# CHAPTER 80
# Obstructive Jaundice

**Francis Aba Uba**
**Mohammed A.Latif Ayad**
**Alaa F. Hamza**

## Introduction

Neonatal cholestasis is defined as prolonged elevation of serum levels of conjugated bilirubin beyond the first 14 days of life. Neonatal hyperbilirubinaemia is usually physiologic, unconjugated, and self-limited. Only 2–15% of neonates remain jaundiced past 2 weeks of life, and just 0.2–0.4% have cholestatic jaundice from either intrahepatic cholestasis or structural abnormalities that cause biliary obstruction. Intrahepatic cholestasis may result from numerous infectious or inflammatory causes, as well as from inherited metabolic defects. The major structural diseases include biliary atresia and choledochal cyst. A variable element of hepatocellular dysfunction is common to all of these, thus rendering initial discrimination between medical and surgical cholestatic disease challenging.

Obstructive jaundice in infancy presents a surgical challenge, not only because of the difficulty in differentiating those cases that are amenable to surgical correction from those that are not, but also because of the desire to improve the persistently low salvage rate obtained even for correctable cases. Only if surgery is undertaken before 3 months of age, and preferably by 2 months of age, can the ravages caused by prolonged obstruction—namely, cirrhosis, portal hypertension, liver failure, and death—be prevented. Survival of patients whose obstruction is surgically relieved after 3 months of age is rare, and when they do survive, many of them (even those operated on before this time) have a severe morbidity or even mortality caused by cirrhosis and, later, portal hypertension. Thus there is only a short time between the appearance of the jaundice (usually between the ages of 4 and 6 weeks) and the optimal time for surgical intervention.

## Aetiology/Pathophysiology

Biliary atresia is the most common cause of obstructive jaundice requiring operation in children, followed by choledochal cyst, cholelithiasis, and spontaneous perforation of the bile ducts. Other causes of obstructive jaundice in infants are infantile obstructive cholangiopathy (biliary hypoplasia or hepatitis syndrome of infants), inspissated bile syndrome, extrinsic compression of the bile duct (e.g., pressure from huge intraabdominal masses), and cholestasis associated with intravenous feeding and gallstones in older children (Table 80.1).

Several hypotheses have attempt to explain the aetiology/pathophysiology of obstructive jaundice in the newborn infant. Biliary atresia and choledochal cyst belong to the same spectrum; they result from a single inflammatory process, probably viral, which leads to progressive destruction of liver parenchymal cells and desquamation of the epithelial lining of incompletely formed extrahepatic ducts late in gestation. Some of the other hypotheses include ischaemic or toxic injury in case of biliary atresia; abnormally long union of the pancreatic and common bile ducts (which permits the reflux of pancreatic secretions in the biliary tree, inducing inflammatory reactions that lead to progressive destruction, obliteration, or local weakening of the ductal walls); and a fault of ductal embryogenesis resulting from failure of the extrahepatic biliary system to develop patency.

At the moment, all of the proposed aetiological factors remain speculative because none of them fully explains the associated polysplenia syndrome, the frequent postnatal onset of jaundice and pale-coloured stools, and the discordance in twins.

*Table 80.1: Most likely causes of cholestasis in infants younger than 2 months of age*

| Disease | Causes |
|---|---|
| Obstructive cholestasis | Biliary atresia<br>Choledochal cyst<br>Gallstones or biliary sludge<br>Alagille syndrome<br>Inspissated bile<br>Cystic fibrosis<br>Neonatal sclerosing cholangitis<br>Congenital hepatic fibrosis/Caroli's disease |
| Hepatocellular cholestasis | Idiopathic neonatal hepatitis<br>Viral infection<br>Cytomegalovirus<br>Human immunodeficiency virus (HIV) |
| Bacterial infection | Urinary tract infection<br>Sepsis<br>Syphilis |
| Genetic/metabolic disorders | $\alpha_1$-antitrypsin deficiency<br>Tyrosinaemia<br>Galactosaemia<br>Hypothyroidism<br>Progressive familial intrahepatic cholestasis (PFIC)<br>Cystic fibrosis<br>Panhypopituitarism |
| Toxic/secondary | Parenteral nutrition–associated cholestasis |

