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Case Series

Obstetrics and Gynaecology Section

Acute Fatty Liver of Pregnancy- A Case Series from a Tertiary Hospital of Kolkata, India: A Case Series

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ABSTRACT

Acute Fatty Liver of Pregnancy (AFLP) is a rare, life-threatening complication of pregnancy that affects women in the third trimester or immediate postpartum period. Although the exact pathogenesis is poorly understood, it has been linked to a deficiency in Long Chain 3-hydroxyacyl-CoA Dehydrogenase (LCHAD) in foetal fatty acid metabolism. The early diagnosis of AFLP can sometimes be challenging due to overlapping features with severe preeclampsia, Haemolysis Elevated Liver Enzymes, Low Platelet (HELLP) syndrome, viral hepatitis, and cholestasis of pregnancy. It is a diagnosis of exclusion when no other known liver diseases are present in the mother. Herein, the authors presented a case series of four cases of AFLP, including their chief complaints, clinicopathological findings, management, and outcomes. Early diagnosis, termination of pregnancy, and multidisciplinary management in the post-delivery period are crucial for improving foetomaternal prognosis.

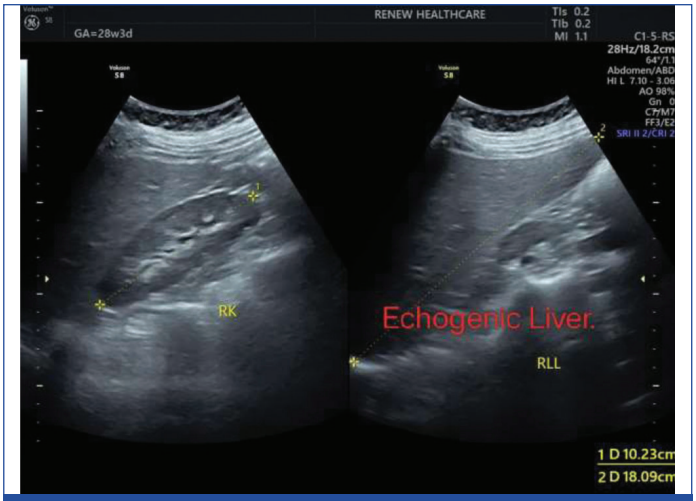
Keywords: Disseminated intravascular coagulopathy, Elevated liver enzymes, Low platelets (HELLP), Long chain 3-hydroxyacyl-CoA dehydrogenase, Multiple organ dysfunction

INTRODUCTION

The AFLP is a rare obstetric emergency characterised by acute liver dysfunction or failure during pregnancy, with a high chances of foetomaternal morbidity and mortality. However, global outcomes have improved due to early diagnosis and timely delivery of the foetus. The incidence of AFLP is estimated to be one in 5,000-20,000 pregnancies [1]. The pathogenesis of AFLP is still poorly understood. The most significant metabolic defect in the foetus is the recessively inherited deficiency of LCHAD. Non metabolised fatty acids from the foetal circulation re-enter the maternal circulation through the placenta and accumulate in haepatocytes, leading to lipotoxicity [2]. It has been observed that mothers with fatty liver of pregnancy often have LCHAD-deficient children with Reye-like syndrome [2,3]. Some identified high-risk factors for AFLP include primigravida, male foetus, previous history of AFLP, and multiple gestation [4].

Case 1

A 29-year-old multipara at 29+5 weeks of gestation presented with progressive nausea/vomiting, high-coloured urine, and yellow discoloration of the eyes for the last seven days. The patient reported no itching or fever and had a previous history of chronic hypertension but was not yet on medication for this pregnancy. Upon examination, patient's blood pressure was 140/90 mmHg and she exhibited icterus. The size of her gravid uterus was consistent with 28-30 weeks. The liver was not palpable. Laboratory parameters at admission revealed anaemia, leukocytosis, serum bilirubin of 5.92 mg/dL, Aspartate Aminotransferase (AST) of 458 IU/L, Alanine Aminotransferase (ALT) of 502 IU/L, and creatinine of 1.8 mg/dL. Tests for hepatitis A, B, C, and E were negative. The patient was prescribed antibiotics, urodeoxycholic acid tablets, and vitamin K injections. An abdominal ultrasound showed an echogenic liver [Table/Fig-1]. Within four days, her bilirubin levels rose to 22.8 mg/dL. The patient gradually developed hypoglycaemia, confusion, drowsiness, and oliguria. Emergency preterm cesarean section was decided upon at 30+3 weeks. The patient delivered a live male foetus weighing 1.05 kg.



