Liver disease during pregnancy

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Inroduction

- Recognizing and managing liver diseases during pregnancy is complex

- Preexisting ,acquired, because of the pregnancy itself

Normal physiology of pregnancy and liver disease

- Increased cardiac output by up to 30%-40% , much occurred during first trimester
- Increase portal venous flow and increased compression of the gravid uterus on iIVC
- Hormonal changes
- Increased in fibrinogen , decreased albumin
- Elevated ALP, normal aminotransferases and bilirubin

Evaluation of a pregnant patient with abnormal liver enzymes

- A new elevation of aminotransferases or bilirubin
- Viral hepatitis , autoimmune hepatitis ,alcohol-related and fatty liver disease , drug induced liver injury
- Timing
- His, ph ex , herbal ,alternatives
- A nonspecific elevation
- Normal INR and PT (however hypercoagulable state)

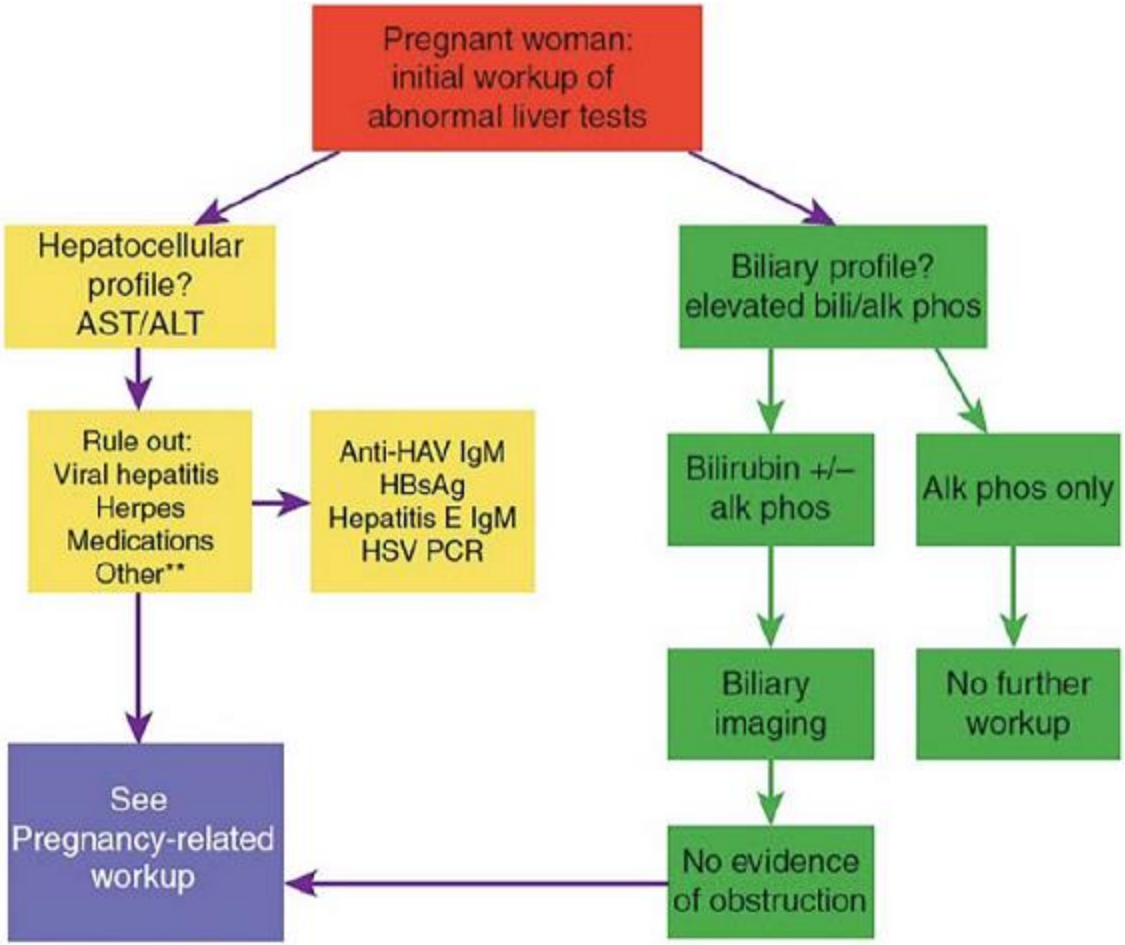

Figure 1. Evaluation of a pregnant patient with abnormal liver enzymes. Reused from Tran TT, Ahn J, Reau NS. ACG clinical guideline: Liver disease and pregnancy. Reprinted with permission from Am J Gastroenterol 2016; 111(2):176–194. doi:10.1038/ajg.2015.430. ALT, alanine transaminase; AST, aspartate transaminase; HSV, herpes simplex virus; IgM, immunoglobulin M.

