Chapter 11

Hepatology

Contents:

Common Liver Diseases in Children

1. ACUTE HEPATITIS

Hepatitis is a non-specific clinical syndrome of variable severity due to inflammation & necrosis of hepatic parenchyma.

Causes may be: infective, toxic, autoimmune, genetically determined, ischemic or cryptogenic.

ACUTE VIRAL HEPATITIS

Viral hepatitis is mostly caused by:

- Hepatotropic viruses (A, B, C, D & E).
- Non-hepatotoxic: Herpes viruses, CMV, EBV, HIV, rubella, mumps & enteroviruses

Hepatitis A

Etiology and epidemiology:

Causative organism	Hepatitis A virus (HAV) is a non-enveloped, single-stranded RNA virus. Only one serotype has been recognized. It is excreted in stool & bile
Route of spread	Fecal-oral.
Source	Case only, HAV causes only acute hepatitis with no carrier state.
Mode of transmission	Transmission by close personal contact and by contaminated food & water. Infection in late pregnancy has not been shown to affect the newborn infant.
Infectivity period	Late in the incubation period & within 2 weeks of clinical onset of hepatitis.

Pathogenesis:

- HAV is mildly cytopathic and the major hepatic injury is due to cell-mediated (cytotoxic T-lymphocytes) immune responses.

Pathology:

- Liver cell damage or necrosis and inflammatory mononuclear cell infiltrate in the hepatic parenchyma and portal tracts.
- Bile duct proliferation with or without bile pigment retention.

Clinical picture:

- Incubation period: from 20-40 days.
- Most children have an asymptomatic subclinical infection.
- Symptomatic infection has **2 phases**:

Pre-icteric phases: Fever, **A**norexia, **H**epatomegaly, **M**alaise (FAHM) + nausea, vomiting, abdominal discomfort, diarrhea.

Icteric phases:

- Jaundice, dark urine & pale stool.
- All symptoms regress & sometimes pruritus occurs.
- Liver is enlarged and tender. Splenomegaly occurs in 20-30% of cases.
- Jaundice may persist for only a few days but fades in the second week.
- Rarely it may persist for months (cholestatic hepatitis).
- Recurrence of cholestasis may also occur (relapsing hepatitis).
- Complete recovery is the rule.

Diagnosis:

1. **History:** Exposure to jaundiced person in family, school or nurseries
2. **Clinical examination.**
3. **Laboratory investigations:**

A-Biochemical:

- Serum biphasic bilirubin level rises.
- ALT & AST levels are elevated several folds the normal values.
- PT to assess the extent of liver injury.

B-Serological:

- IgM anti-HAV antibodies appear in serum at onset of symptoms & disappear after 2 months.
- IgG anti-HAV antibodies appear during convalescence & persist for many years.

Complications:

A- Fulminant hepatic failure (FHF): The most serious complication.

Incidence: 0.5% of cases within 8 weeks of onset of symptoms.

Clinical features:

1. Rapid progression of symptoms.
2. Deepening of jaundice.
3. Reduction of liver size.
4. Development of ascites.
5. Neuro-psychiatric changes (Aggressive behavior, encephalopathy).

Laboratory findings:

1. Prolongation of prothrombin time (not responding to Vit. K).
2. Falling of serum albumin.
3. Raised serum ammonia.

B- Aplastic anemia:

a. Is a very rare complication it is transient but may be fatal.
b. It is due to bone marrow depression.
c. Death is usually due to serous infection due to depressed immunity.

C- Cholestasis:

a. The patient becomes intensely pruritic and jaundiced.
b. It is due to hepatocyte edema which may cause element of obstruction.

D-Relapsing (biphasic) hepatitis:

Treatment:

1. Most children are managed at home except if liver cell failure is suspected.
2. There is no specific therapy for acute viral hepatitis.
3. Balanced diet with low fat intake should be given.

Prevention:

▪ General measures:

Hygienic measures: hand washing & sterilization.

▪ Immunoprophylaxis:

- **Passive:** Human immune serum globulin (ISG): Before exposure (travelers to endemic areas) or after exposure (household & close contacts); Dose: 0.02 ml/kg within 2 weeks of exposure.
- **Active:** Highly immunogenic, formaldehyde-inactivated HAV vaccine given to high-risk children and travelers to endemic areas.
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Dose: children over 2 years: 3-dose regimen (0, 1, 6 months interval) I.M.

