



## ACUTE FATTY LIVER IN PREGNANCY

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### SUMMARY

Acute fatty liver of pregnancy (AFLP) is an obstetric emergency and life threatening condition of the pregnancy. It affects during last trimester of pregnancy and occasionally occurs in postpartum period. It is presented with malaise, nausea, vomiting, and epigastric pain followed by jaundice. Laboratory tests usually derange liver and renal functions with coagulopathy. The incidence of AFLP is approximately 1 in 15,000 pregnancies. We reported the case of a 34-year-old patient, with multiple pregnancy at 35 weeks of gestation presented with dizziness, headache and dyspepsia aggravated by lying down and noted jaundice during operation. She had postpartum haemorrhage after the operation due to coagulopathy and her laboratory investigations findings favoured to diagnosis as AFLP and treated with supportive management at intensive care unit (ICU). Therefore obstetrician must be aware of one of this hepatic problem in pregnant women at late trimester.

**KEYWORDS:** Acute fatty liver of pregnancy; obstetric emergency; delivery.

### INTRODUCTION

The management of pregnant women with liver disease is a common clinical problem and needs to consider not only the expectant mother but also the unborn fetus in treatment decisions. AFLP is a one of the liver diseases which is an uncommon but potentially life-threatening complication that occurs in the third trimester or early postpartum period. It was first described in 1934 by Sheehan as an "acute yellow atrophy of the liver". AFLP is characterized by microvesicular fatty infiltration of hepatocytes without any inflammation or necrosis.<sup>[1]</sup>

It has an incidence of approximately 1 in 15,000 pregnancies.<sup>[2]</sup> This condition occurs more commonly in primigravida, twin pregnancy and pregnancies carrying a male fetus. AFLP presented with nonspecific symptoms such as nausea, vomiting, fatigue, thirst, headache, jaundice, and altered mental status with signs of acute liver failure. If untreated, AFLP can lead to coagulopathy, fulminant hepatic failure, multiple organs dysfunction and death. AFLP is associated with raised bilirubin and transaminase levels. The other possible features include hyperuricemia and thrombocytopenia.<sup>[3]</sup>

It increases a significant perinatal and maternal mortality and can lead to hepatic failure and encephalopathy. If diagnosis is delayed, it may cause death for the fetus and mother.<sup>[4,5]</sup> Once diagnosed, prompt delivery is associated with significantly improvement of outcome

but postpartum management becomes difficult if the patient is complicated with coagulation failure and postpartum haemorrhage. So it is best treated in a center with expertise in high-risk obstetrics management, maternal-fetal medicine, neonatology and hepatology. Experts in liver transplantation may be needed in severe cases.<sup>[6]</sup>

### CASE REPORT

Our patient was a 35 year old lady, G3P2, 35 weeks period of gestation with twin pregnancy was admitted to the hospital for dizziness, headache and dyspepsia aggravated by lying down. She had no complaints of pain in abdomen, bleeding or leaking per vaginam or decreased fetal movement. She was referred from a maternal and child health clinic to antenatal specialist clinic in view of her chief complains.

The physical examination noted there was yellowish discoloration of the scleral on both eyes. Also noted she had discomfort by lying down during ultrasound examination and the cardiotocogram showed shallow decelerations with poor beat to beat variability in first twin for more than half an hour. The specialist decided to do emergency lower segment caesarean section and bilateral tubal ligation after taking blood for completed picture, grouping matching and liver function test. The admission liver function test revealed aspartate transaminase 365 U/L, alanine transaminase 176 U/L,

total bilirubin 115 µmol/l, direct bilirubin 71 µmol/l and alkaline phosphatase 472 U/L. The haemoglobin level was 10.2 g/dl and platelet count was 107x10<sup>9</sup>/L (Figure 1).

After the post spinal, the blood pressure was dropped and vomited once, she was given multiple times of phenylephrine and epinephrine however blood pressure still borderline low and tachycardia. During operation, there was yellowish colouration of the amniotic fluid. The estimated blood loss was 1.2 liters. Both babies were boys and Apgar score at 1 minute was 7 and 5 minutes was 8. The weight of the first twin was 2.56 kg and second twin was 2.28 kg.

