World Journal of Hepatology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.4254/wjh.v8.i36.1593

World J Hepatol 2016 December 28; 8(36): 1593-1601
ISSN 1948-5182 (online)

REVIEW

Biliary atresia: Where do we stand now?

Krishna Kumar Govindarajan

Krishna Kumar Govindarajan, Department of Pediatric Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry 605006, India

Author contributions: The author solely contributed to this manuscript.

Conflict-of-interest statement: None.

Manuscript source: Invited manuscript

Correspondence to: Dr. Krishna Kumar Govindarajan, Department of Pediatric Surgery, Jawaharlal Institute of Postgraduate Medical Education and Research, Pondicherry Road, Puducherry 605006, India. sasisang@rediffmail.com
Telephone: +91-413-2297328
Fax: +91-413-2297325

Received: April 3, 2016
Peer-review started: April 7, 2016
First decision: June 7, 2016
Revised: September 9, 2016
Accepted: November 1, 2016
Article in press: November 2, 2016
Published online: December 28, 2016

Abstract

The pathway from clinical suspicion to establishing the diagnosis of biliary atresia in a child with jaundice is a daunting task. However, investigations available help to point towards the correct diagnosis in reasonable time frame. Imaging by Sonography has identified several parameters which can be of utility in the diagnostic work up. Comparison of Sonography with imaging by Nuclear medicine can bring out the significant differences and also help in appropriate imaging. The battery of Biochemical tests, available currently, enable better understanding of the line-up of investigations in a given child with neonatal cholestasis. Management protocols enable standardized care with optimal outcome. The place of surgical management in biliary atresia is undisputed, although Kasai procedure and primary liver transplantation have been pitted against each other. This article functions as a platform to bring forth the various dimensions of biliary atresia.

Key words: Biliary atresia; Neonatal cholestasis; Kasai procedure; Neonatal jaundice; Hyperbilirubinemia

Core tip: The etiology of biliary atresia is intriguing with a myriad of diagnostics available to work up a child with neonatal jaundice. This article attempts to review the pathogenesis, evaluation, management and outcome for current update of biliary atresia.

Govindarajan KK. Biliary atresia: Where do we stand now? *World J Hepatol* 2016; 8(36): 1593-1601 Available from: URL: http://www.wjgnet.com/1948-5182/full/v8/i36/1593.htm DOI: http://dx.doi.org/10.4254/wjh.v8.i36.1593

INTRODUCTION

Biliary atresia is the commonest surgical cause for neonatal cholestasis, although the diagnosis is one of exclusion of the various causes of neonatal cholestasis which require non-surgical management. Incidence of neonatal cholestasis is noted to be 1 in 2500 newborn children[1]. Among the group of children with neonatal cholestasis, about 34%-42% have been noted to have Biliary atresia[2,3]. The actual incidence is around 1 in

8000-18000 live births[4]. The etio-pathogenesis is not entirely convincing to point towards a particular offending agent, inspite of several studies describing the causal association of infective or autoimmune origin. The investigations for the establishment of the diagnosis are elaborate, and require extensive workup. As timely surgical intervention is essential, an appropriate and prompt work up is required.

ETIOLOGY

For the purpose of better understanding, biliary atresia is categorized into 2 forms, the perinatal or the acquired form and the embryonic or the congenital form. The embryonic form is the less common variant of the two (20%), with a link to syndromic association such as Biliary atresia Splenic Malformation (BASM - polysplenia, intestinal malrotation, preduodenal portal vein, absent inferior vena cava, aberrant hepatic artery, abdominal heterotaxia), known to be due to gene mutations controlling the bile duct development. The commoner perinatal form (80%) is supposed to be the end result of viral trigger and complex interactions between innate and adaptive immune responses[5].

The complete deletion of inversin gene in mice was shown to produce laterality defects in the abdominal organs along with malformations of the hepatobiliary system, similar to that of the fetal form[6]. However, the role of the inversin gene in humans is unlikely in the fetal form of Biliary atresia, as established by Schön *et al*[7].

Several viral agents such as human papilloma virus, cytomegalo virus, respiratory syncytial virus, reovirus, rotavirus[8-12], epstein barr virus, herpes virus, hepatitis B virus[13-15] have been implicated in the past, but none have been consistently and convincingly shown to be associated with the pathogenesis of Biliary atresia in humans.

The cystic biliary atresia is believed to be an exclusive subtype, based on the following observations: (1) jaundice noticed at birth; (2) diagnosed antenatally by the identification of a cystic lesion at the porta on sonography; and (3) intra-operatively a cystic lesion seen, not communicating with intrahepatic ductal system or duodenum.

Reports on cystic type biliary atresia declare that the entity has a better outcome[16].

PATHOGENESIS

To explain the pathogenesis of Biliary atresia, the concept of an initial viral infection damaging the biliary duct, followed by exaggerated autoimmune directed inflammation of biliary ducts and secondary biliary cirrhosis as a result of progressive ductal injury and obstruction has been mooted[17,18].

Interestingly, studies have noted the ability of Rota virus to target cholangiocytes and cause tissue specific inflammation and pathogenic effects in mouse models. The theory of viral mediated damage and progressive obliterative inflammation of bile ductules has been put forward, on the basis of this murine model. The virus is found to be tropic to cholangiocytes, leaving behind gamma interferon producing CD4 and 8 lymphocytes which target the hepatobiliary system, culminating in fibrosis of the injured ductal elements, bearing the striking resemblance to Biliary atresia[19].

Furthermore, it was concluded that the gamma interferon triggered the inflammatory changes responsible for progressive bile duct obstruction and obliteration[19]. It is believed that DNA hypomethylation changes in CD4 lymphocytes leads onto uncontrolled gamma interferon expression[20]. Gamma interferon through release from T lymphocytes, has been projected as the pivotal player, orchestrating the sequence of events, specifically the later occurrence of intraductal inflammation, ductal fibrosis and loss of epithelial integrity. However, the initial response of neutrophilic inflammation to the provoking viral agent was not altered, lending to the surmise that the gamma interferon is responsible for the ultimate damage and loss of extrahepatic bile ducts[21]. It is noteworthy that, in their attempt to achieve viral clearance, the CD8 lymphocytes secondarily cause ductular damage resulting in the experimental type of Biliary atresia[19]. Alpha2 beta1 integrin has been identified to be the medium of interaction responsible for predisposition of the cholangiocytes to Rhesus Rota virus infection[22].

Regulatory T lymphocyte defects in the presence of viral infection, has also found to be contributory to the unchecked bile ductal inflammation and destruction[23].

ANIMAL MODELS

The use of intrahepatic injection of chemicals like carbon tetrachloride, ethanol, formalin have been found to simulate inflammation similar to biliary atresia in adult rat[24,25]. Other animals like lamb fetus has also been studied[26]. Attempted *in vivo* replication of biliary atresia includes bile duct excision or ligation. Sea Lamprey as a model has been propagated with the advantage of seamless progress into biliary atresia without the need for intervention with injection of chemicals or surgical bile duct ligation[27].