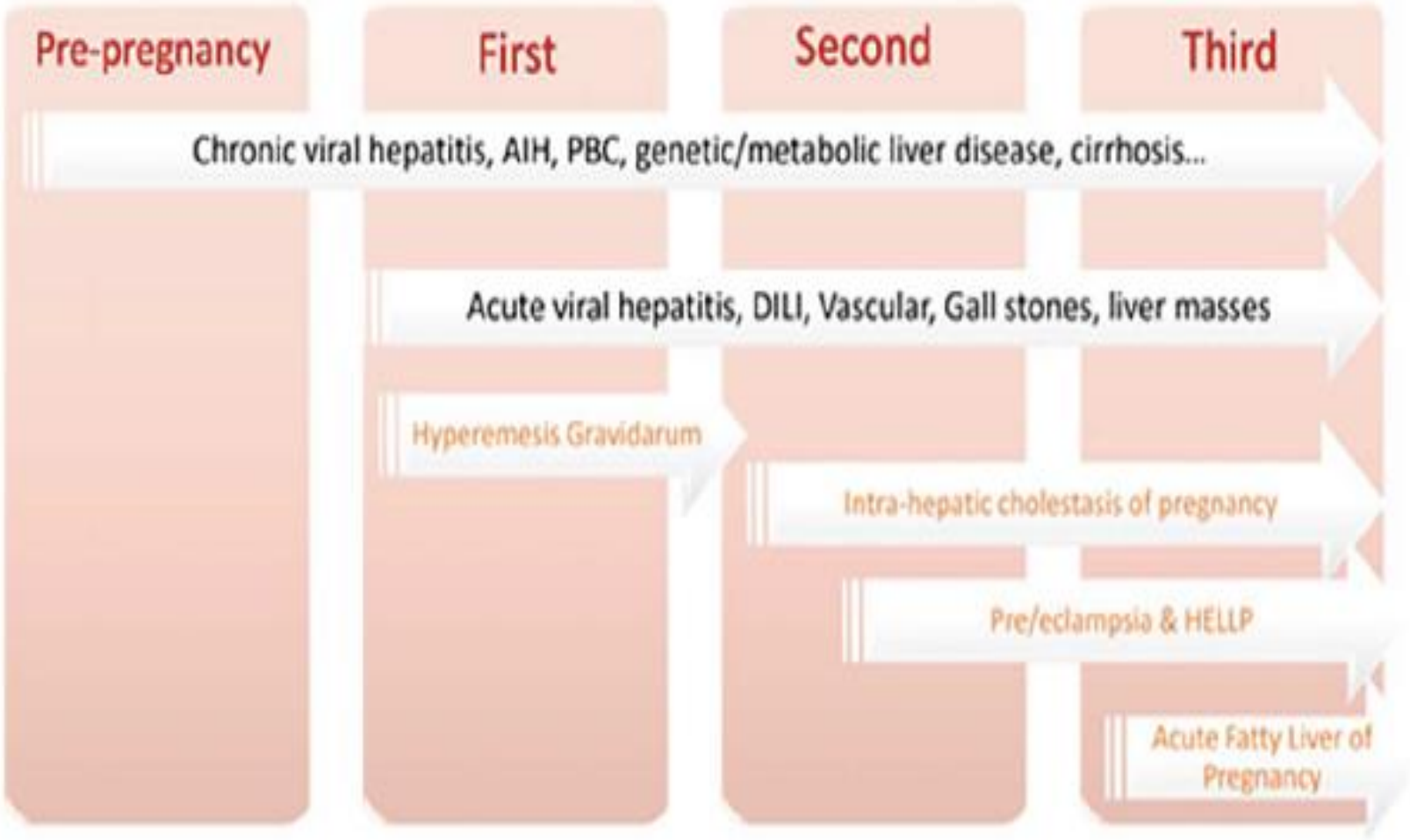

Figure 2. Liver disease unique to pregnancy—trimester-based approach. AIH, autoimmune hepatitis; DILI, drug-induced cholestasis; HELLP, hemolysis, elevated liver enzymes, and low platelets; PBC, primary biliary cirrhosis.

