Neonatal Jaundice

Due to hyperbilirubinemia

- Bilirubin
  - byproduct of RBC breakdown
  - enzyme glucuronyl transferase in liver converts BR into soluble conjugate (conjugated BR) prior to elimination
  - immature enzymatic pathway in neonate

>50% have indirect, unconjugated hyperbilirubinemia

- BR day 2-3, peaks day 5-7
  - FT 12 mg/dL
  - Premature 14 mg/dL

Breastfed babies
- BR up to 2 weeks
- Physiologic jaundice resolves by 7-10 days

Work-Up of Jaundice

Cholestasis

- Onset 1st 24 hours life
- BR rise > 5 mg/dL in 24 hours
- Direct BR > 1 mg/dL anytime
- Persistent or new onset jaundice after 2 weeks

Ultrasound

Differentiate between obstructive and non-obstructive jaundice

Learning Objectives

- List the various causes of jaundice in the neonate
- Describe sonographic features of various obstructive and non-obstructive causes of jaundice in infants and children
- Describe systematic approach to the work-up of neonatal jaundice

Neonates

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Jaundice in Infants*

Neonatal hepatitis

vs

Biliary atresia

vs

Choledochal cyst

vs

Metabolic disease

*Clinical and laboratory features may be similar in hepatocellular and obstructive jaundice

*Early diagnosis (<2-3 mos) essential before irreversible cirrhosis occurs
Other causes bile duct obstruction usually occur later in childhood!

- Cholelithiasis
- Bile duct tumors
- Pancreatic tumors
- Congenital stenosis CBD

Laboratory Evaluation

- Hepatic function tests
- Hepatitis B antigen
- TORCH titers
- α-1-anti-trypsin testing
- Metabolic screening
- Sweat test

US Examination*

- Liver size, texture
- Intra and extrahepatic biliary ducts
- GB size, wall thickness, sludge, stones, pain
- Pancreas size, texture, duct
- Spleen size, texture
- Evidence of portal hypertension
- Ascites
- Abdomen, pelvis for neoplasia

*patients must be NPO 3 hours

US Evaluation Biliary System

Normal Liver
Aorta/celiac/SMA
Celiac axis

Normal Biliary Vascular Anatomy

Hepatic Veins
US Evaluation of the Biliary System

Liver Size
- No valid measurements for pediatric patients
- Neonates: liver 1-2 cm below RCM
- Children: liver not below RCM
- Liver should not extend below right lower renal pole
- Liver and spleen should not touch
- Spuriously large liver with pulmonary hyperinflation

Spleen

Age and Spleen Length

<table>
<thead>
<tr>
<th>Age</th>
<th>Length</th>
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<tbody>
<tr>
<td>0-3 months</td>
<td>6.0 cm</td>
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<tr>
<td>3-6 months</td>
<td>6.5 cm</td>
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<td>6-12 months</td>
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<tr>
<td>10-12 years</td>
<td>11.5 cm</td>
</tr>
<tr>
<td>12-15 years</td>
<td>12.0 cm</td>
</tr>
<tr>
<td>15-20 years</td>
<td>12.0 cm</td>
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</tbody>
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- Female
- Male

Neonatal Jaundice

**hepatocellular damage - cholestasis**

- **Infectious**
  - bacterial (syphilis, Listeria, E.coli, Staph)
  - viral (hepatitis B, hepatitis C, CMV, HIV, rubella, measles, herpes, Epstein-Barr)
  - parasitic (Toxoplasma)

- **Metabolic**
  - α1-anti-trypsin deficiency, galactosemia, glycogen storage disease, tyrosinemia, fructose intolerance, CF, TPN

Neonatal Jaundice

**hepatocellular damage - cholestasis**

- Familial recurrent cholestasis
- Congenital cirrhosis
- Nesidioblastosis (idiopathic hyperinsulin hypoglycemia of infancy)
- Miscellaneous (systemic diseases, shock, sepsis, UTI, CHF, neonatal lupus, histiocytosis, hemolytic diseases)

Neonatal Hepatitis

- Presents at 1-4 wks (< 3 months)
- M > F
- Causative agents via
  - placenta (bacteria, virus, parasite)
  - vagina (infected maternal secretions)
  - catheters
  - blood transfusions
Neonatal Hepatitis
ultrasound findings
- Liver size: normal or increased
- Liver parenchyma coarsely hyperechoic (at times heterogeneous)
- Decreased peripheral portal venous vasculature
- Periportal edema (increased periportal echogenicity)
- GB size: large, normal, small
- GB wall thickened (hypoalbuminemia)
- CBD size: normal
- Periportal lymphadenopathy

CMV Hepatitis

Biliary Atresia
3 types
Type I: Focal (very rare)
- Absence/obliteration lumen extrahepatic and/or intrahepatic bile ducts
- Biliary cirrhosis occurs early
- Etiology
  - in utero insult to hepatobiliary system after bile ducts are formed (infectious, immunologic, toxic, vascular)
  - progressive sclerosis extrahepatic and/or intrahepatic bile ducts

