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Quarterly Review

Obstructive jaundice in neonates

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ABSTRACT:

The causes of jaundice in the first few weeks of life may be categorised into hematologic, enzymatic/metabolic, infectious and obstructive. Obstructive jaundice results from an interruption in the drainage of bile in the biliary system. Surgical causes of jaundice in neonates are biliary atresia, inspissated bile syndrome, intrahepatic hypoplasia, choledochal cyst, Caroli's disease and spontaneous perforation of the bile duct. Pediatricians should be aware of the pernicious consequences of unresolved biliary obstruction and should thus refer neonates or infants with inexplicable jaundice for surgical exploration at an earlier age.

KEYWORDS: surgical jaundice, biliary atresia, inspissated bile syndrome, intrahepatic hypoplasia, choledochal cyst, Caroli's disease, spontaneous perforation of bile duct

Introduction

The causes of jaundice in the first weeks of life can be categorised into hematologic, enzymatic/metabolic, infectious and obstructive.[1,2] Diagnostic tests are definitive and surgical treatment options do not have a role in the first three categories. Operative cholangiography is the next logical step in the diagnosis of obstructive causes.[2,3] Obstructive jaundice is caused by an interruption to the drainage of bile in the biliary system. Surgical causes of jaundice in neonates are biliary atresia, inspissated bile syndrome, intrahepatic hypoplasia, choledochal cyst, Caroli's disease and spontaneous perforation of the bile duct.[1-3]

Biliary atresia (BA)

It is a pathologic process leading to fibrosis and obliteration of the ductal system resulting in obstruction to bile flow, and cholestasis. The aetiology of this entity is unknown. The incidence of BA is high in China and Japan (1:8,000) as compared to Europe (1:17,000 live births), and is more common in girls than in boys.[4-6] A higher incidence is found in infants less than 32 weeks of gestational age, where the maternal age at conception is more than 35 years, and in mothers with parity 4 or more.[7]

Aetiopathogenesis

Evidence suggests that a few cases related to abnormal morphogenesis of the bile ducts occur early in gestation, whilst others appear to arise from damage to the normally developing bile ducts.[4-8] Desmet's theory suggests the interruption of the normal remodelling process of the primitive ductal plate. Local ischemia during foetal hepatobiliary development turns into flow obstruction. As per Howard's hypothesis, bile leakage from abnormal ducts causes inflammatory reaction with subsequent obliteration of the biliary tree.[9]

During pregnancy, exposure to environmental toxins leads to infantile obstructive cholangiopathy. Some commonly involved viruses, reovirus-3, cytomegalovirus, rotavirus C, human papilloma virus and retroviruses have been reported in the literature.[1-3,9] Obstruction to the flow of bile causes progressive cholestasis due to toxic, hydrophobic bile acids. BA may be an acquired rather than a hereditary disease as discordance has been seen in monozygotic twins.[10-15] Approximately 10% of all cases have been associated with anomalies such as polysplenia, asplenia, situs inversus, absence of the inferior vena cava and pre-duodenal portal vein, for which the term biliary atresia splenic malformation (BASM) syndrome has been coined in the literature.[3,16,17] Other associated anomalies are cleft lip, atresia of esophagus, duodenum, and/or jejunum; annular pancreas, malrotation of gut, and polycystic kidney.[5,6]

Pathology

In the intralobular spaces of the liver, bile stasis, distortion, focal necrosis, hemosiderin deposition in liver cells and intralobular fibrosis occur.[18] In the interlobular spaces, widening of portal area, hepatic fibrosis, periportal oedema, ductular proliferation and bile stasis are noted.[19] Even after surgery, when bile flow is regular, intrahepatic bile ducts are not restored to normal morphology; although some reduction in hepatic fibrosis and inflammatory cells is seen. So surgery

is most effective within 60 days of birth, since the hepatic ducts undergo progressive destruction.[4,20-21]

Classification

Biliary atresia is classified as correctable (20%) with distal biliary tree fibrosis and patent intrahepatic bile ducts and proximal biliary tree; and non–correctable (80%) with fibrosis upto the level of the porta hepatis. Anatomical classification based on the pattern of extrahepatic biliary tract remnant is widely accepted. **(Table 1)**[4-6]

Table 1: The Japanese Association of Pediatric Surgeons (JAPS) classification of Biliary Atresia

Type I	Atresia limited to the CBD
Type II	Atresia of intrahepatic bile ducts (common hepatic duct)
Type III	Atresia at the level of porta with Gallbladder, cystic duct and CBD patent

Clinical features

The neonate may present with a history of normal birth weight, varying degrees of jaundice, clay-coloured stools and dark yellow urine. Failure to thrive, coagulopathy and anaemia are also common. On examination, hepatomegaly, signs of advanced disease and cirrhosis, such as ascites, umbilical hernia, prominent abdominal veins and respiratory discomfort may be present.