[Table/Fig-1]: Echogenic liver on ultrasound (kidney echogenicity provided for comparison).

In the Intensive Care Unit (ICU), the patient exhibited signs and symptoms of haepatic encephalopathy (grade 2 according to the West Haven classification system) [5], including disorientation, lethargy, hypersomnia, and marked slowing of mental tasks. The patient also had Disseminated Intravascular Coagulation (DIC) and a haepatic subcapsular bleed, which was managed conservatively. Over the next three days, patient received six units of Packed Red Blood Cells (PRBC), 15 units of Fresh Frozen Plasma (FFP), 12 units of cryoprecipitate, and two units of Single Donor Platelets (SDP) [Table/Fig-2]. Her sensorium, coagulation parameters, liver function, and urine output gradually improved over the course of two weeks. The patient was discharged home on day 30. The Swansea score for this case was 11 [Table/Fig-3,4].

Case 2

A 24-year-old primigravida with a twin pregnancy at 35+5 weeks presented with yellow discoloration of the eyes, nausea, and abdominal pain persisting for five days. The patient had no previous history of hypertension or liver conditions.

Case number	Age (in years)	Gravida	Type of delivery	Gestational age	Foetal gender	Co-morbidities	Swansea criteria score	Peak bilirubin (mg/dL)	Postpartum complications	ICU stay (in days)	Total transfusion units (PRBC, SDP, FFP, cryoprecipitate)	Patient outcome
1	29	2	LSCS	30+3	Male	Chronic hypertension	11	22.8	DIC, hepatic subcapsular bleed	14	35	Alive and healthy
2	24	1 (twin)	LSCS	35+5	Male, Female	Multiple gestation	10	14.0	DIC, rectus muscle haematoma	10	31	Alive and healthy
3	21	1	LSCS	36+4	Male	Gestational hypertension	12	10.8	DIC, MODS, liver failure, sepsis	15	36	Deceased
4	42	1 (twin)	LSCS	32	Male, Male	Twin (IVF) advanced maternal age	7	12.8	PPH, peripartum hysterectomy	5	14	Alive and healthy

[Table/Fig-2]: Clinical parameters of the study patients.
LSCS: Lower segment caesarean section; ICU: Intensive care unit; PRBC: Packed red blood cells; FFP: Fresh frozen plasma; IVF: In-vitro fertilisation; DIC: Disseminated intravascular coagulation; MODS: Multiple organ dysfunction syndrome; PPH: Postpartum haemorrhage

Signs and symptoms	Case 1	Case 2	Case 3	Case 4
Nausea, vomiting	+	+	+	+
Abdominal pain	-	+	-	-
Encephalopathy	+	+	+	-
Polyuria, polydipsia	-	-	-	-
Serum bilirubin >0.8 mg/dL	+	+	+	+
AST/ALT: >42 IU/L	+	+	+	+
Blood sugar <70 mg/dL	+	+	+	-
WBC >11000 mm^3	+	+	+	+
Creatinine>1.7 mg/dL	+	+	+	-
PT >14 sec, APTT >34 s	+	+	+	+
Ammonia >47 mcmol/L	Not done	Not done	Not done	Not done
Uric acid >340 mcmol/L	+	+	+	-
Echogenic liver (USG)	+	-	+	+
Ascites	+	-	+	+
Liver biopsy (Microvesicular steatosis)	Not Done	Not done	+	Not done
Total Swansea score	11	10	12	7

[Table/Fig-3]: Swansea score of the study patients (six or more signs/symptoms to be positive).
AST: Aspartate aminotransferase; ALT: Alanine transaminase; WBC: White blood cells; PT: Prothrombin time; APTT: Activated partial thromboplastin time; USG: Ultrasonography

Parameters	Signs and symptoms
Clinical features	Nausea, vomiting
	Abdominal pain
	Encephalopathy
	Polyuria/polydipsia
Laboratory features	Serum bilirubin: >0.8 mg/dL or >14 mcmol/L
	Blood sugar: <72 mg/dL or <4 mmol/L
	WBC: >11,000 mm^3
	AST/ALT: >42 IU/L
	Creatinine: >1.7 mg/dL
	PT: >14s, APTT: >34 s
	Ammonia >47 mcmol/L
	Uric acid: >340 mcmol/L
Ultrasound features	Ascites Echogenic liver
Histologic features	Microvesicular steatosis (liver biopsy)

[Table/Fig-4]: Swansea criteria for diagnosis of Acute Fatty Liver of Pregnancy (AFLP) (six or more features).
WBC: White blood cells; AST: Aspartate aminotransferase; ALT: Alanine transaminase; PT: Prothrombin time

