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Acute Fatty Liver in Pregnancy

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Abstract

Acute fatty liver in pregnancy (AFLP) is a rare, life-threatening condition that typically occurs in the third trimester, characterized by fat accumulation in the liver. It is associated with high maternal and fetal morbidity, although mortality rates have decreased with improved obstetric care. AFLP's exact cause remains unclear, though it is linked to impaired fatty acid metabolism in the liver. Key risk factors include multiple pregnancies, male fetuses, and metabolic disorders. The condition presents with non-specific symptoms like nausea, jaundice, and abdominal pain, with progression to liver failure and encephalopathy in severe cases. Early diagnosis is critical, and the Swansea Criteria have proven useful. Management focuses on early delivery and supportive care, with cesarean section preferred due to the risk of fetal distress. Liver transplantation may be necessary for severe cases. While maternal and fetal survival rates have improved, the condition still poses significant challenges, emphasizing the need for prompt diagnosis and treatment.

Introduction

Acute fatty liver in pregnancy (AFLP) is a rare but potentially fatal emergency affecting both the mother and the fetus. This serious condition predominantly arises in the third trimester and is marked by the accumulation of fat in the liver, potentially resulting in liver failure and encephalopathy (Ademiluyi et al., 2021; Ibdah, 2006). Its occurrence is approximately one in every 4,000 to 20,000 pregnancies (White et al., 2024). The maternal and fetal death rates have declined, reaching approximately 20% in certain hospitals within developing nations and below 10% in developed nations (Pribadi et al., 2015).

The precise cause of acute fatty liver during pregnancy is not yet fully understood. Molecular research progress indicates that the condition results from impaired beta-oxidation of fatty acids in liver cell mitochondria. This impairment triggers symptoms such as jaundice, coagulopathy, metabolic acidosis, and encephalopathy (Pribadi et al., 2015). Modern obstetric care has enabled a reduction in maternal and fetal mortality rates. The introduction of the Swansea diagnostic criteria, advancements in imaging technology, and liver biopsy support have enhanced treatment strategies for patients with suspected acute fatty liver during pregnancy. The serious outcomes of this condition highlight the critical need for swift diagnosis and treatment. At present, the main approach advised is pregnancy termination along with supportive care for the mother and infant (Liu et al., 2017). This paper will cover key aspects of acute fatty liver in pregnancy, including its definition, epidemiology, risk factors, etiopathogenesis, clinical manifestations, diagnosis, complications, and management. It will

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highlight the importance of prompt diagnosis and treatment, focusing on pregnancy termination and supportive care for both mother and baby.

Definition

Acute fatty liver during pregnancy, also known as acute liver failure of pregnancy (AFLP), was initially described by Tarnier in 1857 as microvesicular fat accumulation in the liver (Hammoud & Ibdah, 2014; Montufar et al., 2021; Pribadi et al., 2015; White et al., 2024). Acute fatty liver during pregnancy typically occurs in the third trimester and is a life-threatening emergency for both the mother and fetus due to its swift progression to coma and potential death (Naoum et al., 2019; Zhong et al., 2020). Women with acute fatty liver in pregnancy frequently need intensive treatment, such as blood transfusions, dialysis, and in some cases, orthotopic liver transplantation (Liu et al., 2017). Acute fatty liver during pregnancy may cause coagulopathy, electrolyte imbalances, and dysfunction in multiple organ systems (Naoum et al., 2019).

Epidemiology

Acute fatty liver in pregnancy is an infrequent condition, with recent studies indicating an incidence of one in every 7,000 to 15,000 births. It is more frequently observed in first-time mothers carrying male fetuses and those with multiple pregnancies (Hammoud & Ibdah, 2014; Liu et al., 2017; Pribadi et al., 2019). A study on the Caucasian population in Minnesota found the incidence of AFLP to be 1 in 15,000, which is rarer than preeclampsia (1 in 15,000) and HELLP syndrome (1 in 15,000) (Ibdah, 2006). No notable ethnic or geographic variations have been found in the severity or incidence of acute fatty liver during pregnancy. However, epidemiological data is limited to certain populations. The condition most commonly occurs in the third trimester, though some cases have been reported in the second trimester (Montufar et al., 2021). Research conducted at Hasan Sadikin Hospital in Bandung, Indonesia, in 2014 found the prevalence of AFLP from 2010 to 2013 to be 1 in 1,538 births (Pribadi et al., 2019).

