

## CASE REPORT

### Acute fatty liver of pregnancy: An atypical case report

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Article Info	ABSTRACT
<p>Received May 22, 2024 Revised Aug 8, 2024 Accepted Aug 16, 2024 Published Dec 1, 2024</p> <p><b>*Corresponding author:</b> Riska Subono subonoriska1985@gmail.com</p> <p><b>Keywords:</b> Acute fatty liver Pregnancy Obstetric emergency Swansea criteria Maternal health</p>	<p><b>Objective:</b> To present an atypical case of acute fatty liver of pregnancy.</p> <p><b>Case Report:</b> A 33-year-old woman was referred to the Emergency department of Dr. Soedarso Tertiary Referral Hospital, Pontianak, Indonesia, previously from the district hospital over 580 KM with diagnosis of multigravida (gravida 3 para 2) at 31 weeks gestation, suspected acute fatty liver disease (AFLP), severe oligohydramnios, and intrauterine growth restriction (IUGR). The patient had a history of nausea, vomiting, epigastric pain, polydipsia and polyuria, and seizure for less than 5 minutes with loss of consciousness. The patient originally did not know she was pregnant and using a contraceptive implant. She missed her period in the last six months ago, which was the first onset of epigastric pain. Further clinical examination resulted in pitting oedema but jaundice as a cardinal sign was not present. Laboratory data showed leukocytosis, normal haemoglobin level, normal blood glucose, hyperuricemia, increased function liver test with high transaminase and bilirubin, normal coagulation profile. Urinalysis showed proteinuria. The viral hepatitis and HIV tests were negative. Transabdominal ultrasound demonstrated a single intrauterine pregnancy with no echogenic liver features. Cardiotocography (CTG) showed category 2. This patient was diagnosed with AFLP based on Swansea Criteria (7 out of 10) and terminated pregnancy two days after diagnosis. A baby boy was born with birth weight 1.100 gr, birth length 34 cm, apgar score (AS) 9 and 10 at 1 and 5 minutes. The mother had a good prognosis, while the baby died on day 23 of life.</p> <p><b>Conclusion:</b> Acute Fatty Liver during Pregnancy is an uncommon but life-threatening obstetric emergency. Early screening, diagnosis, timely handling delivery, and intensive supportive care are essential to decrease morbidity and mortality for both mother and fetus. Multidisciplinary opinion needed for the best management of this case.</p>

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#### Highlights:

1. Acute Fatty Liver of Pregnancy (AFLP) is an uncommon condition but life-threatening obstetric emergency, that increases the risk of fetal death due to preterm birth.
2. AFLP can be challenging for primary health workers (especially for general practitioners (GP) and midwives) since it mimics preeclampsia, viral hepatitis, intrahepatic cholestasis of pregnancy, and HELLPS syndrome, so more concern is needed in this case.



## INTRODUCTION

Acute Fatty Liver of Pregnancy (AFLP) is a life-threatening, uncommon condition in obstetric emergencies. It is estimated to affect 1:7000 – 1:16.000 pregnancies worldwide and is most typically present during the third trimester or early postpartum period.<sup>1</sup> Sheehan first described it in 1940 and was once referred to as "acute yellow atrophy of the liver." In the past, the maternal mortality rate due to AFLP was reported to be quite high, around 75%. Recent studies report a reduction in maternal mortality by an average of 18% with early diagnosis and prompt and appropriate treatment.<sup>2</sup> This is usually due to complications such as DIC, sepsis, shock, and kidney failure. Meng Z et al reported in their study, that in the last 10 years there were 9.4% (10 out of 106) of mothers who died from AFLP, the most maternal complication was acute kidney injury.<sup>3</sup> Chen et al reported that the maternal mortality rate due to AFLP was 36.8%, where the prognosis for AFLP was worsened by complications of hepatic encephalopathy (HE), and the maternal mortality rate due to AFLP related to HE was around 87.5%.<sup>4</sup> A study conducted at one of Indonesia's tertiary hospitals found that maternal mortality due to AFLP was quite high, approximately 66.7%.<sup>5</sup>