CLINICAL PRESENTATION

The consistent passage of clay coloured stools, dark coloured urine, icterus at about 2 wk of age in a neonate should prompt the complete work up for cholestasis, especially biliary atresia.

INVESTIGATIONS

Simple macroscopic examination showing clay coloured acholic stool raises a strong suspicion of biliary atresia. When the stools are not acholic, additional features such as fecal fat and consistency can provide more information. Soil like consistency of stool with massive fat droplets on Sudan Ⅲ stain is a finding which has

high sensitivity, although not specific for biliary atresia detection[28].

Blood biochemistry

Gamma glutamyl transpeptidase (GGT) has been found to be an important parameter in the differential diagnosis of neonatal cholestasis. Children with Biliary atresia consistently had higher GGT levels than those without Biliary atresia (902.7 mmol/L *vs* 263.2 mmol/L)[29]. Tang *et al*[30] demonstrated that an elevated GGT more than 300 IU/L had a specificity of 98% and sensitivity of 38% to differentiate biliary atresia from Neonatal Hepatitis. In addition, the association between GGT and Alanine transferase ALT (GGT/ALT ratio more than 2) was put forth as a useful adjunct in the differential diagnosis of biliary atresia[30].

It is to be noted that, more relevance is placed on the correlation of GGT with age, than an absolute GGT value. To elaborate further, GGT is best diagnostic when evaluating cholestasis in children aged less than 120 d. Among infants aged 31-60 d, GGT levels more than 268 IU/L had a sensitivity of 80.5% and specificity of 75.6%, respectively, with an accuracy of 79.1% in the diagnostic evaluation of Biliary atresia. Recommended cut-off values of GGT for various age groups include 303 IU/L for age 61-90 d, 298 IU/L for age 91-120 d, 252 IU/L for age more than 121 d[31]. Another study brought out the optimal threshold for GGT for various ages, 150 IU/L for age less than 4 wk, 250 IU/L for age between 4-8 wk and 300 IU/L for age more than 8 wk[32].

On the contrary, alkaline phosphatase levels were noted to be higher in those children without biliary atresia[31].

The Apolipoprotein E has been found to be useful in the diagnostic workup as the serum levels have been consistently elevated in biliary atresia[33]. Rafeey *et al*[34] in a recent study showed Apolipoprotein E to have positive predictive value of 71% and negative predictive value of 67% in differentiating biliary atresia from other neonatal cholestatic disorders, indicating that its utility as a stand-alone diagnostic test is limited. Similar results have been seen with procalcitonin, which is an inflammatory marker, synthesized in the liver. Hence it could be used possibly in combination with other tests to improve the diagnostic accuracy[34].

Recently, microRNA assay has been pointed to be a novel method of quick diagnosis of biliary atresia. Injury to liver tissue in biliary atresia is supposed to release certain microRNAs, which are non-coding RNAs regulating target genes. High levels of these micro RNAs are found in the intrahepatic bile ducts confirming the source of release and their specificity. The study by Zahm *et al*[35] has established the high levels of serum miR220b/429 in Biliary atresia patients in comparison to other cholestatic disorders, implying the potential and promising utility of these in aiding in the early diagnosis.

Imaging

Sonography has distinct advantages of being non-invasive, repeatable, less expensive, readily available bedside and non-ionising, although limited by operator dependancy. Hence, this is used as the initial screening modality in the work up of neonatal cholestasis.

The usefulness of sonography, as an initial diagnostic tool is well brought out in several studies. Presence of a triangular cord sign which is the visualization of the fibrotic cord in the portal hilum is one of the hallmarks of sonographic imaging with a positive predictive value of 95%[36]. Triangular or tubular structure with echogenic density cranial to portal vein bifurcation at the liver hilum is indicative of triangular cord sign[37]. Gall bladder (GB) morphology is looked into as the primary diagnostic factor on sonography. If the GB morphology is normal on sonography, the next step of measuring the triangular cord thickness is undertaken, which if more than 3.4 mm, the sonographic diagnosis of Biliary atresia is very likely[38].

In addition, the GB contractility, size and dimension, regular mucosal contour all go together in the diagnostic imaging. Findings pertaining to GB on sonography can be absent/non visualized GB, irregular contour of GB, small shrunken GB, non contractile GB despite 4 h of fasting, cystic structure replacing GB and absent echogenic mucosal lining of GB. The liver echotexture signifying the presence of cirrhosis is another finding useful on sonography for prognostication[39]. At a cut off GB length of 1.5 cm, high index of suspicion for biliary atresia to be kept while evaluating a baby with neonatal cholestasis[40]. In the early stage of the disease, the triangular cord sign may be not prominent, leading to missed diagnosis. Triangular cord sign combined with GB length can act as twin hallmarks in the sonographic diagnosis of biliary atresia. In the setting of periportal inflammation or cirrhosis, sonographic diagnosis may be difficult as triangular cord sign may not be apparent. Utility of the GB ghost triad, including GB length less than 1.9 cm, irregular contour of GB and lack of smooth, regular mucosal echogenicity of GB may be helpful in the above scenario. With an accuracy of 97%, it appears to be an invaluable diagnostic feature on sonography[41].

As adjuncts to the above sonographic parameters, the right hepatic artery diameter more than 1.5 mm and ratio of the right hepatic artery to that of the portal vein more than 0.45 were of use in the sonographic evaluation[42].

The visualisation of hepatic subcapsular flow due to hepatic arteriopathy and fibrosis in biliary atresia is another sonographic feature on colour Doppler study[43]. El-Guindi *et al*[44] in a recent study reported the superiority of demonstration of hepatic subcapsular flow over the other sonographic parameters such as triangular cord sign, GB contractility, GB size and dimensions of hepatic artery. Even when the sonographic hallmark of triangular cord sign could not be satisfactorily demonstrated, presence of hepatic sub capsular flow can be of significant value in sonographic examination[45].

The measurement of liver span below the costal margin by sonography can help in the workup, as consistently "small" livers are seen in non-biliary atresia

children[29].

Using a special transducer sonography probe, it is now possible to measure liver fibrosis, based on the technique of transient elastography. Consequently, prognostication of the state of the advanced liver disease can be predicted in a non-invasive manner. It is predicted to be useful as a follow up tool, without the need to resort to performing a liver biopsy. However, the sensitivity of this test in identifying early stages of liver fibrosis is limited[46].

It is recommended that a confident demonstration of the triangular cord sign can route the algorithm towards operative cholangiography, rather than subjecting to liver biopsy, in view of the accuracy of the sonographic sign[29].

Antenatal diagnosis

The presence of a cystic structure at the porta hepatis without intrahepatic biliary ductular dilatation goes towards the diagnosis of biliary atresia, in the antenatal period. This is also known to be associated with additional anomalies[47,48].

Sonography vs scintigraphy

Compared to nuclear scintigraphy, sonography has better discriminatory value in the differential diagnosis. This is evidenced by the higher specificity of the triangular cord sign (95.8%) against scintigraphy (72.9%). Also, the positive predictive value of the triangular cord sign scoring twice higher than scintigraphy (77.8% *vs* 38.1%) puts sonography ahead, in the correct detection of biliary atresia[49].