Prior to 1970, the maternal and fetal mortality rates in acute fatty liver during pregnancy were as high as 75% and 80%. However, more recent research has shown a significant reduction, with mortality rates now ranging from 8% to 25% (Pribadi et al., 2015). Maternal mortality has decreased to 4% in recent years due to quicker diagnosis and immediate delivery (Hadi & Kupec, 2023). The improved outcomes in cases of acute fatty liver of pregnancy can be attributed to several factors, including the ability to identify less severe cases, timely intervention, and proactive management of potential complications. Early diagnosis and immediate initiation of labor and delivery upon suspicion of AFLP have been shown to significantly reduce the risks of both maternal and fetal mortality. These strategies emphasize the importance of swift action and comprehensive care to enhance survival rates and minimize adverse effects (Naoum et al., 2019). A severe complication that may arise is significant coagulopathy. Following childbirth, coagulation abnormalities typically resolve within one to two days, with liver and kidney function recovering shortly after. This report outlines expected recovery timelines and management approaches for frequently encountered complications. Implementing these strategies has contributed to a reduction in mortality rates from approximately 80% to 10% (Nelson et al., 2021).

Prompt and precise diagnosis, along with timely pregnancy termination and comprehensive multidisciplinary supportive care, play a vital role in managing patients with AFLP (Meng et al., 2021; Qazi et al., 2022; Wang et al., 2020) The method of delivery is determined by maternal and fetal condition, gestational age, fetal position, and the likelihood of successful labor induction (Varlas et al., 2021). If a timely delivery cannot be achieved, a cesarean section is necessary. In recent years, cesarean delivery has been preferred due to its association with improved fetal outcomes and is considered the safest option (Wang et al., 2020). It has shown that cesarean section can reduce maternal mortality by 48% and perinatal mortality by 44%

compared to vaginal delivery. Timely delivery using the safest approach in patients with AFLP plays a crucial role in reducing maternal and fetal mortality and morbidity. This is particularly important when additional complications are present, such as renal dysfunction, diabetes insipidus, coagulopathy, and non-reassuring fetal status, as these conditions can further increase the risks associated with delayed intervention. Therefore, ensuring prompt delivery is essential to improving outcomes (Wang et al., 2020). In addition to the factors mentioned earlier, early screening and comprehensive supportive care play a vital role in minimizing maternal and fetal morbidity and mortality, ensuring better outcomes through timely intervention and appropriate management (Subono & Hikmah, 2024).

Studies have shown that if the fetus is delivered within a week of disease onset, 100% of AFLP patients can survive, whereas if delivery happens more than two weeks after onset, 30% of patients may not survive (Zhong et al., 2020). It is well understood that early diagnosis and prompt initial management, including timely delivery, are crucial treatment strategies for AFLP patients. This is because fulminant liver failure may not be reversible. Research has indicated that if delivery occurs within a week of diagnosis, patient outcomes may improve (Li et al., 2023). A study has shown that prenatal nausea, prolonged prothrombin time (PT), and elevated serum creatinine (Cr) are independent risk factors for maternal mortality in patients with AFLP. A prolonged PT indicates impaired blood clotting, while elevated Cr reflects reduced kidney function, both of which can worsen the prognosis (Meng et al., 2021). Thrombocytopenia may be a risk factor for maternal mortality in AFLP, though further validation through larger-sample studies is necessary. Meanwhile, transaminase levels have not been widely recognized as significant in most liver disease models. However, serum total bilirubin (TBIL) and international normalized ratio (INR) have been identified as reliable indicators for predicting short-term mortality in pregnancy-related liver disease, with follow-up extending up to three months postpartum or until death (Murali et al., 2014).

