

The Challenge in Differentiating Acute Fatty Liver of Pregnancy from Other Hepatic Disorders in Parturient Women – A Case Report

Tiffanie Almas Santoso,¹ Demirel Andrea,¹ Dani Setiawan^{1,2}

¹Department of Obstetrics and Gynecology, General Hospital Sumedang Region, Sumedang, West Jawa, Indonesia

²Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Padjadjaran – Dr. Hasan Sadikin General Hospital, Bandung, Indonesia
Correspondence: Tiffanie Almas Santoso, Email: tiffanie.almas@gmail.com

Abstract

Introduction: Liver disorder during pregnancy can arise from pregnancy-related factors or other underlying causes. One significant example is Acute Fatty Liver of Pregnancy (AFLP), a rare but life-threatening obstetric emergency that typically occurs in the third trimester or early postpartum period. Diagnosis of AFLP is carried out using the Swansea criteria, and its clinical management varies depending on the severity of the condition.

Case Illustration: A 23-year-old woman, at 33–34 weeks of gestation in a multifetal pregnancy, presented with abdominal contractions and jaundice. The patient was diagnosed with AFLP using the Swansea criteria. Following the diagnosis, the patient delivered twins and received multidisciplinary care. After seven days of inpatient care, jaundice improved, symptoms resolved, and there were no signs of coagulation disorders.

Discussion: AFLP is a rare condition that normally occurs in the third trimester, with risk factors including multiple pregnancies and metabolic disorders. Symptoms can be nonspecific but may lead to acute liver failure, thereby timely diagnosis and management are crucial. Treatment primarily involves prompt delivery and supportive care to manage complications such as hypoglycemia and renal failure.

Conclusion: Early identification of AFLP can be challenging due to its similarities with other conditions, but the Swansea criteria can help assess its severity and potential complications for both mothers and fetuses.

Keywords: Acute Fatty Liver of Pregnancy, Diagnosis, First Stage Labor, Liver Disease

Tantangan dalam Membedakan *Acute Fatty Liver* dalam Kehamilan dengan Penyakit Hati Lainnya pada Wanita Parturien – Sebuah Laporan Kasus

Abstrak

Pendahuluan: Penyakit hati selama kehamilan dapat berkaitan dengan kehamilan atau memiliki penyebab lain. AFLP, sebuah keadaan darurat obstetri yang langka dan mengancam jiwa yang terjadi pada trimester ketiga atau periode postpartum awal, didiagnosis menggunakan kriteria Swansea dan memerlukan penanganan klinis yang bervariasi karena spektrum keparahannya.

Ilustrasi Kasus: Seorang wanita berusia 23 tahun pada usia kehamilan 33 – 34 minggu dengan kehamilan multifetal datang dengan kontraksi abdomen dan jaundice. Pasien terdiagnosis *acute fatty liver of pregnancy* (AFLP) dengan menggunakan kriteria Swansea. Pasien melahirkan bayi kembar dan menerima perawatan multidisiplin pascasalin. Setelah tujuh hari perawatan rawat inap, jaundicanya membaik, dan gejalanya menghilang, tanpa tanda-tanda gangguan koagulasi.

Diskusi: AFLP adalah kondisi langka yang biasanya terjadi pada trimester ketiga, dengan faktor risiko termasuk kehamilan ganda dan gangguan metabolik. Gejalanya tidak spesifik, tetapi dapat menyebabkan gagal hati akut sehingga diagnosis dan penanganan yang tepat waktu sangat penting. Perawatan utamanya melibatkan persalinan yang cepat dan perawatan suportif untuk menangani komplikasi seperti hipoglikemia dan gagal ginjal.

Kesimpulan: Identifikasi dini AFLP bisa menjadi tantangan karena kesamaannya dengan kondisi lain, tetapi kriteria Swansea dapat membantu menilai keparahan dan komplikasi potensial bagi ibu dan janin.