The patient was transferred to ICU after the operation with intubation. There was noted postpartum haemorrhage about 500 ml with blood clots evacuated up on vaginal examination. The total estimated blood lost was 2 liters and transfused 2 pints of packed cell with 4 units of fresh frozen plasma at ICU after the uterine massage. The arterial blood gas analysis result showed metabolic acidosis and it was worsening in ICU. The serum ammonia level was 92µmol/l and which was high and urine output was poor therefore referred to nephron team for dialysis in view of worsening metabolic acidosis and poor urine output with increase ammonia, urea and creatinine level. The nephron team gave sodium bicarbonate and started novasource.

The post-operative ultrasound examination of the abdomen noted fatty liver, moderate ascites with no

biliary obstruction. The patient was diagnosed as acute fatty liver of pregnancy because her viral serology tests turned out were negative for hepatitis A, B, C and E and negative test for leptospirosis. The computerized tomogram of the brain showed normal. The impression of the radiologist was hepatic encephalopathy with cerebral decorticate.

The patients' condition was improved at 10<sup>th</sup> post operation day. She was treated with intravenous tazocin for hospital acquired pneumonia infection. The patient was extubated on day 14 after the operation and transferred out to labour ward high dependency unit. The patient was moved to maternity ward in next day. At maternity ward patient unable to ambulate independently and complained of weakness in lower limbs and treated with physiotherapy daily and subcutaneous tinzaparin for thromboprophylaxis. On day 21, the patient complained of itchy rash with discrete papules over the trunk, back, posterior thigh and treated by dermatologist. The patient ambulated with assistance on day 22 and independently on day 23. She was discharged 25 days after the operation and informed the patient to continue thromboprophylaxis treatment, continue to wear Thrombo-Embolus Deterrent (TED) stocking and regular follow-up to check the liver function test. She was notified as high risk e-notification at her discharged summary and informed the family medical specialist of the clinic which was near to the patient's house for home visit.

CHA TD

N 10 labour ward

TEST	Lab Maternity	ICU	Postop and day	Postop day 2	REMARK
FBC	10.2 g/dl	9.1	10.4	10.0	Hep A IgG +ive
TWC	10.0 x 10 <sup>3</sup>	10.2	9.4	50.40	Hep B IgM -ive
PLT	102 x 10 <sup>9</sup>	48	132	459	Hep C IgG serology -ive
PT					ANA -ive
APTT					ICM for both twins - no chn
INR					Leptospira serology -ive
BUSE					
Na	134 mmol/L	130	134	137	
K	4.4	4.2	4.0	3.6	
Cl	106	106	101	106	
UREA	3.6	3.4	1.9	1.7	
SR CREA	16.4 µmol/L	19.8	20	4.1	
URE	47.5	33.8	14.2	4.0	
Ammonia		92 µmol/L	6.0	4.0	
LFT					
TB	115 µmol/L	420	295	259	
DB	71	21.3	124	3.2	
AST	365 U/L	22.3	195	10.6	
ALT	126	12.8	55	6.5	
TP	42 g/L	45		3.1	
ALB	21	21		2.3	
GLO	21	21		2.3	
ALP	472 U/L	351		234	
Ca <sup>2+</sup>					
Corrected					
PO <sub>2</sub>					
Mg <sup>2+</sup>					
CE					
AST					
LDH	912 U/L	942	462	324	
CPK					
CKMB					

Fig. 1: Investigations.

## DISCUSSION

The exact etiology of AFLP is not well known. It may be due to a mitochondrial dysfunction in the oxidation of fatty acids leading to an accumulation in hepatocytes and dysfunction of the hepatocytes. AFLP is highly associated with a fetal homozygous mutation (1528G>C) in the gene that encodes for mitochondrial long-chain hydroxy acyl-CoA dehydrogenase (LCHAD). The mutation in LCHAD results in the accumulation of 3-hydroxy fatty acids, such as 3-hydroxy myristic acid, 3-hydroxy palmitic acid and 3-hydroxy dicarboxylic acid in the placenta, which are then shunted to the maternal circulation leading to the development of acute liver injury observed in patients with AFLP.<sup>[7]</sup> AFLP occurs more commonly in third trimester of pregnancy, twin pregnancy and pregnancies carrying a male fetus as seen in our case.