During clinical examination, icterus, a blood pressure of 122/76 mmHg, and a uterus consistent with term size were observed. The patient appeared drowsy and confused. Laboratory investigations revealed serum bilirubin levels of 14.0 mg/dL, ALT levels of 146 U/L, AST levels of 151 U/L, Total Leucocyte Count (TLC) of 16,810 mm^3/dL, a prothrombin time of 16 seconds, creatinine levels of 1.7 mg/dL, and blood sugar levels of 40 mg/dL. Tests for hepatitis A, E, B, and C were negative. Abdominal ultrasound indicated a normal liver span and echogenicity. An emergency cesarean section was performed, resulting in the delivery of live twins: a male weighing 1.9 kg and a female weighing 1.8 kg. The patient experienced a blood loss of 1200 mL. The patient was transfused three units of PRBC, 16 units of FFP, six units of cryoprecipitate, and six units of Random Donor Platelets (RDP) over a period of three to four days [Table/Fig-1]. On day 3, the patient underwent re-exploratory laparotomy for rectus muscle haematoma. From day 4 onwards, the patient began exhibiting symptoms of haepatic encephalopathy (grade 1 according to the West Haven classification system), including hypersomnia, mild confusion, and slowing of mental tasks [5]. The patient was started on syrup lactulose 30 mL three times daily, tab rifaximin 550 mg twice daily, and injection of vitamin K. Gradually, her sensorium and general health improved, and the patient was discharged home on day 21. The Swansea score for this case was 10 [Table/Fig-3].

Case 3

A 21-year-old primigravida at 36w+4 weeks presented with loss of appetite, yellowing of the eyes, and high-coloured urine since four days. During clinical examination, icterus, pedal oedema, and a blood pressure of 146/98 mmHg (the first elevated blood pressure reading of this pregnancy) were observed. The uterus was consistent with term size, and the foetal heart rate was 138/min.

Laboratory parameters showed a haemoglobin level of 10.0 g/dL, WBC count of 17,180 mm^3, platelet count of 1.35 lac/mm^3, serum bilirubin level of 10.2 mg/dL, AST level of 508 IU/L, ALT level of 645 IU/L, and creatinine level of 1.8 mg/dL. The patient underwent emergency cesarean section the following day due to foetal distress and delivered a male baby weighing 2.0 kg.

Postoperatively, the patient's condition gradually deteriorated due to haepatic encephalopathy (grade 3 according to the West Haven classification system), characterised by disorientation about time and space, hypersomnia, inability to perform mental tasks, and amnesia. The patient also developed DIC, with her haepatic parameters showing a downward trend over the next several days. She experienced anuria, anasarca, abdominal distension, hypotension, and respiratory distress. She received transfusions of six units of PRBC, 12 units of FFP, 12 units of cryoprecipitate, and six units of RDP. Elective ventilation with vasopressor support and Continuous Renal Replacement Therapy (CCRT) were initiated. Despite prone ventilation, she developed worsening Acute Respiratory Distress Syndrome (ARDS). She progressed to Multiple Organ Dysfunction Syndrome (MODS) and slipped into a coma. Extracorporeal Membrane Oxygenation (ECMO) was employed in an attempt to manage her condition. However, despite all measures, the patient succumbed to acute liver failure, sepsis, and MODS on day 15 [Table/Fig-2]. The Swansea score for this case was 12 [Table/Fig-3].

Case 4

A 42-year-old primigravida with a twin gestation (conceived through IVF) at 32 weeks was referred from one of the North Eastern states. The patient had been experiencing symptoms of nausea, yellow discoloration of the eyes, and loss of appetite for four days. During examination, her blood pressure was normal, deep icterus, and mild pallor was observed. Laboratory investigations revealed a serum bilirubin level of 12.8 mg/dL, AST level of 892 IU/L, ALT level of 1002 IU/L, platelet count of 1.5 lac/mm^3, and creatinine level of 1.0 mg/dL. Tests for haepatitis A, E, B, and C were negative. The patient delivered live twin boys weighing 1.5 kg and 1.7 kg via emergency preterm cesarean section. She experienced atonic Postpartum Haemorrhage (PPH) after the cesarean, which did not respond to uterotonics, leading to the performance of a peripartum hysterectomy. Blood loss during the procedure was 1.5 L. The patient received six units of PRBC, four units of FFP, and four units of cryoprecipitate [Table/Fig-2]. With gradual improvement, the patient was discharged home on day 20. The Swansea score for this case was 7 [Table/Fig-3].