Kata kunci: *Acute Fatty Liver* pada Kehamilan; Diagnosis; Parturien; Penyakit Hati

Introduction

Liver disorder during pregnancy can arise from pregnancy-related factors or other underlying causes. This category of disorders includes five conditions, such as hyperemesis gravidarum, intrahepatic cholestasis of pregnancy (ICP), preeclampsia or eclampsia, HELLP disorder, and AFLP. The management of jaundice during pregnancy, specifically in the third trimester, poses a significant challenge for clinicians because of its diverse causes and uncertain prognosis.¹

AFLP is an obstetric emergency characterized by maternal liver failure and can have severe complications for both the mother and fetus, possibly leading to death.² AFLP is a complex disorder representing a spectrum of severe pregnancy-specific liver disorders. It is a rare, life-threatening condition that occurs in the third trimester or early postpartum period and is associated with high maternal and fetal mortality rates.^{2,3}

Acute Fatty Liver of Pregnancy (AFLP) develops rapidly with multi-organ dysfunction and typically presents between the 30th and 38th weeks of pregnancy. The diagnosis of AFLP is carried out based on a series of clinical and laboratory results using the Swansea criteria. The clinical management of women with AFLP varies due to the disorder manifesting as a spectrum from mild metabolic and hemostatic disturbances to liver failure with prominent hepatic encephalopathy and coagulopathy.⁴ This case report discusses the complexities involved in diagnosing and managing a patient with AFLP, particularly in differentiating it from other liver disorders. This distinction is crucial for effective treatment and optimal outcomes for both the mother and the fetus.

Case Report

A 23-year-old woman, G1P0A0, at 33-34 weeks of gestation with a multifetal pregnancy,

presented to the Obstetrics Emergency Department of Sumedang General Hospital with complaints of increasingly frequent abdominal contraction accompanied by fever. Three hours before hospital admission, there was no report of a significant discharge from the birth canal, mixed with blood-tinged mucus, and there was no dysuria or leukorrhoea. Six days before admission, the patient experienced watery stools five times a day, accompanied by nausea, vomiting, epigastric pain, and a bitter taste in the mouth. She denied any headache or blurred vision, and no treatment was administered for these symptoms. Two days before admission, the patient noticed jaundice in her eyes and body, and there was no itching or skin redness. Throughout pregnancy period, the patient had no history of hypertension, diabetes mellitus, or other chronic disorders. At 18 weeks of gestation, the patient was diagnosed with syphilis using a TPHA titer of 1/80 and received treatment with a single dose of 2.4 million IU intramuscular benzathine penicillin. Additionally, lung maturation therapy was initiated using 6 mg intramuscular dexamethasone, administered in four doses one week before hospital admission. This is the patient's first marriage. Ultrasonography carried out between 32-33 weeks of gestation showed live multiple fetuses, dichorionic diamniotic, with the first fetus in cephalic presentation and the second fetus in breech presentation.

Physical examination showed the patient had a febrile body temperature, with other vital signs within normal limits. Conjunctival pallor and icteric sclerae were reported, along with jaundice over the entire body. The thoracic examination was within normal limits. Abdominal examination showed a uterine fundal height of 32 cm, with uterine contractions occurring twice every 10 minutes, each lasting 20 seconds. Foetal heart rate was within normal limits, and genital examination showed a normal

Table 1 Laboratory Examination in a Parturient Patient

Laboratory Aspect	Result	Normal Range
Haemoglobin	10.9 g/dL (low)	12.3-15.3 g/dL
Leukocyte	30.300 /mm ³ (high)	4.500-10.000 /mm ³
Thrombocyte	277.000 /mm ³ (normal)	35-47 /mm ³
Haematocrit	32.9% (low)	35-47%
Random Blood Glucose	50 mg/dL (low)	100-150 mg/dL
Creatinine	1.47mg/dL (increase)	0.5-1.1 mg/dL
SGOT	175 U/L (high)	<31 U/L
SGPT	124 U/L (high)	<32 U/L
Bilirubin Total	7.10 mg/dL (high)	<1 mg/dL
Bilirubin Direct	5.6 mg/dL (high)	0-0.25 mg/dL
Bilirubin Indirect	1.5 mg/dL (high)	0-0.75 mg/dL
APTT	49.7 second (increase)	24-36 second
Natrium	123 mmol/L (low)	135-148 mmol/L
Kalium	3.4 mmol/L (low)	3.5-5.1 mmol/L
Uric Acid	7.8 (increase)	
Proteinuria	+1	negative

vulva and vagina, a thick and soft cervix, and cervical dilation of 3 cm. Urine examination showed bright yellow urine with a volume of 600 cc over 4 hours, and the patient was administered tocolytics and antibiotics. Routine blood tests, liver function tests, random blood glucose, uric acid, coagulation profile, electrolytes, and urinalysis were performed, with results shown in Table 1.