AFLP is rarely seen in practice because initial clinical symptoms may be non-specific. The patient's history, clinical features and biochemical abnormalities manifestations are quite similar as acute hepatitis B virus infection, leptospirosis and preeclampsia. But preeclampsia is not usually present with jaundice as seen in AFLP. The incidence of preeclampsia is much higher 3 in 100 as compared to AFLP 1 in 16,000.<sup>[8,9]</sup> AFLP should be suspected in the following conditions as severe gastrointestinal symptoms, i.e., nausea, vomiting, abdominal pain, and jaundice appearing in late pregnancy, abnormal liver function tests, and thrombocytopenia in third trimester with other associated organs derangements, i.e., renal insufficiency and hepatic encephalopathy. Some of these features are common in severe preeclampsia cases. In our case, the clinical features of severe liver dysfunction appeared at the gestational age of 35 weeks. The clinical and laboratory evidence of primary post-partum haemorrhage, elevation of serum transaminase, and alkaline phosphatase and bilirubin levels with elevated ammonia value favored the diagnosis of AFLP in our case.

## DIAGNOSIS

AFLP is a diagnosis of exclusion and it is challenging and complicated. The characteristic diagnostic investigation showed deranged liver functions, coagulopathy, hypoglycemia, deranged renal function tests, thrombocytopenia and ultrasound imaging showing fatty liver.

Some used Swansea criteria for diagnosis of AFLP<sup>[10]</sup>, these criteria are vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, elevated bilirubin >14 $\mu$ mol/l, hypoglycaemia <4 mmol/l, elevated urea >340  $\mu$ mol/l, leukocytosis >11 $\times$ 10<sup>9</sup>/l, ascites or bright liver on ultrasound scan, elevated transaminases (AST or ALT) >42IU/l, coagulopathy: prothrombin time >14seconds or Activated Partial Thromboplastin Time (APTT) >34seconds, microvesicular steatosis on liver biopsy. The liver biopsy is not necessary to make the diagnosis of AFLP in most case and is only done to

determine the need for early delivery in indeterminate cases.<sup>[11]</sup> The patient with at least six or more criteria confirm the diagnosis of AFLP. One study concluded that the Swansea criteria had 100% sensitivity and 57% specificity with an 85% positive predictive value and a 100% negative predictive value for a sample of 24 patients.<sup>[12]</sup>

## MANAGEMENT

AFLP is associated with a very high maternal and perinatal mortality. Therefore delivery of the fetus is paramount. Even treatment of AFLP is mainly supportive care, the early diagnosis is important because fulminant liver failure due to AFLP may not be reversible.

In the immediate postpartum period, the most common life-threatening conditions associated with AFLP consist of primary postpartum haemorrhage due to disseminated intravascular coagulation, acute liver failure with encephalopathy, acute renal failure and gastrointestinal bleeding.<sup>[13,14]</sup> The patients may require admission to ICU for frequent monitoring for coagulopathy and blood products, aggressive correction of hypoglycemia, and mechanical ventilation for acute respiratory distress syndrome, dialysis, or plasmapheresis. The recurrence of AFLP during subsequent pregnancy may occur about 25%.<sup>[15]</sup>

## CONCLUSION

AFLP is a rare, life-threatening complication of pregnancy with variable presentation and rapid unpredictable complications usually occurs in late pregnancy and occasionally at postpartum. AFLP is an obstetric emergency, therefore, early diagnosis, delivery and management at ICU support may reduce both the mother and perinatal morbidity and mortality. Although our patient presented with vague symptoms of AFLP, we performed an early caesarean section, well managed her postpartum haemorrhage with transfusion of blood products and closed monitoring her conditions at ICU were the key to a good outcome.

## ABBREVIATIONS

AFLP: Acute fatty liver of pregnancy, ICU: Intensive care unit, LCHAD: Long-chain hydroxy acyl-CoA dehydrogenase.

## CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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## COMPETING INTERESTS

The authors declare that they have no competing interest.

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