Magnetic resonance cholangiopancreatography

The utility of Magnetic resonance cholangiopancreatography (MRCP) has not been encouraging in view of the cost, varying results and the need for immobilisation. Negative and positive predictive value have been reported as 91%-100%, 75%-96% respectively[50,51]. The requirement of sedation, preferably general anesthesia is a significant concern in addition to long image acquisition time. In a recent study, the image acquisition time using three dimensional MRCP has been reported to be around 180 s. The sensitivity 99.08% and negative predictive value 96.88% were high but the specificity 36.05% and positive predictive value 65.19% were low[52].

Nuclear scintigraphy

Nuclear scintigraphy is non-invasive, simple and is supposed to have practical utility in view of the logical assumption of the functional ability of liver to take up the tagged agent and subsequent excretion in the intestine, enabling visualization of gut activity. Studies caution regarding excessive reliance of scintigraphy, as it may contribute to misdiagnosis in infants with jaundice[29]. However, in the background of elevated bilirubin levels and likely deranged liver function, ability to take up the agent may be compromised. To overcome this, cholegogues such as Ursodeoxy cholic acid, Phenobarbitone, Phenytoin are used as pre-treatment agents, to ensure adequate "priming"[53].

The value of delayed or 24 h imaging has been pointed out to decrease the false positive results as nearly 50% of the bowel visualization was seen in the delayed image[54]. As an adjunct, SPECT has been put forth in dealing with poor bowel visualization. More studies are required before concluding in favor of its usage[55]. However, arguments against, have discouraged the same citing the poor image resolution with consequent difficult interpretation. Excretion is expected to be less due to reduced uptake primarily, given the background of deranged liver function and high bilirubin levels, competing with the tagged agent effectively to decrease the uptake. Furthermore, it has been proposed that this would be time consuming and lead to more delay in the work up[56].

A recent meta-analysis places the scintigraphy in the correct perspective, at a low specificity of 70.4%, although pooled sensitivity was high at 98.7%. This would mean that almost every case of biliary atresia gets detected, but when the scintigraphy shows no excretion, it does not necessarily diagnose biliary atresia amongst the other causes of neonatal cholestasis[53].

Histology

Liver biopsy is considered as gold standard in the diagnosis of biliary atresia, with an accuracy of 88.2%-96.9%[57,58]. To cope with the delayed referrals and the negative laparotomy rate, histology of liver biopsy is proposed as the best alternative. Also, histology has a definitive role, where the various imaging modalities may not be able to suggest the suitable diagnosis, especially in younger neonatal cholestatic children. Among the several findings in histology, ductular proliferation, bile plugs in the ducts and the ductules and portal fibrosis were found to be statistically significant in the diagnostic workup of biliary atresia. On further multivariate analysis, the ductular proliferation emerged as the sole parameter of paramount importance. Of note, age was not found to be a factor in altering the diagnostic histological features in biliary atresia. Multinucleate giant cell formation and myeloid metaplasia were noted to be seen more commonly in neonatal hepatitis[58]. Utility of the liver biopsy in the work up of neonatal cholestasis has been recommended as a guideline[59].

Histology can also prognosticate in addition to providing a diagnosis, by cirrhosis assessment and ductal plate malformation. Ductal plate malformation which refers to presence of fetal type intrahepatic duct, is identified to be a poor prognostic factor as it is known to be associated with poor bile flow after Portoenterostomy[60].

Ductal diameter less than 100 microns was a feature identified with children requiring liver transplantation[61]. Whereas, when ductal size was more than 150 microns, in combination with a columnar lined epithelium, it was predictive of good prognosis after surgical mana-

gement[62].

Fibrosis as an independent prognostic marker in histological evaluation is established by various studies[63-65]. Also, it has been utilized to predict the long term outcome in post-operative biliary atresia patients[66].

Ductopenia and secondary biliary cirrhosis were consistently found to be late histological features[67].

Endoscopy

Use of endoscopy in biliary atresia is mainly for dealing with the sequelae of portal hypertension and varices. However, endoscopy can be of use in aiding diagnostic workup, in addition to duodenal intubation for bile detection. Sampling of Duodenal contents to improve the accuracy of scintigraphy, as gamma camera may not pick up minimal activity, is a step towards improvisation by means of non-imaging method[68].

Scoring system

Based on the variable nature of the diagnostic tests and their overlapping tendency, it would be best to rely on a combination of investigations with correlation to the clinical condition, to reach a prompt and confident diagnosis in the individual child with neonatal cholestasis. Most investigations by themselves do not point to a clear cut differentiation between biliary atresia and other causes of neonatal cholestasis. Hence this has led to a strategy of mix and match of modalities to evolve a meaningful scoring system to attempt to objectively categorize the children with biliary atresia from the group of Neonatal cholestasis. The proposal of El-Guindi *et al*[69] consists of a twelve-point scoring system, according to clinical, laboratory, ultrasonographic, and histopathological parameters, with a reported accuracy of 98.3% in pin pointing biliary atresia. Strikingly, scintigraphy was not included in their scoring, referring to its low specificity and time lost to prime the patient. Confining to histology, Chen *et al*[70] have evolved a 8-feature (liver fibrosis, portal ductal proliferation, bile plugs in portal ductules, cholestasis, hepatocellular changes inflammatory cells infiltration in portal region, extramedullary hematopoiesis, and ductal plate malformation), 21-point (0 to 21) scoring system declaring an accuracy of 91.9% in correctly identifying biliary atresia[70].

OPERATIVE MANAGEMENT

Surgery is the main stay of treatment in biliary atresia to effectively establish bile drainage and jaundice clearance. Left untreated, there is an incessant progression towards Biliary cirrhosis, end stage liver failure and death by 3 years of age[4]. The hallmark of biliary atresia is the difficulty in prediction of the natural course and outcome, given that it should not be considered a single disease entity with a predictable natural history and stereotypical response to surgery[71].

Kasai portoenterostomy relies on the realization that the microscopic structures in the porta hepatis will act as micro-conduits of bile as an internal biliary fistula is created with a segment of bowel. Use of gall bladder, appendix has been tried earlier as conduits instead of the bowel segment, but none were successful like the bowel. In view of higher revision rates, other conduits except bowel have been abandoned[72].

The extended Kasai procedure attempts at utilising more anastomotic area for achieving effective bile drainage by extending the dissection into the Rex recess (the space between segments Ⅲ and Ⅳ under the liver bridge) and around the bifurcation of the right vascular pedicle of portal hilum[73,74].

Laparoscopic portoenterostomy has not been shown to have better outcome than the open portoenterostomy[75]. Although proponents have defended the minimal access approach with the claim that the risk for damage to small bile ductules around the porta hepatis is minimal, due to avoidance of deep suturing and extensive dissection[76]. The advantage of minimal adhesions after laparoscopic intervention, enabling future liver transplantation has also been negated[77]. Hence, the open portoenterostomy continues to be the gold standard for biliary atresia[78].