The patient's blood glucose was corrected with the administration of 50 mL of Dextrose 40% and an infusion of 500 cc of Dextrose 10%. One hour after the administration of tocolytics, the patient continued to experience increasingly frequent abdominal pain. On examination, the cervix was found to be thin and soft, with 8 cm of dilation. Labor progress was monitored, and after 30 minutes, the first baby was delivered spontaneously in a cephalic presentation. The man infant weighed 1600 grams and cried immediately. Five minutes later, the second baby was delivered spontaneously in a

breech presentation. The man infant weighed 1800 grams and did not cry immediately. Following the postpartum stage, the patient received intensive care with monitoring of the general condition, vital signs, bleeding, and a transfusion of fresh frozen plasma to maintain haemoglobin levels above 9 g/dL. Multidisciplinary care was provided in collaboration with internal medicine and neonatology for the management of the infants.

On the second day postpartum, an ultrasonography of the hepatobiliary system was performed, which reported no abnormalities in liver and spleen, but the presence of ascites, suggestive of pancreatitis and cholecystitis. The patient received the following treatment regimen, including antibiotics (ceftriaxone 2x1 gram and metronidazole 3x500 mg intravenously), antiemetics (ondansetron 3x4mg intravenously), antipyretics (paracetamol infusion 3x1 gram), liver vitamins (Curcuma

Variable	Finding
Vomiting	Positive
Abdominal pain	Positive
Polydipsia or polyuria	Positive
Hepatic encephalopathy	Positive
Bilirubin	> 14 µmol/L
Hypoglycemia	< 4 mmol/L
Uric acid	> 340 µmol/L
Leukocytosis	> 11 × 10 ⁹ /L
Ascites or ultrasound shows bright liver	Positive
ALT	> 42 U/L
Serum ammonia	> 47 µmol/L
Serum creatinine	> 150 µmol/L
Coagulopathy	
PT	> 14 s
APTT	34 s
Liver biopsy	Diffuse micro vesicular steatosis in hepatocytes

ALT: alanine aminotransferase; PT: prothrombin time; APTT: activated partial thromboplastin time

Figure 1 Swansea Criteria⁵

3x1 per oral), packed red cell (PRC) transfusion to achieve target haemoglobin of 9 g/dL, and continuous monitoring of general condition, vital signs, urine output, and bleeding.

The diagnosis for the patient was established using the Swansea criteria (Figure 1), resulting in a total score of 8 based on the presence of nausea and vomiting, abdominal pain, elevated total bilirubin levels, hypoglycaemia, increased uric acid levels, leucocytosis, ascites, and prolonged APTT. Consequently, the patient was diagnosed with acute fatty liver during pregnancy.

The patient received inpatient care for 7 days, during this period, jaundice gradually improved, and symptoms of nausea, vomiting, and fever were resolved. There were no signs of coagulation disorders, and a complete blood count was performed for re-evaluation during her follow-up visit to the

outpatient clinic.

Discussion

AFLP is a rare condition, with an estimated incidence of approximately 1 in 7,000 to 20,000 pregnancies.⁶ Several risk factors are associated with AFLP, and most cases occur in the third trimester, with an average gestational age of around 36 weeks, though some cases have been reported in the second trimester. Risk factors include multiple pregnancies, nulliparity, man fetuses, previous episodes of AFLP, and fetal long-chain 3-hydroxyacyl-CoA dehydrogenase deficiency.² Other risk factors include obesity, metabolic disorders such as diabetes mellitus, and other liver conditions such as intrahepatic cholestasis. Preeclampsia is reported to be associated with an increased risk of AFLP, but the causal relationship is unclear. Multiparous women

are at higher risk due to the higher production of fatty acid metabolites by multiple fetuses. Liver disorder during pregnancy can impact a woman's condition up to the point of AFLP, though the exact relationship remains uncertain. For instance, 20–40% of patients diagnosed with AFLP are also diagnosed with preeclampsia. Approximately, 20% of women with AFLP may also be diagnosed with HELLP disorder, which is related to preeclampsia.^{2,3}

