

Perinatal Outcomes in Patients with Acute Fatty Liver of Pregnancy

Christy Vijay¹, Annamma Thomas², Angeline Yvette Mascarenhas³, Naveen Ramesh⁴

Received on: 06 January 2023; Accepted on: 27 February 2023; Published on: 31 October 2023

ABSTRACT

Introduction: Acute fatty liver of pregnancy (AFLP) is a rare obstetric emergency requiring immediate attention and intensive care to avoid adverse outcomes to the mother and fetus. As this condition poses many complications and is varied in its clinical presentation, we studied the perinatal outcomes in women diagnosed to have AFLP.

Materials and methods: This was a retrospective study that involved all patients over the past 6 years who presented with AFLP. Clinical signs and other altered biochemical parameters were included.

Results: In our study, 19 women were diagnosed to have AFLP. The mean age of the study population was 25.74 ± 3.7 years. 14 (73.68%) women were below the age of 30 years. Gestational age of more than 37 weeks was seen in 13 (68.42%) women. Ten primigravidae (52.63%) and nine multiparous (47.3%) women were found to present with AFLP. The mean blood loss at the time of delivery for a lower section cesarean section and vaginal delivery was 787.5 ± 494.07 mL and 280 ± 44.72 mL, respectively. The preferred treatment at the time of admission was transfusion of fresh frozen plasma (FFP) (Mean: 7.00 ± 9 pints), followed by transfusion of platelet (Mean: 2.37 ± 3.515 pints), transfusion of packed red blood cells (Mean: 2.21 ± 3.691 pints) and cryoprecipitate (Mean: 0.0 ± 2 pints). Nine (47.37%) women were delivered through emergency lower segment cesarean section (LSCS) and all 4 (21.05%) pregnant women who succumbed to AFLP underwent an LSCS. Among the newborn, 13 (65%) of them were low birth weight and 2 (10.53%) had fetal distress.

Conclusion: This study showed a higher maternal mortality rate of 21% in comparison to other studies. Health professionals should be sensitized about this condition and the use of the existing scoring system available to help in detecting AFLP at an early stage to reduce maternal mortality and adverse fetal outcomes.

Keywords: Acute fatty liver of pregnancy, Acute kidney injury, Disseminated intravascular coagulation, Fresh frozen plasma, Lower segment cesarean section, Preeclampsia, Pregnancy, Swansea criteria.

Journal of South Asian Federation of Obstetrics and Gynaecology (2023); 10.5005/jp-journals-10006-2271

INTRODUCTION

Acute fatty liver of pregnancy (AFLP) is a rare obstetric complication.¹ It is a well-known obstetric emergency affecting both the mother and the fetus.¹ This is a life-threatening illness which requires immediate attention and intensive care.¹ High morbidity and mortality are seen among women with AFLP.² This is probably due to liver failure resulting in disseminated intravascular coagulation and decreasing coagulation factors, ultimately culminating in multiorgan failure.² Incidence of AFLP ranges from 1 in 10,000 to 1 in 15,000 pregnancies.³ The illness is so varied that its symptoms override other diagnosis, such as preeclampsia, viral hepatitis, and cholestasis of pregnancy.³ The diagnosis of AFLP always remains a challenge to the medical fraternity.³

Pregnancy, a highly hormonal state is associated with a physiological decrease in the oxidation of long and medium-chain fatty acid.¹ The pathophysiology contributing to AFLP results from fatty acid oxidation between the mother and the fetus.¹ In addition, deficiency of fetal dehydrogenase required for β -oxidation of fatty acids causes accumulation of hepatotoxic fatty acid metabolites which cross the placenta and result in maternal hepatotoxicity.⁴

Acute fatty liver of pregnancy presents commonly in the third trimester, usually manifesting during the 30th to 38th weeks of pregnancy.⁵ It is characterized by nonspecific symptoms, such as nausea, vomiting, anorexia, malaise, abdominal pain, loss of appetite, headache, extreme fatigue, and jaundice.⁵ Severe liver dysfunction due to microvesicular fatty infiltration of hepatocytes

^{1,2}Department of Obstetrics and Gynecology, St. John's Medical College and Hospital, Bengaluru, Karnataka, India

³Department of Emergency Medicine, St. John's Medical College and Hospital, Bengaluru, Karnataka, India

⁴Department of Community Medicine, St. John's Medical College and Hospital, Bengaluru, Karnataka, India

Corresponding Author: Annamma Thomas, Department of Obstetrics and Gynecology, St. John's Medical College and Hospital, Bengaluru, Karnataka, India, Phone: +91 9341899909, e-mail: rejiann@gmail.com

How to cite this article: Vijay C, Thomas A, Mascarenhas AY, et al. Perinatal Outcomes in Patients with Acute Fatty Liver of Pregnancy *J South Asian Feder Obst Gynae* 2023;15(5):538–544.