Liver diseases unique to pregnancy

- Clinical presentation and gestational age

First trimester

- Hyperemesis gravidarum ;mild to mod liver enzyme elevation ,jaundice and hepatic synthetic dysfunction is uncommon

- Resolves as the vomiting stops in second trimester

- Supportive , eating smaller and more frequent meals antiemetics and hydration

Second and third trimesters

- Preeclampsia an eclampsia
- New onset HTN and proteinuria after 20w

- GI consult , RUQ or epigastric pain in the setting of abnormal liver enzymes , (necroinflammatory pattern rather than cholestatic) , exclude other etiologies

- Hepatocytes necrosis , rarely hepatic failure ,subcapsular and intrahepatic hematoma

Preeclampsia an eclampsia

- A baseline imaging study
- Repeat studies
- Delivery in 37
- The only intervention to resolve acute symptoms

The HELLP syndrome

- Third trimester
- Hemolytic anemia
- Elevated liver enzymes > twice the upper limit normal
- Low platelets <100000
- Advanced maternal age , Nulliparity and multiparity
- 20% severe
- Systemic angiopathic inflammatory response

The HELLP syndrome

- Asymptomatic or nonspecific symptoms
- HTN, protenuria , 80%
- Typical laboratory abnormality
- Significant hyperbilirubinemia is uncommon
- Intrahepatic hematoma ,hemorrhages and hepatic infarction
- Ultrasound ,CT or MRI

The HELLP syndrome

- Intrahepatic hematoma , Expectant management
- Percutaneous embolization or surgery

- Hepatic infarction , transplantation

- Glucocoticorticoids and magnesium sulfate and control of the SBP

- Platelat transfusion

Acute fatty liver of pregnancy

- Uncommon
- Third trimester
- High risk of progression to acute liver failure
- Nonspecific symptoms
- Marked elevation of aminotransferases and hyperammonemia
- Twin , low maternal BMI

Acute fatty liver of pregnancy

- Swansea criteria ,6 or more
- Prompt diagnosis , early delivery, ICU care
- Progression to liver failure
- Delivery ,symptomatic care
- Liver transplantation

Table 1. Swansea criteria

Six or more criteria required in the absence of another cause	
Vomiting	
Abdominal pain	
Polydipsia/polyuria	
Encephalopathy	
Elevated bilirubin	>14 μmol/L
Hypoglycemia	<4 mmol/L
Elevated urea	>340 μmol/L
Leukocytosis	$>11 \times 10^6$ cells/L
Ascited or bright liver on ultrasound scan	
Elevated transaminases (AST or ALT)	>42 IU/L
Elevated ammonia	>47 μmol/L
Renal impairment; creatinine	>150 μmol/L
Coagulopathy; prothrombin time	>14 s or APPT >34 s
Microvesicular steatosis on liver biopsy	

ALT, alanine transaminase; APPT, activated partial thromboplastin time; AST, aspartate transaminase.

Intrahepatic cholestasis of pregnancy

- Most common liver disease associated with pregnancy
- Overall prevallance ,0.5 - 5 %
- Onset of pruritus in the second or third trimester ,often in palms and soles
- Without evidence of large bile duct obstruction

Intrahepatic cholestasis of pregnancy

- Jaundice
- Abd pain , uncommon
- Elevated ALP
- AST/ALT levels , normal or moderately elevated
- Elevated serum bile acid
- Advanced maternal age , previous episodes of IHCP ,FH

Intrahepatic cholestasis of pregnancy

- Pruritus ,second or third trimester
- Palms and soles
- Without evidence of biliary obstruction
- Pathogenesis is complex

Intrahepatic cholestasis of pregnancy

- Prematurity ,fetal distress and stillbirth
- Ursodiol (10-15 mg/kg)
- Cholestyramine
- 37 weeks
- Planned fetal delivery in 36 weeks
- Resolution and prevents fetal distress