## Evaluation

The evaluation of the infant with jaundice should follow a logical, cost-effective sequence in a multistep process. Although cholestasis in the neonate may be the initial manifestation of numerous disorders, the clinical manifestations are usually similar and provide very few clues about aetiology. Affected infants have icterus, dark urine, light or acholic stools, and hepatomegaly, all resulting from decreased bile flow due to either hepatocyte injury or bile duct obstruction. Hepatic synthetic dysfunction may lead to hypoprothrombinaemia and a bleeding disorder. Therefore, administration of vitamin K should be the initial treatment of cholestatic infants to prevent haemorrhage.

Most newborn infants whose jaundice is of medical origin tend to be of low birth weight, and most often the jaundice is present at birth. This contrasts with jaundice caused by biliary atresia in the well-fed, healthy-looking newborn, who may have had normal stools at birth with minimal jaundice, but in whom jaundice usually becomes apparent in the first few days and certainly within the first 4 weeks after birth. Most infants with choledochal cyst present with mild intermittent jaundice, which might have been taken for granted for months or years. One-third of patients present with a classic triad of abdominal pain,

jaundice, and abdominal mass, primarily in older children. Other early manifestations are pancreatitis and cholangitis.

The initial step in identification of cholestasis is the finding that more than 20% of the hyperbilirubinaemia is conjugated bilirubin. The next step is to recognize conditions that cause cholestasis and for which specific therapy is available to prevent further damage and avoid long-term complications such as sepsis, an endocrinopathy (hypothyroidism or panhypopituitarism), nutritional hepatotoxicity caused by a specific metabolic illness (galactosaemia), or other metabolic diseases (e.g., tyrosinaemia).

Hepatobiliary disease may be the initial manifestation of homozygous $\alpha_1$-antitrypsin deficiency or of cystic fibrosis. Neonatal liver disease may also be associated with congenital syphilis and specific viral infections, notably echo virus and herpes viruses, including cytomegalovirus (CMV). The hepatitis viruses (A, B, C) rarely cause neonatal cholestasis. The final step in evaluating neonates with cholestasis is to differentiate extrahepatic biliary atresia from neonatal hepatitis.

Urgent diagnosis must be accomplished by radiologic examination of the extrahepatic biliary system because the assistance from the laboratory data is inconclusive. The value of ultrasonography (US) as a rapid, safe, noninvasive means of evaluating the jaundiced infant has been enhanced by the development of high-resolution real-time imaging.

The distinction between jaundice of parenchymal origin and biliary atresia or choldedochal cyst can be accomplished by hepatobiliary imaging by using technetium-99m iminodiacetic acid (IDA). If the nucleotide uptake by the hepatocytes is rapid but excretion into the bowel is absent (even on delayed films), the jaundice is most likely to be due to biliary atresia; when the uptake is delayed by the diseased hepatocytes with poor or nonexcretion into the intestine, the jaundice is likely to be of hepatocellular (parenchymal) origin.

Operative cholangiography is preferred because it helps in proper surgical management decisions, but one-fifth of the interpretations of the cholangiographic films have suggested a diagnosis ultimately found to be incorrect. Other imaging approaches, such as computed tomography (CT), endoscopic retrograde cholangiopancreatography (ERCP), and magnetic resonance cholangiopancreatogram (MRCP), are also useful studies that can contribute to the diagnosis.

Liver biopsy, either percutaneous or open, is both safe and useful as a diagnostic modality. In approximately one-third of the specimens obtained by either method, the histological findings are not clear-cut, so further evaluation is necessary; for example, $\alpha_1$-antitrypsin deficiency can be definitely differentiated from biliary atresia only by determining the $\alpha_1$-antitrypsin level. A combination of open biopsy (with a guaranteed adequacy of size of specimen) and operative cholangiography is recommended as the ideal approach to the obstructed child.

