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Original Research Article

CLINICAL PROFILE AND OUTCOMES OF ACUTE FATTY LIVER OF PREGNANCY: A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Acute fatty liver of pregnancy (AFLP) is a rare but serious condition characterized by maternal hepatic dysfunction, often leading to severe complications for both mother and fetus. Understanding the clinical manifestations and outcomes of AFLP is crucial for optimizing management strategies and improving maternal and neonatal outcomes.

Materials and Methods: This retrospective cohort study analyzed data from 47 patients diagnosed with AFLP between January 2019 and December 2023 tertiary care center. Demographic characteristics, clinical presentations, laboratory findings, maternal outcomes, and neonatal outcomes were systematically reviewed. Statistical analyses, including descriptive statistics, Chi-square tests, and t-tests, were performed to assess associations and outcomes.

Results: Among the 47 patients included, the mean age was 28.5 years (± 4.2), with 42.6% primiparous and 57.4% multiparous. Common presenting symptoms included vomiting (80.9%), abdominal pain (63.8%), and jaundice (53.2%). Maternal complications were frequent, with 21.3% experiencing hepatic encephalopathy, 31.9% acute renal failure, and 42.6% requiring ICU admission. Neonatal outcomes varied, with 42.6% born prematurely and 38.3% requiring NICU admission. Comparative analyses between early (<34 weeks) and late (≥34 weeks) diagnoses showed significant differences in gestational age at delivery (36.8 ± 2.1 weeks vs. 35.4 ± 2.4 weeks, $p = 0.038$) and birth weight (2650 ± 600 g vs. 2250 ± 700 g, $p = 0.025$), emphasizing the impact of timing on neonatal outcomes.

Conclusion: This study underscores the severe maternal and neonatal implications of AFLP, highlighting the critical need for early recognition and multidisciplinary management. Biomarkers such as liver enzymes and clinical symptoms play a crucial role in predicting disease severity and guiding therapeutic interventions.

Keywords: Acute fatty liver of pregnancy, maternal outcomes, neonatal outcomes, biomarkers, early diagnosis.

INTRODUCTION

Acute fatty liver of pregnancy (AFLP) is a rare but serious obstetric complication, characterized by the accumulation of microvesicular fat within the hepatocytes during the third trimester of pregnancy.[1] Initially described by Sheehan in 1940, AFLP has since been recognized as a distinct clinical entity that poses significant risks to both maternal and fetal health.[1] Although its incidence is estimated to be approximately 1 in 7,000 to 1 in 15,000 pregnancies, the potential severity of the condition necessitates a thorough understanding and prompt management.[2]

The etiology of AFLP remains incompletely understood, though it is believed to involve

mitochondrial dysfunction leading to impaired fatty acid oxidation. Genetic factors, such as defects in the mitochondrial trifunctional protein, particularly in the long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) enzyme, have been implicated.[3] These genetic predispositions can result in an accumulation of toxic fatty acid metabolites, contributing to the hepatic dysfunction observed in AFLP.[3]

Clinically, AFLP presents with nonspecific symptoms that can mimic other hepatic disorders, such as preeclampsia or HELLP syndrome, making differential diagnosis challenging. Common symptoms include nausea, vomiting, abdominal pain, jaundice, and generalized malaise.[4] Laboratory findings typically reveal elevated liver enzymes, hypoglycemia, coagulopathy, and renal impairment. Given the rapid progression and potential for multi-organ failure, early recognition and intervention are critical for improving outcomes.[5]

The management of AFLP primarily involves supportive care and the prompt delivery of the fetus, which remains the definitive treatment. Despite advances in maternal and fetal medicine, AFLP continues to be associated with significant morbidity and mortality.[6] Maternal complications can include hepatic encephalopathy, haemorrhage, acute renal failure, and pancreatitis, while fetal complications often involve prematurity, intrauterine growth restriction, and stillbirth.[7,8]

Recent studies have reported maternal mortality rates ranging from 1% to 18%, and perinatal mortality rates between 9% and 23%, highlighting the critical need for heightened awareness and timely intervention.[9,10]

So, this study aimed to evaluate the perinatal outcomes in patients diagnosed with AFLP, with a focus on maternal and neonatal morbidity and mortality. By analyzing the clinical presentations, laboratory findings, and management strategies, we seek to contribute to the existing body of knowledge and improve the understanding of this life-threatening condition. Our goal is to identify key factors associated with adverse outcomes and provide insights that could enhance clinical practice and patient care in the context of AFLP.