Source of support: Nil

Conflict of interest: None

and hemorrhage are the main cause of morbidity and mortality.⁶ This is a result of coagulopathy leading to a vicious cycle of electrolyte imbalance and multiorgan failure.⁶

Acute fatty liver of pregnancy poses a great threat to the fetus, increasing the incidence of perinatal mortality as high as 10–20%.⁴ Increased chances of stillbirths are a result of maternal acidosis, maternal hypoglycemia, and elevated liver enzymes.^{1,7}

Biochemical changes seen in AFLP include hyperbilirubinemia, elevated serum transaminase, increased serum ammonia, lactic acid, leukocytosis, and thrombocytopenia.⁵ Acute fatty liver of

pregnancy is specially characterized by hypoglycemia which helps to differentiate it from other liver conditions during pregnancy.⁶

The treatment of AFLP is crucial and its complications extend even to the first week of the postpartum period.⁷ It has a slow recovery phase following the delivery of the baby.⁷ Deteriorating liver functions can lead to internal hemorrhage, such as gastrointestinal bleeds and pancreatitis which in turn leads to renal failure and circulatory collapse, thus warranting its urgent treatment.⁷

Little is known of its pathophysiology, complications, management, and its outcomes in women with the illness. Hence, the utmost importance to improve treatment and reduce maternal and perinatal mortality is stressed. As very few studies have been done on AFLP in an Indian population, this study was done to assess various perinatal outcomes among women diagnosed with AFLP.

AIMS AND OBJECTIVE(S) OF THE STUDY

To determine the perinatal outcomes among pregnant women diagnosed with AFLP in a tertiary health care hospital, South India.

MATERIALS AND METHODS

This was a retrospective study. Records of all pregnant women diagnosed with AFLP over the past 6 years (January 1, 2014 to 30, December 2020) were studied. Only cases where the diagnosis of AFLP had been established based on standard criteria of thrombocytopenia, deranged liver function tests, and deranged coagulation profile (APTT and prothrombin time) were included. Although there was an overlap with conditions, such as preeclampsia, HELLP syndrome, viral hepatitis, etc. We used the criteria as stated above with the categorization of patients in accordance with the various scoring systems. Ethical approval was obtained from the Institution Ethics Committee before the start of the study (IEC Ref No. Study No. 222/2020).

The presence of clinical signs, symptoms, and altered biochemical parameters were studied. Other causes of icterus and cholestasis in pregnancy (viral hepatitis, gall stones, cholestasis of pregnancy, etc.) were excluded based on the criteria set by Ambros-Rudolph et al. and Kawakita et al.^{8,9}

Detailed information on maternal and fetal variables such as assessment of fetal growth, development of symptoms, such as jaundice, itching (palms and soles), decreased fetal movements, abdominal pain, etc., were noted. Blood parameters, such as complete hemogram, liver function tests, ammonia levels, and renal function tests of the mother at admission and discharge were documented. Pregnancy outcomes such as the need for induction of labor and mode of delivery (vaginal or cesarean) were recorded. Complications such as severe preeclampsia, postpartum hemorrhage (PPH), and the need for admission into the intensive care unit (ICU) were noted. Monitoring of blood loss during vaginal delivery or lower segment cesarean section (LSCS) and quantifying the blood loss at the time of delivery were documented. Perinatal outcomes such as mode of delivery, APGAR, complications at birth, and NICU admission were also studied. Treatment at initial diagnosis, dose of steroids, and other new medications (vitamin K, transfusion of blood products, etc.) were studied.

Comparison of different criteria and classifications were undertaken on the study subjects, using standard guidelines such as the Model for End-Stage Liver Disease (MELD) score for 3-month mortality percent, Swansea criteria (>6 of the criteria satisfied) and Kings College criteria for non-acetaminophen-related acute liver failure and indication for liver transplant.¹⁰⁻¹³

MELD score: A model originally used to predict the outcome of patients undergoing TIPS procedure is now used to assess chronic liver disease and estimate the prognosis along with the possibilities of a liver transplant in patients.¹⁰ It takes into consideration bilirubin levels, serum creatinine, and INR to predict the survival level of the patient.¹⁰ The MELD Score ranges from 6 to 40 indicating the severity of the liver disease with a prediction of 90-day mortality.¹⁰

Swansea Criteria: The Swansea criteria is the main screening tool used for AFLP.¹¹ The criteria consider symptoms, investigatory results along with ultrasonic findings in guiding early diagnosis of AFLP.¹¹ The diagnosis of AFLP is made when a score of 6 is attained in the absence of any other explanations (diagnosis of exclusion).¹¹

King's College Criteria: It is another tool to identify patients with acute liver failure. Patients less than 11 years and greater than 40 years with serum bilirubin levels above 300 mg/dL, INR greater than 3.5 and development of coma have been seen to have a poor prognosis.^{12,13} The criteria takes into consideration coagulopathy and encephalopathy to predict the prognosis of the patients and the success of liver transplant in such patients.^{12,13} All other patients who did not meet the Swansea Criteria were diagnosed as AFLP based on the exclusion of other obstetric and medical diseases. The aid of the other two scoring systems was also used.