The recommendation to perform per op cholangiography directly without a liver biopsy where clinical suspicion is high, reflects the equivocal state of the liver biopsy[3].

Post-operative management

The role of corticosteroids is hotly debated and controversial, as there is no conclusive evidence in terms of long term improved outcome[79]. However, there does seem to be a positive impact of improved clearance of jaundice when steroids are used for a short course in the post-operative period. Thus the lack of translation of beneficial effect with usage of steroids has generally discouraged its prescription in the long term management, although there is a strong link between continuing inflammation, altered immunity and ongoing fibrosis in biliary atresia after Kasai procedure[80]. Unlike steroids, Urso deoxycholic acid does play a positive and significant role in the bile flow and finds a place in the post-operative protocol of Biliary atresia management[81].

OUTCOME

Lower degree of biliary fibrosis, bile ductular proliferation, absence of ductal plate malformation, large ducts more than 150 μm and younger age were found to be associated with better long term outcome[66].

The cystic dilatation of the intrahepatic biliary system on sonography following Kasai during long term follow-up, is considered as a poor prognostic feature lowering the survival rate with native liver[82].

The children with BASM tend to have a poorer prognosis[83,84]. Younger age at Kasai was linked with better outcome in those with the cystic type biliary atresia and BASM. Whereas younger age at surgery was not a determining factor in isolated biliary atresia[83].

The long term survival with native liver is significantly lower, establishing the dictum that liver transplant is the

ultimate recipe for biliary atresia management. Adult outcome studies in Biliary atresia patients quote the survival with native liver at 20% in the adults 20 years post Kasai and 10% among those who are 30 years post Kasai[85,86].

Centralisation of services, such that biliary atresia surgery is managed at select centres, has been shown to remarkably increase surgical outcome and overall survival. Standardisation of protocolised management with uniform pre operative work up, surgical technique, post operative management and follow-up seem to be the cohesive factors towards achieving a better outcome. To quote the Finnish study, jaundice clearance rate improved from 27% to 75% and overall survival from 64% to 92% with all the above measures[87].

Kasai portoenterostomy effectively acts as a bridging procedure, enabling retention of native liver in about a quarter of patients and maintaining the rest till an organ is available for transplant in the long term[88]. The importance of surveillance is underlined by the fact that majority of the patients (58.3%) after Kasai procedure develop features of chronic liver disease such as Cirrhosis and Portal hypertension[89].

Early neonatal screening with stool charts has a beneficial effect as evidenced by the fact that 5 year survival with native liver increased from 27.3% to 64.3%[90].

Nutritional management for optimal outcome would include feeding regime with a medium chain triglyceride formula. Also, the follow-up of these children should monitor the regular vitamin supplementation of fat soluble vitamins. However, the question of nutritional resuscitation is relevant from the point of view of those awaiting liver transplant[4].

SCREENING

Various screening methods other than stool charts have been studied, but none are effective as a simple, cost effective and useful tool in screening general population. Serum bile acid, direct bilirubin, Apo CⅡ/CⅢ proteins, urine sulfated bile acid, fecal bilirubin and fat[91-95] were some of the biomarkers used in the literature for screening of Biliary atresia.

CONCLUSION

Biliary atresia is a multifactorial disorder with varied outcome depending upon the time of surgical treatment and histology. Strict adherence to protocols in the form of investigations would lead to seamless progression from diagnosis to management. Post operative management with appropriate medications is required to ensure an optimal outcome. Long term follow-up is essential as the native liver can fail over a period of time requiring the need for liver transplantation. Although advances regarding understanding of progressive inflammation after portoenterostomy have been made, translation into significant treatment has not evolved yet.

REFERENCES

1 **Poddar U**, Thapa BR, Das A, Bhattacharya A, Rao KL, Singh K. Neonatal cholestasis: differentiation of biliary atresia from neonatal hepatitis in a developing country. *Acta Paediatr* 2009; **98**: 1260-1264 [PMID: 19469771 DOI: 10.1111/j.1651-2227. 2009.01338.x]

2 **Indian Academy of Pediatrics. Pediatric Gastroenterology Subspecialty Chapter.** Consensus report on neonatal cholestasis syndrome. Pediatric Gastroenterology Subspecialty Chapter of Indian Academy of Pediatrics. *Indian Pediatr* 2000; **37**: 845-851 [PMID: 10951633]

3 **Shah I**, Bhatnagar S, Dhabe H. Clinical and biochemical factors associated with biliary atresia. *Trop Gastroenterol* 2012; **33**: 214-217 [PMID: 23600053]

4 **Sokol RJ**, Mack C, Narkewicz MR, Karrer FM. Pathogenesis and outcome of biliary atresia: current concepts. *J Pediatr Gastroenterol Nutr* 2003; **37**: 4-21 [PMID: 12827000]

5 **Mack CL**, Feldman AG, Sokol RJ. Clues to the etiology of bile duct injury in biliary atresia. *Semin Liver Dis* 2012; **32**: 307-316 [PMID: 23397531 DOI: 10.1055/s-0032-1329899]

6 **Mazziotti MV**, Willis LK, Heuckeroth RO, LaRegina MC, Swanson PE, Overbeek PA, Perlmutter DH. Anomalous development of the hepatobiliary system in the Inv mouse. *Hepatology* 1999; **30**: 372-378 [PMID: 10421642 DOI: 10.1002/hep.510300223]

7 **Schön P**, Tsuchiya K, Lenoir D, Mochizuki T, Guichard C, Takai S, Maiti AK, Nihei H, Weil J, Yokoyama T, Bouvagnet P. Identification, genomic organization, chromosomal mapping and mutation analysis of the human INV gene, the ortholog of a murine gene implicated in left-right axis development and biliary atresia. *Hum Genet* 2002; **110**: 157-165 [PMID: 11935322 DOI: 10.1007/s00439-001-0655-5]

8 **Drut R**, Drut RM, Gómez MA, Cueto Rúa E, Lojo MM. Presence of human papillomavirus in extrahepatic biliary atresia. *J Pediatr Gastroenterol Nutr* 1998; **27**: 530-535 [PMID: 9822318]

9 **Fischler B**, Ehrnst A, Forsgren M, Orvell C, Nemeth A. The viral association of neonatal cholestasis in Sweden: a possible link between cytomegalovirus infection and extrahepatic biliary atresia. *J Pediatr Gastroenterol Nutr* 1998; **27**: 57-64 [PMID: 9669727]

10 **Nadal D**, Wunderli W, Meurmann O, Briner J, Hirsig J. Isolation of respiratory syncytial virus from liver tissue and extrahepatic biliary atresia material. *Scand J Infect Dis* 1990; **22**: 91-93 [PMID: 2320967]

11 **Morecki R**, Glaser JH, Cho S, Balistreri WF, Horwitz MS. Biliary atresia and reovirus type 3 infection. *N Engl J Med* 1982; **307**: 481-484 [PMID: 6285193 DOI: 10.1056/NEJM198208193070806]