Biochemical tests

A rise in total bilirubin and fall in proteins (albumin) with reversal of the albumin/globulin ratio is noted in advanced cases. Levels of alkaline phosphatase and transaminases (ALT, AST) are also raised. Deranged LFTs correspond to the degree of parenchymal damage and not to the duration of disease. Hepatitis A, B, and C serology; TORCH titres, alpha-1-antitrypsin, gamma glutamyl transpeptidase (GGPT), and serum lipoprotein-X estimates are carried out to negate the possibility of other causes of cholestasis.[4]

Ultrasonography

Shrunken, non-distended gallbladder without visible common duct structure is the usual picture. Triangular cord sign, more than 4 mm thickness of echogenic anterior wall of the right portal vein on longitudinal scan, is most indicative of BA.[22,23] This modality may also be used for the differential diagnosis of cholestasis, choledochal cyst, and the polysplenia syndrome.

Duodenal fluid aspiration test

Duodenal intubation may be carried out for 7-24 hours with a Ryle's tube and the aspirated fluid examined; the presence of yellow bilirubin pigment, rules out BA.[24] Severe neonatal cholestasis can generate false negative results.

Nuclear imaging

It differentiates obstructive from parenchymal causes of jaundice. Non-appearance of the isotope in the intestine is specific for biliary atresia in upto 50-75% cases only, because severe intrahepatic cholestasis and paucity syndrome may yield similar results.[25]

Operative cholangiography

The gold standard for the diagnosis of BA and widely employed as a more practical tool is operative cholangiography.[26] The gallbladder appears small and fibrotic and the dye fails to enter proximally into the hepatobiliary tree.

Percutaneous liver biopsy

This is usually carried out prior to surgery but may be done peroperatively as well. It has a diagnostic accuracy of 90%.[27] It reveals portal tract oedema, fibrosis, inflammation, intracellular and canalicular cholestasis, and proliferation of bile ductules.

Management

Currently BA is managed in two phases;[3-4,21] the first phase comprises the Kasai procedure, which aims to restore bile flow. In the second phase liver transplantation is considered, if bile flow is not restored by the Kasai procedure or life-threatening complications of cirrhosis ensue. In patients presenting late with advanced cirrhosis, liver transplantation is done as the primary procedure.

Kasai procedure (hepato-porto-enterostomy) has been the standard for non-correctable BA since 1958.[28] Extended right subcostal incision cholangiography and liver biopsy are done. The fibrous remnant of the CBD is dissected beyond the confluence and the transected liver hilum anastomosed with Roux-en-Y loop of jejunum. Many technical variations are possible, according to the anatomical pattern of the biliary remnant.[20,21]

Type 1 : Cholecystoenterostomy, or hepaticoenterostomy
Type 2 : Cystoenterostomy where the hilar cyst communicates with the dystrophic intrahepatic bile ducts, demonstrated on cholangiography
Type 3 : Hepatoportocholecystostomy

In portocholecystostomy, the gall bladder is used for drainage, and requires a patent cystic duct and CBD. Complications such as bile leak, gallbladder obstruction, cholangitis, and kinking of the CBD are more frequent.[29-31] Liver transplantation is indicated after portoenterostomy. The five-year survival after transplantation is 80-90%.[30-32]

Postoperatively during the evaluation phase of biliary atresia, the infant's diet is typically not altered; breastfeeding is encouraged where possible, but an energetic supplementation may be required to obtain a 150-180 Kcal/kg/day intake. As long as cholestasis persists, supplementation of fat-soluble vitamins is necessary. Administration of choleretics like ursodeoxycholic acid 20 mg/kg/day has been studied with benefits;[33] prednisolone use remains controversial.[34]

Complications

Cholangitis is the most common complication with an incidence of 40-60% following surgery. It can be reduced by lengthening of 50-70 cm of the roux-en-Y jejunum loop and

total diversion of biliary conduit;[35] and construction of the intestinal valve by removing a segment of seromuscular layer of the bowel wall and intussuscepting the denuded mucosa as a nipple.[36] Other complications are portal hypertension, nutritional deficiencies like rickets, pulmonary arteriovenous fistula, ectopic variceal bleed, hepatopulmonary syndrome, pulmonary hypertension and malignancy.