DISCUSSION

The AFLP is a rare obstetric emergency with features of acute liver dysfunction/failure during pregnancy, which poses a high-risk of morbidity and mortality for both the mother and foetus. However, global outcomes have improved due to early diagnosis and prompt delivery of the foetus. The condition was first described by Sheehan in 1940, and its incidence ranges from one in 5,000 to 20,000 pregnancies [1].

The pathogenesis of AFLP is not well understood. LCHAD deficiency, a recessively inherited metabolic defect, is considered the most important factor in foetal development. Non metabolised fatty acids from the foetal circulation re-enter the maternal circulation through the placenta and accumulate in haepatocytes, leading to lipotoxicity [2]. It has been observed that mothers with fatty liver of pregnancy often have children with LCHAD deficiency and Reye-like syndrome [2,3]. Some identified high-risk factors for AFLP include primigravida, male foetus, previous history of AFLP, and multiple gestation [4].

Fatty liver of pregnancy presents with a spectrum of clinical severity. Symptoms may include persistent nausea/vomiting, malaise, anorexia, and progressive jaundice of varying degrees [1]. Many patients also exhibit signs and symptoms overlapping with severe preeclampsia, such as hypertension, proteinuria, low platelet count (HELLP syndrome), and oedema. Laboratory parameters typically show hyperbilirubinaemia, elevated liver transaminases, hypoglycaemia, leukocytosis, increased creatinine levels, and prolonged clotting times [4,6]. Profound activation of endothelial cells with capillary leakage can lead to hemodynamic instability, acute kidney injury, ascites, and pulmonary oedema. Decreased uteroplacental flow can also jeopardize foetal well-being [7].

Due to its relative rarity, there have been few large case series reported in the literature. Liu G et al., described a series of 15 patients over a period of 10 years and concluded that early diagnosis and prompt delivery can improve prognosis [4]. The Swansea diagnostic criteria, developed by Ch'ng CL et al., in 2002 at Swansea NHS Trust hospitals, are widely used worldwide for the diagnosis of AFLP since their proposal [6-8]. The clinical presentation and laboratory findings of AFLP are vague and non specific, which poses a diagnostic challenge [1]. A case reported by Ziki E et al., in 2019 highlighted the importance of timely diagnosis in AFLP to prevent poor maternal outcomes [9]. Over the past two decades, the incidence of AFLP and its associated foetomaternal morbidity has decreased due to better knowledge, early diagnosis, and termination of pregnancy [10,11].

Marked progressive hyperbilirubinaemia, deranged renal function tests, hypoglycaemia with normal platelet count, and elevated serum bile acids should raise suspicion of AFLP and shift focus from HELLP syndrome and cholestasis of pregnancy [10,12]. Liver biopsy was only performed postmortem for one patient in the present study due to coagulopathy issues. The mode of delivery is a dilemma and should be decided based on cervical findings, foetal compromise, coagulation parameters, and the patient's general condition [7,11]. Management of AFLP requires a multidisciplinary approach and should ideally be done at a tertiary centre. Although the initial postpartum period can be challenging, with good supportive care, most patients show uphill trend. Sivakumar S reported on three cases of AFLP with significant complications due to renal dysfunction, coagulopathy, and encephalopathy. These cases, like present case showed improved outcomes with early diagnosis, delivery of the foetus, and multidisciplinary supportive care [13]. Ling W et al., reported a series of three patients who were referred with different complaints, but early suspicion of AFLP and subsequent multidisciplinary management led to positive outcomes [14].

Full clinical recovery from AFLP usually takes several weeks with no long-term sequelae, although histological changes in the liver may persist for months. Patients should be informed about the association between various defects in fatty acid oxidation in offspring and liver disease in the mother. Babies born to mothers with AFLP should be under follow-up [1,4]. Utsa IM et al., reported a series of 14 cases several years ago, with favourable outcomes attributed to early diagnosis and termination of pregnancy [11]. The key to early diagnosis lies in maintaining a high index of suspicion and excluding common liver disorders of pregnancy, like viral hepatitis, cholestasis of pregnancy, severe preeclampsia, HELLP syndrome, dengue, and malaria [15,16].

CONCLUSION(S)

There are many etiologies for jaundice in pregnancy, but one of the most life-threatening conditions is AFLP. However, due to its rarity, the diagnosis can be missed, leading to high morbidity and mortality among pregnant women, especially in low-resource settings. Therefore, early suspicion and diagnosis, prompt multidisciplinary team management, early termination of pregnancy, and robust intensive care support are crucial for improving foetomaternal outcomes.

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