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# Therapeutic Plasma Exchange in Acute Fatty Liver of Pregnancy with Acute Kidney Injury: A Case Report

**[1]Dr. Snehal Mishra, [2]Dr. Manisha Khande, [3]Dr. Shraddha Goswami**

[1,2]Senior Resident, Department of Nephrology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, India

[3]Professor and HOD, Department of Nephrology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, India

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**Corresponding Author:** Dr. Manisha Khande, Senior Resident, Department of Nephrology, Sri Aurobindo Medical College and Post Graduate Institute, Indore, India

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## ABSTRACT

Acute fatty liver of pregnancy (AFLP) is characterised by acute liver failure that occurs most commonly in the third trimester of pregnancy. Prompt delivery reverses liver failure in most cases. Rarely, termination of pregnancy may not reverse liver failure, and adjunct interventions may be required. Therapeutic plasma exchange (TPE) has been described in AFLP in very few case reports. We describe a patient in whom liver failure and extrahepatic organ failure persisted even after delivery for which she underwent TPE which resulted in expedititious clinical improvement. We propose that TPE be considered as a measure to salvage AFLP patients with liver failure that does not reverse after termination of pregnancy.

**Keywords**

Acute fatty liver of pregnancy (AFLP), Therapeutic plasma exchange (TPE), Hemolysis, Elevated liver enzymes, Low platelet syndrome (HELLP).

## BACKGROUND

Acute fatty liver of pregnancy (AFLP) is a mitochondrial hepatopathy characterized by hepatic microvesicular steatosis in late pregnancy. It is a rare obstetric emergency with 5 cases per 100,000 maternities in the United Kingdom. Fulminant liver failure can result. The disorder has been linked to fetal

homozygosity for beta-fatty acid oxidation disorders. This leads to an excessive, fatty acid load in the mother which results in hepatotoxicity and liver dysfunction.

Diagnosis of AFLP is made using the Swansea criteria which requires a combination of six clinical features of AFLP in the absence of another possible cause.

Markers of disease severity relate to impaired intrinsic liver function and include the development of encephalopathy, recalcitrant hypoglycaemia or coagulopathy, lactic acidosis, and hyperbilirubinaemia, rather than the level of transaminases.[1]

Conditions unique to pregnancy that cause liver dysfunction include intrahepatic cholestasis of pregnancy, pre-eclampsia, Haemolysis Elevated Liver enzymes Low Platelet count (HELLP) syndrome and AFLP.

While intrahepatic cholestasis of pregnancy (ICP) and preeclampsia are frequently seen, AFLP is rare and potentially life-threatening. The pathogenesis of AFLP remains unclear but there is emerging evidence of the genetic basis of AFLP where defective mitochondrial fatty acid beta-oxidation in the foetus is implicated in some cases of AFLP. [2,3]

**CASE PRESENTATION**

An 18-year-old primiparous female with an estimated gestational age (EGA) of 35 weeks and 15 days presented with complaints of nausea, vomiting and yellowish discolouration of sclera and urine since 4-5 days without any pruritus. She was a booked case and the Antenatal Clinic (ANC) visits were unremarkable. She had no history of fever or loose motions. Human Immunodeficiency Virus (HIV) status was negative. She had no chronic illnesses and gave no history of paracetamol, asprin, sodium valproate or alternative medicine ingestion. Clinical examination revealed a deeply jaundiced patient who was fully conscious on examination. The blood pressure, pulse and temperature were 116/68mmHg, 104 bpm and 37.2 degrees Celsius respectively. Respiratory and cardiovascular examinations were normal. The abdomen was soft and there was no hepatomegaly or splenomegaly. The fundal height was 35 weeks and the foetal heart sound was absent. She was draining thin meconium stained liquor at presentation and underwent preterm vaginal delivery with intrauterine death. The vital signs remained normal but the patient was deeply icteric.