## Choledocholithiasis

Common bile duct stones are rare, but are relatively more frequent in infants and children with sickle cell disease. Obstructive jaundice, cholangitis, and/or pancreatitis are typical presenting features in symptomatic cases. Although US (conventional or endoscopic), MRCP, and CT may be helpful in diagnosis, ERCP offers the possibility of both diagnosis and treatment. ERCP and sphincterotomy with stone retrieval can be performed before or after laparoscopic cholecystectomy. Early ERCP is recommended for common duct stones associated with obstructive jaundice (bilirubin >100 $\mu$mol/L) and/or cholangitis, but not for most cases of gallstone pancreatitis because the stone usually passes spontaneously. Laparoscopic cholecystectomy with intraoperative cholangiography is usually undertaken a few weeks after the episode of gallstone pancreatitis.

Choledocholithiasis can be treated by open exploration of the common bile duct; laparoscopic common duct exploration; or ERCP, sphincterotomy, and stone extraction. In some centers, percutaneous techniques are used. In small infants, cholecystotomy and irrigation may be successful. An initial short period of observation may be worthwhile if the infant is well without evidence of sepsis or progressive obstruction because some stones will pass spontaneously.

## Idiopathic Perforation of Extrahepatic Bile Ducts

Spontaneous perforation of the extrahepatic bile ducts should always be considered in a young infant who develops obstructive jaundice after an initial period of good health or who presents with progressive ascites. The majority of infants present subacutely within 3 months of birth with mild, fluctuating, obstructive jaundice and slowly progressive biliary ascites. An acute presentation with abdominal distention and tenderness is rare.

The typical site of bile duct perforation is at the junction of the cystic and common bile ducts. The cause is unknown, but biliary obstruction from inspissated bile in the distal common bile duct or from ampullary stenosis may account for some cases. The differential diagnosis includes bile duct perforation secondary to trauma, choledochal cyst, or necrotising enterocolitis.

Abdominal US may show a complex loculated collection of bile around the common bile duct (which may be mistaken for a choledochal cyst) and within the lesser sac and/or generalized ascites. A hepatobiliary radionuclide scan confirms intraabdominal extravasation of bile.

Operative cholangiography via the gallbladder will confirm the site of perforation and assess the patency of the common bile duct. Definitive treatment is dictated by the findings. Cholecystectomy is sufficient for rare instances of cystic duct perforation, but for the usual site of perforation, tube cholecystostomy and simple drainage are appropriate if there is free flow of contrast into the duodenum. If there is distal common bile duct obstruction, catheter irrigation may clear inspissated bile, but drainage should be combined with cholecystostomy. If a distal bile duct stricture is demonstrated, hepaticojejunostomy is indicated.

## Inspissated Bile Syndrome

Inspissated bile within the distal common bile duct may cause obstructive jaundice in newborns. It can be due to haemolysis, diuretic therapy, parenteral nutrition, prematurity, or cystic fibrosis. Inspissated bile plug syndrome may be difficult to distinguish from biliary atresia. In both conditions, there may be jaundice and acholic stools, conjugated hyperbilirubinaemia, and no biliary excretion on a radionuclide scan. However, US usually reveals dilated proximal bile ducts and inspissated bile.

Spontaneous resolution may occur. Treatment with ursodeoxycholic acid may help. More persistent obstruction can be cleared by percutaneous, transhepatic irrigation of the bile ducts, ERCP and retrograde irrigation, or cholecystectomy and bile duct irrigation. Occasionally, transduodenal sphincteroplasty may be required to remove an impacted mass of material or stones.

## Biliary Hypoplasia

Biliary hypoplasia is a unique classification within the cholestatic spectrum. The liver histology is characterized by a paucity of intrahepatic ducts (i.e., a significantly decreased ratio of the number of interlobular bile ducts to the number of portal tracts). Biliary hypoplasia is best regarded as a condition secondary to decreased bile flow from the liver rather than a primary structural abnormality of the ducts. Biliary hypoplasia is either syndromic (Alagille syndrome) or nonsyndromic.