The fetal mortality rate in infants born to mothers with AFLP ranges from 10% to 20%, with the majority of cases leading to stillbirth. Fetal complications include acidosis and prematurity (Naoum et al., 2019). The mortality rates for both the mother and fetus are lower in cesarean deliveries than in those who undergo spontaneous labor (Pribadi et al., 2019). Fetal death was primarily observed in cases where the gestational age was 36 weeks or less, while no fatalities occurred beyond this gestational period. This suggests that a gestational age of less than 36 weeks may be a potential risk factor for fetal mortality (Samuel et al., 2018). With increased awareness of AFLP and advancements in prenatal care, the condition is now detected earlier. As a result, the mortality rate has significantly declined to approximately 2%, largely due to early diagnosis, timely delivery, and improved supportive care. However, despite better early detection, the ability to recognize and manage AFLP still varies across hospitals. Standardizing clinical management practices is essential to enhancing maternal and neonatal outcomes (Li et al., 2021).

With widely accepted standardized criteria for diagnosing AFLP, numerous studies have provided insights into maternal and perinatal outcomes. Despite advancements in early detection and management, AFLP remains a serious condition with life-threatening complications. Across all previous research, three primary causes of maternal morbidity and mortality have been consistently identified which were hemorrhage, liver failure, and acute kidney injury. Hemorrhage, often due to coagulation abnormalities such as disseminated intravascular coagulation (DIC), significantly increases the risk of severe bleeding, particularly postpartum, necessitating intensive transfusion support and surgical interventions. Liver failure, a hallmark of AFLP progression, leads to hepatic dysfunction, jaundice, encephalopathy, and multi-organ failure, making it a major contributor to maternal mortality. Additionally, acute kidney injury (AKI) commonly occurs due to hypovolemia, hypotension, or sepsis, further complicating patient management and sometimes requiring renal replacement

therapy .(Chang et al., 2020; Cheng et al., 2014; Vigil-de Gracia & Montufar-Rueda, 2011; Zhang et al., 2016). The long-term outcomes for the fetus largely depend on the timely identification of fatty acid oxidation defects. Early detection allows for dietary and lifestyle adjustments that can help reduce morbidity and mortality. Preventing prolonged fasting is essential to avoid reliance on fatty acid oxidation for energy. Nutritional management should include a balanced diet with a steady intake of carbohydrates, sufficient medium-chain triglycerides (MCTs), and a reduced intake of long-chain fatty acids to support metabolic stability and overall health (White et al., 2024).

Risk Factors

Factors linked to the occurrence of acute fatty liver in pregnancy include fetal fatty acid oxidation defects, multiple pregnancies, and male fetuses. Other minor contributing factors include metabolic disorders, obesity, and liver conditions like intrahepatic cholestasis during pregnancy. Some studies also indicate an elevated risk of AFLP in patients with a BMI below 20. Though preeclampsia is associated with the condition, the exact causal link is not yet definitive (Liu et al., 2017; Montufar et al., 2021; Naoum et al., 2019; White et al., 2024). A clinical review identified multigravida and metabolic conditions like type 2 diabetes as risk factors for acute fatty liver in pregnancy. AFLP is diagnosed in 20-40% of preeclampsia cases, with or without organ damage such as thrombocytopenia, liver and kidney dysfunction, pulmonary edema, and visual disturbances. About 20% of women with AFLP also have HELLP syndrome, and there is a rarer link with intrahepatic cholestasis during pregnancy (Liu et al., 2017).

Etiopathogenesis

Hormonal changes in normal pregnancy reduce the oxidation of long- and medium-chain fatty acids, affecting serum levels. Increased lipase activity in fat tissues, adrenal glands, gonads, heart, and skeletal muscles, along with insulin resistance, raises triglycerides, which are broken down into free fatty acids in the maternal blood. This increases susceptibility to fatty acid metabolism issues, potentially causing liver toxicity in at-risk pregnancies. A key marker is multi-organ fat infiltration, with microvesicular steatosis impairing liver function, including cholesterol, fibrinogen, and bilirubin processing. Fatty acid metabolites can damage pancreatic tissue, leading to pancreatitis. Elevated placental fatty acids impair oxygen delivery to the fetus, while fibrin deposits in chorionic villi reduce blood flow, causing fetal hypoxia (Naoum et al., 2019).

