



4th International
Hepatology Conference
DHAKA 2016

NUHS
National University
Health System

Practical approach to liver diseases in pregnancy

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Research

Clinical Care

Education



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BODY DOUBLE



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Structure of this presentation

- The Liver in Normal Pregnancy
- Liver Diseases/Dysfunction Specific to Pregnancy
- Incidental Liver Disease during Pregnancy
- Pregnancy in patients with Chronic Liver Disease
- A Practical *Approach* to Liver Disease in Pregnancy



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The Liver in Normal Pregnancy

- Physical Examination
 - Spider naevi, Palmar erythema
 - Liver palpation difficult, but palpable liver abnormal
- Ultrasound Examination
 - Biliary tract normal
 - Fasting Gall Bladder volume increased
- Liver Function Tests
 - Serum albumin *lower*
 - Serum alkaline phosphatase 2-4 times *higher*
 - Serum GGT lower & 5'Nucleotidase slightly *higher*
 - Serum bilirubin, ALT, AST, Bile acids within *normal* range



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Liver Disease/Dysfunction Specific to Pregnancy

- Hyperemesis Gravidarum
- Severe Pre-eclampsia
- HELLP syndrome
- Intra-hepatic Cholestasis of Pregnancy (IHCP)
- Acute Fatty Liver of Pregnancy (AFLP)

(All tend to recur in subsequent pregnancies)



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Incidental Liver Disease during Pregnancy

- Viral Hepatitis
- Gallbladder disease & Cholelithiasis
- Thrombotic disease – Budd-Chiari syndrome
- Drug toxicity

Pregnancy in patients with Chronic Liver Disease

- Auto-immune hepatitis
- Cirrhosis
- Non-cirrhotic portal hypertension
- Wilson's disease
- Liver transplantation



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Hyperemesis & Liver Dysfunction

- Severe nausea & vomiting in 1st Trimester
- sometimes continues into 2nd Trimester
- Tends to recur in pregnancies
- Biochemical hyperthyroidism
- Elevated bilirubin & transaminases (ALT rises more than AST; usually not over 200 units)
- Need to exclude other causes of liver dysfunction & failure
- Otherwise supportive treatment and self limiting



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Severe Preeclampsia and HELLP syndrome

- Hypertension (BP > 140/90 mm Hg) with Proteinuria = Preeclampsia
- Hepatic dysfunction (Transaminitis) is a sign of Severe PE and indication to deliver. Bilirubin is usually normal.
- Subcapsular bleeding and stretching of liver capsule and epigastric pain is a sign of impending eclampsia.
- HELLP (Hemolysis, Elevated Liver enzymes & Low Platelets) is a variety of severe PE.



Intrahepatic cholestasis of Pregnancy (IHCP) *aka Obstetric Cholestasis (OC)*

- Presents with generalized pruritus without a rash
- 10% may have jaundice, dark urine and pale stools
- Usually in second half of pregnancy
- Elevated Transaminases &/or bile acids
- Hep C is commoner
- Increased risk of IUD after 37W (unknown cause)
- Increased risk of Preterm Labour and meconium stained amniotic fluid
- Increased risk of post-partum haemorrhage (PPH)
- 90% risk of recurrence in subsequent pregnancy



Intrahepatic cholestasis of Pregnancy (IHCP) aka *Obstetric Cholestasis (OC)*

- Ursodeoxycholic acid (UDCA) 500 mg BD (up to 2 G/day)
 - causes symptomatic improvement and reduction of AST/ALT/Bile acids
- Anti Histamines like cetirizine sometimes help with symptoms
- Vitamin K 10 mg orally daily for a week before delivery
- Dexamethasone, Cholestyramine not useful
- Close fetal monitoring
- Deliver at 38 wks



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Acute Fatty Liver of Pregnancy (AFLP)

- Usually in 3rd Trimester
- Rare (1:13000)
- Can lead to hepatic failure, encephalopathy and mortality
- Typically present with nausea, vomiting, malaise & jaundice
- Often associated pre-eclampsia
- Lab changes:
 - Elevated WBC
 - Decreased Glucose
 - Elevated Transaminases & Bilirubin
 - Elevated Uric Acid
 - Decreased Platelets
 - Elevated Ammonia
 - Prolonged INR