Outcome after successful Kasai operation

If the Kasai operation succeeds in restoring bile flow, the evolution of biliary cirrhosis is prevented or at least delayed, and survival with the native liver has been reported up to adulthood. Factors influencing prognosis are the patient's age at the time of surgery, extension of liver fibrosis at surgery, degree of intrahepatic bile duct injury, number of episodes of ascending cholangitis, the surgeon's expertise and the site of bile duct obstruction.[30-32,37-38]

Choledochal cysts

These are congenital conditions associated with benign cystic dilatation of the bile ducts. Its incidence, although as high as 1:1000 in the Asian (Japan) population, is only 1:150 000 in the West.[3] They are more frequently seen in female cases than in male cases. About 60% are diagnosed during the first decade of life, whilst 20% remain undiagnosed until adulthood.

The preponderance in Asia suggests a role for either genetic or environmental factors. Anomaly of the pancreaticobiliary junction results in a long common channel and reflux of pancreatic enzymes into the CBD, leading to mucosal breakdown and dilatation.[39] This can present early (in children) with high grade reflux or later (adulthood) with low grade reflux.[40,41]

There can be abnormal autonomic innervation of the extrahepatic biliary tree and weakening of the duct wall due to increased proximal pressure, because of distal obstruction, which is also responsible for the formation of choledochal cysts.[42,43]

Table 2: Todani's choledochal cyst classification

Type I	Cystic dilatation of entire common bile duct (most common, 50–85%)
	IA: Cystic
	IB: Fusiform
	IC: Saccular
Type II	Diverticulum of the extrahepatic biliary tree (<5%)
Type III	Cystic dilatation of the intraduodenal portion of CBD (Choledochocele)
Type IV	Multiple cysts of the intrahepatic and extrahepatic biliary tree
	IVA: Both intrahepatic and extrahepatic cysts (30–40%)
	IVB: Multiple extrahepatic cysts without intrahepatic
Type V	Isolated intrahepatic biliary cystic disease (Caroli's disease)

The traditional classification system devised by Alonso-Lej[44] exclusively involved the extrahepatic duct. The clinical classification was revised in 1977 by Todani and colleagues. **(Table 2)**[45]

The patient usually presents with a classical triad of abdominal pain, cholestatic jaundice (80%), and abdominal mass (30%).[2] In patients over 2 years of age, abdominal pain is the most common presenting symptom. Bile and pancreatic juice reflux and bile stasis lead to chronic inflammation, stone and stricture formation. This in turn leads to recurrent cholangitis, hepatic abscesses and pancreatitis, resulting in significant pain and jaundice.[46-52] The main diagnostic tool for detection of a choledochal cyst, especially in childhood, is ultrasonography. In adults, computed tomography can confirm the diagnosis; however, endoscopic retrograde cholangiography or magnetic resonance cholangiography, are considered the gold standard.[53]

Surgery is the treatment of choice;[2] excision of the cyst and reconstruction of the biliary tree by choledochal/hepatojejunostomy with a roux-en-Y loop is the standard procedure for types I and II.[54-56] Type III cysts 3 cm or less in size are managed with endoscopic sphincterotomy and cysts more than 3 cm in size require surgical excision with transduodenal sphincteroplasty. In Type IVA cysts, for the extraphepatic component, excision and hepaticojejunostomy is done; however, for the intrahepatic component hepatic resection with hepaticojejunostomy is the treatment of choice. Transhepatic intubation may be used for intrahepatic cysts. In Type IVB cysts, excision of the cyst with hepaticojejunostomy and transduodenal sphincteroplasty is carried out. For Type V cysts restricted to one lobe, hepatic resection and liver transplantation are preferred. Bilobar disease represents an especially challenging problem. Roux-en-Y intrahepatic cholangiojejunostomy or transhepatic silastic intubation for 6-12 months may be indicated to improve biliary drainage.