Beta-oxidation of fatty acids provides energy for the heart and skeletal muscles, mainly in the liver during fasting, illness, or muscle activity. It generates ketone bodies like 3-hydroxybutyrate and acetoacetate as alternative energy sources for organs like the brain during low blood sugar. This mitochondrial process involves transport stages and four enzymatic reactions, releasing acetyl coenzyme in two-carbon units (Ibdah, 2006). The fetal-placental unit metabolizes fatty acids to support fetal growth. Placental enzymes, including lipoprotein lipase, break down triglycerides, while transport proteins aid in transferring fatty acids to the fetus. Disruptions in the fatty acid oxidation pathway lead to fatty acid accumulation in the maternal bloodstream. This, along with reactive oxygen species (ROS), triggers liver inflammation and cell necrosis (Liu et al., 2017; Montufar et al., 2021). Deficient antioxidant function and cytotoxic lipid peroxidation products disrupt metabolism and activate inflammation (Naoum et al., 2019).

AFLP is strongly associated with fetal long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, found in 20% of cases. Studies show a 50-fold increased risk of liver disease in pregnant individuals with a fetus deficient in LCHAD (White et al., 2024). LCHAD deficiency results from defects in the mitochondrial trifunctional protein and the mitochondrial membrane, especially in the C-terminal of the alpha subunit. A common defect in LCHAD

deficiency is the nucleotide change from G to C at position 1528 in exon 15 of the alpha subunit, leading to the E474Q mutation, where glutamate is replaced by glutamine at amino acid 474. LCHAD catalyzes the third stage of long-chain fatty acid oxidation, and its deficiency leads to the accumulation of toxic long-chain 3-hydroxy-fatty acyl intermediates in the liver (Hammoud & Ibdah, 2014; Ibdah, 2006; Liu et al., 2017; Montufar et al., 2021; Pribadi et al., 2015; White et al., 2024). However, a study of 10 AFLP cases found no G1528C mutation in fetuses, and a Japanese study reported similar results, suggesting other causes for AFLP (Liu et al., 2017).

LCHAD deficiency is inherited autosomal recessively. If the mother carries the homozygous gene, the fetus experiences fatty acid oxidation issues. Unmetabolized fatty acids accumulate in hepatocytes, causing liver damage, jaundice, elevated liver enzymes, bilirubin, and coagulation abnormalities (Liu et al., 2017; Naoum et al., 2019; Pribadi et al., 2019). Environmental stress can increase toxic metabolite buildup in genetically vulnerable mothers, causing liver disease during pregnancy (Hammoud & Ibdah, 2014; Ibdah, 2006). Fetal fatty acid oxidation defects (FAOD) are thought to be linked to AFLP. Along with LCHAD, deficiencies in other enzymes involved in fatty acid oxidation, such as medium-chain acyl-CoA dehydrogenase (MCAD), very long-chain acyl-CoA dehydrogenase (VLCAD), short-chain acyl-CoA dehydrogenase (SCAD), and carnitine palmitoyltransferase 1 (CPT1), can also increase the risk of AFLP. While MCAD deficiency is rarely associated with AFLP, VLCAD deficiency has been found to be unrelated to AFLP (Liu et al., 2017; Montufar et al., 2021).

Clinical Manifestations

The prodromal symptoms in AFLP patients are non-specific and resemble other liver conditions in pregnancy. Common symptoms include nausea and vomiting (70%), encephalopathy, upper right abdominal pain or heartburn (50-80%), jaundice (70%), headaches, polydipsia, and polyuria. AFLP typically begins in the late second trimester, between weeks 27 and 38. Maternal complications such as hypoglycemia, kidney failure, and coagulopathy are present in 90% of cases. Hepatic encephalopathy occurs in advanced stages, making AFLP a potential diagnosis. Most patients improve within 1-4 weeks after delivery (Hammoud & Ibdah, 2014; Ibdah, 2006; Liu et al., 2017; Naoum et al., 2019; Pribadi et al., 2015). Hypertension, edema, ascites, and preeclampsia are common in AFLP. Severe untreated cases can lead to rapid liver failure, coma, hypoglycemia, hyperammonemia, kidney failure, and severe bleeding, risking death for both mother and fetus (Hammoud & Ibdah, 2014).