The pathogenesis of AFLP remains unclear, though abnormalities in fatty acid metabolism during pregnancy are believed to play an important role. Free fatty acids typically increase during pregnancy, specifically in the later trimesters, to meet the needs for fetal and placental growth and development. If maternal-fetal fatty acid metabolism is abnormal, intermediate metabolic products can accumulate in the mother's blood and hepatocytes, leading to maternal hepatocyte damage.⁷ A presumptive diagnosis of AFLP is clinically established based on the presence of symptoms, including nausea, vomiting, abdominal pain, fatigue, and/or anorexia in a pregnant woman with significant liver dysfunction in the second trimester after other potential causes have been ruled out.^{1,2} AFLP, HELLP disorder, and severe preeclampsia present with overlapping clinical features, which complicates their differentiation. Multisystem involvement, including acute kidney injury, encephalopathy, coagulopathy, pancreatitis, pulmonary edema, and/or adult respiratory distress disorder, supports an AFLP diagnosis.^{3,8} The diagnosis of AFLP in this case were established by several symptoms appear but in acute onset such as nausea and vomiting. The multisystem failure did not occur in this patient because the diagnosis was made early, as soon as the symptoms were recognized.

Early symptoms of AFLP may be nonspecific (e.g., nausea, vomiting, abdominal pain, fatigue, and/or anorexia), but

manifestations of acute liver failure, including jaundice, encephalopathy, coagulopathy, and/or hypoglycaemia, can develop. In patients with clinical and laboratory results consistent with AFLP, prompt resuscitation, and management should be initiated without waiting for biopsy confirmation.⁷ Biopsy may be rarely needed if liver function does not normalize postpartum or in very early stages of AFLP when the diagnosis is uncertain.⁹

Several differential diagnoses, such as viral hepatitis, HELLP disorder, cholelithiasis, and intrahepatic cholestasis of pregnancy (IHCP), might be taken into consideration in parturient women who may have liver failure.¹⁰ Differentiation becomes challenging since the clinical symptoms and test results associated with these disorders are frequently ambiguous and imprecise. The primary symptom of IHCP is itching, and blood bilirubin levels often rise above 5 mg/dL. Ultrasonography is used to identify cholelithiasis, which can manifest as fever and pain in the right upper quadrant at any stage of pregnancy.¹¹ Any trimester can also experience acute viral hepatitis, which manifests as fever, nausea, vomiting, exhaustion, and jaundice in addition to markedly high AST levels.^{9,10} Pre-eclampsia with liver involvement, HELLP disorder, and AFLP can all occur in the third trimester. When compared to AFLP, HELLP disorder is more prevalent. When all other potential causes have been excluded, pregnant women exhibiting diagnostic symptoms and with significant liver impairment may receive an initial diagnosis of AFLP.¹²

Although distinguishing AFLP from HELLP disorder or severe preeclampsia can be challenging, these conditions require similar clinical management. Therefore, treatment should not be delayed to obtain a definitive diagnosis. In order to diagnose AFLP, the "Swansea criteria" were put forth and verified in a sizable cohort in the United Kingdom. If there is no other recognized

BOX 1 Swansea criteria for diagnosis of acute fatty liver of pregnancy (meet six or more criteria)
1. Elevated transaminases (AST or ALT >42 IU/L)
2. Elevated bilirubin (>14 μmol/L or 0.8 mg/dL)
3. Elevated ammonia (>47 μmol/L or 80.04 μg/dL)
4. Elevated urate (>340 μmol/L or 5.7 mg/dL)
5. Hypoglycemia (<4 mmol/L or 72 mg/dL)
6. Coagulopathy (PT >14s; aPTT >34s)
7. Renal injury (creatinine >1.7 mg/dL or 150 μmol/L)
8. Ascites/bright liver on ultrasound
9. Microvesicular steatosis on liver biopsy
10. Vomiting
11. Abdominal pain
12. Polydipsia/polyuria
13. Encephalopathy
14. Leukocytosis (>11 × 10 ⁹ /L)

Note: Criteria 10–14 (in italics) are non-specific and subjective and may be considered for change. For criteria 1–7, consider weighted points based on severity.
Abbreviations: ALT, alanine aminotransferase, aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; PT, prothrombin time.