Complications are commonly observed with types I, IV, and V, the overall morbidity rate is less than 10%. Post-surgical complications include cholangitis, biliary stones, anastomotic stricture, residual debris, pancreatitis, and intrahepatic bile duct dilatation.[54] It is important to operate on cholodochal cysts as there is a 20- to 30-fold higher risk in these patients than the general population for cholangiocarcinoma. Complete excision of these lesions is recommended as soon as possible, preferably before puberty, in order to decrease the chance of developing cancer; the risk remains high even after surgery.[57]

Caroli's Disease

In 1958 Caroli[58] described a congenital anomaly of the biliary tree characterised by multiple cystic dilatations of the intrahepatic bile ducts. In infants, almost all cases of congenital intrahepatic bile duct dilatation appear to be associated with the choledochal cyst. The intra-hepatic component is frequently asymmetrical, involving predominantly one major intrahepatic branch. Neonates present with jaundice in the early period which is indistinguishable from presentation of the simple choledochal cyst. Ultrasound, CT scan, percutaneous transhepatic cholangiography, endoscopic cholangiopancreatography and magnetic resonance cholangiopancreatography are performed to establish the diagnosis.[59-61]

Definitive surgery for most patients is impossible since adequate drainage of intrahepatic cysts is difficult to achieve. At the moment, hepatic resection, liver transplantation and roux-en-Y intrahepatic cholangiojejunostomy at the liver hilum provide the best chance for unimpeded bile flow.[61] Transhepatic intubation is recommended as internal drainage is associated with frequent postoperative complications like recurrent cholangitis, biliary lithiasis, and hepatic abscess. Malignant degeneration has also been reported.[62]

Inspissated bile plug

There is mechanical obstruction of the extrahepatic bile ducts by inspissated bile.[63] Inspissated bile syndrome, a misnomer for a common sequel of erythroblastosis fetalis, results from massive hemolysis due to Rh or ABO blood group incompatibility.[64] Obstruction is secondary, as a consequence of the earlier excessive bile pigment excretory load; it may proceed to the production of bile pigment stones.[65]

There is persistent jaundice in newborns with hemolytic anaemia, with elevation of both direct and indirect bilirubin components. Operative cholangiography is required for diagnosis. Simple irrigation of the extrahepatic bile ducts is curative. If choledocholithiasis is present, manual extraction of biliary stones or duodenotomy and sphincterotomy may be done.[66] The incidence has fallen due to early diagnosis of blood group incompatibility and prompt exchange transfusion.[63]

Intrahepatic hypoplasia

Biliary hypoplasia is not a discrete clinical entity; it is an operative or radiographic finding found in a variety of hepatobiliary disorders. It is a rare cause of neonatal jaundice.[2-4] Affected children have absent or reduced bile ductules with normal branche distributions of the portal vein and hepatic artery within the liver parenchyma. Biliary hypoplasia is also identified as paucity of interlobular bile ducts (PILBD) and two types have been described.

Syndromic biliary hypoplasia (Alagille's syndrome) is characterised by hyperbilirubinemia, characteristic facial appearance, pulmonic artery stenosis, vertebral anomalies, embryotoxon and delayed weight-height development.[67] Non-syndromic biliary hypoplasia is usually clinically indistinguishable from biliary atresia. Cholangiography and liver biopsy show diminutive intra- and extra-hepatic biliary tree. However, management is conservative and includes predigested formulae, ursodeoxycholic acids, phenobarbitone, and vitamin A, D, K, E replacement. PILBD has better long-term prognosis.[68]

Spontaneous perforation of the bile duct (SPBD)

Though uncommon, it is potentially fatal and occurs with sufficient frequency to be considered in the differential diagnosis of neonatal jaundice.[69] Predisposing factors for perforation are portal bacteremia, stone disease, protein plugs, distal atresia and viral gastroenteritis. Sites of perforation are the cystic duct, common hepatic duct, and the CBD; the commonest site is at the junction of the cystic and hepatic ducts.[70,71] The perforation is most often pinhole in size, consequently, bile extravasation is gradual, permitting the formation of a biliary pseudocyst. Jaundice is the usual clinical manifestation of the disease which becomes apparent during the first three months of life. Systemic signs may be minimal and thus the infant easily blends into the diagnostic mix of surgical jaundice in infancy.[72]

Sonography shows either generalised ascitis or localised collection of fluid, the biliary tree is usually not dilated. Scintigraphy and abdominal paracentesis demonstrate that the intraperitoneal fluid originates from the biliary tract. Intraoperative cholangiography is carried out for confirmation of diagnosis at surgery. It can be misinterpreted as a choledochal cyst, which is disastrous if an intestinal anastomosis is performed on the pseudocyst.

Simple peritoneal drainage (percutaneous tube drainage) of the area of ductal perforation is sufficient in the majority of cases.[73,74] Peritoneal drainage is followed by spontaneous closure of the perforation, resolution of the biliary pseudocyst and cure of the "mechanical obstruction" (probably bile sludge) of the distal common duct. Definitive treatment involves surgery, and repair of perforation.[69,74] Since the perforation of the common duct appears to be the only fault in biliary embryogenesis, the long term prognosis is excellent.