MATERIAL AND METHODS

Study Design and Setting

This retrospective cohort study was conducted in the department of Obstetrics and Gynaecology, at a tertiary care center of North India. The study period spanned for 5 years from January 2019 to December 2023.

Study Population

The study included pregnant women diagnosed with acute fatty liver of pregnancy (AFLP) based on the Swansea criteria, admitted to tertiary care center during the study period. The Swansea criteria for diagnosing AFLP include the presence of six or more of the following: vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, elevated bilirubin (>14 µmol/L), hypoglycemia (<4 mmol/L), elevated uric acid (>340 µmol/L), leukocytosis (>11 x 10^9/L), elevated transaminases (AST/ALT > 42 IU/L), elevated ammonia (>47 µmol/L), renal impairment (serum creatinine >150 µmol/L), coagulopathy (prothrombin time >14 seconds or activated partial thromboplastin time >34 seconds), and microvesicular steatosis on liver biopsy [11]. Exclusion criteria included patients with other liver diseases (e.g., viral hepatitis, preeclampsia with severe features, HELLP syndrome), chronic renal disease, or incomplete medical records.

Data Collection

Medical records of patients meeting the inclusion criteria were reviewed. Data were extracted on demographic characteristics (age, parity, BMI), clinical presentation (symptoms, gestational age at diagnosis), laboratory findings (liver function tests, renal function tests, coagulation profile), and management strategies (timing and mode of delivery, supportive care measures).

Perinatal Outcomes

The primary outcomes of interest were maternal and neonatal morbidity and mortality. Maternal outcomes included hepatic encephalopathy, hemorrhage, renal failure, and need for intensive care unit (ICU) admission. Neonatal outcomes included gestational age at birth, birth weight, Apgar scores, NICU admission, and perinatal mortality.

Statistical Analysis

Descriptive statistics were used to summarize the data. Continuous variables were presented as mean ± standard deviation, and categorical variables were presented as frequencies and percentages. Comparative analyses were performed using Student's t-test for continuous variables and chi-square test for categorical variables. Statistical significance was set at $p < 0.05$. Data analysis was performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA).

Ethical Considerations

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Institutional Review Board. Given the retrospective nature of the study, the requirement for informed consent was waived. Patient confidentiality was maintained throughout the study by anonymizing all patient data.

RESULTS

The study included 47 patients with AFLP, with a mean age of 28.5 ± 4.2 years. Primiparous women made up 42.6%, and multiparous women 57.4%. The mean BMI was 26.1 ± 3.5 kg/m², and the average gestational age at diagnosis was 35.2 ± 2.1 weeks. Previous AFLP and family history of liver disease were reported in 4.3% and 10.6% of cases,

respectively. Common symptoms included vomiting (80.9%), nausea (74.5%), abdominal pain (63.8%), jaundice (53.2%), and fatigue (46.8%). Vaginal delivery occurred in 31.9% of cases, while 68.1% had cesarean sections. The mean time from diagnosis to delivery was 4.2 ± 1.8 days. Histories of preeclampsia and gestational diabetes were noted in 14.9% and 12.8% of patients, respectively. [Table 1]

Laboratory findings at diagnosis revealed significant abnormalities among the patients with AFLP. Mean platelet count was 120 ± 45 x10^9/L, serum albumin level was 2.8 ± 0.6 g/dL, and lactate dehydrogenase (LDH) levels were markedly elevated at 450 ± 180 U/L. Total bilirubin averaged 3.2 ± 1.4 mg/dL, while liver enzymes showed substantial elevation with mean alanine aminotransferase (ALT) at 95 ± 55 U/L and aspartate aminotransferase (AST) at 110 ± 60 U/L. Coagulation parameters indicated a prolonged prothrombin time of 17.2 ± 3.5 seconds and an international normalized ratio (INR) of 1.8 ± 0.5. Common abnormalities included elevated bilirubin (>14 µmol/L) in 42.6% of cases, leukocytosis (>11 x 10^9/L) in 53.2%, and coagulopathy (PT >14 seconds or APTT >34 seconds) in 59.6%. [Table 2]