Figure 2 Swansea Criteria for AFLP Diagnosis¹⁴

cause of liver dysfunction, six or more of the following criteria must be met for a diagnosis made using the Swansea criteria.^{12,13}

Early diagnosis, timely delivery, and intensive supportive care are essential components of AFLP management, as they significantly reduce maternal and infant mortality. The cornerstone of treatment is the fetus's quick birth. Complications such as hypoglycemia, acute respiratory distress disorder (ARDS), hepatic encephalopathy, disseminated intravascular coagulation (DIC), renal failure, and hepatic failure necessitate extensive supportive care and medication.^{13,14}

The limitation of this study was that we did not conduct other supportive examinations, such as a liver biopsy, which is considered the gold standard for diagnosing AFLP. However, the Swansea criteria demonstrated good predictive value for diagnosing AFLP.

Conclusion

In conclusion, AFLP had similarities to other

frequent liver dysfunction conditions such as pre-eclampsia, viral hepatitis, and pregnancy-related cholestasis, early identification can occasionally be challenging. AFLP is an uncommon, life-threatening condition that occurs in the third trimester of pregnancy or the early postpartum phase. In addition to being able to partially anticipate difficulties for both mothers and fetuses, the Swansea criteria score may help determine the severity of the condition in patients with AFLP.

Acknowledgment Patient Consent

Written informed consent was obtained from the patient for publication of the case report. The authors state that the patient gave her informed consent to have this case report published.

Conflict of Interest

The authors declare there are no competing financial interests or personal relationships that could have appeared to influence the

work reported in this paper.

Reference

1. Guntur MRN, Kholili U. A patient with acute fatty liver of pregnancy (AFLP) with acute pancreatitis manifestations. *Bali Med J.* 2023;12(2):1538–42.
2. Nelson DB, Byrne JJ, Cunningham FG. Acute Fatty Liver of Pregnancy. *Obstet Gynecol.* 2021;137:535–46.
3. Liu J, Ghaziani T, Wolf J. Acute Fatty Liver Disease of Pregnancy: Updates in Pathogenesis, Diagnosis, and Management. *Am J Gastroenterol.* 2017;112(6):838–46.
4. Casey LC, Fontana RJ, Aday A, Nelson DB, Rule JA, Gottfried M, et al. Acute Liver Failure (ALF) in Pregnancy: How Much Is Pregnancy Related? *Hepatology.* 2020 Oct 1;72(4):1366–77.
5. Meng, Z. et al. Risk factors for maternal and fetal mortality in acute fatty liver of pregnancy and new predictive models [Preprint]. 2021. doi:10.21203/rs.3.rs-590345/v1.
6. Morton A, Laurie J. Physiological changes of pregnancy and the Swansea criteria in diagnosing acute fatty liver of pregnancy. *Obstet Med.* 2018 Sep 1;11(3):126–31.
7. de Oliveira CV, Moreira A, Baima JP, Franzoni L de C, Lima TB, Yamashiro F da S, et al. Acute fatty liver of pregnancy associated with severe acute pancreatitis: A case report. *World J Hepatol.* 2014;6(7):527–31.
8. Yemde A, Kawathalkar A, Bhalerao A. Acute Fatty Liver of Pregnancy: A Diagnostic Challenge. *Cureus.* 2023 Mar 26;
9. Sinha S, Yadav J, Pradhan T. A Case Report on Acute Fatty Liver of Pregnancy: A Difficult Differential Diagnosis of Liver Disorder. *Cureus.* 2023 Jul 31;15(7).
10. Tran TT, Ahn J, Reau NS. ACG clinical guideline: Liver disease and pregnancy. *Vol. 111, Am J of Gastroenterol.* 2016. p. 176–94.
11. Hay JE. Liver disease in pregnancy. *Vol. 47, Hepatology.* 2008. p. 1067–76.
12. Patidar R, Gowdra Revannasiddappa K, Ghazanfer M. Key Components of Successful Management of Acute Fatty Liver of Pregnancy: A Case Report and Literature Review. *Cureus.* 2024 Feb 9;
13. Ronen J, Shaheen S, Steinberg D, Justus KR. Acute Fatty Liver of Pregnancy: A Thorough Examination of a Harmful Obstetrical Syndrome and Its Counterparts. *Cureus.* 2018 Feb 6;
14. Nelson DB, Yost NP, Cunningham FG. Acute fatty liver of pregnancy: Clinical outcomes and expected duration of recovery. In: *Am J of Obstet and Gynecol.* Mosby Inc.; 2013. p. 456.e1-456.e7.