Analysis

Data were entered into Microsoft Excel and analyzed using IBM Statistical Packages for Social Sciences (SPSS) version 16.0. Interquartile ranges were deduced for various variables, such as gestational age, gestational age of diagnosis, and blood investigations for the analysis of perinatal outcomes in AFLP. All categorical data were presented using frequency, percentages, and all continuous measurements are summarized using mean \pm standard deviation or Median (IQR) based on the distribution. The Chi-square test or Fisher's exact test was applied to assess the association of categorical demographic characteristics. The continuous measurements of maternal characteristics were compared between age, gestational age, and obstetric score, using independent sample *t*-test or Mann-Whitney *U* test based on the normality assumption. *P*-value was considered significant at 5% level of significance for all comparisons.

RESULTS

A total of 19 pregnant women were diagnosed with AFLP out of the 18,058 deliveries over the past 6 years. Hence, the prevalence of AFLP in our population was 0.10% in the study period. The mean age of the patients at diagnosis was 25.74 ± 3.7 years. Of most women, 14 (73.68%) were below the age of 30 years. 68.42% of women were <37 weeks of gestational age. Of most women, 16 (84.21%) had no previous obstetric history of pre-eclampsia and preterm delivery. Ten primigravidae (52.63%) and nine multiparous (47.3%) women were found to present with AFLP (Table 1).

The study revealed that the presenting maternal complaints remained vague and nonspecific. Thirteen women presented with Icterus and one patient was febrile. Eight (42.11%) patients complained of vomiting. Only a small percentage of women presented with problems, such as abdominal pain 7 (36.84%), fever 5 (26.32%), itching 3 (15.79%), and others presented with high blood pressure 2 (10.53%), decreased urine output 2 (10.53%) and reduced fetal movements 2 (10.53%). A history of preeclampsia in prior pregnancies was seen in 3 (15.79%) pregnancies. One (5.26%) woman had signs of fetal compromise, such as oligohydramnios,

Table 1: Descriptive statistics of the study population

Variables	Frequency (N)	Percent (%)
Age		
<30 yrs	14	73.68
>30 yrs	5	26.32
Gestational age		
<37 weeks	13	68.42
>37 weeks	6	31.58
Obstetrics – SCORE		
Primigravidae	10	52.6
Multigravidae	9	47.4
Obstetric complication		
Preeclampsia	8	42.11
Meconium-stained liquor	7	36.84
Fetal distress	2	10.53
Previous LSCS	2	10.53
Oligohydraminos	1	5.26
IUD	1	5.26
Abruption	1	5.26
Medical complication		
AKI	7	36.84
Hypertensive retinopathy	3	15.79
Disseminated intravascular coagulation	4	21.05
Anemia	1	5.26
Hepatitis E	1	5.26
Pancreatitis	1	5.26
Maternal mortality	4	21.05

Table 2: Biochemical profile of patients with AFLP

Variables	Mean (at admission)	Mean (at discharge)
Random blood sugar (mg/dL)	73.57 ± 17.28	–
Uric acid (mg/dL)	7.22 ± 3.65	–
Blood urea (mg/dL)	32.00 ± 43	32.45 ± 38.25
Creatinine (mg/dL)	1.60 ± 2.13	1.55 ± 1.98
Sodium (mEq/L)	132.73 ± 5.28	136.158 ± 6.03
Potassium (mEq/L)	4.58 ± 0.77	4.0500 ± 0.60
Chloride (mEq/L)	106.89 ± 7.06	106.895 ± 8.66
Total protein (gm/dL)	5.77 ± 0.74	4.9484 ± 0.72
Albumin (gm/dL)	2.47 ± 0.66	1.968 ± 0.56
Total bilirubin (mg/dL)	9.72 ± 4.82	8.5737 ± 5.50
AST (U/L)	154.00 ± 23	67.00 ± 101.5
ALT (U/L)	131.00 ± 267.5	57.00 ± 67
ALP (U/L)	471.00 ± 467.5	265.00 ± 229.5
GGT (U/L)	82.00 ± 99.5	73.00 ± 87
LDH (U/L)	572.50 ± 588.7	413.400 ± 475.40
Prothrombin time (seconds)	21.30 ± 19	19.411 ± 7.0
APTT (seconds)	51.52 ± 22.52	50.141 ± 24.46
INR	1.70 ± 1.68	1.6542 ± 0.59
NH ₃ mmol/L	62.8 ± 20.70	–
AFI (cm)	11.32 ± 4.24	–

