Chapter 104
Approach to Liver Dysfunction in Pregnancy in the ICU

104.1 Introduction

Liver dysfunction during pregnancy is a challenging clinical scenario with a wide range of potential causes, varying in severity and urgency. It affects approximately 3% of pregnancies in developed countries, highlighting its clinical significance. Early recognition and appropriate management are critical to minimizing maternal and fetal morbidity and mortality. Management often requires a multidisciplinary approach involving hepatologists, obstetricians, and neonatologists to optimize outcomes for both mother and child [1, 2].

Pregnancy-specific liver disorders include hyperemesis gravidarum (HG), intrahepatic cholestasis of pregnancy (ICP), HELLP syndrome, and acute fatty liver of pregnancy (AFLP). In addition, non-pregnancy-specific causes such as viral hepatitis, autoimmune hepatitis, and biliary obstruction may mimic or exacerbate pregnancy-related liver dysfunction [Ref: Algorithm 104.1].

104.2 Normal Physiological Changes in Pregnancy

Understanding normal physiological changes in liver function tests during pregnancy is essential to differentiate between physiological alterations and pathological conditions.

- Serum Albumin: Decreased serum albumin levels occur due to hemodilution and increased plasma volume.
- Alkaline Phosphatase (ALP): ALP levels increase significantly because of placental production, which can elevate levels up to two to four times the normal upper limit.

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- Aminotransferases (AST/ALT) and Bilirubin: Generally, remain within normal limits during pregnancy. Any elevation should prompt further investigation as they may indicate underlying pathology [3].

104.3 Initial Assessment

Clinical Symptoms

Presenting symptoms often include nausea, vomiting, jaundice, pruritus, abdominal pain, and fatigue. These symptoms may overlap with normal pregnancy physiology or signal significant pathology.

Initial Laboratory Tests

- Liver Function Tests (LFTs): ALT, AST, bilirubin, ALP
- Coagulation Profile: To assess synthetic liver function
- Complete Blood Count (CBC): To identify associated hematologic abnormalities like anemia or thrombocytopenia [4]

104.4 Timing of Symptoms

Determining the gestational age and timing of symptoms can provide clues about the etiology:

- First Trimester Symptoms: Often linked to hyperemesis gravidarum
- Late Second/Third Trimester Symptoms: Consider ICP, HELLP syndrome, or AFLP
- Postpartum Symptoms: Evaluate for chronic liver disease, genetic predispositions, or autoimmune conditions [5]

104.5 Specific Disorders by Presentation

A. First Trimester: Hyperemesis Gravidarum (HG)

Key Features

- Persistent Nausea and Vomiting: With associated weight loss and dehydration
- LFTs: Elevated ALT > AST with mild jaundice
- Transient Hyperthyroidism: Occurs in up to 60% of cases due to high levels of hCG stimulating the thyroid

Action

- Supportive Care:
- IV Fluids: Rehydration is essential.

- Antiemetics: Medications like ondansetron and metoclopramide can be used to control nausea and vomiting. However, European medicines agency does not allow use of ondansetron in the first trimester due to risk of newborns with defects such as cleft palate and cardiac septal defects (although <1%). Vitamin B6/Pyridoxine and Doxylamine (Antihistamine/H1 antagonist) combination can be used to reduce nausea during the first trimester of pregnancy.
- Nutritional Support: In severe cases, enteral or parenteral nutrition may be necessary.
- Rule Out Other Causes: If symptoms are atypical or severe, consider other diagnoses.

B. Pruritus and Hallmark Symptoms: Intrahepatic Cholestasis of Pregnancy (ICP)

Key Features

- Intense Pruritus: Especially on the palms and soles, without rash.
- Elevated Bile Acids: Levels are typically elevated (>10 μmol/L).
- Mild AST/ALT Elevation.
  Action
- Treatment:
- Ursodeoxycholic Acid (UDCA): To reduce bile acids and alleviate symptoms.
- Hydroxyzine (25 mg/d) or an aqueous cream with 1% menthol may be used to alleviate pruritus.
- Administration of *S*-adenosyl methionine in combination with ursodeoxycholic acid may increase its benefit.
- Monitoring:
- Regular Bile Acid Levels: Close monitoring is essential.
- Delivery Timing:
- Early Delivery Consideration: If bile acid levels exceed 40 μmol/L, consider early delivery after 37 weeks (no later than 38 weeks) to reduce the risk of stillbirth.
- Urgent Action: Bile acid levels ≥100 μmol/L may necessitate delivery as early as 34–36 weeks.
- Genetic Testing:
- ABCB11 and ABCB4 Mutations: In severe or recurrent cases, genetic testing may help identify mutations associated with bile salt transporters [6].