Iatrogenic

Rarely some cases have been reported in the literature of neonatal obstructive jaundice caused by a malpositioned gastrostomy tube (Foley's catheter).[75-77]

Conclusion

Pediatricians should be aware of the pernicious consequences of unresolved biliary obstruction and should thus refer neonates or infants with inexplicable jaundice for surgical exploration at an earlier age than was previously considered appropriate. The specific operations advocated for congenital malformation of the biliary tract are 1) Correctable biliary atresia: roux-en-Y choledochojejunostomy 2) Non-correctable biliary atresia: Kasai's hepatic portoenterostomy operation. In the few patients in whom the gallbladder and the distal biliary tree are still patent, hepatic portocholecystostomy is advocated 3) Billary hypoplasia: Hepatic portoenterostomy 4) Choledochal cyst: Total excision and choledochojejunostomy (roux-en-Y) 5) Caroli's disease: Resection of the dilated portion of the extra-hepatic bile duct and roux-en-Y choledochojejunostomy. Hepatic resection is done for intrahepatic cystic disease limited to a single segment or lobe 6) Inspissated bile plug: Irrigation of the extrahepatic bile ducts and for choledocholithiasis, manual extraction of biliary calculi. 7) Spontaneous perforation of the common bile duct: Simple peritoneal drainage at the site of ductal perforation and cholecystostomy.

References:

1. Balistreri WF. Neonatal cholestasis. *J Pediatr*. 1985;**106**:171–84.
2. Howard ER. Choledochal cysts. In: Howard ER, (ed) Surgery of liver disease in children. *Oxford: Butterworth-Heinemann*; 1991:78–90.
3. Davenport M, Betalli P, D'Antiga L, Cheeseman P, Mieli-Vergani G, Howard ER. The spectrum of surgical jaundice in infancy. *J Pediatr Surg*. 2003;**38**:1471–9.
4. Haber BA, Russo P. Biliary atresia. *Gastroenterol Clin North Am*. 2003;**32**:891–911.
5. Sinha CK, Davenport M. Biliary atresia. *J Indian Assoc Pediatr Surg*. 2008;**13**:49–56.
6. Carmi R, Magee CA, Neill CA, Karrer FM. Extrahepatic biliary atresia and associated anomalies: etiologic heterogeneity suggested by distinctive patterns of associations. *Am J Med Genetics*. 1993;**45**:683–93.
7. Fischler B, Haglund B, Hjern A. A population based study on the incidence and possible pre- and perinatal etiologic risk factors of biliary atresia. *J Pediatr*. 2002;**141**:217–22.
8. Brunero M, De Dreuzy O, Herrera JM, Gauthier F, Valayer L. Prenatal detection of a cyst in the liver hilum. Interpretation for an adequate treatment. [Article in Italian] *Minerva Pediatr*. 1996;**48**:485–94.