Type II: Intrahepatic biliary atresia (uncommon)
- Paucity intrahepatic bile ducts

Type III: Extrahepatic biliary atresia (most common)
- Atresia CBD, patent proximal biliary ductal system

Biliary Atresia
Type III - subtype 1
- Perinatal type (66%)
  - Occurs late fetal life/postnatally
  - Jaundice after 2 weeks
  - Bile duct remnant present in porta hepatitis
  - No associated malformations

Biliary Atresia
Type III - subtype 2
- Embryonic/fetal type (34%)
  - Normal decline BR does not occur
  - No bile duct porta hepatitis
  - Associated with polysplenia syndrome
  - Biliary atresia
  - Polysplenia
  - Situs inversus
  - Symmetric bilobed liver
  - Interrupted IVC
  - Azygous continuation
  - Preduodenal PV
  - Intestinal malrotation
  - Bilobed right lung
  - Cardiac malformation
Biliary Atresia

ultrasound findings

- Liver size normal or increased
- Liver parenchymal diffusely coarse, hyperechoic
- Decreased visualization peripheral portal venous vasculature

Biliary Atresia

ultrasound findings

- Bile duct remnant may be present
- “Triangular cord” in porta hepatitis
  (fibrotic remnant obliterated cord)
- GB small (<1.5 cm long) or absent
- Cystic areas within liver with cholangitis

Newborn with Jaundice

Biliary Atresia

hepatobiliary scan

< 3 mo
- Normal hepatic extraction
- Absent tracer passage into small bowel

> 3 mo
- Decreased hepatic extraction
- Absent tracer passage into small bowel

*bile-stimulating effect of phenobarbital administered 3-5 days prior to scan
**Hepatitis**

- Hepatic parenchymal disruption/lobular disarray
- Relatively little bile within canaliculi
- Multinucleated giant cells
- Mononuclear lobular infiltrate
- Pseudoductular formation

**Biliary Atresia:**

- Bile duct proliferation
- Periportal fibrosis
- Acute or chronic portal inflammation

**MR cholangiography in neonates and infants:**

Feasibility and preliminary applications.


**Biliary Atresia cholangiography**

- Performed when imaging and pathologic findings suggest biliary atresia
- If biliary atresia, Kasai* portoenterostomy
  (jejunal loop transposed to liver after Roux-en-Y anastomosis and any patient bile “ductules” at liver hilum)

* Untreated, babies die within years
* Best results < 60 days of age
* 75% require liver transplantation by 20 yrs

**Alagille Syndrome**

- May present with neonatal cholestatic jaundice
- US findings similar to biliary atresia
- Paucity/hypoplasia interlobular ducts
- Autosomal dominant
- Associated congenital anomalies
  - abnormal facies (large forehead, small pointed chin, hypertelorism, poorly developed nasal bridge)
  - butterfly/hemivertebrae,
  - pulmonary artery hypoplasia/stenosis
  - complex congenital heart disease
  - ocular abnormalities
  - renal abnormalities infrequently

**Choledochal Cyst**

- Uncommon cause jaundice
- F > M
- Asian
- Presenting features:
  - Jaundice
  - Pain
  - RUQ mass
- Abnormal insertion CBD into pancreatic duct
**Choledochal Cyst**

**Todani classification**

- **Type I** - Fusiform (80-90%)
  - I-A: Cystic dilatation CBD
  - I-B: Focal segmental dilatation CBD
  - I-C: Fusiform choledochal dilatation

- **Type II** - Diverticulum (2%)

- **Type III** - Choledochocele (1.4-5%)
  (dilated intraduodenal CBD)

**Choledochal Cyst**

**US findings**

- Cystic mass porta hepatis separate from GB
- No change in mass following milk feeding
- CBD, CHD or cystic duct communicates with cyst
- Intrahepatic ducts may be dilated
- Intrahepatic bile ducts not dilated when associated biliary atresia
- Hepatomegaly with abnormal liver texture

**Choledochal Cyst**

**Type 1**

**Newborn with jaundice**

Choledochal Cyst with Intrahepatic Biliary Atresia

Intraoperative cholangiogram

MRI Choledochal Cyst

Type IV A
- IV A: Multiple intrahepatic/extrahepatic biliary cysts
- IV B: Normal intrahepatic bile ducts/multiple biliary cysts

Choledochocele type III

Type IV

Courtesy Harriet Paltiel, MD
Choledochal Cyst

Type V - Caroli Disease
- Single/multiple intrahepatic cysts (represent saccular dilatation bile ducts) converge toward porta hepatitis
- Portal radicals partially/completely surrounded by dilated ducts
- CBD may be dilated
- Associated with hepatic fibrosis/portal HPTN/PCKD
- Rarely seen at birth
- Most patients: young adults, fever, pain, transient jaundice

Carol’s Disease:
“central dot sign”
portal venule seen as small dot nondependent part of dilated bile duct

Carol’s Disease
associated abnormalities
- Stone formation, cholangitis, abscess
- Hepatic fibrosis
- Choledochal cyst
- Medullary sponge kidney
- Infantile polycystic kidney disease
- Nephronophthisis