12 **Riepenhoff-Talty M**, Gouvea V, Evans MJ, Svensson L, Hoffenberg E, Sokol RJ, Uhnoo I, Greenberg SJ, Schäkel K, Zhaori G, Fitzgerald J, Chong S, el-Yousef M, Nemeth A, Brown M, Piccoli D, Hyams J, Ruffin D, Rossi T. Detection of group C rotavirus in infants with extrahepatic biliary atresia. *J Infect Dis* 1996; **174**: 8-15 [PMID: 8656017]

13 **Mahjoub F**, Shahsiah R, Ardalan FA, Iravanloo G, Sani MN, Zarei A, Monajemzadeh M, Farahmand F, Mamishi S. Detection of Epstein Barr virus by chromogenic in situ hybridization in cases of extra-hepatic biliary atresia. *Diagn Pathol* 2008; **3**: 19 [PMID: 18442403 DOI: 10.1186/1746-1596-3-19]

14 **Domiati-Saad R**, Dawson DB, Margraf LR, Finegold MJ, Weinberg AG, Rogers BB. Cytomegalovirus and human herpesvirus 6, but not human papillomavirus, are present in neonatal giant cell hepatitis and extrahepatic biliary atresia. *Pediatr Dev Pathol* 2000; **3**: 367-373 [PMID: 10890252]

15 **Landing BH**. Considerations of the pathogenesis of neonatal hepatitis, biliary atresia and choledochal cyst--the concept of infantile obstructive cholangiopathy. *Prog Pediatr Surg* 1974; **6**: 113-139 [PMID: 4856850]

16 **Caponcelli E**, Knisely AS, Davenport M. Cystic biliary atresia: an etiologic and prognostic subgroup. *J Pediatr Surg* 2008; **43**: 1619-1624 [PMID: 18778995 DOI: 10.1016/j.jpedsurg.2007.12.058]

17 **Mack CL**, Sokol RJ. Unraveling the pathogenesis and etiology of biliary atresia. *Pediatr Res* 2005; **57**: 87R-94R [PMID: 15817506