9. Bassett MD, Murray KF. Biliary atresia: recent progress. *J Clin Gastroenterol*. 2008;**42**:720–9.
10. Gunasekaran TS, Hassall EG, Steinbrecher UP, Yong SL. Recurrence of extrahepatic biliary atresia in two half sibs. *Am J Med Genet*. 1992;**43**:592–4.
11. Lachaux A, Descos B, Plauchu H, Wright C, Louis D, Raveau J, et al. Familial extrahepatic biliary atresia. *J Pediatr Gastroenterol Nutr*. 1988;**7**:280–3.
12. Smith BM, Laberge JM, Schreiber R, Weber AM, Blanchard H. Familial biliary atresia in three siblings including twins. *J Pediatr Surg*. 1991;**26**:1331–3.
13. Silveira TR, Salzano FM, Howard ER, Mowat AP. Extrahepatic biliary atresia and twinning. *Braz J Med Biol Res*. 1991;**24**:67–71.
14. Hyams JS, Glaser JH, Leichtner AM, Morecki R. Discordance for biliary atresia in two sets of monozygotic twins. *J Pediatr*. 1985;**107**:420–2.
15. Poovorawan Y, Chongsrisawat V, Tanunytthawongse C, Norapaksunthorn T, Mutirangura A, Chandrakamol B. Extrahepatic biliary atresia in twins: Zygosity determination by short tandem repeat loci. *J Med Assoc Thai*. 1996;**79** Suppl 1:119–24.
16. Davenport M, Savage M, Mowat AP, Howard ER. The biliary atresia splenic malformation syndrome. *Surgery*. 1993;**113**:662–8.
17. Davenport M, Tizzard SA, Underhill J, Mieli-Vergani G, Portmann B, Hadziæ N. The biliary atresia splenic malformation: A 28 year single center retrospective review. *J Pediatr*. 2006;**149**:393–400.
18. Sokol RJ, Mack C, Narkewicz MR, Karrer FM. Pathogenesis and outcome of biliary atresia: current concepts. *J Pediatr Gastroenterol Nutr*. 2003;**37**:4–21.
19. Okazaki T, Miyano G, Yamataka A, Kobayashi H, Koga H, Lane GJ, et al . Diagnostic laparoscopy-assisted cholangiography in infants with prolonged jaundice. *Pediatr Surg Int*. 2006;**22**:140–3.
20. Chardot C, Carton M, Spire-Bendelac N, Le Pommelet C, Golmard JL, Auvert B. Prognosis of biliary atresia in the era of liver transplantation: French national study from 1986 to 1996. *Hepatology*. 1999;**30**:606–11.
21. Gauthier F, Luciani JL, Chardot C, Branchereau S, de Dreuzy O, Lababidi A, et al. Determinants of life span after Kasai operation at the era of liver transplantation. *Tohoku J Exp Med*. 1997;**181**:97–107.
22. Kanegawa K, Akasaka Y, Kitamura E, Nishiyama S, Muraji T, Nishijima E, et al. Sonographic Diagnosis of Biliary Atresia in Pediatric Patients Using the Triangular Cord Sign Versus Gallbladder Length and Contraction. *AJR Am J Roentgenol*. 2003;**181**:1387–90.
23. Farrant P, Meire HB, Mieli-Vergani G. Improved diagnosis of extrahepatic biliary atresia by high frequency ultrasound of the gallbladder. *Br J Radiol*. 2001;**74**:952–4.
24. Meisheri IV, Kasat LS, Kumar A, Bahety G, Sawant V, Kothari P. Duodenal intubation and test for bile: a reliable method to rule out biliary atresia. *Pediatr Surg Int*. 2002;**18**:392–5.
25. Gilmour SM, Hershkop M, Reifen R, Gilday D, Roberts EA. Outcome of hepatobiliary scanning in neonatal hepatitis syndrome. *J Nucl Med*. 1997;**38**:1279–82.
26. Meyers RL, Book LS, O'Gorman MA, White KW, Jaffe RB, Feola PG, et al. Percutaneous cholecysto-cholangiography in the diagnosis of obstructive jaundice in infants. *J Pediatr Surg*. 2004;**39**:16–8.
27. Zerbini MC, Gallucci SD, Maezono R, Ueno CM, Porta G, Maksoud J, et al. Liver biopsy in neonatal cholestasis: a review on statistical grounds. *Mod Pathol*. 1997;**10**:793–9.
28. Kasai M, Suzuki S. A new operation for non-correctable biliary atresia-hepatic portoenterostomy. *Shujitsu* 1959;**13**:733–9.
29. Lilly JR. Hepatic portocholecystostomy for biliary atresia. *J Pediatr Surg*. 1979;**14**:301–4.
30. Freitas L, Gauthier F, Valayer J. Second operation for repair of biliary atresia. *J Pediatr Surg*. 1987;**22**:857–60.
31. Karrer FM, Lilly JR, Stewart BA, Hall RJ. Biliary atresia registry, 1976 to 1989. *J Pediatr Surg*. 1990;**25**:1076–80.