Hepatic Fibrosis

US findings
- Hepatomegaly
- Heterogeneously increased echogenicity
- Increased echogenicity portal triads
- Poorly defined portal vessels
- Large cysts if associated with Caroli’s disease
- Spleen size dependent on presence/absence portal HPTN

Complications of Choledochal Cyst
- Cholelithiasis
- Choledocholithiasis
- Pancreatitis
- Ascending cholangitis
- Intrahepatic abscess
- Spontaneous cyst rupture
- Biliary cirrhosis
- Carcinoma biliary tree
Cystic Lesions Confused with Choledochal Cyst

- Hepatic cysts
- Enteric duplication cyst
- Pancreatic pseudocyst
- HA aneurysm
- Spontaneous perforation CBD

Spontaneous Perforation Extrahepatic Bile Duct

- Rare
- Infants < 3 months
- Presents with jaundice, ascites, pseudocyst porta (bilia)
- Pathogenesis: Bile duct weakened from dilatation (stenosis, stricture, stone, inspissated bile, congenital weakness)
- Junction cystic and CBD
- May have gallstones GB and distal CBD
- Biliary tree not dilated
- Elevated BR, liver f nl
- Hepatobiliary scintigraphy confirms

Tumors rarely cause Jaundice!

- Benign Neoplasms
  - Hemangioendothelioma
  - Cavernous hemangioma
  - Mesenchymal hamartoma
  - Focal nodular hyperplasia
  - Hepatic adenoma
  - Nodular regenerative hyperplasia
  - Fatty tumors (angiomyolipoma, lipoma)
  - Cyst

Hemangioendothelioma

- Most common benign hepatic tumor neonates
- High output failure
- Hepatomegaly
- Thrombocytopenia
- Commonly involutes in 12 – 18 months
- Solitary or diffuse
- Slow internal circulation
Mesenchymal Hamartoma
- Benign well-circumscribed multilocular septated cystic mass usually in right lobe
- M > F, usually 2-3 year olds
- Developmental anomaly originating in connective tissue along portal tracts
- Composed of bile ducts and mesenchymal tissue
- Asymptomatic abdominal mass or abdominal distention
- Rarely undergoes malignant transformation

Hepatoblastoma
- < 3 yrs
- Heterogeneous mass
- Often right lobe
- Variable echogenicity
- Well circumscribed/infiltrating
- Calcifications 50%
- May be highly vascular
- Vascular invasion common
- Elevated α-fetoprotein 60-70%
- Metastasizes to lungs/portal hepati
- Less often to brain and skeleton

Hepatoblastoma
- < 3 yrs
- Beckwith-Weidemann syndrome
  - Hypoglycemia, macroglossia, visceromegaly, hemihypertrophy, umbilical hernia or omphalocele
- Isolated sexual precocity
- Fetal alcohol syndrome
- Familial polyposis coli
- Gardner’s syndrome

Secondary Hepatic Neoplasms
- Metastases
  - Wilms’
  - Neuroblastoma
  - Leukemia
  - Lymphoma

Portal Hypertension (increased R)
- altered portal, hepatic venous and arterial flow
- Obstruction
  - Extrahepatic (level PV or HVs)
  - Intrahepatic (hepatocellular disease)
- Clinical signs
  - Splenomegaly
  - Ascites
  - Prominent abdominal vev (caput medusae, systemic portosystemic shunts)
  - Hematemesis (varices)
  - Hepatic encephalopathy
  - Hypersplenism

Cirrhosis
- Liver cell necrosis and degeneration
- Diffuse fibrosis and regenerating nodules
- Causes in pediatric age range
  - Chronic hepatitis
  - Congenital hepatic fibrosis
  - Biliary atresia
  - Cystic fibrosis
  - Metabolic disease (Wilson’s, glycogen storage disease, tyrosinemia, galactosemia, α-1-antitrypsin deficiency)
  - Budd-Chiari syndrome
  - Drugs
Cirrhosis
US findings
- Small right lobe/medial segment left lobe
- Compensatory hypertrophy lateral segment left lobe/ caudate lobe
- Nodular liver margins
- Coarsened/heterogeneous texture
- Decreased beam penetration
- Regenerating nodules
- Displace/compress HV/PV radicals
- GB small/not visualized
- Other signs: ascites, splenomegaly, varices

Collateral Flow
- Tributary
  - Normally drain into PV (left gastric/coronary v, short gastric vv/SMV/IMV)
- Developed
  - Recanalized preexisting vessels (paraumbilical v, splenorenal, ductus venosus)

Gastroesophageal Varices

Recanalized Paraumbilical Vein

Recanalized Ductus Venosus

Figu Splenorenal Shunt re 14.7 i
Summary

- Discussed the various causes of jaundice in the neonate
- Described the sonographic features of various obstructive and non-obstructive causes of jaundice (cholestasis) in infants and children
- Discussed systematic approach to the work-up of neonatal jaundice

Thank You