Hepatitis B

Etiology and epidemiology:

Causative organism	Hepatitis B virus (HBV) is an enveloped, double-stranded DNA virus. HBV is composed of 3 antigens: surface (HBsAg), core (HBcAg) and envelope (HbeAg).
Route of spread	HBV has been found in almost all body secretions, but only blood, serum, semen and vaginal secretions have been shown to be infectious. HBV is transmitted parenterally by needle and intravenous equipment, perinatally, unscreened blood products and sexually.
Source	HBsAg positive family member or other close contacts, drug abusers, homosexuals, hemodialysis patients. Blood products, particularly clotting factor concentrates. Medical personnel and institutionalized children are susceptible.
Mode of transmission	**Perinatal transmission:** From infected HBsAg positive mother to infants (10-40%) during delivery. Risk of infection increases to 70-90% if the mother is also HbeAg positive. Chronic hepatitis and chronic carrier state develop in >90% of infected infants. **Parenteral:** In patient receiving transfusion of contaminated blood or blood products, renal dialysis, dental care and through contaminated syringes and needles. **Child to child transmission:** It may occur through biting of insects, ear perforation, drooling and shared chewing gums. Although HBV was detected in breast milk of infected mother there is no role of breast milk to transmit the infection.

Pathogenesis:

Hepatocellular injury in HBV is the result of humoral and cellular immune responses.

Clinical picture:

Incubation period: 30-180 days (mean 90 days). Many cases are asymptomatic. Symptomatic cases with jaundice occur in 25% of patients.

1. **Prodromal phase**: lasts 2-3 weeks

   - FAHM + nausea.
   - Serum sickness-like illness: in a few children
   - Fever, abdominal pain, arthralgia, pruritic urticarial or maculopapular skin rash.
   - Papular acrodermatitis: erythematous papular eruption on face and extremities and lymphadenopathy.

2. **Icteric phase**: lasts from 4-6 weeks. Jaundice, hepatomegaly and splenomegaly.

Diagnosis:

- Clinical.
- Laboratory Investigations.

Laboratory investigations:

Serological tests:

- HBs Ag can be detected in serum 1-4 weeks before liver enzyme elevation or appearance of clinical symptoms.
- Anticore antibodies appear in the serum after 4 weeks and followed by antisurface antibodies (HBs Ab).

Complications:

Fulminant hepatitis:

It occurs more frequently with HBV than other viruses (1%). Risk increases when there is co-infection or super infection with hepatitis D virus. Mortality is 70%.

Chronic hepatitis:

This develops in >90% of neonates and 10-20% in older children.

Types: chronic persistent and chronic active hepatitis. Chronic hepatitis may progress to cirrhosis and hepatocellular carcinoma.

Treatment:

1. Supportive treatment.
2. Interferon-∝-2b is useful for treatment of children with recent HBV infection and active viral replication (25-40% recovery rate). However, it is less successful in children with long-standing HBV infection.
3. Liver transplantation is used in end stage liver failure (ESLF) caused by HBV infection.

Prevention:

General measures:

- Screening for HBV of blood and plasma-derived products.
- Use of disposable needles, sterilization of equipments and safe handling of all clinical specimens.

Immunoprophylaxis:

- **Passive:** Hepatitis B immune globulin (HBIG) containing high titers of anti-HBs given at a dose of 0.04-0.06 ml/kg as early as possible or after exposure for household and sexual contacts and perinatal exposure.
- **Active:** 2 types of vaccines:
  1. Plasma-derived: inactivated HBs Ag particles obtained from plasma of HBV carriers.
  2. Recombinant yeast-derived vaccines (Recombivax HB, Engerix B). A highly immunogenic effective and safe vaccine.
- **Indications:** Universal infant immunization and Children.

Dose: three IM dose (initial injection, repeated 1 and 6 months later). Neonates of HBs Ag-positive mother should receive HBIG (0.5 ml) + HB vaccine (5ug) IM within 12 hours of birth and repeated at l and 6 months.

Prognosis:

1. Recovery may be complete. 2-The child may remain as an asymptomatic carrier. 3- Or chronic patient for months or years.

