholic stool and dark urine usually accompany jaundice, with acholic stool usually presenting at 2 weeks of age that is almost indisputable at one month of age. The color of the stool may sometimes be light and not definitely acholic, and the recognition of acholic stool by parents may be delayed if the diaper is stained with dark urine (Bezerra et al., 2021).

Babies with BA are usually term and of normal birth weight. In the most common perinatal type, weight gain is normal in the first weeks but begins to decrease in untreated patients. Bleeding may occur due to vitamin K malabsorption; hepatomegaly and splenomegaly are signs of cirrhosis and portal hypertension, and ascites will be observed in decompensated cases (Napolitano et al., 2021).

Diagnosis

1- Antenatal Diagnosis

Biliary atresia may be suspected prenatally, when a cystic structure is observed in the portahepatis. In this condition; further investigations must be performed rapidly after birth, in order to distinguish a choledochal cyst, which does not require immediate intervention, from the cystic form of BA, which calls for urgent surgical treatment (Hinds et al., 2024).

2- Newborn Screening

In order to improve outcome of BA patients, that is, to reduce the need for early liver transplant in these children, and last but not least, measures must be taken towards an early diagnosis of BA. Many screening programs for BA have been proposed, such as early measurement of serum bile acid, serum direct bilirubin, serum Apo C-II and III proteins, urinary sulfated bile acid, and fecal bilirubin and fat; however, none has been put into practice extensively, due to both cost and technical complexity (Zhou et al., 2022).

A much simpler method, based on the detection of neonatal cholestasis through examination of the baby's stool color, represents an extremely

attractive alternative; pale, grey-pigmented stool is readily identified in 95.2% of children with BA in early infancy. Such screening, which can rely on the use of a very simple stool color card, is easy and inexpensive. Both the parents and the pediatrician can easily detect pathologic stool pigmentation by confronting the baby's feces with color indicators on the card; an examination that optimally should be performed during the first month of life in order to have enough time for confirming the diagnosis and performing an early portoenterostomy (Wildhaber BE, 2021).

The stool color card was thus proven to be a simple, noninvasive, efficient, low-cost, and applicable mass screening method for early diagnosis and management of BA, hence an ideal mean to help identify a devastating disease, that, if not treated early in life, inexorably leads to the need to overly precocious and risky liver transplant in infancy, secondarily depriving the community of most precious organs for transplantation. The benefit of this BA screening program is thus not only paramount for the child and his family, but also for society in general (Wildhaber BE, 2021).

Figure 2: (Biliary Atresia Home Screening, Stool Color Card, Effective January 2023)

3- Laboratory Investigations:

Biliary atresia is usually diagnosed by performing liver enzymes, direct& indirect bilirubin. Levels of (GGT) and (Alk-p), are higher than hepatocellular enzymes, such as (ALT) and (AST). Special attention should be paid to GGT, since Alk-p is originated in bones. Liver function, assessed by albumin and clotting function, is normal in the initial stages of the disease but the international normalized ratio (INR) may be abnormal due to vitamin K deficiency. hypoalbuminemia and coagulopathy (may be observed in patients with end-stage cirrhosis) (Davenport 2019).

4- Imaging:

a) Abdominal ultrasound:

Ultrasonography is useful in the initial evaluation of neonatal cholestasis, although it is not diagnostic for biliary atresia but it is the most commonly used noninvasive radiological investigation for the preoperative diagnosis of BA (Mittal V et al., 2021).

The triangular cord sign (TC sign) at the portahepatis is one of the direct and specific objective criteria for BA. It's a circumscribed, focal, triangular or tubular echogenic density more than 3 mm thick located cranial to the portal vein bifurcation corresponding to fibrosis of the extra hepatic biliary system (Li SX et al., 2018).

b) Hepatobiliary scintigraphy:

Hepatobiliary scintigraphy using following phenobarbitone pretreatment (5mg/kg/day for 3-5 days) is of limited value. But may be of value in determining patency of the biliary tract,

in cases in which a radiotracer is detected in the intestine (Moyer et al., 2024).

c) Cholangiography:

If there is still doubt about the possibility of BA, the performance of cholangiography is indicated (Sydney 2023).

1) Endoscopic Retrograde Cholangiopancreatography:

Endoscopic retrograde cholangiopancreatography (ERCP) has been recommended by some services, but it is not performed on a routine basis for the differential diagnosis of neonatal cholestasis, since it requires appropriate material and qualified personnel, in addition to being an invasive and costly exam (Iinuma et al., 2020).

