



Clinical Characteristics and Obstetric Outcome in Women with Acute Fatty Live of Pregnancy: A Retrospective Review of 36 Cases

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Abstract

Objective: To describe the clinical characteristics of women diagnosed with acute fatty liver of pregnancy (AFLP) and to describe the maternal and perinatal outcome in these women.

Methods: Retrospective review of 36 cases of women diagnosed with AFLP from a teaching hospital from Southern India.

Results: The occurrence of AFLP during the study period was 2.4/10,000 deliveries. Majority were nulliparous (61.1%) and all of them presented in third trimester. The Swansea criteria 6 and above used to diagnose AFLP was present in 77.8% of women and the common symptoms at admission were jaundice (100%), nausea/vomiting (77.8%) and malaise (69.4%). The maternal mortality rate was 38.9% and perinatal mortality rate was 50%. The most common complications were coagulopathy (n = 19), post-partum hemorrhage (n = 17), acute kidney injury (n = 17) followed by encephalopathy (n = 13).

Conclusion: AFLP is a rare obstetric emergency which invariably presents in third trimester. The adverse maternal and perinatal outcomes are inevitable as disease progresses. Late presentation is often leads to increased maternal and perinatal mortality. Early diagnosis, multidisciplinary care and timely termination are the key factors in improving obstetric outcome in women with AFLP.

Keywords: Jaundice; Acute Fatty Liver of Pregnancy; Pregnancy Specific Liver Disease; Maternal Outcome; Perinatal Outcome

Introduction

Acute fatty liver of pregnancy (AFLP) is a potentially dangerous condition and its incidence varies between 1 in 5000 and 20,000 pregnancies [1,2]. The maternal and perinatal outcome are worse in AFLP when compared to other pregnancy specific liver disorders (P-sLD) which include hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome, intrahepatic cholestasis of pregnancy (IHCP) and hyperemesis gravidarum (HG) [3]. It is commonly seen in third trimester when the energy demand of pregnancy is more and its frequency increases in elderly gravidae, pregnant women carrying male fetus and multiple pregnancy [4,5]. However, the exact reason is not clear. Over the period of time, multi-disciplinary care and early atraumatic delivery has brought improved the maternal and perinatal outcome in many countries [1,6,7]. It is also not clear whether the caesarean delivery has led to this im-

proved outcome seen in the recent days. Moreover, there is a paucity of data on maternal and perinatal outcome from developing countries which continued to have increased maternal mortality.

Methodology

This was a retrospective observational study conducted at women and children hospital, Jawaharlal Institute of Post graduate Medical education and Research, Puducherry located in Southern part of India. It is one of the largest teaching hospital with annual delivery rate of 15,000-18,000. The study was conducted over the period of 10 years from January 2010 to December 2019. The medical records of all women admitted with jaundice during the study period were examined. Those with the final diagnosis of acute fatty liver of pregnancy (AFLP) in the case records were included in the study. The demographic details, clinical characteristics, labora-

tory parameters, clinical course, the complications/recovery and the final outcome were noted from the case records. There were a total of 36 cases with AFLP were included and the characteristics including maternal and perinatal outcome are described. The schematic flow of the study is described as a flow chart in figure 1. All pregnant women who were admitted with jaundice underwent thorough evaluation at admission to arrive at an appropriate diagnosis. This include detailed clinical history, examination, laboratory parameters like complete blood picture, renal/liver function tests, blood glucose, coagulation profile, viral markers especially hepatitis/leptospira, urine microscopic examination including protein creatinine ratio, fundoscopic examination if needed and ultrasound abdomen for liver and thorough fetal evaluation. All of there were managed by multi-disciplinary team involving obstetrician, obstetric physician, critical care physician, anaesthesiologist, gastroenterologist and nursing team.