Pregnant patients with preexisting liver disease

Viral hepatitis

- Screening , HCV Ab and HBs Ag, HBs Ab
- Vaccination
- Does not affect the mode of delivery or breastfeeding

Viral hepatitis

Viral hepatitis B

- Well tolerated
- HBV DNA
- Treatment consideration , decrease the risk of transmission
- Antiviral therapy
- AST/ALT , Cirrhosis

Viral hepatitis B

- HBIG and HBV vaccination in 12 hrs
- > 1000000 in third trimester
- Tenofovir
- Close monitoring

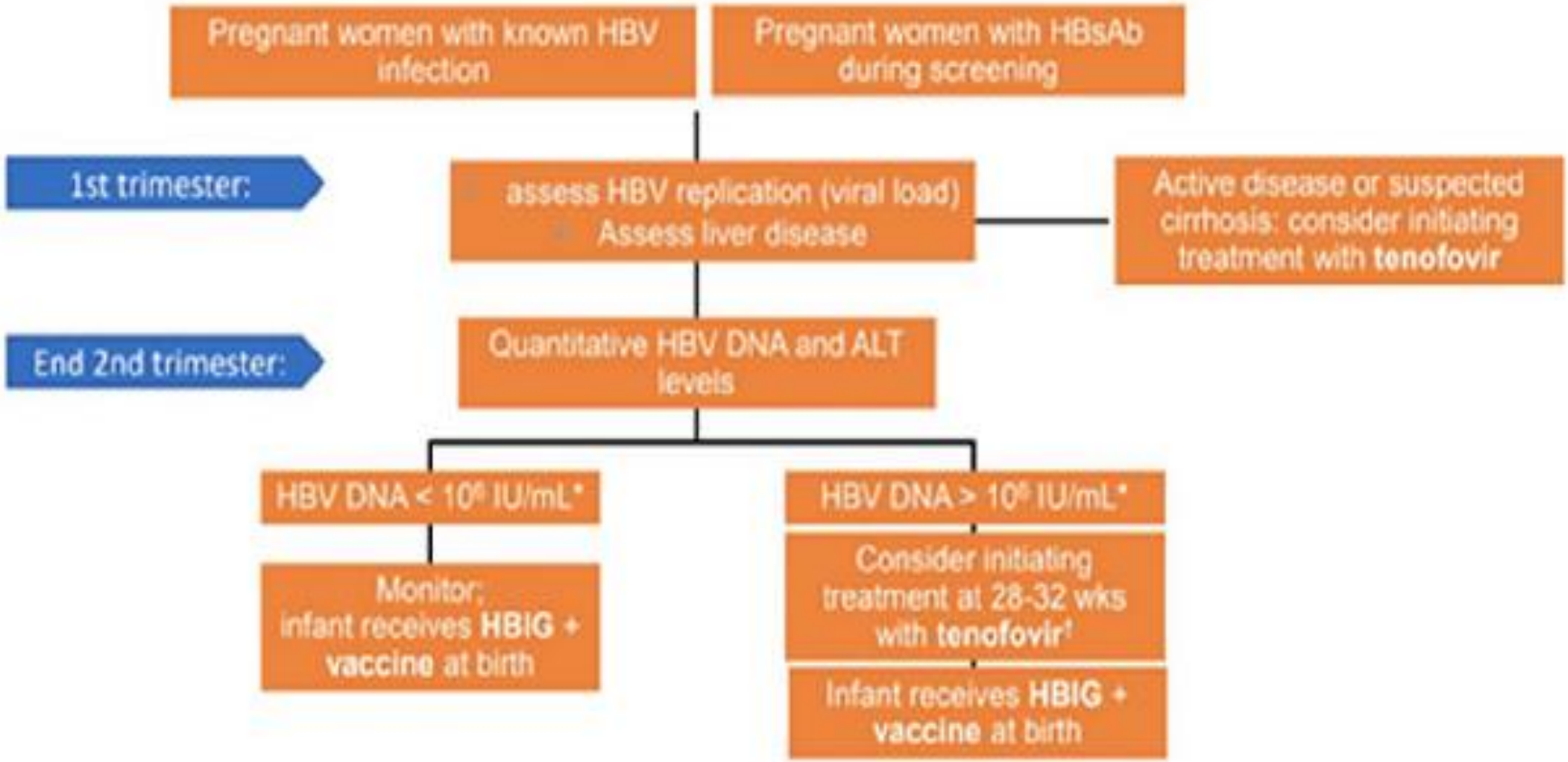

Figure 3. HBV management in patients during pregnancy. *HBV DNA from 6 to 8 $\log_{10}$ IU/mL can be considered for therapy based on physician and patient preference. †Tenofovir is preferred if treatment is expected to be >12 weeks of if treatment is expected to continue while breast-feeding. Lamivudine and Telbivudine are also safe during pregnancy but have risk of resistance with prolonged exposure. ALT, alanine transaminase; HBV, hepatitis B virus; HBsAb, hepatitis B surface antibody.

Viral hepatitis

Viral Hepatitis C

- Screening is recommended
- HCV RNA
- No effects on hepatitis C
- Higher rates of IHCP and preterm labor
- MTCT 5%
- Treatment not recommended

Viral Hepatitis C

- Mode of delivery
- HIV / HCV coinfection

Chronic nonviral liver disease

Nonalcolic fatty liver disease

- One-third
- PCOS
- GDM ,hypertensive complication ,postpartum hemorrhage ,and preterm birth

Chronic nonviral liver disease

Autoimmune hepatitis

- Usually well-controlled during pregnancy
- Highest risk of flare in 3 months after delivery
- Flare ,cirrhosis ,decompensation ,fetal loss or still birth
- Continued immune suppression at lowest dose
- Liver enzyme monitoring

Chronic nonviral liver disease

Wilson disease

- Chelating agents (reduce dose), teratogenicity
- Zinc ,no decrease ,preferred
- Avoid overchelation
- Balance to breastfeed on chelation
- Cerulop lasmin measurement for newborn

Chronic nonviral liver disease

- Benign hepatic lesions
- Hemangioma ,hepatic cysts ,FNH
- Adenoma ,special attention
- >5 cm ,risk of tumor rupture
- Resection or embolization

BEST PRACTICE RECOMMENDATIONS

- ✓ Multidisciplinary comanagement by hepatology, maternal fetal medicine, and pediatrics is recommended for any pregnant patient with liver disease.