The laboratory findings in AFLP patients are characteristic of acute liver dysfunction, including transaminitis, hyperbilirubinemia, high gamma-glutamyl transferase (GGT), elevated ammonia levels, increased alkaline phosphatase (AFP), hyperuricemia, rising creatinine and blood urea nitrogen, leukocytosis with neutrophilia and toxic granulation, hypocholesterolemia, prolonged prothrombin time, low fibrinogen, thrombocytopenia, hypoglycemia, and elevated lipase. As the disease progresses, hemolysis with reticulocytosis, nucleated red blood cells, echinocytes, and elevated fibrin-fibrinogen split products can be seen (Naoum et al., 2019). AFLP diagnosis doesn't require a routine liver biopsy. Histologically, it shows microvesicular steatosis, with dense hepatocyte nuclei and no widespread inflammation. Fat accumulation is more in pericentral areas. This pattern can also occur in other liver diseases, like Reye's syndrome or tetracycline-induced liver damage, requiring clinical correlation for proper interpretation (Hammoud & Ibdah, 2014; Liu et al., 2017; Ronen et al., 2018) There is a case report of an 18-year-old primigravida at 35 weeks with suspected AFLP developed symptoms of nausea, vomiting, and jaundice, worsening postpartum and leading to death. Lab results showed elevated leukocytes, low hemoglobin, and altered liver enzymes. Postmortem liver examination revealed shrunken, pale tissue with macrovesicular and microvesicular steatosis and minimal inflammation (Ziki et al., 2019).

Diagnosis

The Swansea Criteria have been validated prospectively and are useful for diagnosing AFLP. Recognizing the absence of standardized diagnostic criteria for acute fatty liver of pregnancy, Ch'ng et al. proposed the Swansea criteria based on a retrospective analysis of multiple case series. These criteria rely on characteristic clinical presentation, the exclusion of alternative diagnoses, and specific laboratory findings observed in patients with acute fatty liver of pregnancy. The 15-month study in a Welsh obstetric unit found that 3% of 4,377 pregnant women had abnormal liver function tests, with most cases linked to preeclampsia and HELLP syndrome. Five women were diagnosed with acute fatty liver of pregnancy (AFLP), a higher incidence than previously reported. The Swansea criteria were introduced to diagnose AFLP without requiring liver biopsy, which is risky in coagulopathic and thrombocytopenic patients. These criteria consist of 14 clinical, pathological, and radiological features, with the presence of six or more, in the absence of another cause, supporting an AFLP diagnosis. Sensitivity and specificity vary among criteria components—abdominal pain is common in both HELLP syndrome and AFLP, transient diabetes insipidus is specific but rare, ascites occurs in severe preeclampsia and AFLP, and a bright liver on ultrasound appears in only 25% of cases. The Swansea criteria use reference values based on the non-pregnant state (Ch'ng, 2002). The Swansea criteria were later prospectively validated by Knight et al. (2008).

In a retrospective study of 24 patients with suspected pregnancy-related liver disease, these criteria were assessed against the diagnostic gold standard diffuse or perivenular microvesicular hepatic steatosis on liver biopsy obtained either in the immediate postnatal period or post-mortem (Goel et al., 2011). This validation demonstrated that antenatal application of the Swansea criteria, even without liver biopsy (requiring at least 6 of the remaining 13 criteria), is effective in diagnosing acute fatty liver of pregnancy and predicting microvesicular steatosis on biopsy (Wang et al., 2017). A patient is considered to have AFLP if they meet at least 6 of the 15 criteria. These criteria were developed for patients without other liver diseases, such as HELLP or preeclampsia, making their use challenging in patients with additional conditions (Liu et al., 2017; Pribadi et al., 2019). A study of 24 patients found that these criteria have a 100% sensitivity, 57% specificity, an 85% positive predictive value, and a 100% negative predictive value (Knight et al., 2008).