### Alagille syndrome

Alagille syndrome is a genetic disorder that affects the liver, heart, and other systems of the body. Problems associated with the disorder generally become evident in infancy or early childhood. The disorder is inherited in an autosomal dominant pattern, and its estimated prevalence is 1 in every 100,000 live births. The severity of the disorder can vary within the same family, with symptoms ranging from being so mild as to go unnoticed to severe heart and/or liver disease requiring

transplantation. Signs and symptoms arise from liver damage, cholestasis, and deposits of cholesterol in the skin xanthomas. Other signs of Alagille syndrome include congenital heart problems, tetralogy of Fallot, and vertebral arch defects with failure of anterior vertebral arch fusion (butterfly vertebrae). Many people with Alagille syndrome have similar facial features, including a broad prominent forehead; deep-set, widely spaced eyes; a long straight nose; and a small pointed chin with underdeveloped mandible. The kidneys and central nervous system may also be affected.

### Nonsyndromic biliary hypoplasia

Nonsyndromic patients may initially be confused with those who have biliary atresia. Differentiation is crucial because transplantation is the only appropriate therapy for the end-stage liver disease in biliary hypoplasia. Percutaneous liver biopsy samples from affected infants lack the hepatic fibrosis and ductal proliferation characteristic of biliary atresia. The liver is smooth and often chocolate brown. Cholangiography demonstrates a diminutive biliary tree. Outcomes range from clinical improvement with resolution of cholestasis to end-stage liver disease with progressive cirrhosis.

## Evidence-Based Research

Endoscopic ultrasonography (EUS) is a major advance in gastrointestinal imaging. It is used to image suspected pathology in the gastrointestinal tract and in the adjacent organs. It is a less invasive modality and may be equal or superior to ERCP in visualising the biliary tree. Its diagnostic accuracy in the evaluation of pancreatico-biliary diseases exceeds 90%. Its role and feasibility in children need to be accurately defined. Table 80.2 presents a study comparing EUS and ERCP in children with chronic liver disease.

*Table 80.2: Evidence-based surgery.*

| | |
|---|---|
| **Title** | A comparative study of EUS versus ERCP in children with chronic liver disease (CLD) |
| **Authors** | El-Karaksy HM, El-Koofy NM, Okasha H, Kamal NM, Naga M |
| **Institution** | Department of Pediatrics and Department of Internal Medicine, Cairo University, Cairo, Egypt |
| **Reference** | Ind J Med Sci 2008; 62:345–351 |
| **Problem** | The primary aim is to evaluate the role of EUS in comparison to ERCP in the pancreatico-biliary assessment of children with CLD. The secondary aim is to compare the findings obtained by EUS with those obtained by conventional abdominal ultrasound. |
| **Intervention** | Children with sonographic or histopathological evidence of biliary pathology, autoimmune hepatitis, cryptogenic CLD, and neonatal cholestasis underwent EUS and ERCP. |
| **Comparison/ control (quality of evidence)** | A descriptive comparative study carried out on 40 children older than 4 years of age suffering from CLD. All patients were subjected to EUS, ERCP, and abdominal ultrasound. |
| **Outcome/ effect** | EUS was equal to ERCP in diagnosis of biliary pathology. However, one false positive case was described to have dilatation and tortuosity of the pancreatic duct by EUS as compared to ERCP. EUS could detect early pancreatitis in five cases. One case with cryptogenic liver disease proved to have sclerosing cholangitis diagnosed by both EUS and ERCP. |
| **Historical significance/ comments** | In this study, EUS proved to be superior in detecting the cause of common bile duct (CBD) dilatation in patients in whom US could not demonstrate the cause of dilatation or in whom US revealed equivocal results. EUS was superior to ERCP in diagnosing chronic pancreatitis. In addition, negative cases should not be subjected to further evaluation by ERCP. ERCP should be performed if pancreatic duct pathology needs further assessment or if intervention is planned. More studies are needed to justify accurately the role of EUS in children with CLD and to highlight the feasibility of its usage for young ages. |

## Key Summary Points

1. Neonatal cholestasis is a prolonged elevation of serum levels of conjugated bilirubin beyond the first 14 days of life.
2. From 0.2% to 0.4% of neonates have cholestatic jaundice from either intrahepatic cholestasis or structural abnormalities that cause biliary obstruction.
3. Obstructive jaundice in infancy presents a surgical challenge; differentiation and surgical correction should be done by the age of 2 months.
4. Biliary atresia is the most common cause of obstructive jaundice requiring operation in children.
5. Evaluation of the jaundiced infant should follow a logical, cost-effective sequence in a multistep process.

## Suggested Reading


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