AFI, amniotic fluid index; ALT, alanine transaminase; ALP, alkaline phosphatase; AST, aspartate transaminase; APTT, activated partial prothrombin time; GGT, gamma glutamyl transferase; INR, international normalized ratio; LDH, lactate dehydrogenase; NH₃, Ammonia; RBS, random blood sugar; TSH, Thyroid stimulating hormone

intrauterine death, and abruption. Fetal distress was noticed in 2 (10.53%) pregnancies. However, a higher number of women were found to have preeclampsia or HELLP syndrome 8 (42.11%), complicating the condition, making it necessary for intensive care and immediate termination of pregnancy through LSCS. Acute kidney injury (AKI) was seen in 7 (36.84%) women, and 6 (33.33%) of these women required hemodialysis. This study showed a higher maternal mortality rate of 21.05%.

Patients presented with a mean systolic and diastolic blood pressure of 127.8 ± 14.7 mm Hg and 86.0 ± 10.4 mm Hg respectively. The pulse rate, respiratory rate, and temperature were within normal limits at admission, being 91.7 ± 12.9 beats per minute, 20.8 ± 5.0 breaths per minute and 98.1 ± 0.4 Fahrenheit. It was noticed that 4 (21.05%) women had SPO₂ levels of >95% and <99%, and were supported by oxygen or continuous positive airway pressure (CPAP).

The investigations among women with AFLP showed characteristic changes which distinguished AFLP from other hepatic disorders in pregnancy. A significant number of women had thrombocytopenia with a platelet count of less than 1 lakh. The mean total bilirubin at the time of admission was as high as 9.73 (±4.82) mg/dL showing some recovery at the time of discharge. An elevated prothrombin time of 19.41 (±7) seconds, along with an increased APTT of 51.52 (±22.53) seconds and INR of 1.7 (±0.59) was seen. However, liver enzymes, such as AST, ALP, and GGT were not remarkably raised in contrast to illnesses like eclampsia or HELLP syndrome. LDH levels were also raised, ranging from 379 to 797 U/L as given in Tables 2 and 3. All patients were tested for hepatitis markers, to rule out viral hepatitis (Hepatitis A, B, C, D,

and E). One patient had co-existent viral Hepatitis E. A liver biopsy was contraindicated in all our patients because of a deranged coagulation profile. Hence, a liver biopsy could not be done.

In Table 4, MELD score predicted a 42.2% 3-month mortality (52.6–74.5%) as seen in our study. However, the Swansea Criteria exhibited only 13 women to satisfy the criteria to be diagnosed as AFLP. Only one patient fulfilled the criteria for the need for liver transplantation as per the Kings College Criteria. The deficits of preexisting scoring systems in accurately assessing morbidity or mortality in-patients with AFLP, warrants development of a scoring system that would alleviate this deficit. The prognostic scores parameters (King's College Criteria and MELD score) and the diagnostic score parameters (Swansea Criteria) were calculated at the time of admission for comparison of the different score types. As AFLP warrants liver transplant as a final measure of treatment for survival, the King's College score was used to take a decision on the need for transplant in conjunction with the MELD score to view the absolute need for the procedure, considering the high risks of liver transplant surgery.

Reviewing the outcomes of women diagnosed with AFLP, although different modes of induction were attempted, most women were taken up for an emergency LSCS on an account of worsening maternal condition with 100% of them requiring transfusion. AFLP was found in 11 (57.8%) O group individuals and Rhesus positivity in 18 (94.7%) individuals.

The mean blood loss at the time of delivery for a Lower Section Caesarian Section and vaginal delivery was 787.5 ± 494.07 mL and 280 ± 44.72 mL respectively. Three women with LSCS had

Table 3: Comparison of various biochemical parameters

Variable	Age		Gestational age		Obstetric score		(p-value)*
	<30 years	>30 years	<37 weeks	>37 weeks	Primigravidae	Multigravidae	
RBS (mg/dL)	9.57	11.20	9.73	10.58	10.00	10.00	<0.999
BU (mg/dL)	10.46	8.70	9.65	10.75	12.9	6.78	0.018*
Creatinine (mg/dL)	10.79	7.80	10.31	9.33	11.90	7.89	0.121
Total bilirubin (mg/dL)	10.07	9.80	9.92	10.17	12.2	7.56	0.072
Direct bilirubin (mg/dL)	10.29	9.20	9.65	10.75	12.6	7.11	0.034*
AST (U/L)	10.21	9.40	9.92	10.17	11.1	8.78	0.369
ALT (U/L)	10.57	8.40	9.77	10.50	10.2	9.78	0.870
ALP (U/L)	11.43	6.00	9.27	11.58	13.45	6.17	0.005*
PT (seconds)	10.64	8.20	9.62	10.83	9.15	10.94	0.487
INR	10.46	8.70	9.23	11.67	9.65	10.39	0.775
APTT (seconds)	8.77	11.40	9.69	9.00	9.80	9.12	0.487