32. Shinkai M, Ohhama Y, Take H, Kitagawa N, Kudo H, Mochizuki K, et al. Long-term outcome of children with biliary atresia who were not transplanted after the Kasai operation: >20-year experience at a children's hospital. *J Pediatr Gastroenterol Nutr*. 2009;**48**:443–50.
33. Balistreri WF. Bile acid therapy in pediatric hepatobiliary disease: the role of ursodeoxycholic acid. *J Pediatr Gastroenterol Nutr*. 1997;**24**:573–89.
34. Muraji T, Higashimoto Y. The improved outlook for biliary atresia with corticosteroid therapy. *J Pediatr Surg*. 1997;**32**:1103–6.
35. Bu LN, Chen HL, Chang CJ, Ni YH, Hsu HY, Lai HS, et al. Prophylactic oral antibiotics in prevention of recurrent cholangitis after the Kasai portoenterostomy. *J Pediatr Surg*. 2003;**38**:590–3.
36. Muraji T, Tsugawa C, Nishijima E, Satoh S, Takamizawa S, Ise K, et al. Surgical management for intractable cholangitis in biliary atresia. *J Pediatr Surg*. 2002;**37**:1713–5.
37. Saeki M, Nakano M, Hagane K, Shimizu K. Effectiveness of an intussusceptive antireflux valve to prevent ascending cholangitis after hepatic portojejunostomy in biliary atresia. *J Pediatr Surg*. 1991;**26**:800–3.
38. Sokol RJ, Mack C, Narkewicz MR, Karrer FM. Pathogenesis and outcome of biliary atresia: current concepts. *J Pediatr Gastroenterol Nutr*. 2003;**37**:4–21.
39. Gigot J, Nagorney D, Farnell M, Moir C, Ilstrup D. Bile duct cysts: a changing spectrum of disease. *J Hepatobiliary Pancreat Surg*. 1996;**3**:405–11.
40. Babbitt DP. Congenital choledochal cysts: new etiological concept based on anomalous relationships of the common bile duct and pancreatic bulb. *Ann Radiol (Paris)*. 1969;**12**:231–40.
41. Jeong IH, Jung YS, Kim H, Kim BW, Kim JW, Hong J, et al. Amylase level in extrahepatic bile duct in adult patients with choledochal cyst plus anomalous pancreatico-biliary ductal union. *World J Gastroenterol*. 2005;**11**:1965–70.
42. Yotsuyanagi S. Contribution to aetiology and pathology of idiopathic cystic dilatation of the common bile duct with report of three cases. *Gann: Japanese Journal of Cancer Research*. 1936;**30**:601–752.
43. Davenport M, Basu R. Under pressure: choledochal malformation manometry. *J Pediatr Surg*. 2005;**40**:331–5.
44. Alonso-Lej F, Rever W, Pessagno DJ. Congenital choledochal cyst, with a report of 2, and an analysis of 94 cases. *Int Abstr Surg*. 1959;**108**:1–30.
45. Todani T, Watanabe Y, Narusue M, Tabuchi K, Okajima K. Congenital bile duct cysts: Classification, operative procedures, and review of thirty-seven cases including cancer arising from choledochal cyst. *Am J Surg*. 1977;**134**:263–9.
46. 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**:113–39.
47. Shi LB, Peng SY, Meng XK, Peng CH, Liu YB, Chen XP,, et al. Diagnosis and treatment of congenital Choledochal cyst: 20 years' experience in China. *World J Gastroenterol*. 2001;**7**:732–4.
48. Lipsett PA, Pitt HA, Colombani PM, Boitnott JK, Cameron JL. Choledochal cyst disease: a changing pattern of presentation. *Ann Surg*. 1994;**220**:644–52.
49. Rattan KN, Magu S, Ratan S, Chaudhary A, Seth A. Choledochal cyst in children: 15 year experience. *Ind J Gastroenterol*. 2005;**24**:178.
50. Sela-Herman S, Scharschmidt BF. Choledochal cyst, a disease for all ages. *Lancet*. 1996;**347**:779.
51. Büyükyavuz Y, Ekinci S, Ciftçi AO, Karnak I, Senocak ME, Tanyel FC. A retrospective study of choledochal cyst: clinical presentation, diagnosis and treatment. Turk *J Pediatr*. 2003;**45**:321–5.
52. de Vries JS, de Vries S, Aronson DC, Bosman DK, Rauws EA, Bosma A, et al. Choledochal cysts: age of presentation, symptoms, and late complications related to Todani's classification. *J Pediatr Surg*. 2002;**37**:1568–73.
53. Kim MJ, Han SJ, Yoon CS, Kim JH, Oh JT, Chung KS, et al. Using MR cholangiopancreatography to reveal anomalous pancreaticobiliary ductal union in infants and children with Choledochal cysts. *AJR Am J Roentgenol*. 2002;**179**:209–14.
54. Nagorney D M. Bile duct cysts in adults. In: Blumgart LH, Fong Y, editors. Surgery of the Liver and Biliary Tract and Pancreas. 3rd edition. Saunders, UK; 2001;1229-1244.

