Liver Failure in Pregnancy

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KEYWORDS

• Pregnancy • Liver failure • Acute fatty liver of pregnancy • HELLP syndrome
• Viral infections

KEY POINTS

- Acute liver failure in pregnancy should be evaluated for both pregnancy-related and non–pregnancy-related causes.
- Acute fatty liver of pregnancy is rare but has a high maternal and fetal mortality rate, so acute liver failure in pregnancy should include evaluation for this disorder.
- HELLP (hemolysis, elevated liver enzymes, low platelet) syndrome occurs in less than 1% of all pregnancies but may be seen in up to 20% of pregnancies complicated by preeclampsia, and can lead to acute liver failure especially with associated liver hematomas or liver rupture.
- Therapy should be similar to that for the nonpregnant patient, and no life-saving intervention should be withheld from a patient with acute liver failure in pregnancy.

INTRODUCTION

Acute liver failure (ALF), also known as fulminant hepatic failure, is an uncommon but life-threatening condition[1] caused by an acute hepatic insult or injury with subsequent development of encephalopathy and coagulopathy.[1–3] The underlying hepatic cell necrosis, apoptosis, and inflammatory response may precipitate multiorgan failure.[4] ALF can further be broken down into hyperacute (0–1 weeks), acute (1–4 weeks), and subacute (4–12 weeks) phases according to the onset of symptoms and development of encephalopathy.[1,5] Although severe liver disease and ALF are rare, there is still an estimated worldwide incidence of 1 to 10 cases per million persons per year.[1,2] Survival rates have increased in the last decade because of improved understanding of the underlying disease processes and advances in critical care. Although ALF in pregnancy is extremely rare, the outcomes, both maternal and fetal, can be devastating. It is estimated that liver disease occurs in approximately 3% of pregnancies, although the true incidence of ALF in pregnancy is unknown. Most often, pregnancy-related diseases

Authorship Disclosures: None.
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Crit Care Clin 32 (2016) 61–72
http://dx.doi.org/10.1016/j.ccc.2015.08.005 criticalcare.theclinics.com
0749-0704/16/$ – see front matter

such as acute fatty liver of pregnancy (AFLP) and hemolysis, elevated liver enzymes, and low platelet (HELLP) syndrome are the origin of liver failure in pregnancy.

This review provides an overview of the normal liver changes that occur during pregnancy, and describes the most common conditions of ALF and general management strategies of ALF during pregnancy. Preeclampsia and eclampsia are discussed in detail in separate reviews.

NORMAL LIVER FUNCTION DURING PREGNANCY

Despite increases in cardiac output, blood flow to the liver remains essentially unchanged (approximately 25%–33% of cardiac output) during pregnancy.[6,7] The liver may be slightly elevated within the abdomen with increasing gestation, owing to displacement by the enlarging uterus.[8] However, hepatomegaly is abnormal and should prompt an immediate evaluation of underlying liver disease. Liver enzymes including alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT), and bilirubin remain normal or may decrease about 20% in pregnancy compared with the nonpregnant patient.[6,7] Alkaline phosphatase (ALP) increases with advancing gestation as a result of placental production, and high levels should not be considered abnormal. Total protein decreases during pregnancy, primarily because of a decrease in serum albumin. Increased levels of estrogen cause an increase in fibrinogen and other clotting factors (factors VII, VIII, IX, and X).[9] Ceruloplasmin and transferrin are also elevated during pregnancy.

Suspicions for a pathologic process should be raised with elevations in liver markers during pregnancy. In general, elevations in ALT, a more specific liver marker, and AST are caused by hepatocyte necrosis after injury and enzyme release into the circulation.[6] However, while minor elevations may suggest liver disease, slight elevations (less than 1.5 times the upper limit of normal) in ALT and AST may also represent normal distribution.[6] These values are also known to be higher in obese individuals and a small number of people with a defect in enzyme clearance.

PREGNANCY-RELATED CAUSES OF LIVER FAILURE

Acute Fatty Liver of Pregnancy

AFLP occurs in 1 of 7000 to 16,000 pregnancies, primarily in the third trimester (**Table 1**).[7,10] The incidence is higher in primigravid women, multiple gestations, and pregnancies with a male fetus. The exact pathophysiology is unknown. It is thought that AFLP is caused by microvesicular fatty infiltration of the hepatocytes.[10] More specifically, recent data suggest the defects in long-chain fatty acid oxidation attributable to a deficiency in the enzyme long-chain 3-hydroxyacyl coenzyme A dehydrogenase (LCHAD) in fetal mitochondria result in accumulation of fatty acids in the maternal circulation and hepatocytes.[11,12] This accumulation results in hepatotoxicity and eventually leads to liver failure. Though rare, the maternal and neonatal mortality rates are high, up to 18% and 55%, respectively.[10] Sixteen cases of AFLP were identified in a 10-year review from 3 tertiary care centers.[10] The majority, 69%, of patients developed AFLP during pregnancy, with the remaining cases identified within 4 postpartum days. In this review, 12.5% of the patients died and there were 3 fetal deaths. Pereira and colleagues[13] found a similar mortality rate in their 10-year single-institution review. In a large retrospective study from the Netherlands, the maternal mortality ratio from AFLP was 0.13 per 100,000 births, and the incidence of severe maternal morbidity (including admission to intensive care unit, uterine rupture, eclampsia/HELLP syndrome with liver hematoma, and hemorrhage requiring transfusion) was 3.2 per 100,000 deliveries.[14]