Comparison of haematological and renal tests were done on admission and then 48 h later showed a rising white blood cell count (WBC) (10,000 to 17,000 cells/mm3), falling haemoglobin (8.6 to 7.5 g/dl), Platelets (PLT) had fallen (74,000 to 64,000/microlit), rising urea (43 to 105) and creatinine (2.36 to 2.84), hyponatremia (sodium 138 to 130 mmol/l), rising potassium (3.10 to 4.5 mmol/l). The liver function tests showed elevated alkaline phosphatase (ALP) (330 IU/L and 466 IU/L) and gamma glutamyl transpeptidase (GGT) (49 IU/L) with minimally elevated aspartate aminotransferase (AST) (52 U/l) and alanine aminotransferase (ALT) (32 U/l). Total serum protein and albumin were 4.92 g/dl and 2.56 g/dl respectively. Total bilirubin was 16.81 mg/dl and direct bilirubin 13.49 mg/dl. Hepatitis A and B were negative. Rapid Diagnostic Test (RDT) for malaria was negative. The urine was dark and urinalysis showed trace proteinuria, RBC 2-3/HPF, WBC 3-4/HPF and Epithelial cells 2-3/HPF. She had repeated episodes of hypoglycaemia which were corrected with

50% dextrose followed by infusion of 10% dextrose 8 hourly. Coagulation profile was deranged with raised fibrin degradation products (FDP) 4038 ng/ml, D-dimer 2019ng/ml, APTT 27.3 seconds, PT 28 seconds and INR 2.2. Uric acid was 11.2mg/dl. Her urine and blood cultures were negative on admission. Repeat Liver function tests after 72 hours showed rise in total bilirubin levels (19.18 mg/dL) and direct bilirubin 16.87 mg/dL.

USG whole abdomen revealed fatty liver grade 2, mild to moderate ascites with no features of chronic liver disease. The kidney size were normal with raised parenchymal echogenicity and maintained cortico-medullary differentiation. Ascitic fluid analysis showed high SAAG (serum albumin ascitic fluid gradient) with no evidence of peritonitis.

Among the pregnancy related syndromes, AFLP was considered more likely than HELLP syndrome and pre-eclamptic liver dysfunction in view of coagulopathy and absence of pregnancy-induced hypertension. She fulfilled 8 of 14 Swansea diagnostic criteria for AFLP including vomiting, hypoglycemia, hyperbilirubinemia, elevated transaminase levels, coagulopathy, deranged renal function, leucocytosis, ascites.

She was given empirical antibiotics and other supportive treatment after drawing blood cultures. Urine output and blood sugars were regularly monitored.

Due to persistent organ dysfunction despite termination of pregnancy, she was offered sessions of Therapeutic Plasma Exchange - on postpartum days 3,5 and 7. TPE was done with membrane filtration technique via standard Hemodialysis (Fresenius HD Machine). In each session, 2 litres of plasma was removed and replaced by Fresh Frozen Plasma (FFP) at the rate of 45 ml/minute without periprocedural complications. Patient received 24 units of FFP, 4 units of Packed cell transfusion, 8 units of cryoprecipitate & 4 units IV Human albumin (20%) transfusion.

Post TPE, she had sustained clinical improvement with resolution of ascites and gradual improvement of biochemical parameters (Total serum bilirubin 3.2 mg/dL, AST 40 U/L, ALT 38 U/L), coagulation profile (PT 12 seconds & INR 1.0) and normalization of renal parameters (Serum creatinine 0.64 mg/dL & urea 25 mg/dL) after two weeks and discharged after three weeks of hospitalization.

**DISCUSSION**

We described a case of a patient with AFLP with persistent acute liver failure despite termination of pregnancy, where timely TPE lead to prompt recovery. This case highlights the importance of a high index of suspicion of the condition in women presenting with jaundice in pregnancy. Other differential diagnosis of jaundice occurring during pregnancy include viral hepatitis, preeclampsia, cholelithiasis and intrahepatic cholestasis of pregnancy (ICP) [(4)]. The clinical presentation and laboratory findings of AFLP are vague and nonspecific, and pose a diagnostic challenge [(5)]. It is important to always consider life threatening differentials which may require prompt delivery and intensive care.

Whilst HELLP syndrome and AFLP usually complicate the third trimester of pregnancy, HELLP syndrome (1 in 5000) is seen more frequently than AFLP (1 in 13000)[(4,6)]. In our case, the patient was at risk for both conditions as she was young and

nulliparous. The blood pressure was however normal and urinalysis had trace proteinuria. Key features of jaundice and the episodes of hypoglycemia, raised ALT, AST and high WBC as well as the coagulopathy shown by deranged coagulation profile made the diagnosis of AFLP more likely. These tests have aided in the diagnosis of the coagulopathy and timely supportive care with blood products. Viral hepatitis also presents with jaundice but is characterised by a generally unwell patient with fever, nausea, vomiting and markedly elevated aminotransferases. Patients with intrahepatic cholestasis of pregnancy commonly complain of pruritus and their serum bilirubin levels do not usually exceed 6 mg/dl[(2)]. Ingestion of drugs and herbal remedies that could lead to hypoglycemia were ruled out from the history. Cholelithiasis and viral hepatitis may occur at any time during pregnancy unlike AFLP which is usually diagnosed in the third trimester[(7)]. Other differential diagnoses were excluded in our case based on the symptoms, the timing of the presentation and investigations that were available. The definitive management of AFLP is prompt delivery of the foetus and supportive intensive care.