2) Magnetic Resonance Cholangiography:

According to services which employ this method, MRC should be incorporated as a routine procedure in cases of neonatal cholestasis. BA can be ruled out if the complete extrahepatic biliary duct is identified at MR cholangiography (Han et al., 2022).

3) Intraoperative Cholangiography (IOC):

Intraoperative cholangiography is performed when other methods do not permit a definitive diagnosis. Intraoperative cholangiography should be performed at a medical center which is capable of performing the Kasai portoenterostomy immediately if necessary. It can be used in combination with the above diagnostic methods (Sydney 2023). The surgeon performs an intraoperative cholangiogram during gallbladder surgery. The surgeon inserts a flexible tube through an incision (surgical cut) in the skin and inject contrast dye through it, into bile ducts. The surgeon then uses an X-ray machine to send images of the bile duct to a monitor. Contrast dye is a liquid that either blocks or absorbs more X-rays than the tissue around it, which makes structures in the body defined and more easily seen on medical imaging (Temperley et al., 2023).

d) Echocardiography:

Echocardiography also plays an important role in the assessment of associated cardiac anomalies, such as in biliary atresia splenic malformation (BASM) syndrome (De Carvalho et al., 2017).

e) Duodenal intubation:

A nasogastric tube is put into the distal portion of the duodenum and the liquid collected for 24 hours. If no bile fluid is seen, the test is prolonged for a further 24 hours. The administration of magnesium sulfate at 25%, with a dosage of 1 ml/kg, or cholecystokinin, can be performed when biliary fluids are negative, 24 hours after the collection of the duodenal liquid (Sydney 2023).

The tube test is also used in investigation of the radioactivity of gastroduodenal juices, after the performance of scintigraphy using

DISIDA Tc99m, with the intention of increasing the specificity of this test, the maximum activity found was below 500 cpm/ 100mcl/ mCi dose (Larrosa-Haro et al., 2015).

In a recent study, the duodenal tube test as a diagnostic instrument for BA showed a sensitivity level of 100%, and specificity of 100%, a positive predictive value of 100% and a negative predictive value of 100%. The authors of this study indicated operative cholangiography in cases of duodenal tube test results negative for bile (El-Guindi et al., 2018).

f) Liver Biopsy:

Longitudinal studies have shown the progressive nature of the pathological changes in biliary atresia even with surgical therapy.

g) Diagnostic Laparoscopy

A coarse, irregular, greenish-brown liver with some degree of fine angiomatous development and an atretic GB were found laparoscopically in some infants with BA. However, in case of NH, the liver was smooth, sharp-edged, and chocolate brown in color. Simultaneous IOC showed the passage of the contrast material into the proximal biliary tract and the intestinal system. Laparoscopic guided puncturing with a needle was used to swash the bile duct from the GB to decrease jaundice in patients with bile plug syndrome, thus unnecessary laparotomy was avoided in 25% of the patients (Tang et al., 2015).

h) Biliary Atresia Score

A study was done at National Liver Institute in Menoufia University by El-Guindi et al., 2015 to determine the biliary atresia score. The total score ranged from 0 to 37.18 and a cut-off value of >23.927 to discriminate BA from other causes of neonatal cholestasis with sensitivity and specificity of 100% each.

Conclusion

Children with biliary atresia are in intense need for planned nursing care such as hand washing, promoting child rest, measuring vital signs, growth measurements, feeding, medication administration, prevention of dehydration and blood gases.

References

Bezerra JA, Asai A, Tiao G, Mullapudi B, Balistreri WF. 2021. Biliary Atresia and Other Disorders of the Extrahepatic Bile Ducts. In: Suchy FJ, Sokol RJ, Balistreri WF, Bezerra JA, Mack CL, Shneider BL, editors. Liver Disease in Children 5th ed. Cambridge: Cambridge University Press; 162-181.

Biliary Atresia Home Screening, Stool Color Card, Effective January 2023.

Blumgart LH. Biliary atresia. In: Jarnagin WR, Blumgart LH, Belghiti J, Buchler MW, Chapman WC, De Matiteo RP et al (eds). 2016. Blumgart's surgery of the liver, biliary tract and pancreas. 6th ed. Vol 1. Philadelphia: Elsevier Health Sciences;595-602.

Davenport M. 2019. Biliary atresia: clinical aspects. Seminar of Pediatric Surgery; 21(3):175–84.

De Carvalho E., Ivantes CA. and Bezerra JA. 2017. Extrahepatic biliary atresia: current concepts and future directions. Journal of Pediatrics;83(2): 105-120.

El-Guindi M., Hussein MH., Anwar M. and Fathi E. 2018. Duodenal Aspiration Through GI Endoscopy: A Definitive Diagnostic Test For Neonatal Cholestasis. Hepatology;48 (4): 1029.