Hepatitis C

Etiology and epidemiology:

Causative organism	HCV is a small, lipid-enveloped single stranded RNA virus It has six genotypes and several subtypes. It has not been isolated, but cloned using recombinant DNA Technology.
Route of spread	Parenteral.
Source	HCV positive patient, drug abusers, hemodialysis. Contaminated blood products, particularly clotting factor concentrates. Medical personnel and institutionalized children are susceptible.
Mode of transmission **Prevalence**	**i)** Intravenous drug use 40%. **ii)** Transfusion of blood and blood products 10%. **iii)** Occupational and sexual exposure 10%. **iv)** No obvious risk factor 40%. **v)** Perinatal transmission is uncommon. **a)** Chronic hepatitis in most infected infants. **b)** Breast-feeding does not transmit HCV. Hemophiliacs 90%, Thalassemics 10-50%, Hemodialysis patients 40%.

Clinical picture:

Incubation period: 2 weeks - 6 months (average 7 weeks). Most cases are symptomatic, Jaundice occurs in 20% of those infected. Acute HCV is usually mild and course is more indolent:

i. **Preicteric phase:** (FAHM) + nausea, vomiting and abdominal pain.

ii. **Icteric phase:** jaundice and dark urine.

Laboratory investigations:

- **Serum transaminases:** SGPT and SGOT are moderately elevated and fluctuate for long time.
- **Serologic tests:** Detection of anti-HCV: by enzyme -linked immunoassay (ELISA-2) and recombinant immuno Blot assay (RIBA) (confirmatory) / Positive by 2-4 weeks post infection.
- **Detection and quantitative measurement** of HCV RNA: by polymerase chain reaction (PCR) positive by 1-3 weeks after exposure.

Complications:

- Fulminant hepatitis**:** rare - mortality 90%.
- Chronic hepatitis: **occurs** in 70% of cases. Half of those cases develop cirrhosis.
- Hepatocellular carcinoma may occur.
- Extrahepatic complications: Aplastic anemia, pancreatitis and glomerulo-nephritis.

Prevention:

Reduction of risk factor exposure:

1- **Screening** of blood donors for Anti HCV, Use of disposable needles, and sterilization of equipments and safe handling of all clinical specimens.

2- **Immunoprophylaxis:** Neither passive nor active immunization against HCV is currently available.

3- Children with HCV and their household contacts should be **vaccinated against hepatitis A and B virus** to prevent worsening or catching of liver disease. There is no need to prevent children with HCV infection from attending daycare.

4- **Breastfeeding** is not contraindicated for mothers with HCV infection.

Treatment:

- The antiviral therapy (peginterferon–ribavirin) may be recommended for children older than 3 years with CHC who have a persistently elevated serum ALT level, portal or bridging fibrosis, and at least moderate inflammation and necrosis at liver biopsy. However, this is a difficult decision.
- Oral new treatment options are now developing and include several potent oral directly-acting antiviral drugs such as (sofosbuvir/daclatasvir, sofosbuvir /ledipasvir or sofosbuvir/velpatasvir combined oral therapy ± ribavirin) with great success in adults. However its role and safety in pediatric HCV infection (for those <18 year) as are not yet established.

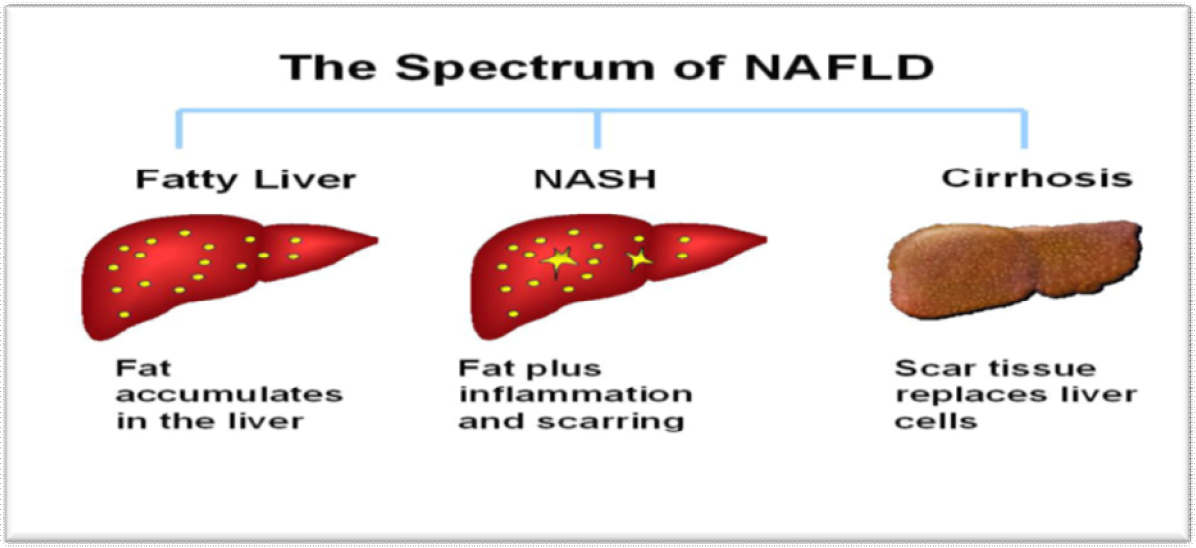
2. NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Definition and spectrum:

- Paralleling the epidemic of childhood obesity, pediatric NAFLD has emerged as a growing global health problem worldwide and is considered the most common cause of CLD in pediatrics nowadays.

- It can range from fatty liver alone (steatosis) to a triad of fatty infiltration, inflammation, and fibrosis that is called nonalcoholic steatohepatitis (NASH) that resembles alcoholic liver disease but occurs with no exposure to alcohol.

- The pathogenesis of NAFLD is multifactorial; it is strongly associated with obesity/overweight and insulin resistance. Also, in addition to environmental factors, there is strong genetic predisposition to NAFLD & NASH.



Prevalence: Liver histology from autopsy data suggest that 10% of children and 38% of obese children aged 2-18 yrs. might have NAFLD.

Risk factors: include children with overweight or central obesity, insulin resistance, type 2 diabetes mellitus, male gender, hypertriglyceridemia. The risk is higher in white or Hispanic ethnicity, but lower in African-American children.

Clinical picture and course: Many patients are asymptomatic. Enlarged liver can be present in a minority of cases. Hepatic steatosis alone may be benign, but up to a quarter of patients with NASH can develop progressive fibrosis with resultant cirrhosis and portal hypertension with its sequelae.

Diagnosis:

-**All** other **causes of CLD and steatosis must be excluded firstly.**

-Elevated serum aminotransferase levels are not sensitive or specific markers for NAFLD. A normal serum ALT level is present in 21-23% of pediatric patients with NAFLD.

-Imaging procedures: Although ultrasonography, MRI and MRS can detect most NAFLD cases, no current imaging modalities can distinguish between steatosis and NASH.

-Liver stiffness measurement by elastography (FibroScan) can be used to predict liver fibrosis stages in cases with NASH.

-A liver biopsy may be required for definitive diagnosis especially for those with persistently elevated liver enzymes.

Treatment:

-Lifestyle modification (low calorie diet and exercise) is the main line of therapy.

-Some antioxidants like vitamin E and vitamin C may provide additional benefit to the efficacy of this line in improving liver histology and biochemical abnormalities.
- Metformin has produced mixed results in the treatment of NAFLD.

3- Cholestasis in infants and children

Definition:

Reduction in bile flow with retention of substances normally excreted in the bile (e.g. bilirubin, bile acids & cholesterol) with histopathologic features reflecting nature & degree of disturbances.

The mechanisms of cholestasis can be broadly classified into:

A- Hepatocellular cholestasis: Where an impairment of bile formation occurs.

B- Obstructive cholestasis: Where impedance to bile flow occurs after it is formed.

Causes:

I. Extrahepatic biliary obstruction:

1. Extrahepatic biliary atresia (EHBA).
2. Choledochal cyst.
3. Spontaneous rupture of the bile duct.
4. Extrinsic compression.

II. Intrahepatic biliary hypoplasia or paucity of interlobar bile ducts (PIBD):

1- Alagille's syndrome.

2- Non syndromic ductal paucity.

III. Hepatocellular disease:

1- Neonatal hepatitis.

2- ∝1antitrypsin deficiency, Cystic fibrosis.

3- Inborn errors of bile acid synthesis.

4- Drug induced cholestasis.

5- Total parenteral nutrition.

6- Progressive familial intraheptic cholestasis (PFIC).

7- Inections: TORSCH, Sepsis.

Approximately 75% of all cases of neonatal cholestasis are due to EHBA or neonatal hepatitis.