These criteria include clinical symptoms, laboratory tests, imaging findings, and pathological examination results. Some studies suggest that the Swansea criteria score may serve as a useful clinical tool for assessing disease severity (Wang et al., 2017). However, clinical symptoms often lack specificity, and pathological examination is rarely feasible for most patients. As a result, laboratory test results are considered the most crucial component for diagnosis and evaluation (Tan et al., 2022). Although not intended for early detection, these criteria are useful and possess a strong negative predictive value (Zhong et al., 2020). In rare cases, a woman may experience persistent nausea, vomiting, abdominal pain, jaundice, and encephalopathy, making the diagnosis relatively clear. However, more frequently, the initial clinical features overlap with other obstetric conditions, are not specific to acute fatty liver of pregnancy, and may persist for several weeks (Byrne et al., 2022). Laboratory evaluation is crucial for confirming a diagnosis of acute fatty liver of pregnancy. However, clinical findings and initial laboratory results indicate the condition in most cases, prompting further targeted investigations. The main objective of these tests is to identify liver dysfunction, a key feature of acute fatty liver. Affected patients typically present with transaminitis and hyperbilirubinemia (Abbassi-Ghanavati et al., 2009). Coagulation tests may show abnormalities, such as a prolonged prothrombin time, partial thromboplastin time, and an increased international normalized ratio. If handled correctly, serum ammonia levels are typically elevated (Nelson et al., 2013).

Some recommend conducting imaging studies (Liu et al., 2017). Ultrasonographic findings are part of the Swansea criteria; however, a prospective evaluation reported that only a quarter of women with acute fatty liver of pregnancy exhibited the characteristic findings, such as ascites or a bright liver (Knight et al., 2008). Liver biopsy was once deemed essential for diagnosing acute fatty liver during pregnancy. However, it is now considered unnecessary when characteristic clinical and laboratory findings are present. It may still be useful in cases where the diagnosis remains uncertain. Characteristic histopathologic features include swollen hepatocytes with central nuclei and microvesicular fatty infiltration. Notably, hepatocyte necrosis is minimal, with periportal areas remaining unaffected, distinguishing it from the periportal necrosis seen in preeclampsia. In some instances, fat droplets may not be readily visible on hematoxylin and eosin staining, requiring the use of oil red O stain on frozen sections, which highlights neutral triglycerides and lipids in red (Nelson et al., 2021).

Table 1. The Swansea criteria

Swansea Criteria
Vomiting
Abdominal pain
Excessive thirst and urination
Brain dysfunction
Bilirubin >0.8 mg/dl
Blood sugar <72 mg/dl
Urea >950 mg/dl
White blood cell count >11x10^9 /l
Fluid accumulation in the abdomen
ALT >42 U/I
Ammonia >66 µmol
Acute kidney injury (Cr >1.7 mg/dl)
Coagulopathy or prolonged prothrombin time (>14 seconds)
Ultrasound shows "bright liver"
Liver biopsy shows microvesicular steatosis

Source: (Liu et al., 2017).

Medical history, comorbidities, and diagnostic tests help identify the cause of illness. Pregnant women with abnormal liver function should be evaluated for viral infections, autoimmune conditions, coagulation issues, and undergo imaging to rule out conditions like liver bleeding or rupture. Ultrasound, though with low sensitivity, may detect ascites or a "bright liver." CT scans can reveal liver infiltration but are not sensitive for detecting fatty liver. MRI is proposed as an alternative to biopsy, detecting excess liver fat in some AFLP cases (Naoum et al., 2019). Liver biopsy is rarely performed during pregnancy due to high risks. In HELLP syndrome, it is controversial, as it isn't needed for management and may cause bleeding due to liver failure and coagulopathy (Liu et al., 2017; Naoum et al., 2019). A biopsy is needed for unclear symptoms to determine delivery and may be considered if the mother's condition doesn't improve post-delivery or if other diseases are suspected (White et al., 2024).