There is usually improvement of symptoms 1 to 2 days after delivery but for patients with liver failure and extrahepatic organ failure, we propose that TPE be considered as a measure to salvage AFLP patients.

The decision to perform TPE in our patient was based on worsening clinical condition despite termination of pregnancy. Table 1 describes the Swansea criteria used for diagnosis of AFLP and Table 2 summarises existing literature on TPE in AFLP [(4,6,11-17)]. Similar to our observation, these reports have shown benefit of TPE in AFLP in the form of rapid normalisation of laboratory parameters, shorter hospital stay, reversal of multiorgan failure and decreased mortality. Larger prospective studies may better elucidate the impact of TPE on maternal survival in AFLP, but the rarity of the disease limits the feasibility of such studies. Hence, we suggest TPE as a therapeutic option to salvage AFLP patients with inadequate clinical improvement despite termination of pregnancy.

**Table 1. Swansea diagnostic criteria[3]**

| Laboratory | Clinical | Other |
|---|---|---|
| Bilirubin >14 µmol/L | Vomiting | Ultrasound showing ascites/ bright liver |
| Hypoglycaemia <4 mmol/L | Abdominal pain | Histology showing microvesicular steatosis |
| Uric acid >340 µmol/L | Polydipsia and polyuria | |
| Leukocytosis >11x10⁶/L | Encephalopathy | |
| AST/ALT >42 IU/L | | |
| Ammonia >47 µmol/L | | |
| Creatinine >150 µmol/L | | |
| Coagulopathy, PT >14 s | | |

AST= aspartate transaminase; ALT= alanine transaminase; PT= prothrombin time.

**Table 2:** Summary of Studies Done in Plasma Exchange for Acute Fatty Liver of Pregnancy

| Authors | Type of publication | Patients and interventions | Indication for TPE | Results |
|---|---|---|---|---|
| Tang et al | Non randomised control trial | N=28 TPE, n=13 Conventional treatment, n=15 Cultured hepatocytes were treated with the plasma of patients before and after TPE and also the TPE waste replacement fluid Delivery to TPE interval= 6 hours Number of TPE sessions=1-3 | Proportions of various organ failure in each group not mentioned separately | No mortality in either groups TPE group had lesser hospital stay, lower ICU stay and faster recovery of hepatic function Serum of patients in TPE group showed lower levels of Malonaldehyde (Oxidative markers), Caspase-2 and Caspase -9(apoptosis markers) after first TPE sessions compared to before TPE. |
| Jin et al | Retrospective series | N=39 All underwent TPE Delivery to TPE interval= 1-5 days Number of TPE sessions=1-4 | Encephalopathy (n=14) AKI (n=19) DIC (n=20) | Survival in 37(94.8%) patients Earlier initiation of TPE led to quicker recovery with lesser sessions |
| Martin et al | Case series | N=6 All patients underwent TPE Delivery to TPE interval= 2-9 days Number of TPE sessions= 2-4 | Liver failure, Renal failure (n=6) Respiratory failure (n=3) Circulatory failure (n=2) | Survival 100% Improvement in multiorgan failure |
| Chu et al | Retrospective series | N=11 All patients underwent combined TPE and CHDF Delivery to TPE interval= 0-3 days Number of TPE sessions=2-8 | Liver failure, renal failure (n=11) Respiratory failure (n=4) | Survival in 10 patients Resolution of multiorgan dysfunction No significant procedure related complications |
| Ding et al | Retrospective study | N=22 Conventional treatment, n=16 TPE+ PP, n=6 Delivery to TPE interval= 2 weeks Number of TPE sessions=2-8 | Liver failure (n=6) DIC(n=2) | 83.3% survival in TPE+PP group 18% survival in conventional therapy group |

**CONCLUSION**

AFLP is a rare, life-threatening complication of third trimester of pregnancy which requires a high index of suspicion for early diagnosis. Urgent delivery and maximum supportive care should be instituted to prevent poor outcomes. In rare instances where organ failure persists, TPE may be a readily available modality to prevent maternal mortality.

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