*p-value: Mann-Whitney U test; ALT, alanine transaminase; ALP, alkaline phosphatase; APTT, activated partial prothrombin time; AST, aspartate transaminase; BU, blood urea; FBS, fasting blood sugar; GGT, gamma glutamyl transferase; INR, international normalized ratio; LDH, lactate dehydrogenase; PPBS, postprandial blood sugar; PT, prothrombin time; RBS, random blood sugar; TSH, thyroid stimulating hormone

Table 4: Comparison of score classifications of AFLP

MELD score	Numbers (n = 19)	
3-month mortality %		%
1.9–3.7	0	0
6–20	3	15.8
19.6–45.5	7	36.8
52.6–74.5	8	42.2
71–100	1	5.2
Swansea Criteria (>6 of the criteria satisfied)		
AFLP diagnosed as per the criteria	13	68.4
AFLP patients who did not fulfil the criteria	6	31.6
Kings College Criteria for Non-acetaminophen related acute liver failure and Indication for Liver Transplant		
Need for liver transplantation	1	5.2

PPH of >1000 mL. The best treatment during admission was a transfusion of fresh frozen plasma (FFP) (mean: 7.00 ± 9) based on the derangement of coagulation profile and derangement of bleeding etc. excess bleeding prevaginal etc., followed by transfusion of platelet (mean: 2.37 ± 3.515), transfusion of packed red cell (mean: 2.21 ± 3.691) and transfusion of cryoprecipitate (mean: 0.0 ± 2) as depicted in Table 5.

Acute fatty liver of pregnancy had a predilection to occur among women who gave birth to male babies 12 (57.15%). Fourteen (66.67%) babies were found to have low birth weight (<2.5 kg). APGAR score recorded at 1 minute of <8 was in over 90% of the babies. The APGAR score at 5 minutes of life improved in 8 babies who had poor scores at 1 minute of life (Table 6).

Table 7 depicts the investigations and clinical descriptions of the four women who succumbed to their illness. All the four women underwent an LSCS. Two out of the four women underwent hemodialysis. One patient has a twin pregnancy, with a boy and a girl baby. The other two women had a singleton pregnancy with two boys and a girl baby, respectively. The morbidity of the illness was seen in 15 (78.94%) women, in terms of ICU stay, prolonged hospital stay, need for massive transfusions, and high costs of hospital stay.

Table 5: Intrapartum outcomes of pregnancy in women with AFLP

Induction	Numbers (n = 19)	%
PGE1	1	5.26
PGE2	7	36.84
PGE1 and PGE2	1	5.26
Indication of induction		
AFLP	7	36.84
Meconium-stained liquor grade 3	1	5.26
Decreased fetal movements	1	5.26
Mode of delivery		
FTVD	3	15.79
PTVD	7	36.84
Emergency LSCS	9	47.37
Elective LSCS	0	0
Indication for LSCS		
Worsening maternal condition	5	25
Abruption	1	5
Fetal distress	1	5
Nonprogress of labor	1	5
Severe preeclampsia	1	5
Transfusion	19	100
Hemodialysis	6	33.33

FTVD, full-term vaginal delivery; LSCS, lower segment caesarean section; PGE1, misoprostol; PGE2, dinoprostone; PTVD, preterm vaginal delivery

DISCUSSION

Acute fatty liver of pregnancy has been known to be a potentially fatal and an uncommon illness.¹⁴ It complicates the third trimester of pregnancy which progresses to fulminant hepatic failure with encephalopathy.¹⁴ AFLP is estimated to affect 1/7,000–1/16,000 of all deliveries as stated by Reyes et al. as early as in the year 1994.¹⁵ In our study, 19 pregnant women were diagnosed with AFLP in the last 6 years.

Early diagnosis and treatment have been difficult because the symptoms of AFLP mimic symptoms of other common conditions encountered in obstetrics, such as preeclampsia, HELLP syndrome,

viral hepatitis, and cholestasis of pregnancy.^{1,3} Clinical symptoms such as nausea and vomiting are the most common symptoms which can be routinely missed.¹⁰ A study in China reported about 23% of the women with AFLP presented with nausea and vomiting.¹³ In comparison to our study which reported nausea and vomiting to present in 42% of the women. Hence, a differential diagnosis of AFLP with other possible conditions needs to be kept in mind with women presenting with nausea and vomiting, especially in their third trimester.