Acute Fatty Liver of Pregnancy (AFLP)

- Supportive treatment & stabilization
- Delivery
- Usually recovery of liver function occurs within a week following delivery
- Baby may have LCHAD (Long-chain 3-Hydroxy Acyl Co-enzyme A Dehydrogenase deficiency) and mother may be a carrier
- Risk of recurrence in next pregnancy



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Disease	Trimester			Laboratory studies		Differential diagnosis	Prognosis	
	1	2	3	PP	Aminotransferase levels (int. unit/L)			Other findings
Hyperemesis gravidarum					Mean ALT: 45 may be normal or >500	Bilirubin usually normal	Gastroenteritis, cholecystitis, hepatitis, peptic ulcer disease, pancreatitis, appendicitis, diabetic ketoacidosis, hyperthyroidism, drug toxicity	No maternal or fetal mortality; may recur with subsequent pregnancies
HELLP syndrome					AST >70, marked elevations in the setting of hepatic infarction	Platelets <100,000/mm ³ LDH >600 int. units/L	Acute fatty liver of pregnancy, gastroenteritis, hepatitis, appendicitis, cholelithiasis, immune thrombocytopenia, hemolytic uremic syndrome	Maternal mortality is low, but complication rates are high; fetal mortality may be as high as 35%; recurs in 3 to 27% of subsequent pregnancies
Intrahepatic cholestasis of pregnancy					ALT/AST are usually <500; occasionally they are >1000	Bile acid concentration elevated	Cholelithiasis, viral hepatitis, primary biliary cirrhosis, drug hepatotoxicity, urinary tract infection. Urinary tract infection or other sepsis may either cause or worsen cholestasis.	No maternal mortality; associated with premature delivery and stillbirth (fetal mortality 1 to 2%); recurs in 60 to 70% of subsequent pregnancies
Acute fatty liver of pregnancy					Modest elevations, up to 500 int. unit/L	Elevated WBC count Elevated INR Decreased platelets Decreased glucose Elevated uric acid Elevated ammonia	HELLP syndrome, drug toxicity, fulminant viral hepatitis	Maternal and fetal mortality is low if prompt stabilization and delivery; recurrence may be seen in subsequent pregnancies