DOI: 10.1203/01.PDR.0000159569.57354.47]
18 **Asai A**, Miethke A, Bezerra JA. Pathogenesis of biliary atresia: defining biology to understand clinical phenotypes. *Nat Rev Gastroenterol Hepatol* 2015; **12**: 342-352 [PMID: 26008129 DOI: 10.1038/nrgastro.2015.74]
19 **Shivakumar P**, Sabla G, Mohanty S, McNeal M, Ward R, Stringer K, Caldwell C, Chougnet C, Bezerra JA. Effector role of neonatal hepatic CD8+ lymphocytes in epithelial injury and autoimmunity in experimental biliary atresia. *Gastroenterology* 2007; **133**: 268-277 [PMID: 17631148 DOI: 10.1053/j.gastro.2007.04.031]
20 **Dong R**, Zhao R, Zheng S. Changes in epigenetic regulation of CD4+ T lymphocytesin biliary atresia. *Pediatr Res* 2011; **70**: 555-559 [PMID: 21857377 DOI: 10.1203/PDR.0b013e318232a949]
21 **Shivakumar P**, Campbell KM, Sabla GE, Miethke A, Tiao G, McNeal MM, Ward RL, Bezerra JA. Obstruction of extrahepatic bile ducts by lymphocytes is regulated by IFN-gamma in experimental biliary atresia. *J Clin Invest* 2004; **114**: 322-329 [PMID: 15286798 DOI: 10.1172/JCI21153]
22 **Jafri M**, Donnelly B, Allen S, Bondoc A, McNeal M, Rennert PD, Weinreb PH, Ward R, Tiao G. Cholangiocyte expression of alpha2beta1-integrin confers susceptibility to rotavirus-induced experimental biliary atresia. *Am J Physiol Gastrointest Liver Physiol* 2008; **295**: G16-G26 [PMID: 18436621 DOI: 10.1152/ajpgi.00442.2007]
23 **Brindley SM**, Lanham AM, Karrer FM, Tucker RM, Fontenot AP, Mack CL. Cytomegalovirus-specific T-cell reactivity in biliary atresia at the time of diagnosis is associated with deficits in regulatory T cells. *Hepatology* 2012; **55**: 1130-1138 [PMID: 22105891 DOI: 10.1002/hep.24807]
24 **Tatekawa Y**, Nakada A, Nakamura T. Intrahepatic biliary ablation with pure ethanol: an experimental model of biliary atresia. *Surg Today* 2013; **43**: 661-669 [PMID: 23073846 DOI: 10.1007/s00595-012-0379-2]
25 **Dumont M**, D'Hont C, Moreau A, Mbape H, Feldmann G, Erlinger S. Retrograde injections of formaldehyde into the biliary tree induce alterations of biliary epithelial function in rats. *Hepatology* 1996; **24**: 1217-1223 [PMID: 8903401 DOI: 10.1053/jhep.1996.v24.pm0008903401]
26 **Spitz L**. Ligation of the common bile duct in the fetal lamb: an experimental model for the study of biliary atresia. *Pediatr Res* 1980; **14**: 740-748 [PMID: 7383750 DOI: 10.1203/00006450-198005000-00007]
27 **Chung-Davidson YW**, Yeh CY, Li W. The Sea Lamprey as an Etiological Model for Biliary Atresia. *Biomed Res Int* 2015; **2015**: 832943 [PMID: 26101777 DOI: 10.1155/2015/832943]
28 **Okajima K**, Nagaya K, Azuma H, Suzuki T. Biliary atresia and stool: its consistency and fat content, another potentially useful clinical information. *Eur J Gastroenterol Hepatol* 2016; **28**: 118 [PMID: 26594917 DOI: 10.1097/MEG.0000000000000504]
29 **Sun S**, Chen G, Zheng S, Xiao X, Xu M, Yu H, Dong R. Analysis of clinical parameters that contribute to the misdiagnosis of biliary atresia. *J Pediatr Surg* 2013; **48**: 1490-1494 [PMID: 23895960 DOI: 10.1016/j.jpedsurg.2013.02.034]
30 **Tang KS**, Huang LT, Huang YH, Lai CY, Wu CH, Wang SM, Hwang KP, Huang FC, Tiao MM. Gamma-glutamyl transferase in the diagnosis of biliary atresia. *Acta Paediatr Taiwan* 2007; **48**: 196-200 [PMID: 18265540]
31 **Chen X**, Dong R, Shen Z, Yan W, Zheng S. Value of Gamma-Glutamyl Transpeptidase for Diagnosis of Biliary Atresia by Correlation With Age. *J Pediatr Gastroenterol Nutr* 2016; **63**: 370-373 [PMID: 26963938 DOI: 10.1097/MPG.0000000000001168]
32 **Rendón-Macías ME**, Villasís-Keever MA, Castañeda-Muciño G, Sandoval-Mex AM. Improvement in accuracy of gamma-glutamyl transferase for differential diagnosis of biliary atresia by correlation with age. *Turk J Pediatr* 2010; **50**: 253-259 [PMID: 18773671]
33 **Wang H**, Malone JP, Gilmore PE, Davis AE, Magee JC, Townsend RR, Heuckeroth RO. Serum markers may distinguish biliary atresia from other forms of neonatal cholestasis. *J Pediatr Gastroenterol Nutr* 2010; **50**: 411-416 [PMID: 20216099 DOI: 10.1097/MPG.0b013e3181cb42ee]
34 **Rafeey M**, Saboktakin L, Shoa Hassani J, Farahmand F, Aslanabadi S, Ghorbani-Haghjou A, Poorebrahim S. Diagnostic value of procalcitonin and apo-e in extrahepatic biliary atresia. *Iran J Pediatr* 2014; **24**: 623-629 [PMID: 25793072]
35 **Zahm AM**, Hand NJ, Boateng LA, Friedman JR. Circulating microRNA is a biomarker of biliary atresia. *J Pediatr Gastroenterol Nutr* 2012; **55**: 366-369 [PMID: 22732895 DOI: 10.1097/MPG.0b013e318264e648]
36 **Park WH**, Choi SO, Lee HJ. Technical innovation for noninvasive and early diagnosis of biliary atresia: the ultrasonographic "triangular cord" sign. *J Hepatobiliary Pancreat Surg* 2001; **8**: 337-341 [PMID: 11521178 DOI: 10.1007/s0053410080337]
37 **Sun Y**, Zheng S, Qian Q. Ultrasonographic evaluation in the differential diagnosis of biliary atresia and infantile hepatitis syndrome. *Pediatr Surg Int* 2011; **27**: 675-679 [PMID: 21207229 DOI: 10.1007/s00383-010-2814-z]
38 **Lee SM**, Cheon JE, Choi YH, Kim WS, Cho HH, Kim IO, You SK. Ultrasonographic Diagnosis of Biliary Atresia Based on a Decision-Making Tree Model. *Korean J Radiol* 2015; **16**: 1364-1372 [PMID: 26576128 DOI: 10.3348/kjr.2015.16.6.1364]
39 **Li SX**, Zhang Y, Sun M, Shi B, Xu ZY, Huang Y, Mao ZQ. Ultrasonic diagnosis of biliary atresia: a retrospective analysis of 20 patients. *World J Gastroenterol* 2008; **14**: 3579-3582 [PMID: 18567090]
40 **Tan Kendrick AP**, Phua KB, Ooi BC, Subramaniam R, Tan CE, Goh AS. Making the diagnosis of biliary atresia using the triangular cord sign and gallbladder length. *Pediatr Radiol* 2000; **30**: 69-73 [PMID: 10663514 DOI: 10.1007/s002470050017]
41 **Tan Kendrick AP**, Phua KB, Ooi BC, Tan CE. Biliary atresia: making the diagnosis by the gallbladder ghost triad. *Pediatr Radiol* 2003; **33**: 311-315 [PMID: 12695863 DOI: 10.1007/s00247-003-0867-z]
42 **Kim WS**, Cheon JE, Youn BJ, Yoo SY, Kim WY, Kim IO, Yeon KM, Seo JK, Park KW. Hepatic arterial diameter measured with US: adjunct for US diagnosis of biliary atresia. *Radiology* 2007; **245**: 549-555 [PMID: 17890351 DOI: 10.1148/radiol.2452061093]
43 **Lee MS**, Kim MJ, Lee MJ, Yoon CS, Han SJ, Oh JT, Park YN. Biliary atresia: color doppler US findings in neonates and infants. *Radiology* 2009; **252**: 282-289 [PMID: 19561262 DOI: 10.1148/radiol.2522080923]
44 **El-Guindi MA**, Sira MM, Konsowa HA, El-Abd OL, Salem TA. Value of hepatic subcapsular flow by color Doppler ultrasonography in the diagnosis of biliary atresia. *J Gastroenterol Hepatol* 2013; **28**: 867-872 [PMID: 23425046 DOI: 10.1111/jgh.12151]
45 **Ramesh RL**, Murthy GV, Jadhav V, Ravindra S. Hepatic subcapsular flow: An early marker in diagnosing biliary atresia. *Indian J Radiol Imaging* 2015; **25**: 196-197 [PMID: 25969645 DOI: 10.4103/0971-3026.155875]
46 **Shin NY**, Kim MJ, Lee MJ, Han SJ, Koh H, Namgung R, Park YN. Transient elastography and sonography for prediction of liver fibrosis in infants with biliary atresia. *J Ultrasound Med* 2014; **33**: 853-864 [PMID: 24764341 DOI: 10.7863/ultra.33.5.853]
47 **Hinds R**, Davenport M, Mieli-Vergani G, Hadzić N. Antenatal presentation of biliary atresia. *J Pediatr* 2004; **144**: 43-46 [PMID: 14722517 DOI: 10.1016/j.jpeds.2003.09.027]
48 **Casaccia G**, Bilancioni E, Nahom A, Trucchi A, Aite L, Marcellini M, Bagolan P. Cystic anomalies of biliary tree in the fetus: is it possible to make a more specific prenatal diagnosis? *J Pediatr Surg* 2002; **37**: 1191-1194 [PMID: 12149700]
49 **Imanieh MH**, Dehghani SM, Bagheri MH, Emad V, Haghighat M, Zahmatkeshan M, Forutan HR, Rasekhi AR, Gheisari F. Triangular cord sign in detection of biliary atresia: is it a valuable sign? *Dig Dis Sci* 2010; **55**: 172-175 [PMID: 19229615 DOI: 10.1007/s10620-009-0718-3]
50 **Han SJ**, Kim MJ, Han A, Chung KS, Yoon CS, Kim D, Hwang EH. Magnetic resonance cholangiography for the diagnosis of biliary atresia. *J Pediatr Surg* 2002; **37**: 599-604 [PMID: 11912518]
51 **Norton KI**, Glass RB, Kogan D, Lee JS, Emre S, Shneider BL.