Classically AFLP presents with jaundice and lethargy as the main clinical manifestations in pregnancy; which should alert the treating obstetrician.¹¹ Our study had 13 women presenting with jaundice which accounted for about 68% of the women. Similar results (63%) were seen in another retrospective study conducted in tertiary care hospitals in China.¹⁴ This shows a similarity in the presentation of AFLP among women of Asian origin.

In our study, the age of diagnosis of AFLP was comparatively lower, being 25.74 ± 3.7 years. The most probable reason being early marriages and childbearing among the women of India, having a negative effect on maternal reproductive health and the overall well-being of mother and child.¹⁶

Taking into consideration various risk factors, Mikolasevic et al. enumerated a few risks factor for AFLP, such as multigravida, preeclampsia, multigestation, and male fetus.¹⁷ Our study confirmed such findings in all parameters except in terms of gravida. In

contrast, our study had 52.6% of primi gravida who presented with AFLP, the probable reason for such presentation is to be explored.

A retrospective analysis of 56 AFLP cases in West China showed that male fetuses (64%) and twin pregnancies (9%) showed a higher likelihood of developing AFLP. Majority of the pregnant women with AFLP in our study gave birth to a male fetus (57.15%).

Insufficient understanding of the disease makes the diagnosis and effective treatment challenging.¹³ The early recognition of AFLP cases and prompt progressive management, including early termination of pregnancy and large amounts of titrated infusion of fresh frozen plasma, obviously improves the outcomes.¹⁸ In our study, all 19 women were managed with transfusion of fresh frozen plasma, PRBC, platelets, and cryoprecipitate, thus improving patient outcomes. With no fixed protocol in treating women with AFLP, the management always should be customized according to the patient's needs and requirements. For example, the mode of delivery depends on a number of maternal and fetal factors.¹⁹ Nine emergency cesarean sections were conducted due to worsening maternal conditions and signs of increasing fetal distress in our study.

In our study, we identified that blood group 'O' and Rh-positive individuals had a higher chance of presenting with AFLP. Three out of the four women who succumbed to the illness were O-positive blood group individuals. Hence, we suggest further research to look into the association of O-positive blood group with the presentation of AFLP.

Overall, our study showed a higher maternal mortality rate of 21% which when compared with other studies conducted in China showed a death rate of 5.5%.²⁰ Thus, making AFLP a highly fatal condition requiring prompt management to improve outcomes.

An Indian case report study found a 20-year-old primigravidae at 37 weeks of gestation to deliver a male baby with poor APGAR scores.²¹ Loganathan et al. found a similar presentation of coagulopathy in two of the cases seen in India.²² Our study like the above two Indian reports shows the need for immediate treatment of coagulopathy which seems to be the leading cause of morbidity and mortality in such women.

Hong-Yan Wang et al. studied the effect of cesarean section on maternal and fetal outcomes in AFLP.²³ The meta-analysis on 9959 patients from several studies showed a positive association between cesarean section for termination of pregnancy and perinatal outcomes in AFLP.²³ The study observed that cesarean section exhibited positive effects in terms of maternal mortality rate being 44% lower [relative risk (RR), 0.56 (0.41–0.76)] and perinatal mortality rate being reduced [RR, 0.52 (0.38–0.71)] when compared with vaginal delivery.²³ There were no associations

Table 6: Neonatal outcomes and complications in mothers with AFLP

	Numbers of babies (n = 21)	%
Fetal outcomes		
Boy	12	57.15
Girls	9	42.85
Twin delivery (out of 19 deliveries)	2	10.52
Birthweight		
<2.5 kgs	14	66.67
>2.5 kgs	7	33.33
APGAR 1 minute		
<8	19	90.47
>8	2	9.53
APGAR 5 minute		
<8	11	52.39
>8	10	47.61

Table 7: Mortality description of women who succumbed to AFLP

Patient Sl. No.	GA weeks + days	Obstetric score/ pregnancy	Uric acid (mg/dL)/creatinine (mg/dL)	Total bilirubin (mg/dL)	AST (U/L)/ ALT (U/L)	Blood group	PT (seconds)/ INR	Neonatal outcome/ Gender	APGAR 5 minutes
1	35 + 4	Primigravidae/ Twins	1.7/3.86	14.05	154/131	O+	180/12	Alive Boy/Girl	<5
2	33 + 4	Primigravidae/ Singleton	9/3.78	10.9	323/190	O+	14.9/1.3	Dead Boy	<5
3	36 + 5	Primigravidae/ Singleton	9.6/1.45	7.9	178/300	B+	20/1.66	Alive Boy	7–8
4	35 + 4	Multigravidae/ Twins	10/2.71	9.46	334/299	O+	18/1.4	Dead Girl/ Girl	>8