Uptodate



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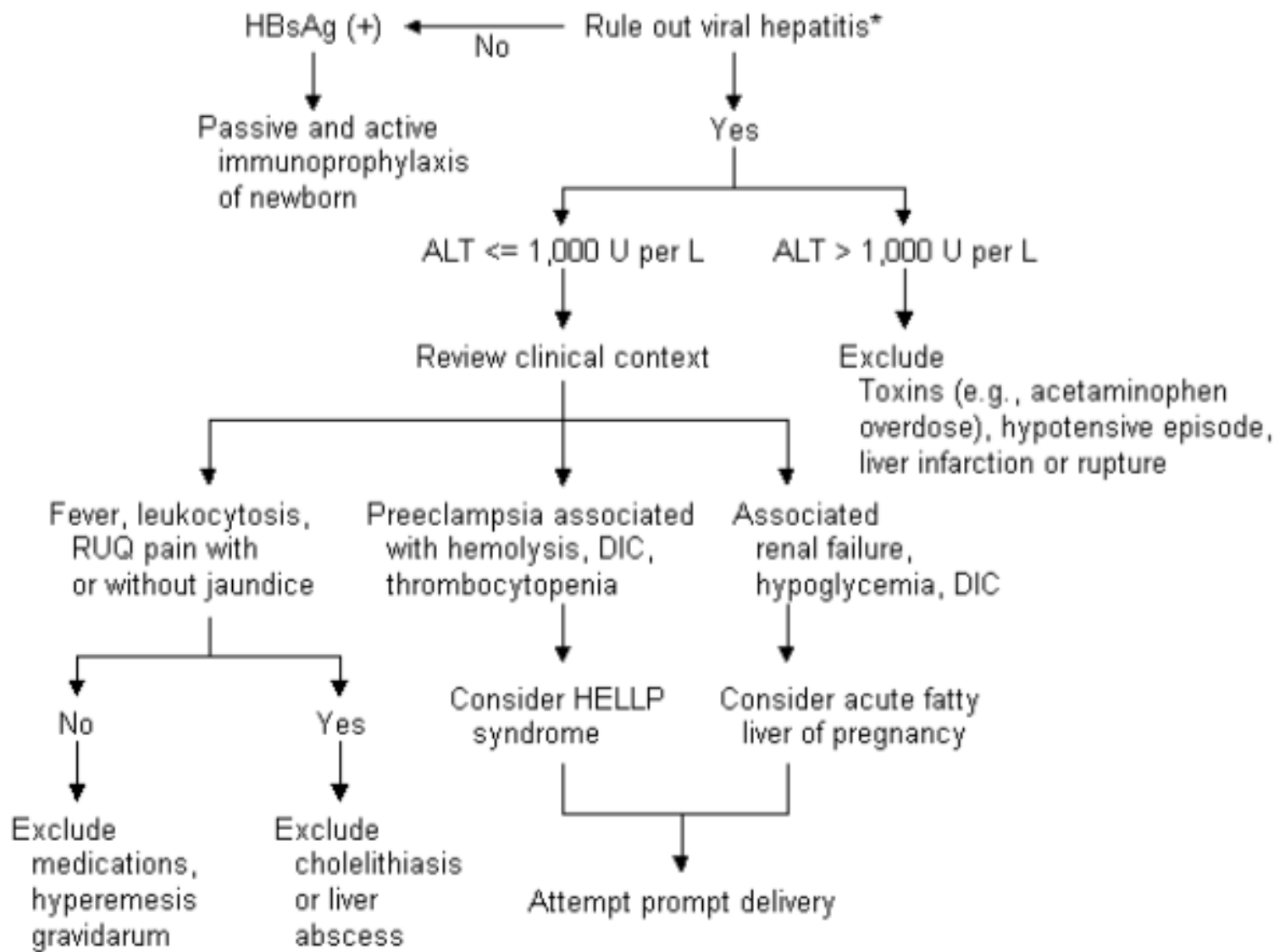
Laboratory work-up of icteric pregnant patient

- FBC
- LFT – Bilirubin, AST, ALT, GGT
- Fasting glucose
- PT/PTT
- Viral Hepatitis screen (screen for Hep A,B,C,E. HSV, CMV,EBV)
- Autoimmune Hepatitis screen
- Hepato-biliary ultrasound



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Algorithm for elevated ALT





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SCREENING

VIRAL HEPATITIS	AUTOIMMUNE HEPATITIS
Hep A IgM	Serum antinuclear antibody (ANA)
Hep B S Ag	Anti-smooth muscle antibody (ASMA)
Hep B Core Ab	Liver-kidney microsomal type 1 (LKM-1) antibody
Hep C Ab	Serum protein electrophoresis (SPEP)
Hep E IgM	Quantitative immunoglobulins
CMV IgM	
HSV IgM	
EBV IgM	



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Viral Hepatitis in Pregnancy

- Commonest cause of Jaundice in Pregnancy
- Course of most Viral Hepatitis (A, B,C,D) unaffected by pregnancy
- Hep C carriers have higher risk of IHCP
- Hep E and Disseminated HSV run a more severe course in pregnancy. Acute liver failure & Maternal mortality 10-20% in Hep E and nearly 50% in disseminated herpes simplex.