Differentiating AFLP from conditions like preeclampsia/eclampsia and HELLP is essential in diagnosis, as each condition requires different management. Immediate delivery is recommended for AFLP, and liver transplantation may be necessary if the disease progresses. Both AFLP and HELLP share symptoms such as elevated transaminases, preeclampsia/eclampsia, and proteinuria (White et al., 2024). To distinguish acute fatty liver of pregnancy from HELLP syndrome, a cohort of 67 women with each condition was studied. The diagnosis of acute fatty liver of pregnancy was confirmed using the Swansea criteria. In 10 cases, microvesicular fatty infiltration was verified through liver biopsy or autopsy. Both

groups showed no significant differences in age, race, or parity. Nonspecific symptoms such as fatigue, malaise, and pruritus were observed in both conditions. While nearly all women with HELLP syndrome had hypertension, only 70% of those with acute fatty liver of pregnancy were hypertensive. Headache was more common in HELLP syndrome, whereas hepatic encephalopathy developed in 15% of cases with acute fatty liver of pregnancy. Other notable differences included variations in the incidence of proteinuria, nausea, vomiting, and jaundice. (Byrne et al., 2022).

Several laboratory parameters differed significantly between the two groups at admission, particularly those indicating hepatic and renal dysfunction. Due to impaired hepatic synthesis, women with acute fatty liver of pregnancy had lower plasma fibrinogen levels than those with HELLP syndrome. Notably, over one-third of these patients had fibrinogen levels below 150 mg/dL, with 25% falling below 100 mg/dL. In contrast, all women with HELLP syndrome had fibrinogen levels exceeding 200 mg/dL. Additional indicators of hepatic dysfunction included lower serum cholesterol and higher bilirubin levels in the acute fatty liver group. Regarding renal impairment, acute kidney injury was more frequent and severe in cases of acute fatty liver of pregnancy (Byrne et al., 2022). Furthermore, AFLP can be distinguished from HELLP or preeclampsia by hypoglycemia, elevated INR, and liver dysfunction signs, but it doesn't exclude other liver disorders in pregnancy (Liu et al., 2017; Pribadi et al., 2015).

The diagnosis of acute fatty liver of pregnancy impacts delivery, genetic screening, child health, and recurrence risk. It primarily involves hepatocellular damage and impaired liver function, with nearly all cases showing elevated transaminases, hyperbilirubinemia, and coagulopathy absence of these suggests an alternative diagnosis. Encephalopathy, elevated ammonia, hypoglycemia, and transient diabetes insipidus strongly indicate hepatic injury but are less common. Coagulopathy and low antithrombin III help differentiate it from HELLP syndrome, while further research on cholesterol levels may provide additional insights. If diagnostic uncertainty remains, early delivery should be prioritized due to significant maternal and fetal risks (Morton & Laurie, 2018).

Complications

Patients with AFLP may experience complications such as acute kidney failure, ascites, encephalopathy, acute respiratory distress syndrome, and bleeding due to disseminated intravascular coagulation. The most frequent complications are acute kidney failure, disseminated intravascular coagulation, and hypoglycemia. Hypoglycemic patients should be observed and treated with dextrose infusion. Moreover, infection risks should be monitored, and broad-spectrum antibiotics should be administered if necessary. Serum lipase levels should be monitored for potential pancreatitis, especially if the patient reports epigastric pain (White et al., 2024). A study at Hasan Sadikin Hospital in Indonesia, from 10 patients between 2010 and 2013, found complications including acute kidney failure, metabolic acidosis, pulmonary edema, shock, respiratory distress, and death. Six patients died, and others experienced kidney failure, coagulation issues, and acidosis (Pribadi et al., 2015).