Pathology of cholestasis:

I-Gross Pathology of cholestasis:

-Irrespective of the cause, the changes depend on the duration of cholestasis.

-Early, the liver is enlarged with a smooth surface, rounded border and its cutsection is greenish in color.

-In prolonged cholestasis: Secondary Biliary cirrhosis develops and pathological changes appear in different organs. In cirrhosis the liver shows nodular surface and sharp border with variable size.

II-Microscopic pathology of cholestasis:

i-Early cholestasis: Both hepato-cellular and canalicula cholestasis, hepatocellular necrosis, giant cell transformation, and fibrosis. However, special histological findings may help in the diagnosis of some causes.

ii- In late or complicated of cholestasis: Regenerating nodules are present**.**

Histological DD of Hepatocellular vs Obstructive cholestasis:

A- Hepatocellular cholestasis:

-Presence of bile within hepatocytes and canalicular spaces.

-Generalized cholate injury.

B- Obstructive cholestasis:

-Bile plugging of the interlobular bile ducts. -Portal expansion

-Bile duct proliferation (This pathological change is not seen in cases with PIBD)

-Centrilobular cholate injury.

Complications of cholestasis:

Malabsorption, growth retardation, secondary biliary cirrhosis, portal hypertension and endstage liver cell failure (ESLF).

Clinical picture of cholestasis:

The common clinical manifestations and consequences of cholestasis are classified into:

A- Early cholestasis:

I. Retention / Regurgitation of the different components of the bile:

-Conjugated Bilirubin ⟶ Jaundice with changes in color of urine and or stool.

-Bile acid⟶ Pruritus, Bradycardia.

-Cholesterol⟶ Xanthomatosis.

II. Decreased bile salts in intestine:

-Malabsorption of long-chain triglycerides→Growth retardation, diarrhea / steatorrhea
-Vit.A rnalabsorption→ Thick skin, Night blindness.
-Vit.D rnalabsorption→ Metabolic bone disease (Osteoporosis, rickets).
-Vit.E rnalabsorption→ Hemolytic anemia, Neuromuscular degeneration.
-Deficiencies of Vit.K-dependent coagulation factors→ bleeding tendency.

B-Late or complicated cholestasis:

III- Biliary liver cirrhosis.

IV- Portal hypertension with development of gastroesophageal varices.

V- Liver cell failure.

Diagnosis of Cholestasis

I. History:
II. Physical Examination:
III. Investigations:

The initial step in identification of cholestasis is the finding that the conjugated (direct) bilirubin is more than 20% of the significantly elevated level of total bilirubin (conjugated hyperbilirubinemia).

-The next step: Is the early recognition of the treatable medical or surgical causes of cholestasis.

A- Medical causes (sepsis, endocrinopathy e.g. hypothyroidism or panhypopituitarism, or galactosemia).

B- Surgical causes (e.g. extrahepatic biliary atresia as early surgical correction of the lesion within the first 2 months after birth will save the liver cells from early cirrhosis.

Investigations include:

A-Laboratory procedures: Serum bilirubin fractionation, Hepatic synthetic function (albumin, coagulation profile), Liver enzymes (ALT, AST, ALP, GGT), Exam of aspirated duodenal fluid for presence of bile, TORSCH screening, Sepsis work-up, Hepatitis markers, Urine/serum bile acids measurement, Urine/serum amino acids measuremen and urine reducing substances, α1-antitrypsin phenotype, Thyroxine and TSH, Sweat chloride/mutation analysis,.

B-Imaging procedures: -Abd Ultrasonography -MRI of liver & biliary ducts (MRCP).

C- Hepatobiliary scintigraphy (HIDA scan).

D- Liver biopsy.

E- Intraoperative cholangiography (IOC) for suspected cases of EHBO only.

Management of infantile cholestasis:

A- Surgical Correction for EHBO:

1. **Correctable lesions** (i.e. distal atresia with patent proximal portion of the extra hepatic duct): Direct drainage of the biliary system into the intestine (hepatico-jejunostomy).

2. **Non-correctable lesions** (i.e. No patent extra hepatic bile duct): Hepatic portoenterostomy (Kasai procedure) is performed before the age of 2 months before development of liver cirrhosis.