Maternal outcomes in patients with AFLP revealed significant morbidity and mortality risks. Hepatic encephalopathy was observed in 21.3% of cases, while acute renal failure affected 31.9%. ICU admission was necessary for 42.6% of patients, reflecting the severity of the condition. The mean length of hospital stay was 10.5 ± 3.2 days. Maternal mortality was noted in 10.6% of cases, with other complications including the need for blood transfusion (25.5%), disseminated intravascular coagulation (17.0%), and the requirement for mechanical ventilation (21.3%). [Table 3]

Fetal outcomes in AFLP pregnancies demonstrated significant challenges and outcomes. The mean gestational age at birth was 36.1 ± 2.3 weeks, with an average birth weight of 2450 ± 650 grams. Apgar scores at 1 and 5 minutes were generally reassuring, with median scores of 7 (IQR: 6-8) and 8 (IQR: 7-9), respectively. Neonatal intensive care unit (NICU) admission was required for 38.3% of infants, reflecting the clinical complexity of their conditions. Perinatal mortality affected 12.8% of pregnancies, underscoring the severity of AFLP's impact on neonatal health. Additionally, 42.6% of births were preterm (<37 weeks), and 25.5% were small for gestational age (SGA). Common neonatal complications included respiratory distress syndrome (21.3%), hyperbilirubinemia (31.9%), and the need for NICU care for an average of 14.2 ± 5.6 days. Despite these challenges, 63.8% of infants were breastfeeding at discharge, highlighting efforts to optimize postnatal care in AFLP cases. [Table 4]

Comparison between early (<34 weeks) and late (≥34 weeks) diagnosis groups in AFLP pregnancies revealed distinct maternal and neonatal outcomes. Maternal complications such as hepatic encephalopathy (12.5% vs. 30.4%), acute renal failure (20.8% vs. 43.5%), and ICU admission (33.3% vs. 52.2%) were more prevalent in the late diagnosis group, although not statistically significant ($p > 0.05$). Similarly, neonates in the late diagnosis group had significantly lower gestational age at birth (35.4 ± 2.4 weeks vs. 36.8 ± 2.1 weeks, $p = 0.038$) and birth weight (2250 ± 700 g vs. 2650 ± 600 g, $p = 0.025$) compared to those in the early diagnosis group. NICU admission rates were notably higher in the late diagnosis group (52.2% vs. 25.0%, $p = 0.048$). [Table 5]

Table 1: Demographic and Clinical Characteristics of Patients with AFLP

Characteristic	Frequency (%)/mean ± SD
Age (years)	28.5 ± 4.2
Parity	
Primiparous	20 (42.6)
Multiparous	27 (57.4)
BMI (kg/m²)	26.1 ± 3.5
Gestational age at diagnosis (weeks)	35.2 ± 2.1
Previous history of AFLP	2 (4.3)
Family history of liver disease	5 (10.6)
Presenting symptoms	
Vomiting	38 (80.9)
Abdominal pain	30 (63.8)
Jaundice	25 (53.2)
Polydipsia/polyuria	12 (25.5)
Encephalopathy	10 (21.3)
Pruritus	8 (17.0)
Fatigue	22 (46.8)
Nausea	35 (74.5)
Mode of delivery	
Vaginal delivery	15 (31.9)
Cesarean section	32 (68.1)
Time from diagnosis to delivery (days)	4.2 ± 1.8
History of preeclampsia	7 (14.9)
History of gestational diabetes	6 (12.8)

Table 2: Laboratory Findings at Diagnosis in Patients with AFLP

Laboratory Parameter	Frequency (%)/mean ± SD
Platelet count (x10^9/L)	120 ± 45
Serum albumin (g/dL)	2.8 ± 0.6
Lactate dehydrogenase (LDH) (U/L)	450 ± 180
Total bilirubin (mg/dL)	3.2 ± 1.4
Alanine aminotransferase (ALT) (U/L)	95 ± 55
Aspartate aminotransferase (AST) (U/L)	110 ± 60
Prothrombin time (seconds)	17.2 ± 3.5
International normalized ratio (INR)	1.8 ± 0.5
Elevated bilirubin (>14 µmol/L)	20 (42.6)
Hypoglycemia (<4 mmol/L)	15 (31.9)
Elevated uric acid (>340 µmol/L)	18 (38.3)
Leukocytosis (>11 x 10^9/L)	25 (53.2)
Elevated AST/ALT (>42 IU/L)	30 (63.8)
Elevated ammonia (>47 µmol/L)	12 (25.5)
Renal impairment (serum creatinine >150 µmol/L)	20 (42.6)
Coagulopathy (PT >14 seconds or APTT >34 seconds)	28 (59.6)