- ✓ Any abnormalities in transaminases or bilirubin during pregnancy require further evaluation
- ✓ The key principle of management of patients with acute fatty liver of pregnancy is early delivery and treatment of acute liver failure as necessary. Newborns should be monitored for manifestations of LCHAD enzyme deficiency.
- ✓ Prompt delivery after 34–36 weeks is advised for pregnant patients with the HELLP syndrome and preeclampsia-associated liver disease.
- ✓ Patients may present with liver disease and overlapping features of preeclampsia, the HELLP syndrome, and fatty liver of pregnancy.
- ✓ Patients with ICP should have weekly bile acid testing. Total serum bile acids greater than 100 μmol/L are associated with poor fetal prognosis in cholestasis of pregnancy.
- ✓ HBsAg, HBsAb, and HCV-Ab should be tested during the first trimester for all pregnant patients. A viral load (HBV DNA or HCV RNA) should be performed in any patient who is positive for HCV-Ab or HBsAg.
- ✓ HCV during pregnancy is associated with higher rates of ICP. If pruritus occurs, bile acids should be tested.
- ✓ Invasive procedures should be deferred if possible, and mode of delivery should not be affected by viral hepatitis. Neither HBV nor HCV are contraindicated during lactation.
- ✓ Chelation therapy for WD should be reduced during pregnancy; however, there is no adjustment needed for zinc.
- ✓ AIH flares are associated with a higher risk for maternal/fetal complications. Disease flares are less common in patients who have been in remission on stable immune suppression for a year before conceptions. Immune suppression should be continued during pregnancy wth the exception of mycophenolate mofetil, which is contraindicated.
- ✓ There is an increased risk of liver decompensation and portal hypertensive complications, especially variceal bleeding, in pregnant patients with cirrhosis.
- ✓ Management of liver-related complications in pregnancy follows typical societal guidelines in place for nonpregnant patients with cirrhosis.
- ✓ Although fertility rates are decreased in advanced cirrhosis, premenopausal patients should be counseled on the risks of pregnancy and for the need of involving high-risk obstetricians and maternal fetal medicine specialists as members of their multidisciplinary team.