Early detection and diagnosis are crucial to decrease the risk of fatal complications. However, it can be challenging for primary health workers since it mimics preeclampsia, viral hepatitis, intrahepatic cholestasis of pregnancy, and HELLP syndrome.<sup>6</sup> Despite that, the diagnosis can be made based on Swansea criteria, a combination of clinical, laboratory, and imaging features. The cornerstone of management of AFLP is prompt termination of pregnancy and intensive supportive care with a multidisciplinary approach.<sup>7,8</sup>

Therefore, this study aimed to report an atypical case of AFLP with good maternal prognosis, while the baby was born preterm and died. AFLP is uncommon but life threatening so that requires more concern for rapid assessment, diagnosis, and comprehensive management to avoid complications and death.

## CASE REPORT

A 33-year-old woman was referred to the Emergency department of Dr. Soedarso Tertiary Referral Hospital, Pontianak, Indonesia, previously from the district hospital over 580 KM with a diagnosis of multigravida (gravida 3 para 2) at 31 weeks gestation, suspected acute fatty liver disease (AFLP), severe oligohydramnios, and intrauterine growth restriction (IUGR). She had a history of nausea, vomiting,

epigastric pain, polydipsia and polyuria, and seizure for less than 5 minutes with loss of consciousness. The patient did not know she was pregnant before and using a contraceptive implant. She missed her period in the last six months ago, which was the first onset of epigastric pain. On admission, the vitals were stable, but her blood pressure was 165/105 mmHg, and her heart rate was 100 beats per minute—further clinical examination resulted in pitting edema in both hand and foot with no jaundice.

Laboratory data in our hospital showed leukocytosis (11.33 x 10<sup>3</sup>/ μL), average hemoglobin level (13.6 mg/dL), and thrombocytopenia (26.000/ μL). The biochemical markers showed the following: total bilirubin 5.13 mg/dL, direct bilirubin 1.92 mg/dL, aspartate transaminase (AST) 102.9 IU/L, alanine transaminase (ALT) 127.1 IU/L, albumin 3.60 g/dL, serum urea level 70.1 mg/dL, serum creatinine level 0.89 mg/dL, total cholesterol 249 mg/dL, blood glucose level 121 mg/dL, hyperuricemia 10.5 mg/dL, hyponatremia 131.88 mmol/L, and hypocalcemia 0.91 mg/dL. The coagulation profile was average: prothrombin time (PT) 11.3 sec, activated partial thromboplastin (APTT) 30.9 sec, and INR 0.77. A D-dimer test was also done and revealed 836.17 ng/mL FEU. Urinalysis showed proteinuria. The viral hepatitis and HIV tests were negative. Transabdominal ultrasound demonstrated a single intrauterine pregnancy with no echogenic liver features. Cardiotocography (CTG) showed category 2. The diagnosis of AFLP is based on Swansea criteria, at least having 6 of 14 combinations of clinical and laboratory features. This patient has seven as follows: nausea and vomiting, abdominal pain, polydipsia/polyuria, bilirubin >0.8 mg/dL, WBC >11x10<sup>9</sup>/L, AST or ALT >24 units/L, and urate >340 μmol/L or >5.7 mg/dL.

For this case, we held a conference to obtain a multidisciplinary opinion for the best management of this patient. The pregnancy would be terminated with cesarean section after receiving 12 units of thrombocyte concentrates and reaching the target of platelets >50.000/L, would be in an intensive care unit pre-and post-surgery, echocardiography examination would be carried out and showed normal, and the baby would be treated in the neonatal intensive care unit (NICU) because of very preterm and meager birth weight. After the multi-department conference, the patient underwent an elective cesarean section on the day-2 admission. The outcome was a live male baby with a 9/10 Apgar score, birth weight of 1.100 gr, and birth length of 34 cm. On day two after surgery, the surgical wound was good, and there was no hemorrhage postpartum and no wound dehiscence. The mother had a good prognosis, while the baby died on day 23 of life.