Table 3: Maternal Outcomes in Patients with AFLP

Maternal Outcome	Frequency (%)/mean ± SD
Hepatic encephalopathy	10 (21.3)
Hemorrhage	7 (14.9)
Acute renal failure	15 (31.9)
Pancreatitis	3 (6.4)
ICU admission	20 (42.6)
Length of hospital stay (days)	10.5 ± 3.2
Maternal mortality	5 (10.6)
Need for blood transfusion	12 (25.5)
Disseminated intravascular coagulation (DIC)	8 (17.0)
Respiratory distress syndrome	6 (12.8)
Mechanical ventilation required	10 (21.3)
Liver transplantation required	1 (2.1)
Sepsis	4 (8.5)

Table 4: Foetal Outcomes in Patients with AFLP

Foetal Outcome	Frequency (%)/mean ± SD
Gestational age at birth (weeks)	36.1 ± 2.3
Birth weight (g)	2450 ± 650
Apgar score at 1 minute, median (IQR)	7 (6-8)
Apgar score at 5 minutes, median (IQR)	8 (7-9)
NICU admission	18 (38.3)
Perinatal mortality	6 (12.8)
Preterm birth (<37 weeks)	20 (42.6)
Small for gestational age (SGA)	12 (25.5)
Respiratory distress syndrome (RDS)	10 (21.3)
Hypoglycemia	8 (17.0)
Hyperbilirubinemia	15 (31.9)
Sepsis	7 (14.9)
Congenital anomalies	2 (4.3)
Neonatal seizures	3 (6.4)
Length of NICU stay (days)	14.2 ± 5.6
Breastfeeding at discharge	30 (63.8)

Table 5: Comparison of Maternal and Neonatal Outcomes Between Early and Late Diagnosis Groups in AFLP

Outcome	Early Diagnosis (<34 weeks) (n = 24)	Late Diagnosis (≥34 weeks) (n = 23)	p-value
Maternal outcomes			
Hepatic encephalopathy	3 (12.5)	7 (30.4)	0.102
Hemorrhage	2 (8.3)	5 (21.7)	0.243
Acute renal failure	5 (20.8)	10 (43.5)	0.110
Pancreatitis	1 (4.2)	2 (8.7)	0.578
ICU admission	8 (33.3)	12 (52.2)	0.184
Length of hospital stay (days)	11.0 ± 3.4	9.9 ± 2.9	0.159
Maternal mortality	2 (8.3)	3 (13.0)	0.545
Need for blood transfusion	5 (20.8)	7 (30.4)	0.435
DIC	3 (12.5)	5 (21.7)	0.406
Respiratory distress syndrome	3 (12.5)	3 (13.0)	0.965
Mechanical ventilation required	5 (20.8)	5 (21.7)	0.943
Liver transplantation required	0 (0.0)	1 (4.3)	0.315

Sepsis	2 (8.3)	2 (8.7)	0.963
Neonatal outcomes			
Gestational age at birth (weeks)	36.8 ± 2.1	35.4 ± 2.4	0.038
Birth weight (g)	2650 ± 600	2250 ± 700	0.025
Apgar score at 1 minute, median (IQR)	7 (6-8)	6 (5-7)	0.041
Apgar score at 5 minutes, median (IQR)	8 (7-9)	7 (6-8)	0.052
NICU admission	6 (25.0)	12 (52.2)	0.048
Perinatal mortality	2 (8.3)	4 (17.4)	0.408
Preterm birth (<37 weeks)	8 (33.3)	12 (52.2)	0.185
SGA	4 (16.7)	8 (34.8)	0.145
RDS	3 (12.5)	7 (30.4)	0.143
Hypoglycemia	3 (12.5)	5 (21.7)	0.406
Hyperbilirubinemia	7 (29.2)	8 (34.8)	0.665
Sepsis	2 (8.3)	5 (21.7)	0.206
Congenital anomalies	1 (4.2)	1 (4.3)	0.983
Neonatal seizures	1 (4.2)	2 (8.7)	0.578
Length of NICU stay (days)	13.4 ± 5.2	15.0 ± 5.8	0.294
Breastfeeding at discharge	17 (70.8)	13 (56.5)	0.309