C. Hypertension or Severe Symptoms: HELLP Syndrome

Key Features

- Majority present in the third trimester (28–36 weeks)
- Hemolysis:
- Peripheral Smear: Schistocytes, indicating microangiopathic hemolytic anemia
- Low Haptoglobin: Due to hemolysis
- Elevated Liver Enzymes:
- AST/ALT: Elevated (>70 IU/L) is significant.
- Low Platelets:

- Thrombocytopenia: Platelet counts <100,000/mm^3.
  Action
- Immediate Stabilization:
- Magnesium Sulfate: For seizure prophylaxis if there is a risk of eclampsia.
- Blood Pressure Control: Using antihypertensive agents like labetalol or hydralazine.
- Corticosteroids:
- Role in Management: May improve maternal platelet counts and hepatic function, although their efficacy is still under investigation.
- Expedite Delivery:
- Definitive Treatment: Delivery of the fetus is the only cure and should be considered once the maternal condition is stabilized, regardless of gestational age.
  Complications
- Intra-parenchymal hemorrhage
- Liver infarction
- Subcapsular hematoma
- Hepatic rupture
- Hepatic failure

D. Acute Fatty Liver of Pregnancy (AFLP)

Key Features

- Symptoms:
- Nausea, vomiting, abdominal pain, and jaundice.
- Hypoglycemia: Due to impaired gluconeogenesis. It indicates a poor prognosis.
- Coagulopathy: Elevated PT/INR.
- Hyperbilirubinemia: Usually not >5 mg/dL
- Transaminitis: AST and ALT are elevated to around 300–500 times (lower than acute viral hepatitis levels)
- Imaging:
- Ultrasound or MRI: May reveal fatty infiltration of the liver.
  Swansea diagnostic criteria
  Six or more of the following without any alternative explanation:

1. Vomiting
2. Abdominal pain
3. Polydipsia/polyuria
4. Encephalopathy
5. High bilirubin (>14 mg/dl)
6. Hypoglycemia (< 70 mg/dl)
7. High uric acid (>340 μmol/L)
8. Leucocytosis (>11 × 10^6/L)
9. Ascites or bright liver on ultrasound
10. High AST/ALT (>42 IU/L)
11. High ammonia (>47 μmol/L)
12. High ammonia (>47 μmol/L)

13. Renal impairment (creatinine >150 μmol/L)
14. High ammonia (>47 μmol/L)
15. Coagulopathy (PT >14 s or aPTT>34 s)
16. Microvesicular steatosis on liver biopsy

Action

- Immediate Stabilization:
- IV Glucose: To correct hypoglycemia
- Correction of Coagulopathy: Using plasma products as needed
- Supportive Care: Intensive monitoring in a high-dependency unit
- Urgent Delivery:
- Definitive Treatment: Prompt delivery is necessary to prevent further maternal and fetal complications.
- Long-Term Follow-Up:
- Mitochondrial Dysfunction: AFLP is associated with defects in mitochondrial fatty acid oxidation, particularly LCHAD deficiency. Both mother and child may require genetic counseling and long-term monitoring.

4. Nonspecific Liver Abnormalities

If no clear etiology is identified, assess for conditions unrelated to pregnancy:

- Viral Hepatitis:
- Serologies: For HBV, HCV, HAV, HEV
- Autoimmune Hepatitis:
- Autoantibodies: ANA, SMA, anti-LKM1
- IgG Levels: May be elevated
- Biliary Obstruction:
- Ultrasound: To evaluate for gallstones or cholestasis
- Other Conditions:
- Budd-Chiari Syndrome: Hepatic vein thrombosis presenting with abdominal pain and hepatomegaly
- Autoimmune Liver Diseases: Such as primary biliary cholangitis
- Noninvasive Assessment:
- Elastography: Can assess liver fibrosis or steatosis safely during pregnancy Action
- Treat Underlying Condition:
- Antiviral Therapy: For viral hepatitis, considering pregnancy safety profiles
- Immunosuppressants: For autoimmune hepatitis, balancing maternal benefits and fetal risks
- Interventional Procedures: For biliary obstruction, such as ERCP if necessary

5. Postpartum and Chronic Liver Disease

Persistent symptoms beyond delivery may signal chronic liver disease or an underlying genetic predisposition:

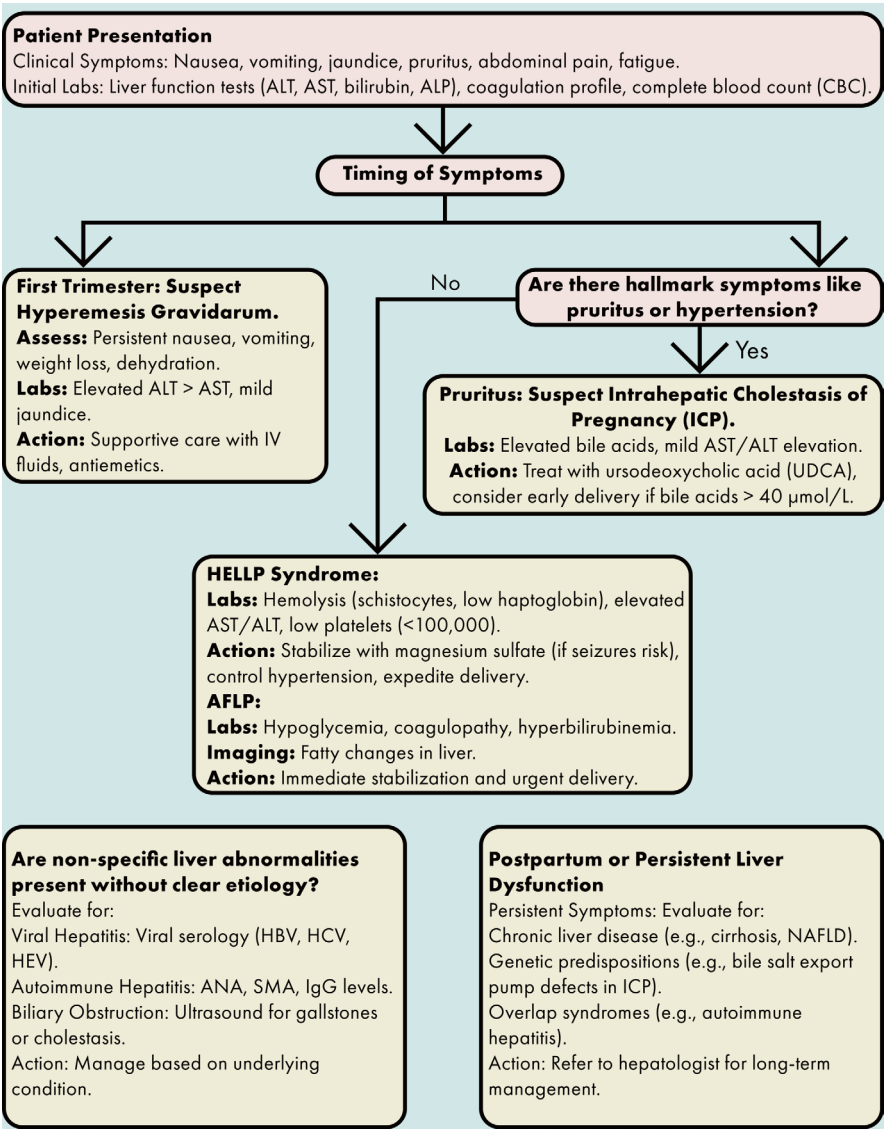
- Conditions to Consider:
- Nonalcoholic Fatty Liver Disease (NAFLD)

- Autoimmune Hepatitis
- Chronic Viral Hepatitis
- Risk of Future Liver Disease:
- ICP: Women with a history of ICP have a higher risk of developing gallstones, hepatitis C, or NAFLD.
  Action
- Long-Term Follow-Up:
- Hepatology Referral: For ongoing management and monitoring
- Lifestyle Modifications: Diet and exercise recommendations
- Genetic Counseling: For conditions like AFLP or recurrent ICP

104.6 Conclusion

The management of liver dysfunction in pregnancy requires a systematic approach grounded in gestational age, symptomatology, and laboratory findings. Understanding normal physiological changes is crucial to differentiate between pathological and physiological alterations. Early identification of pregnancy-specific conditions such as hyperemesis gravidarum, ICP, HELLP syndrome, and AFLP is essential for optimal outcomes. A multidisciplinary team involving hepatologists, obstetricians, and neonatologists can provide comprehensive care. Postpartum follow-up is equally important to address persistent or chronic liver dysfunction and to mitigate future risks.

Algorithm 104.1: Approach to liver dysfunction in pregnancy in the ICU



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