MR cholangiography in the evaluation of neonatal cholestasis: initial results. *Radiology* 2002; **222**: 687-691 [PMID: 11867786 DOI: 10.1148/radiol.2223010969]
52 **Liu B**, Cai J, Xu Y, Peng X, Zheng H, Huang K, Yang J. Three-dimensional magnetic resonance cholangiopancreatography for the diagnosis of biliary atresia in infants and neonates. *PLoS One* 2014; **9**: e88268 [PMID: 24505457 DOI: 10.1371/journal.pone.0088268]
53 **Kianifar HR**, Tehranian S, Shojaei P, Adinehpoor Z, Sadeghi R, Kakhki VR, Keshtgar AS. Accuracy of hepatobiliary scintigraphy for differentiation of neonatal hepatitis from biliary atresia: systematic review and meta-analysis of the literature. *Pediatr Radiol* 2013; **43**: 905-919 [PMID: 23519699 DOI: 10.1007/s00247-013-2623-3]
54 **Stipsanelli K**, Koutsikos J, Papantoniou V, Arka A, Palestidis C, Tsiouris S, Manolaki A, Zerva C. Hepatobiliary scintigraphy and gamma-GT levels in the differential diagnosis of extrahepatic biliary atresia. *Q J Nucl Med Mol Imaging* 2007; **51**: 74-81 [PMID: 17220819]
55 **Yang JG**, Ma DQ, Peng Y, Song L, Li CL. Comparison of different diagnostic methods for differentiating biliary atresia from idiopathic neonatal hepatitis. *Clin Imaging* 2009; **33**: 439-446 [PMID: 19857804 DOI: 10.1016/j.clinimag.2009.01.003]
56 **Guan YX**, Chen Q, Wan SH, Huang JS, Yang XQ, Pan LJ, Zhang QI, Zhang Q, Ou YJ, Peng XW, Liu SZ, Chen QJ, Lou J. Effect of different time phases of radionuclide hepatobiliary scintigraphy on the differential diagnosis of congenital biliary atresia. *Genet Mol Res* 2015; **14**: 3862-3868 [PMID: 25966156 DOI: 10.4238/2015.April.22.15]
57 **Dehghani SM**, Haghighat M, Imanieh MH, Geramizadeh B. Comparison of different diagnostic methods in infants with Cholestasis. *World J Gastroenterol* 2006; **12**: 5893-5896 [PMID: 17007060]
58 **Rastogi A**, Krishnani N, Yachha SK, Khanna V, Poddar U, Lal R. Histopathological features and accuracy for diagnosing biliary atresia by prelaparotomy liver biopsy in developing countries. *J Gastroenterol Hepatol* 2009; **24**: 97-102 [PMID: 19196397 DOI: 10.1111/j.1440-1746.2008.05737.x]
59 **Moyer V**, Freese DK, Whitington PF, Olson AD, Brewer F, Colletti RB, Heyman MB. Guideline for the evaluation of cholestatic jaundice in infants: recommendations of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2004; **39**: 115-128 [PMID: 15269615]
60 **Shimadera S**, Iwai N, Deguchi E, Kimura O, Ono S, Fumino S, Higuchi K. Significance of ductal plate malformation in the postoperative clinical course of biliary atresia. *J Pediatr Surg* 2008; **43**: 304-307 [PMID: 18280279 DOI: 10.1016/j.jpedsurg.2007.10.023]
61 **Baerg J**, Zuppan C, Klooster M. Biliary atresia--a fifteen-year review of clinical and pathologic factors associated with liver transplantation. *J Pediatr Surg* 2004; **39**: 800-803 [PMID: 15185199]
62 **Gautier M**, Eliot N. Extrahepatic biliary atresia. Morphological study of 98 biliary remnants. *Arch Pathol Lab Med* 1981; **105**: 397-402 [PMID: 6894845]
63 **Kang N**, Davenport M, Driver M, Howard ER. Hepatic histology and the development of esophageal varices in biliary atresia. *J Pediatr Surg* 1993; **28**: 63-66 [PMID: 8429476]
64 **Wildhaber BE**, Coran AG, Drongowski RA, Hirschl RB, Geiger JD, Lelli JL, Teitelbaum DH. The Kasai portoenterostomy for biliary atresia: A review of a 27-year experience with 81 patients. *J Pediatr Surg* 2003; **38**: 1480-1485 [PMID: 14577071]
65 **Arii R**, Koga H, Arakawa A, Miyahara K, Lane GJ, Okazaki T, Urao M, Yamataka A. How valuable is ductal plate malformation as a predictor of clinical course in postoperative biliary atresia patients? *Pediatr Surg Int* 2011; **27**: 275-277 [PMID: 21069347 DOI: 10.1007/s00383-010-2793-0]
66 **Mukhopadhyay SG**, Roy P, Chatterjee U, Datta C, Banerjee M, Banerjee S, Basu AK, Ganguli M. A histopathological study of liver and biliary remnants in the long-term survivors (& gt; 10 years) of cases of biliary atresia. *Indian J Pathol Microbiol* 2014; **57**: 380-385 [PMID: 25118727 DOI: 10.4103/0377-4929.138722]
67 **Kahn E**. Biliary atresia revisited. *Pediatr Dev Pathol* 2004; **7**: 109-124 [PMID: 14994122 DOI: 10.1007/s10024-003-0307-y]
68 **Liu SX**, Huang ZH. The value of radionuclide hepatobiliary scintigraphy in combination with determination of bilirubin from duodenal drainage in differential diagnosis of infantile persistent jaundice. *Front Med China* 2010; **4**: 342-345 [PMID: 21191842 DOI: 10.1007/s11684-010-0099-1]
69 **El-Guindi MA**, Sira MM, Sira AM, Salem TA, El-Abd OL, Konsowa HA, El-Azab DS, Allam AA. Design and validation of a diagnostic score for biliary atresia. *J Hepatol* 2014; **61**: 116-123 [PMID: 24657403 DOI: 10.1016/j.jhep.2014.03.016]
70 **Chen G**, Xue P, Zheng S, Chen L, Ma Y. A pathological scoring system in the diagnosis and judgment of prognosis of biliary atresia. *J Pediatr Surg* 2015; **50**: 2119-2123 [PMID: 26577909 DOI: 10.1016/j.jpedsurg.2015.08.041]
71 **Davenport M**, Grieve A. Maximizing Kasai portoenterostomy in the treatment of biliary atresia: medical and surgical options. *S Afr Med J* 2012; **102**: 865-867 [PMID: 23116745]
72 **Zhao R**, Li H, Shen C, Zheng S, Xiao X. Hepatic portocholecystostomy (HPC) is ineffective in the treatment of biliary atresia with patent distal extrahepatic bile ducts. *J Invest Surg* 2011; **24**: 53-58 [PMID: 21345004 DOI: 10.3109/08941939.2010.530737]
73 **Endo M**, Katsumata K, Yokoyama J, Morikawa Y, Ikawa H, Kamagata S, Nakano M, Nirasawa Y, Ueno S. Extended dissection of the portahepatis and creation of an intussuscepted ileocolic conduit for biliary atresia. *J Pediatr Surg* 1983; **18**: 784-793 [PMID: 6663407]
74 **Kobayashi H**, Yamataka A, Urao M, Okazaki T, Yanai T, Koga H, Lane GJ, Miyano T. Innovative modification of the hepatic portoenterostomy. Our experience of treating biliary atresia. *J Pediatr Surg* 2006; **41**: e19-e22 [PMID: 16677870 DOI: 10.1016/j.jpedsurg.2005.12.056]
75 **Sun X**, Diao M, Wu X, Cheng W, Ye M, Li L. A prospective study comparing laparoscopic and conventional Kasai portoenterostomy in children with biliary atresia. *J Pediatr Surg* 2016; **51**: 374-378 [PMID: 26589186 DOI: 10.1016/j.jpedsurg.2015.10.045]
76 **Yamataka A**. Laparoscopic Kasai portoenterostomy for biliary atresia. *J Hepatobiliary Pancreat Sci* 2013; **20**: 481-486 [PMID: 23572285 DOI: 10.1007/s00534-013-0607-1]
77 **Oetzmann von Sochaczewski C**, Petersen C, Ure BM, Osthaus A, Schubert KP, Becker T, Lehner F, Kuebler JF. Laparoscopic versus conventional Kasai portoenterostomy does not facilitate subsequent liver transplantation in infants with biliary atresia. *J Laparoendosc Adv Surg Tech A* 2012; **22**: 408-411 [PMID: 22577810 DOI: 10.1089/lap.2012.0077]
78 **Lishuang M**, Zhen C, Guoliang Q, Zhen Z, Chen W, Long L, Shuli L. Laparoscopic portoenterostomy versus open portoenterostomy for the treatment of biliary atresia: a systematic review and meta-analysis of comparative studies. *Pediatr Surg Int* 2015; **31**: 261-269 [PMID: 25627699 DOI: 10.1007/s00383-015-3662-7]
79 **Sarkhy A**, Schreiber RA, Milner RA, Barker CC. Does adjuvant steroid therapy post-Kasai portoenterostomy improve outcome of biliary atresia? Systematic review and meta-analysis. *Can J Gastroenterol* 2011; **25**: 440-444 [PMID: 21912769]
80 **Bezerra JA**, Spino C, Magee JC, Shneider BL, Rosenthal P, Wang KS, Erlichman J, Haber B, Hertel PM, Karpen SJ, Kerkar N, Loomes KM, Molleston JP, Murray KF, Romero R, Schwarz KB, Shepherd R, Suchy FJ, Turmelle YP, Whitington PF, Moore J, Sherker AH, Robuck PR, Sokol RJ. Use of corticosteroids after hepatoportoenterostomy for bile drainage in infants with biliary atresia: the START randomized clinical trial. *JAMA* 2014; **311**: 1750-1759 [PMID: 24794368 DOI: 10.1001/jama.2014.2623]
81 **Willot S**, Uhlen S, Michaud L, Briand G, Bonnevalle M, Sfeir R, Gottrand F. Effect of ursodeoxycholic acid on liver function in children after successful surgery for biliary atresia. *Pediatrics* 2008; **122**: e1236-e1241 [PMID: 19029197 DOI: 10.1542/peds.2008-0986]
82 **Shimadera S**, Iwai N, Deguchi E, Kimura O, Ono S, Furukawa T, Fumino S. Predicting factors on the occurrence of cystic dilatation