B-Medical Treatment of Cholestasis:

1. Adequate calories for maintenance of good nutrition.
2. Malnutrition due to malabsorption of dietary long-chain triglyceride: Replace with dietary formula or supplements containing readily absorbed medium-chain triglycerides.
3. Large doses of fat-soluble vitamins (A, D, E and K) to correct malabsorption of these vitamins.
4. Retention of biliary constituents such as bile acids and cholesterol (itch/xanthomata): Administer choleretics such as ursodeoxycholic acid (5-10 mg/kg/day) or phenobarbital or bile acid binders (cholestyramine 8-16 g/day).

C-Liver transplantation: if ESLF occurs.

4. Liver Cirrhosis

Definition:

It implies chronic irreversible liver damage defined histologically as a diffuse hepatic process characterized by necrosis of hepatocytes and fibrosis of whatever etiology with the conversion of normal liver architecture into malfunctioning regenerating nodules. The progression of liver injury to cirrhosis may occur over weeks to years. It results in disturbances of the normal lobular and vascular pattern of the liver. It may be compensated or de compensated. Also, It may be active or in active.

Causes of cirrhosis in childhood:

I. Post-necrotic cirrhosis:

1- Post-hepatitic:

1. Viral hepatitis (B, C, D).
2. Idiopathic neonatal hepatitis.

2- Venous congestion:

- Tricuspid regurgitation/right heart failure (cardiac cirrhosis)
- Budd-Chiari syndrome
- Hepatic veno-occlusive disease

3- Toxins:

- Drug induced hepatitis: actinomycin D, methotrexate amiodarone.
- Alfatoxin.
- Chronic alcoholism.

II. Biliary cirrhosis:

- Extrahepatic biliary atresia, Intrahepatic biliary hypoplasia, Cystic fibrosis, Biliary stenosis, Familial intrahepatic cholestasis, Primary sclerosing cholangitis, Choledochal cyst.

III. Genetic or metabolic causes:

- NASH, ∝1-Antitrypsin deficiency, Wilson disease, Galactosemia, some glycogen storage diseases, hemochromatosis, Gaucher disease, Niemann-Pick disease, Sickle cell anemia, Thalassemia, etc.

IV- Cryptogenic cirrhosis

Pathology:

Regardless of etiology, in all cirrhotic patients, the triad of liver cell necrosis, regenerating nodules and fibrosis is present.

Pathophysiologic consequences of cirrhosis:

- **Alteration of hepatic blood flow: -** Portal hypertension.
- **Reduction in functional liver cell mass:**

a. Decreased synthesis: Albumin, coagulation proteins, other proteins.

b. Decreased detoxification and conjugation of: bilirubin, ammonia, methyl mercaptan, drugs and hormones.

Investigations of cirrhosis:

1. Laboratory Investigations:

- Liver function tests that may be entirely normal in a patient with cirrhosis (inactive). CBC, Urea and creatinine.

2. Imaging Investigations: ultrasound with Doppler, FibroScan, CT, MRI.

3. Upper GIT endoscopy to diagnose varices.

4. Liver biopsy.

5. Etiological investigations:

- Serological tests for viral hepatitis.
- Serum immunological tests for autoimmune chronic active hepatitis.
- Special tests for metabolic disorders: Wilson's disease, Alpha 1 anitrypsin deficiency, hemochromatosis, etc.

Treatment of cirrhosis

1. Supportive therapy:

- Provide sufficient calories, proteins, essential fatty acids, minerals, trace elements and vitamins for growth and normal activities.
- Proteins: High biological value protein. The protein is not restricted except with clinical and biochemical evidence of hepato-cellular failure.
- Vitamin supplements: Daily requirements of both water-soluble and fat-soluble vitamins should be taken.

2. Management of complications:

- Hepatic encephalopathy, Ascites, Bleeding varices, Hypersplenism.

5. PORTAL HYPERTENSION (PH)

Definition:

- PH exists when pressure in portal venous system rises above 10-12 mmHg.

Pathology:

- Increased vascular resistance caused by obstruction of portal blood flow leads to hemodynamic changes.
- Increased COP with decreased splanchnic arteriolar vasodilatation leads to increased portal inflow resulting in increased portal pressure (PH).
- Increased portal blood flow and resistance lead to formation of porto-systemic collaterals that divert portal blood flow to the systemic circulation, bypassing the liver.

Etiological classification:

Causes of PH are classified according to the anatomic location of the disease:

Pre-hepatic obstruction:

A-Portal vein occlusion:

- Thrombosis (umbilical sepsis, umbilical venous catheterization in the neonate).
- Extrinsic compression.