ALT, alanine transaminase; AST, aspartate transaminase; GA, gestational age; INR, international normalized ratio; "+", positive; "-", negative; PT, prothrombin time



between cesarean section, perinatal neonatal mortality type, and maternal multiple organ complications.²³ The study emphasized the significant prognostic value and clinical implications of cesarean section in AFLP.²³ In our study, we observed 47.37% of the women with AFLP to undergo LSCS. All were emergency LSCS. The chance of increased bleeding with a deranged coagulation profile and the option of vaginal delivery, as opposed to LSCS must be made. All patients were transfused with FFP before attempting a LSCS to prevent the anticipated torrential bleeding that would be encountered when a patient is in DIC. Similar thoughts were opined by Ashish et al. as studied at CMC Vellore, Tamil Nadu, India.²⁴ The study stated that although the risks of LSCS in AFLP were present, the decrease in the duration of delivery was beneficial and was the dictum practiced in many centers.²⁴

von Meijenfheldt et al. studied the prophylactic use of fresh frozen plasma and platelet transfusion to have a prothrombotic effect in patients with liver disease.²⁵ The study found 19 patients who were transfused with prophylactic FFP transfusion as requested by their treating physician. Thirteen of the patients were prescribed platelet transfusion.²⁵ The study observed that following FFP transfusion, thrombin generation significantly increased.²⁵ Platelet counts were also found to increase ($p < 0.01$).²⁵ In our study, seldom was there a need to prophylactically transfuse patients as most of them were indicated transfusions based on deranged biochemical parameters and clinical features. von Meijenfheldt et al. contemplated the need for prophylactic transfusions and questioned their clinical relevance.²⁵

CONCLUSION

Acute fatty liver of pregnancy in pregnancy poses risks to mothers in terms of maternal mortality and morbidity. The prevalence of AFLP in our population was 0.10%. This study showed a higher maternal mortality rate of 21.05%. Most women had no previous obstetric history of preeclampsia and preterm delivery. Preeclampsia or HELLP syndrome complicates the condition in terms of clinical presentation and decision-making, warranting the need for intensive care and immediate termination of pregnancy. Acute kidney injury is an anticipated complication in these women requiring hemodialysis.

Health professionals should be sensitized about this condition and the use of the existing scoring system available to help in detecting AFLP at an early stage to reduce maternal mortality and adverse fetal outcomes. Although LSCS was the mode of delivery for obstetric indications in our institution, we feel the decision for LSCS has to be made on an individual patient to patient basis. Blood loss at the time of delivery makes it imminent to arrange for appropriate treatment and supportive care in the management of the patient, which includes fresh frozen plasma transfusion which was found beneficial in our patients.

Scope for the Future

In view of India planning to achieve SDGs with regard to maternal mortality, it is imperative that Maternal and Child Health Mission should accentuate the need for consideration of a separate scheme for AFLP, with incentives to relieve the burden of illness on mothers and their families in terms of expenditure on laboratory tests and need for expensive treatment in tertiary care hospitals.

Limitations

Since AFLP is a very rare phenomenon, we relied on records to calculate the incidence.

This study is one among the first few papers where the outcomes of pregnancy in AFLP have been studied in detail including the outcomes of various treatment options in an Indian setting. This study is one of the few studies that compare various scoring systems in the diagnosis of AFLP in pregnancy and determines the need to devise a more universal system to prevent the non-identification of cases.