55. Lipsett PA, Pitt HA. Surgical treatment of choledochal cysts. *J Hepatobiliary Pancreat Surg*. 2003;**10**:352–9.
56. Metcalfe MS, Wemyss-Holden SA, Maddern GJ. Management dilemmas with choledochal cysts. *Arch Surg*. 2003;**138**:333–9.
57. Kobayashi S, Asano T, Yamasaki M, Kenmochi T, Nakagohri T, Ochiai T. Risk of bile duct carcinogenesis after excision of extrahepatic bile ducts in pancreaticobiliary maljunction. *Surgery*. 1999;**126**:939–44.
58. Caroli J, Soupault R, Kossakowski J, Plocker L, Paradowska. Congenital polycystic dilation of the intrahepatic bile ducts; attempt at classification. *Sem Hop*. 1958;**34**:488–95/SP.
59. Lopez CA, Munoz BA, Herrera MD, Moreno SO, Flores MM, Perez JJ. Diagnosis of Caroli's disease with conventional ultrasonography and echo-Doppler. *Rev Esp Enferm Dig* 1994;**85**:387–9.
60. Benhidjeb T, Muller JM, Gellert K, Zanow J, Rudolph B. Current therapy of bile duct cysts II. Intrahepatic cysts (Caroli syndrome). [Article in German] *Chirurg*. 1996;**67**:238–43.
61. Lendoire J, Schelotto PB, Rodríguez JA, Duek F, Quarin C, Garay V, et al. Bile duct cyst type V (Caroli's disease): surgical strategy and results. *HPB* (Oxford). 2007;**9**:281–4.
62. Balsells J, Margarit C, Murio E, Lazaro JL, Charco R, Vidal MT, et al. Adenocarcinoma in Caroli's disease treated by liver transplantation. *HPB Surg*. 1993;**7**:81–6.
63. Kondo M, Kunikata T, Onishi S. Inspissated bile syndrome. [Article in Japanese] *Ryoikibetsu Shokogun Shirizu*. 1996;**9**:524–7.
64. Dunn P. Obstructive jaundice and haemolytic disease of the newborn. *Arch Dis Child* 1963;**38**:596–9.
65. Grosfeld JL, Rescorla FJ, Skinner MA, West KW, Scherer LR 3rd. The spectrum of biliary tract disorders in infants and children. Experience with 300 cases. *Arch Surg*. 1994;**129**:513–20.
66. Gunnarsdottir A, Holmqvist P, Arnbjornsson E, Kullendorff CM. Laparoscopic aided cholecystostomy as a treatment of inspissated bile syndrome. *J Pediatr Surg*. 2008;**43**:e33–5.
67. Alagille D, Estrada A, Hadchouel M, Gautier M, Odièvre M, Dommergues JP. Syndromic paucity of interlobular bile ducts (Alagille syndrome or arteriohepatic dysplasia): review of 80 cases. *J Pediatr*. 1987;**110**:195–200.
68. Kahn E, Daum F, Markowitz J, Teichberg S, Duffy L, Harper R, et al. Nonsyndromatic paucity of interlobular bile ducts: Light and electron microscopic evaluation of sequential liver biopsies in early childhood. *Hepatology*. 2005:**6**;890–901.
69. Kasat LS, Borwankar SS, Jain M, Naregal A. Spontaneous perforation of the extrahepatic bile duct in an infant. *Pediatr Int*. 2001;**17**:463–4.
70. Stringel G, Mercer S. Idiopathic perforation of the biliary tract in infancy. *J Pediatr Surg*. 1983;**18**:546–50.
71. Chardot C, Iskandarani F, De Dreuzy O, Duquesne B, Pariente D, Bernard O, et al. Spontaneous perforation of the biliary tract in infancy: a series of 11 cases. *Eur J Pediatr Surg*. 1996;**6**:341–6.
72. Konoija RP, Shandip KS, Rawat J, Wakhlu A, Kureel S, Tandom R. Spontaneous biliary perforation in infancy and childhood: clues to diagnosis. *Indian J Pediatr*. 2007;**74**:509–10.
73. Lilly JR, Weintraub WH, Altman RP. Spontaneous perforation of the extrahepatic bile ducts and bile peritonitis in infancy. *Surgery*. 1974;**75**:664–73.
74. Prevot J, Babut JM. Spontaneous perforations of the biliary tract in infancy. *Prog Pediatr Surg*. 1970;**3**:187–208.
75. Sebastian MV, Coley BD. Neonatal obstructive jaundice caused by a malpositioned gastrostomy tube. *AJR* 2005;**184**:S132–3.
76. Konda J, Ruggle P. Prolapse of Foley catheter gastrostomy tube causing obstructive jaundice. *Am J Gastroenterol*. 1981;**76**:353–5.
77. Abu Zidan F, Kumar M, Hassan I, Samhan M, Dadah S. Iatrogenic obstructive jaundice caused by the balloon of a Foley catheter. *Clin Nucl Med*. 1991;**16**:757–9.