## DISCUSSION

The sex hormones estrogen and progesterone progressively increase in pregnancy, leading to physiological changes that affect hepatic metabolic, synthesis, and excretory functions. These physiological changes promote fetal growth and development. Hepatic disorders in pregnancy often occur in approximately 3% of pregnancies in developing countries.<sup>2</sup> Reports of AFLP cases in Indonesia are scarce, but it is reported increasing 2-3 issues per year at Dr. Soetomo General Academic Hospital Surabaya, Indonesia. AFLP incidence at dr Hasan Sadikin General Hospital Bandung-Indonesia from 2010-2013 is ten pregnancies of 10.766 (1: 1538 or 0.065%), and at Dr Soetomo General Hospital Surabaya-Indonesia from 2011-2015 is 18 pregnancies.

Several liver diseases during pregnancy often have similar features, which makes it challenging to identify.<sup>10</sup> Herein, we report on a case of atypical acute fatty liver of pregnancy. Our patient presented at 31 weeks of pregnancy – the third trimester with gastrointestinal symptoms as the patient's main complaint. A retrospective study showed the average gestational age for AFLP is 36 weeks (32-38 weeks)<sup>11</sup>, and a survey from Dr. Soetomo General Academic Hospital showed the average is 33 weeks (20-45 weeks). However, a case occurred at 19 weeks gestation.<sup>5</sup>

The initial symptoms of AFLP are non-specified, with frequent gastrointestinal symptoms such as nausea, vomiting, abdominal pain/epigastric pain. Several studies revealed jaundice as a cardinal sign of AFLP.<sup>11</sup> Nausea and vomiting occur several days or 1-2 weeks before jaundice, commonly present lately.<sup>12</sup> A study at Parkland Hospital showed patients with nausea, vomiting 57%, abdominal pain 53%, and jaundice 33% on admission.<sup>13</sup> Based on studies in Indonesia, the presentation of jaundice is relatively high, 100% at Dr. Soetomo General Academic Hospital and 70% at Dr Hasan Sadikin General Hospital.<sup>5,14</sup> Shi Y et al. showed jaundice (69%), fatigue (62%), nausea and vomiting (46%) being the most common signs and symptoms of AFLP.<sup>15</sup>

Recently, diagnosis of AFLP was made by a minimum of 6 of 14 Swansea Criteria. Our patient was diagnosed with Swansea criteria for AFLP, which met the required minimum features, 7 out of 14 parts. Her blood glucose level, hemostatic test (PT or APTT), and renal function remained normal, and she was not jaundiced and encephalopathic in perpetuum. No biopsy was performed, considering an invasive procedure despite being a gold standard diagnostic for AFLP.

Swansea criteria were used for presumptive diagnosis of AFLP with a high negative predictive value (100%) in diagnosing microvesicular steatosis, so it is not precise for early diagnosis. Several signs and symptoms will appear in line with AFLP progressions, such as encephalopathy, coagulopathy, or ascites. Likewise, laboratory and radiology findings such as bright liver on ultrasonography or profound hypoglycemia that occurs if liver function gets worse.

A study showed that aminotransferase, liver function, and coagulation tests are essential for diagnosing AFLP. Patients with GI symptoms, abnormal liver function tests, and coagulopathy without liver disease history had a high risk for AFLP. This study demonstrated several diagnostic criteria and levels of sensitivity and specificity. GI symptoms, elevated transaminase, elevated bilirubin, and prolongation of PT/APTT have a sensitivity of 97.6% and specificity of 97.1% for AFLP.<sup>16</sup> Dwivedi et al., AFLP most often occurs with jaundice, elevated bilirubin, and moderately elevated transaminase.<sup>11</sup>

Our patient did not meet the cardinal criteria, such as jaundice, like some previous studies that reported atypical AFLP. Onwuagbu et al. reported an atypical presentation of AFLP, which did not meet the required minimum Swansea Criteria, at 21 weeks gestation with no jaundice, developed anasarca, blood glucose, and renal function remained regular, unstable liver function tests, thrombocytopenia, and there was elevated international normalized ratio of 3.72 on day 12 admission. In this study, AFLP was confirmed by core liver biopsy that showed the presence of microvesicular steatosis (ballooning and feathery degeneration of hepatocytes) on day 17 admission.<sup>17</sup> In our patient, a liver biopsy was not carried out because of hemorrhage risk and limited time. Our patient also had a seizure pre-hospital. Although seizures are more common in preeclampsia, they are also reported to occur in around 15% of AFLP cases at Dr Hasan Sadikin Bandung-Indonesia.<sup>14</sup> Moreover, experiencing preeclampsia had a 50% risk for AFLP.<sup>11</sup>