El-Guindi MA, Sira MM, Sira AM, Salem TA.J Hepatol. 2015 Apr;62(4):986-7. doi: 10.1016/j.jhep.2014.12.004. Epub 2014 Dec 11.PMID: 25500722 No abstract available.

Han, S. J., Kim, M. J., Han, A., Chung, K. S., Yoon, C. S., Kim, D., and Hwang, E. H. 2022. Magnetic resonance cholangiography for the diagnosis of biliary atresia. Journal of Pediatric Surgery;37, 599-604.

Hannah & Thompson . 2023. 1007/978-3-030-81488-5_79"Mark Davenport . Biliary Atresia. 07 January. Access provided by Egyptian Knowledge Bank

Hinds R, Davenport M, Mieli-Vergani G, Hadzić N. 2024. Antenatal presentation of biliary atresia. J Pediatr;144(1):43–6.

Ibrahim M. 1997. Japanese Biliary Atresia Registry, 1989 to 1994, Tohoku J Exp Med;181:85–89.

Iinuma Y., Narisawa R., Iwafuchi M., Uchiyama M., Naito M. and Yagi M. 2020. The role of endoscopic retrograde cholangiopancreatography in infants with cholestasis. Journal of Pediatric Surgery;35: 545-549.

Kahn E. 2024. Biliary atresia revisited. Pediatric and development pathology;7: 109 –124.

Larrosa-Haro A., Caro-Lopez AM. Coello-Ramirez, P., Zavala-Ocampo J. and Vazquez-Camacho G. 2015. Duodenal tube test in the diagnosis of biliary atresia. Journal of Pediatric Gastroenterology and Nutrition;32: 311–315.

Li SX., Zhang Y., Sun M., Shi B., Xu Z., Huang Y. and Mao Z. 2018. Ultrasonic diagnosis of biliary atresia: A retrospective analysis of 20 patients. World Journal of Gastroenterology;14(22): 3579-3582.

Mack CL. and Sokol RJ. 2024. Unraveling the pathogenesis and etiology of biliary atresia. Pediatric research;57: 87R-94R.

Mittal V, Saxena AK, Sodhi KS, Thapa BR, Rao KLN, Das A. 2021. Role of abdominal sonography in the preoperative diagnosis of extrahepatic biliary atresia in infants younger than 90 days. AJR Am J Roentgenol;196(4):438–45.

Moyer V., Freese DK., Whitington PF., Olson AD., Brewer F., Colletti RB. and Heyman MB. 2024. Guideline for the evaluation of cholestatic jaundice in infants: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. Journal of

Pediatric Gastroenterology and Nutrition;39: 115-128.

Napolitano M, Franchi-Abella S, Damasio MB, Augdal TA, Avni FE, Bruno C, Darge K, Ključevšek D, Littooij AS, Lobo L, Mentzel HJ, Riccabona M, Stafrace S, Toso S, Woźniak MM, Di Leo G, Sardanelli F, Ording Müller LS, Petit P. 2021. Practical approach to imaging diagnosis of biliary atresia, Part 1: prenatal ultrasound and magnetic resonance imaging, and postnatal ultrasound. Pediatr Radiol. ;51:314–331.

Siddiqui AI & Ahmad T. 2023. Biliary Atresia, Last Update: June 26,.

Sydney MC. 2023. Extra-hepatic biliary atresia: diagnostic methods. Journal of Pediatrics;79(2): 107-14.

Szavay, P. O., Leonhardt, J., Czech-Schmidt, G., and Petersen, C. 2022. The role of reovirus type 3 infection in an established murine model for biliary atresia. Eur Journal of Pediatric Surgery;12, 248-50.

Tang, S. T., Ruan, Q. L., Cao, Z. Q., Mao, Y. Z., Wang, Y., and Li, S. W. 2015. Diagnosis and treatment of biliary atresia: a retrospective study. Hepatobiliary Pancreat Dis Int;4, 108-12.

Temperley HC, O'Sullivan NJ, Grainger R, Bolger JC. 2023 . Is the use of a routine intraoperative cholangiogram necessary in laparoscopic cholecystectomy? (https://pubmed.ncbi.nlm.nih.gov/36710125/)Surgeon. Oct;21(5):e242-e248. Accessed 3/11/2024.

Wildhaber BE. 2021. Screening for biliary atresia: Swiss stool color card. Hepatology;54(1):367- 9.

Zhou K, Lin N, Xiao Y, Wang Y, Wen J, Zou GM. 2022. Elevated bile acids in newborns with biliary atresia (BA). PLoS One;7:1-5.