B-Splenic vein thrombosis:

This might be a congenital anomaly or acquired.

Hepatic obstruction:

- Cirrhosis: post-necrotic, biliary, cardiac, autoimmune, drug-induced, cryptogenic.
- Schistosomiasis.
- Congenital hepatic fibrosis.
- Veno-occlusive disease.

Post-hepatic obstruction:

- Budd-chiari syndrome.
- Right ventricular failure.
- Constrictive pericarditis.

Clinical picture:

1. Features of the underlying hepatic disease.
2. GIT bleeding: hematemesis or melena.
3. Splenomegaly with features of hypersplenism (low Hb concentration, low total white count and thrombocytopenia).
4. Liver size is normal in pre-hepatic obstruction whereas in hepatic and post-hepatic obstruction the liver may be enlarged, normal-sized or shrunken depending on the stage of the underlying disease.
5. Dilated cutaneous collateral vessels.
6. Ascites.
7. Failure to thrive due to malabosrption and porto-systemic shunts.
8. Hepatic encephalopathy due to porto-systemic shunts.

Diagnosis:

A-Non-Invasive Investigations of PH (routinely done):

- Initial Lab Investigations: full blood count, liver and renal function tests.
- Ultrasonography with Doppler: to assess liver size, echogenicity, intrahepatic bile ducts, Patency and diameter of portal vein, velocity and direction of blood flow, Extent of collaterals, splenomegaly and ascties.
- Liver stiffness measurement by ultrasound-based elastography (FibroScan) or by MRI- based elastography to predict liver fibrosis stages and the presence of varices.
- Endoscopy of upper GIT: to detect esophageal varices, gastric varices, peptic ulcers, PH gastropathy.

B-Invasive Measurements of PH (not-routinely done).

- Operative portal vein measurement.
- Percutaneous transhepatic measurement.
- Transjugular measurement.
- Hepatic vein catheterization.
- Intrasplenic measurement.

Treatment:

i) **Gastrointestinal bleeding:** it requires emergency treatment (Resuscitation of the patient followed by urgent endoscopic variceal sclerotherapy or endoscopic variceal band ligation).

ii) **Hepatic encephalopathy:** Nasogastric administration of neomycin or lactulose, I.V vitamin K, Restriction of protein intake and control of any triggering factors.

iii)**Surgical procedures in portal hypertension:**

- Porto-systemic shunts (selective or non-selective).
- Transjugular intrahepatic portosystemic shunting (TIPS).
- Liver transplantation: if ESLF occurs.

6. ASCITES

Definition:

Ascites is accumulation of fluid in the peritoneal cavity.

Etiology:

Transudate	Heart failure, Nephrotic syndrome, Liver cirrhosis, Constrictive pericarditis.
Exudate	Peritonitis, Tuberculosis, Malignancy e.g. neuroblastoma, Polyserositis.
Haemorrhagic	Trauma, Bleeding tendency, Malignancy.
Biliary	Spontaneous perforation of common bile duct, Post-operative, Congenital obstruction.
Chylous	Trauma, Malignant infiltration, Thoracic duct obstruction.

Pathogenesis of ascites in hepatic cirrhosis:

1. Two main factors in liver disease favor the development of ascites:

a. **Hypoalbuminemia:** reduced albumin synthesis lowers plasma osmotic pressure, allowing the transfer of fluid into the tissue spaces and hence into the peritoneal cavity.

b. **Intra-hepatic vascular obstruction:** leads to increased portal venous pressure.

2. The above mechanisms lead to

a. **Accumulation of fluid in peritoneal cavity (ascites),** this may lead to reduced plasma volume and so reduced glomerular filtration.

b. **This results in increased aldosterone** and retention of sodium and water leads more ascites.

c. **Increased hepatic lymph formation** due to the increase in intra-sinusoidal pressure and this adds to the ascites.

Clinical picture:

Ascites may appear insidiously or may develop suddenly when hepatocelluar function is reduced e.g. by hemorrhage, shock and infection.

The symptoms of ascites include: Abdominal distension, abdominal pain and discomfort.

Clinically ascites can be detected by the following methods:

A- Abdominal percussion in knee- chest position can detect minimal ascites, but abdominal ultrasound is easy and accurate than this discomfortable test.