of intrahepatic biliary system in biliary atresia. *Pediatr Surg Int* 2010; **26**: 611-614 [PMID: 20428877 DOI: 10.1007/s00383-010-2601-x]

83 **Davenport M**, Caponcelli E, Livesey E, Hadzic N, Howard E. Surgical outcome in biliary atresia: etiology affects the influence of age at surgery. *Ann Surg* 2008; **247**: 694-698 [PMID: 18362634 DOI: 10.1097/SLA.0b013e3181638627]

84 **Shneider BL**, Brown MB, Haber B, Whitington PF, Schwarz K, Squires R, Bezerra J, Shepherd R, Rosenthal P, Hoofnagle JH, Sokol RJ. A multicenter study of the outcome of biliary atresia in the United States, 1997 to 2000. *J Pediatr* 2006; **148**: 467-474 [PMID: 16647406 DOI: 10.1016/j.jpeds.2005.12.054]

85 **Lykavieris P**, Chardot C, Sokhn M, Gauthier F, Valayer J, Bernard O. Outcome in adulthood of biliary atresia: a study of 63 patients who survived for over 20 years with their native liver. *Hepatology* 2005; **41**: 366-371 [PMID: 15660386 DOI: 10.1002/hep.20547]

86 **Howard ER**, MacLean G, Nio M, Donaldson N, Singer J, Ohi R. Survival patterns in biliary atresia and comparison of quality of life of long-term survivors in Japan and England. *J Pediatr Surg* 2001; **36**: 892-897 [PMID: 11381420 DOI: 10.1053/jpsu.2001.23965]

87 **Lampela H**, Ritvanen A, Kosola S, Koivusalo A, Rintala R, Jalanko H, Pakarinen M. National centralization of biliary atresia care to an assigned multidisciplinary team provides high-quality outcomes. *Scand J Gastroenterol* 2012; **47**: 99-107 [PMID: 22171974 DOI: 10.3109/00365521.2011.627446]

88 **Karrer FM**, Price MR, Bensard DD, Sokol RJ, Narkewicz MR, Smith DJ, Lilly JR. Long-term results with the Kasai operation for biliary atresia. *Arch Surg* 1996; **131**: 493-496 [PMID: 8624194]

89 **Lee S**, Park H, Moon SB, Jung SM, Kim JM, Kwon CH, Kim SJ, Joh JW, Seo JM, Lee SK. Long-term results of biliary atresia in the era of liver transplantation. *Pediatr Surg Int* 2013; **29**: 1297-1301 [PMID: 23948814 DOI: 10.1007/s00383-013-3366-9]

90 **Lien TH**, Chang MH, Wu JF, Chen HL, Lee HC, Chen AC, Tiao MM, Wu TC, Yang YJ, Lin CC, Lai MW, Hsu HY, Ni YH. Effects of the infant stool color card screening program on 5-year outcome of biliary atresia in Taiwan. *Hepatology* 2011; **53**: 202-208 [PMID: 21140377 DOI: 10.1002/hep.24023]

91 **Matsui A**, Kasano Y, Yamauchi Y, Momoya T, Shimada T, Ishikawa T, Abukawa D, Kimura A, Adachi K, Tazuke Y. Direct enzymatic assay of urinary sulfated bile acids to replace serum bilirubin testing for selective screening of neonatal cholestasis. *J Pediatr* 1996; **129**: 306-308 [PMID: 8765633]

92 **Akiyama T**, Yamauchi Y. Use of near infrared reflectance spectroscopy in the screening for biliary atresia. *J Pediatr Surg* 1994; **29**: 645-647 [PMID: 8035274]

93 **Mushtaq I**, Logan S, Morris M, Johnson AW, Wade AM, Kelly D, Clayton PT. Screening of newborn infants for cholestatic hepatobiliary disease with tandem mass spectrometry. *BMJ* 1999; **319**: 471-477 [PMID: 10454398]

94 **Mowat AP**, Davidson LL, Dick MC. Earlier identification of biliary atresia and hepatobiliary disease: selective screening in the third week of life. *Arch Dis Child* 1995; **72**: 90-92 [PMID: 7717750]

95 **Song Z**, Dong R, Fan Y, Zheng S. Identification of serum protein biomarkers in biliary atresia by mass spectrometry and enzyme-linked immunosorbent assay. *J Pediatr Gastroenterol Nutr* 2012; **55**: 370-375 [PMID: 22569524 DOI: 10.1097/MPG.0b013e31825bb01a]

P- Reviewer: Liu HY, Santetti D **S- Editor**: Gong ZM **L- Editor**: A
E- Editor: Li D

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com