Hypertension, average blood glucose, regular coagulation test, and no encephalopathy presence in this patient made it more challenging to differentiate from other liver diseases in pregnancy. Hypertension occurs most often in HELLP syndrome and can differentiate between these two, but several studies report the incidence of hypertension in approximately 57% of AFLP cases.<sup>5,13,16</sup> Laboratory tests in AFLP usually demonstrate hypoglycemia in about 12% of patients with baseline <72 mg/dl. Hypoglycemia in a non-diabetes mellitus/gestational diabetes pregnant woman

and abnormal liver dysfunction and thrombocytopenia give a clue for AFLP. Profound hypoglycemia occurs in line with liver function progression. Hypoglycemia can also occur in HELLP syndrome, but in a small number, likewise coagulopathy.<sup>11,16,18</sup> Several signs and symptoms present at the late phase, such as encephalopathy, ascites, and bright liver on ultrasonography. Hyperuricemia and thrombocytopenia can be additional signs in cases of AFLP.

Differential diagnoses resembling AFLP are preeclampsia, HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) syndrome, viral hepatitis, and intrahepatic cholestasis.<sup>17,19</sup> Preeclampsia presents in the second/third trimester with hypertension occurring after 20 weeks, edema and proteinuria, and neurological deficits can be found (headaches, seizures, coma).<sup>19</sup> HELLP syndrome commonly presents in the third trimester between 28 and 36 weeks with mildly elevated transaminase, earlier elevated blood pressure, coagulation function, and hypoglycemia rarely changes. The symptoms of viral hepatitis are almost the same as AFLP, but the patient must have a history of previous liver disease, especially hepatitis B. In Intrahepatic cholestasis, occurring in the second and third trimester with commonly elevated bile acid, jaundice <25% of patients, pruritus of palms and soles, and mild liver dysfunction, but the coagulation test was rarely changed besides severe hypertension or elevated bile acid.<sup>16,18-20</sup>

AFLP had no specific signs and symptoms, making diagnosing it challenging. CSOG MFM Committee Guideline and previous studies recommend prenatal AFLP screening for outpatients at 34-37 of pregnancy. First-grade screening indications are gastrointestinal symptoms, complete blood count, liver function test, and coagulant test. Then, continue with second-grade screening, which includes renal function test, blood sugar, and ultrasonography.<sup>16,21</sup> Zhong et al. made a diagnostic procedure for AFLP; pregnant women with gastrointestinal symptoms in the third trimester should be suspected of AFLP, and an assessment of liver disease history, blood pressure, liver function, and coagulation function is carried out.<sup>16</sup> When the diagnosis of AFLP has been established, the definitive treatment is delivery.<sup>22</sup> Studies reported that if delivery is carried out within a week of the onset of diagnosis, the survival rate can be up to 100%. In comparison, 30% of cases had poor prognosis if delivery was carried out beyond two weeks after onset.<sup>21,23</sup>

Uncommon but life-threatening cases should concern health workers, especially in the first line, general practitioners (GP) and midwives. AFLP should be suspected in third-trimester pregnancy with gastrointestinal symptoms, abnormal liver function, and

coagulopathy without liver disease history. Education to primary health workers must also be carried out that hyperemesis gravidarum with gastrointestinal main complaints is only limited to 14-15 weeks of pregnancy; if more than 14-15 weeks, then AFLP is suspected.<sup>5,16</sup>

## CONCLUSION

Acute Fatty Liver during Pregnancy is an uncommon but life-threatening obstetric emergency. Early screening, diagnosis, timely handling delivery, and intensive supportive care are essential to decrease morbidity and mortality for both mother and fetus.

## DISCLOSURES

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### Conflict of interest

The authors declare that they have no conflict of interest.

### Patient consent for publication

The patient has signed the informed consent form and agreed that her case is to be published in a case report.

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### Author contribution

All authors have contributed to all processes in this research and approval for publication of this manuscript.

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