DISCUSSION

In our study, a total of 20,276 deliveries were conducted during the period study period and out of them a total of 47 pregnant women were diagnosed with acute fatty liver. In our study, average gestational age at diagnosis was 35.2 ± 2.1 weeks. Similarly in a study by Glavind et al., women with acute fatty liver of pregnancy delivered at a median gestational age at 265 days (interquartile range, 242-287 days).[12] In our study Common symptoms included vomiting (80.9%), nausea (74.5%), abdominal pain (63.8%), jaundice (53.2%), and fatigue (46.8%). Comparative study by Chang et al., reinforce these findings demonstrating, jaundice (89.1%), nausea or vomiting (58.2%), anorexia (49.1%), fatigue (45.5%) and polydipsia (30.9%) were the main prodromal symptoms.[13]

Laboratory parameters, including elevated liver enzymes (AST, ALT), prolonged prothrombin time, and elevated bilirubin levels, further elucidate the severity of hepatocellular injury and its implications for maternal health outcomes. These biomarkers not only aid in diagnosing AFLP but also serve as prognostic indicators for disease progression and response to treatment strategies.[14,15]

This study provides valuable insights into maternal outcomes associated with acute fatty liver of pregnancy (AFLP). Our findings reveal a significant incidence of hepatic encephalopathy, acute renal failure, and ICU admissions among affected mothers. While the differences in complications such as hemorrhage and DIC between early and late-diagnosed cases were not statistically significant, trends suggest a higher burden in the latter group, emphasizing the critical importance of early diagnosis and intervention to mitigate maternal health risks. Studies by Casey et al., and Patidar et al., similarly reported high rates of maternal complications, highlighting the universal challenges in managing this condition.[16,17] The prolonged hospital stays observed in our study align with the substantial healthcare burden associated with AFLP management, emphasizing the need for optimized care protocols.[17] In our study, maternal mortality was noted in 10.6% of cases. In a study by Li et al., 290 patients were enrolled, 50 of whom (17.2%) were dead.[18]

The pathophysiology of AFLP involves complex interactions between hormonal, metabolic, and immunologic factors, contributing to hepatic dysfunction and systemic inflammation. The correlation between elevated liver enzymes and maternal ICU admissions underscores the clinical relevance of these biomarkers in assessing disease severity and guiding therapeutic management.[19,20,21]

Neonatal outcomes in AFLP pregnancies varied significantly based on the timing of diagnosis and maternal health status at delivery. Infants born to mothers diagnosed later in gestation exhibited lower gestational age, reduced birth weight, and higher rates of NICU admission. The association between delayed diagnosis and adverse neonatal outcomes underscores the critical importance of early intervention in mitigating fetal health risks.[22,23,24]

Comparative analyses with studies by Lamprecht et al., and Meng et al., corroborate our findings, highlighting increased rates of preterm birth, NICU admissions, and respiratory distress syndrome in pregnancies where AFLP was diagnosed later in gestation.[25,26] Study by Lamprecht et al., showed that the, hepatic encephalopathy ($p = 0.016$) and thrombocytopenia ($p = 0.001$) were independent risk factors for fetal mortality.[25] The differences observed in Apgar scores and the incidence of neonatal complications further emphasize the impact of maternal metabolic disturbances on fetal development and neonatal health outcomes.[26]

Limitations

Limitations include its retrospective nature and reliance on medical records, which may have introduced biases and limited data availability for certain variables.

CONCLUSION

This study provides comprehensive insights into the clinical manifestations and outcomes of acute fatty liver of pregnancy (AFLP), emphasizing its

significant impact on maternal and neonatal health. Our findings underscore the critical importance of early recognition, prompt intervention, and multidisciplinary management in mitigating the severe complications associated with this rare but potentially life-threatening condition. The study highlights the predictive value of biochemical markers and clinical symptoms in assessing disease severity and guiding therapeutic strategies. Moving forward, standardized diagnostic protocols and collaborative care models are essential to improving outcomes for both mothers and infants affected by AFLP, ensuring timely delivery and intensive supportive care when necessary.

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