Acute liver damage is linked to reduced production of coagulation factors and procoagulant proteins, causing coagulopathy with hypercoagulability. Platelet dysfunction may arise from uremia and endothelial abnormalities, correlating with the severity of liver dysfunction. Decreased fibrinogen production, lower antifibrinolytic pathway components, and increased tissue plasminogen activator regulation can lead to hyperfibrinolysis and disseminated intravascular coagulation (Naoum et al., 2019; White et al., 2024) Coagulopathy worsens bleeding from causes like uterine atony, surgical bleeding, and lacerations. Intra-abdominal bleeding is a poor prognosis indicator in AFLP, with 65% of patients needing transfusions. Non-obstetric bleeding, like Mallory-Weiss tears, may also occur (Chang et al., 2020; Naoum et al., 2019). Kidney complications in AFLP can range from mild to severe, with some

requiring hemodialysis. Hepatorenal syndrome and transient diabetes insipidus may occur. Encephalopathy can cause seizures and coma, requiring intensive monitoring and treatment. Infections like sepsis and pneumonia, along with respiratory distress, may require ventilation (Naoum et al., 2019).

Management

The clinical approach to managing AFLP can differ because of the broad spectrum of symptoms, which may range from mild metabolic issues and coagulopathy to severe liver damage and hepatic encephalopathy. Key management strategies involve early identification and evaluation of the mother and fetus, planning for supportive care to address coagulopathy, prompt preparation for delivery, and post-delivery supportive treatment. Liver damage is expected to persist, along with its harmful effects, until the fetus is delivered. After birth, the metabolic irregularities in the mother typically resolve gradually, requiring supportive care for several days to weeks (Ko & Yoshida, 2006; Montufar et al., 2021).

The main focus in treating acute fatty liver during pregnancy is to deliver the baby promptly once the mother's condition is stabilized, either with or without steroid treatment to aid fetal lung development. Stabilizing the mother involves managing her airway, controlling hypertension, correcting low blood sugar, balancing electrolytes, and addressing coagulopathy issues. Regular monitoring of the mother's vital signs, mental status, and the fetus's well-being is necessary. While terminating the pregnancy is the definitive approach, the timing and delivery method need to be carefully considered. A sign of liver recovery is an improvement in prothrombin time, and liver transplantation may be considered for those who do not recover after childbirth (Hammoud & Ibdah, 2014; Naoum et al., 2019; White et al., 2024). Without coagulopathy, cesarean section is recommended for AFLP cases. Prompt termination and cesarean delivery reduce maternal and fetal mortality (Ko & Yoshida, 2006; Pribadi et al., 2019).

While vaginal delivery is possible, cesarean section is preferred in most cases due to frequent fetal distress related to maternal metabolic acidosis and reduced blood volume from endothelial dysfunction (Ko & Yoshida, 2006; Montufar et al., 2021). Inducing labor after diagnosis lowers maternal and fetal mortality. If spontaneous labor isn't possible, induction should be attempted, with cesarean section as a backup. There's insufficient evidence to link delivery method to bleeding in AFLP. In emergencies, cesarean section shows higher intra-abdominal bleeding than vaginal delivery. Although cesarean has higher mortality in some cases, choosing the best method remains challenging due to varying severity in studies (Naoum et al., 2019).

AFLP increases risks of postpartum bleeding, DIC, acute kidney failure, and GI bleeding, needing intensive care. Regular checks on hematology, liver, and kidney function should be done every 6 hours in the first 1-2 days. Anemia may require transfusions, and blood glucose should be monitored frequently; if below 60 mg/dl, IV glucose is necessary (Montufar et al., 2021). Newborns from AFLP mothers should be screened for LCHAD deficiency and other fatty acid oxidation defects due to risks of metabolic crises. Early intervention with high-carb, low-fat diets is essential. AFLP recurrence in future pregnancies is rare but higher in women with LCHAD mutations, and genetic counseling is advised. Prenatal diagnosis through chorionic villus sampling can identify AFLP risks. With early management, outcomes can be positive for patients with previous AFLP (Liu et al., 2017; Montufar et al., 2021; Pribadi et al., 2015; White et al., 2024).

Conclusion

Acute fatty liver of pregnancy (AFLP) is a rare but serious condition in the third trimester, caused by genetic mutations in enzymes responsible for fatty acid metabolism, leading to enzyme deficiencies and metabolite buildup in the mother's blood. Common symptoms include nausea, vomiting, jaundice, and hypertension, with lab findings showing elevated

transaminases and bilirubin. Early diagnosis and prompt delivery improve outcomes, while supportive care for both mother and baby is crucial to reduce mortality.

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