REFERENCES

- Liu J, Ghaziani TT, Wolf JL. Acute fatty liver disease of pregnancy: updates in pathogenesis, diagnosis, and management: *Am J Gastroenterol* 2017;112(6):838–846. DOI: 10.1038/ajg.2017.54.
- Natarajan S, Ibdah J. Role of 3-hydroxy fatty acid-induced hepatic lipotoxicity in acute fatty liver of pregnancy. *Int J Mol Sci* 2018;19(1):322. DOI: 10.3390/ijms19010322.
- Westbrook RH, Dusheiko G, Williamson C. Pregnancy and liver disease. *J Hepatol* 2016;64(4):933–945. DOI: 10.1016/j.jhep.2015.11.030.
- Naoum EE, Leffert LR, Chitilian HV, et al. Acute fatty liver of pregnancy. *Anesthesiol* 2019;130(3):446–461. DOI: 10.1097/ALN0000000000002597.
- Ronen J, Shaheen S, Steinberg D, et al. Acute fatty liver of pregnancy: a thorough examination of a harmful obstetrical syndrome and its counterparts. *Cureus* 2018;10(2):e2164. DOI: 10.7759/cureus.2164.
- Dekker RR, Schutte JM, Stekelenburg J, et al. Maternal mortality and severe maternal morbidity from acute fatty liver of pregnancy in the Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2011;157(1):27–31. DOI: 10.1016/j.ejogrb.2011.02.015.
- Ko H, Yoshida EM. Acute fatty liver of pregnancy. *Can J Gastroenterol* 2006;20(1):25–30. DOI: 10.1155/2006/638131.
- Ambros-Rudolph CM, Glatz M, Trauner M, et al. The importance of serum bile acid level analysis and treatment with ursodeoxycholic acid in intrahepatic cholestasis of pregnancy: A case series from central Europe. *Arch Dermatol* 2007;143(6):757–762. DOI: 10.1001/archderm.143.6.757.
- Kawakita T, Parikh LI, Ramsey PS, et al. Predictors of adverse neonatal outcomes in intrahepatic cholestasis of pregnancy. *Am J Obstet Gynecol* 2015;213(4):570.e1–e8. DOI: 10.1016/j.ajog.2015.06.021.
- Fesenmeier MF, Coppage KH, Lambers DS, et al. Acute fatty liver of pregnancy in 3 tertiary care centers. *Amer J Obstet Gynecol* 2005;192(5):1416–1419. DOI: 10.1016/j.ajog.2004.12.035.
- Reyes H, Sandoval L, Wainstein A, et al. Acute fatty liver of pregnancy: A clinical study of 12 episodes in 11 patients. *Gut* 1994;35(1):101–106. DOI: 10.1136/gut.35.1.101.
- Ibdah JA. Acute fatty liver of pregnancy: an update on pathogenesis and clinical implications. *World J Gastroenterol* 2006;12(46):7397–7404. DOI: 10.3748/wjg.v12.i46.7397.
- Zhang YP, Kong WQ, Zhou SP, et al. Acute fatty liver of pregnancy: a retrospective analysis of 56 cases. *Chin Med J (Engl)* 2016;129(10):1208–1214. DOI: 10.4103/0366-6999.181963.
- Kaplan MM. Acute fatty liver of pregnancy. *New England Journal of Medicine*. 1985;313(6):367–370. DOI: 10.1056/NEJM198508083130606.
- Rajasri AG, Srestha R, Mitchell J. Acute fatty liver of pregnancy (AFLP)—an overview. *J Obstet Gynaecol* 2007;27(3):237–240. DOI: 10.1080/01443610701194705.
- Prakash R, Singh A, Pathak PK, et al. Early marriage, poor reproductive health status of mother and child well-being in India. *J Fam Plann Reprod Health Care*. 2011;37(3):136–145. DOI: 10.1136/jfprhc-2011-0080.
- Mikolasevic I, Filipec-Kanizaj T, Jakopic I, et al. Liver disease during pregnancy: a challenging clinical issue. *Med Sci Monit* 2018;24:4080–4090. DOI: 10.12659/MSM.907723.
- Mjahed K, Charra B, Hamoudi D, et al. Acute fatty liver of pregnancy. *Arch Gynecol Obstet* 2006;274(6):349–353. DOI: 10.1007/s00404-006-0203-6.
- Glavind J, Boie S, Glavind E, et al. Risk of recurrent acute fatty liver of pregnancy: survey from a social media group. *Am J Obstet Gynecol MFM* 2020;2(2):100085. DOI: 10.1016/j.ajogmf.2020.100085.

20. Chang L, Wang M, Liu H, et al. Pregnancy outcomes of patients with acute fatty liver of pregnancy: A case control study. *BMC Pregnancy Childbirth*. 2020;20(1):282. DOI: 10.1186/s12884-020-02980-2.
21. Dey M, Kumar R, Narula GK, et al. Acute fatty liver of pregnancy. *Med J, Armed Forces India* 2014;70(4):392–393. DOI: 10.1016/j.mjafi.2012.06.013.
22. Loganathan G, Eapen CE, Chandy RG, et al. Acute fatty liver of pregnancy: a report of two cases. *Natl Med J India* 2002;15(6):336–338. PMID: 12540067.
23. Wang HY, Jiang Q, Shi H, et al. Effect of caesarean section on maternal and foetal outcomes in acute fatty liver of pregnancy: A systematic review and meta-analysis. *Sci Rep* 2016;6:28826. DOI: 10.1038/srep28826.
24. Goel A, Ch'ng CL, Eapen CE, et al. Acute fatty liver of pregnancy better understanding of pathogenesis and earlier clinical recognition results in improved maternal outcomes. *EMJ Hepatol* 2018;6(1):72–79. DOI: 10.33590/emjhepatol/10314416.
25. von Meijenfeldt FA, van den Boom BP, Adelmeijer J, et al. Prophylactic fresh frozen plasma and platelet transfusion have a prothrombotic effect in patients with liver disease. *J Thromb Haemost* 2021; 19(3):664–676. DOI: 10.1111/jth.15185.