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Vertical transmission in Viral Hepatitis

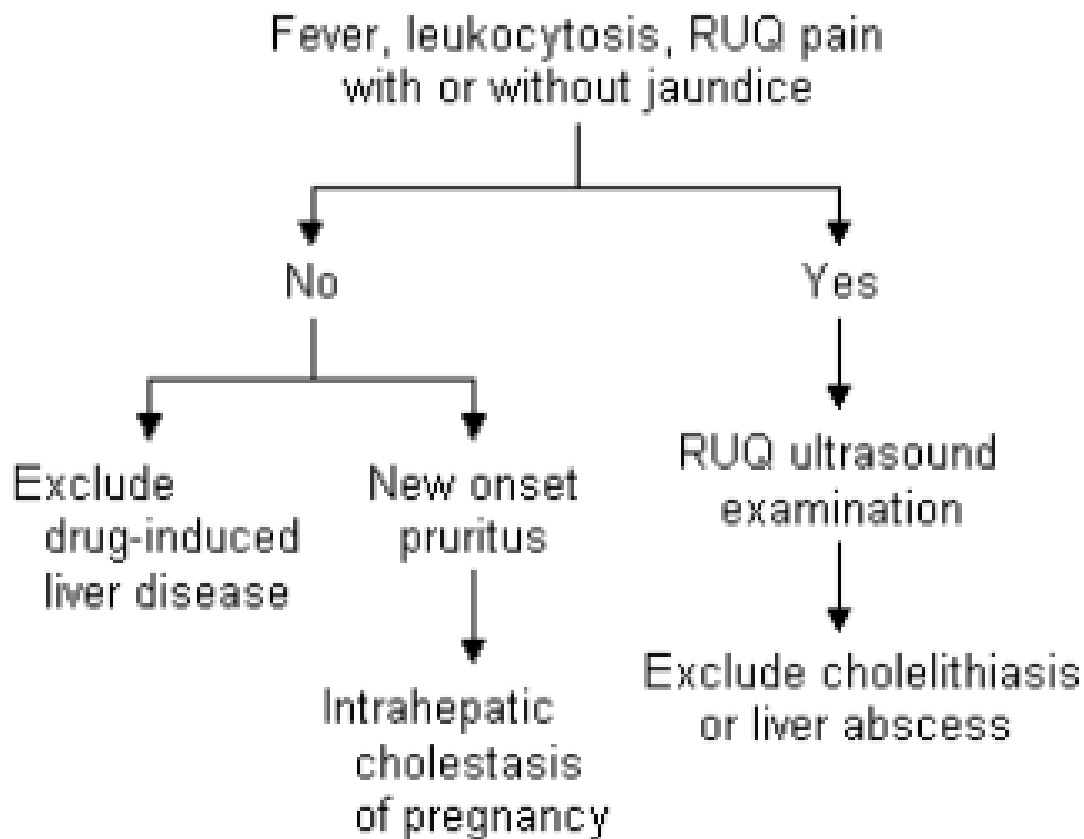
Hep A	No increased fetal risk. Transmission at birth possible but rare.	If mother has active Hep A in labor, non-specific IgG for baby.
Hep B	In acute Hep B 10% risk in 1 st TM and 90% in 3 rd TM. For chronic Hep B 90% risk if Hep e Ag positive.	Lamivudine to mother if HepB DNA load high to reduce vertical transmission. Combined HBIG and Hep B vaccine immunoprophylaxis at birth. 93% effective. BF safe.
Hep C	Transmission risk low if mother has low viral count. Risk higher if co-infection with HIV.	Mode of delivery or BF does not influence risk of transmission.
Hep E	Premature labour in 66% & vertical transmission in 33%.	Affected babies (1/3 rd) have high neonatal mortality (33%).



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Cholestasis during pregnancy

Assessed by elevated 5' nucleotidase, GGT and Bilirubin
ALP not useful unless more than 4 times elevated





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Women with Liver Transplant

- Pregnancy outcome worse if conceive within 2Y of transplant.
- Higher risk of miscarriage, CMV infection, preterm labor, preclampsia, IUGR.
- Cyclosporin, Tacrolimus, Azathioprine should not be stopped.
- Deterioration of Liver function suggests graft rejection (but could be due to IHCP or Preeclampsia).
- NIPT results may be inconclusive.



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Dhan'yabāda



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**Thank you
for your warm invitation and kind attention**

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