B - Shifting dullness which can detect moderate ascites.

C -Transmitted thrill in cases of massive ascites.

Differential diagnosis:

Ascites should be differentiated from:

1. Gases.
2. Obesity.
3. Abdominal cysts.
4. Full urinary bladder.
5. Ascites of liver cirrhosis should be differentiated from other causes of ascites:

A - Tuberculous ascites

B - Malignant ascites:

i. There may be symptoms and localizing signs due to primary tumor.

ii-The ascetic fluid is exudates, may be sanguineous and may contain malignant cells.

C - Constrictive pericarditis:

i. Diagnostic points include the very high jugular venous pressure and the paradoxical pulse.

ii. The radiological demonstration of a calcified pericardium and characteristic ECG and echocardiographic changes.

Diagnosis:

- **Abdominal ultrasonography** to detect the degree of ascites.
- **Ascetic fluid tabbing** for chemical & cytological examination.
- **Liver function tests:** Usually show impaired levels of transaminases, Low plasma albumin.

Treatment:

1. Sodium restriction.
2. Diuretics: used cautiously because they may lead to hypovolemia. Start with spironolactone, but furosemide can be used in combination with spironolactone in severe cases.

3- IV Albumin infusion + IV Furosemide ± therapeutic paracentesis for refractory symptomatic severe cases with ascites.

7. Causes and Investigations of Hepatomegaly in Children

A- Mechanisms of Hepatomegaly and Representative Diseases	
MECHANISM	**REPRESENTATIVE DISEASES**
Inflammation/ Infections	• **Infections:** -Viral (hepatitis A, B, C, D, E, Cytomegalovirus, Ebstein-Barr virus, etc.) -Bacterial (sepsis, pyogenic liver abscess, miliary TB, Brucellosis, typhoid fever) -Parasitic (Schistosomiasis, malaria, hepatic amebiasis, hydatid cyst, visceral larva migans, Fasciola hepatica, etc.) • Toxins • Drugs • Idiopathic neonatal hepatitis • Autoimmune liver disease • Kupffer cell heperplasia
Inappropriate Storage	• Glycogen: Glycogen storage disease, diabetes mellitus, parenteral nutrition. • Lipids: Neimann-Pick disease, Gaucher disease, Wolman disease • Fat: Fatty acid oxidation defect, obesity, diabetes mellitus, parenteral nutrition, mucopolysaccharidoses • Metals: Copper: Wilson disease Iron: hemochromatosis • Abnormal proteins: Alpha-1-antitrypsin deficiency

Infiltration	• Primary neoplastic tumors Hepatoblastoma/Hepatocellular carcinoma • Primary non-neoplastic tumors Hemangioma, hemangioendothelioma, teratoma, focal nodular hyperplasia • Metastatic or disseminated tumors Leukemia, lymphoma, neuroblastoma, histiocytosis • Cysts Parasitic cyst, choledochal cyst, polycystic liver disease • Hemophagocytic syndromes. • Extramedullary hematopoiesis.
Vascular Congestion	• Suprahepatic Congestive heart failure, Restrictive pericardial disease, Suprahepatic web Hepatic vein thrombosis (Budd-Chiari syndrome) • Intrahepatic Veno-occlusive disease
Biliary Obstruction	• Cholelithiasis • Choledochal **cyst** • Biliary **atresia** • Tumors (Hepatic, Biliary, Pancreatic, Duodenal)

B- Investigations of Hepatomegaly:

I. Non-invasive Investigations:

i -Laboratory:

A- Stool & urine analysis.

B- Liver & renal function tests.

C- CBC, serum electrolytes, serum lactate & pyruvate and ABG if indicated.

D- Disease-specific markers**:** (viral markers, TORSCH screaning, sepsis workup, serology of hepatic parasites, autoimmune markers, immunological markers, screening markers for suspected metabolic disorders, tumors markers).

ii-Imaging procedures:

(Abdominal ultasound with Doppler, Abdominal CT, MRI, or MRCP, FibroScan)

II. Invasive Investigations:

- **GIT Endoscopy:** (Uppper GIT Endoscopy, Colonoscopy, Enteroscopy, ERCP, Endoscopic ultasonography, Capsule endoscopy).
- **Histopathological tissue diagnosis :** (liver biopsy, lymph node biopsy, bone marrow aspiration or biopsy) .