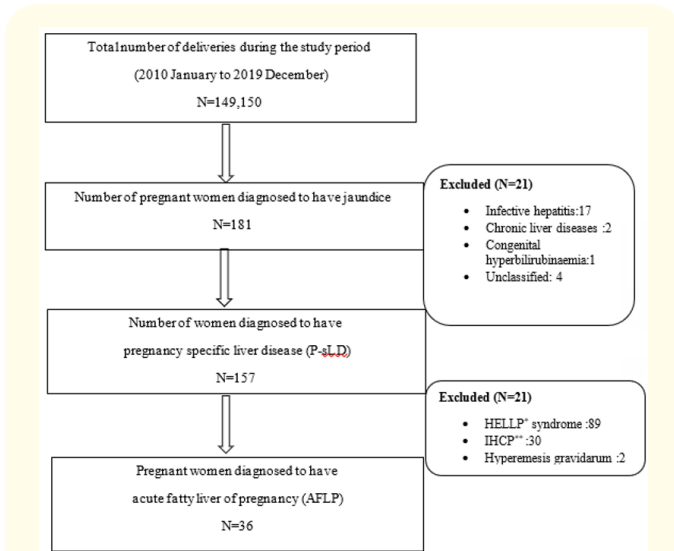


Figure 1: Schematic representation of study subjects.

*HELLP syndrome: Hemolysis, elevated liver enzymes, low platelet count; **IHCP: Intrahepatic cholestasis of pregnancy.

The continuous variables are described as mean with standard deviation or median with inter quartile ratio as appropriate. The categorical values are described as percentages. The differences in frequency distribution of maternal and perinatal outcome among women with AFLP was analyzed using Fisher exact Chi-square test). The p value of <0.05 was considered as statistical significance. The results were analyzed using software (version 25.0; New York, USA, IBM).

Results

The number of women who were diagnosed to have AFLP based on the final diagnosis after thorough evaluation of case records were found to be 36 and the incidence was 2.4/10,000 deliveries. The general demographic characteristics and clinical symptoms of all women with AFLP are shown in table 1. Majority of them were nulliparous (61.1%) with the mean maternal age of 28.3 ± 6.8years (ranging from 19-36 years). All of them presented in third trimester and the gestational age ranging from 32 to 39 weeks. The most common symptom at admission was jaundice (100%) followed by nausea/vomiting (77.8%) and malaise (69.4%). More than half of the women had coexisting preeclampsia (PE) at admission or during the course of hospital stay. Almost two thirds of the women had the Swansea criteria of 6 and above (77.8%). The distribution various components of Swansea criteria for all women diagnosed with AFLP is shown in figure 2.

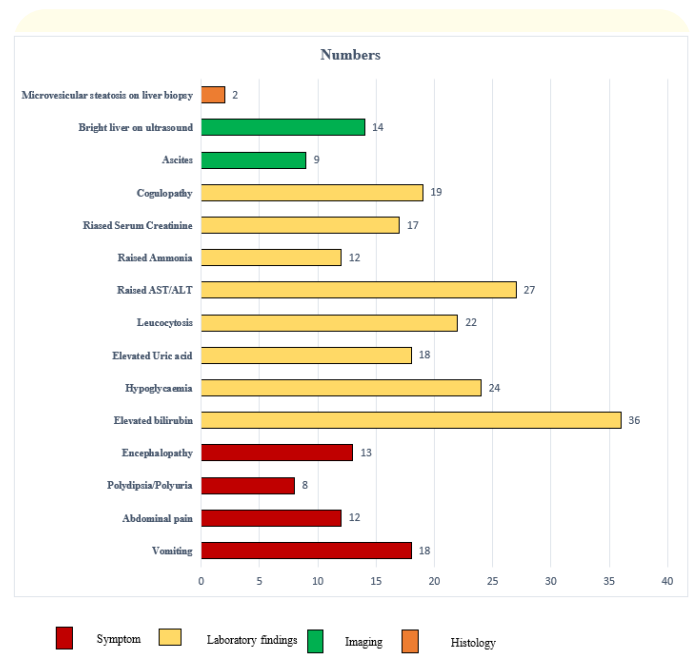


Figure 2: Bar diagram shows Swansea criteria among 36 women with acute fatty liver of pregnancy.

The main laboratory findings are described in table 1; all of them had raised serum bilirubin and the mean value was 10.8 ± 5.9 mg/dl. The mean prothrombin time was 28.4 ± 11.6. The maternal and perinatal outcomes are described in table 2. The most

S. No	Characteristics	Frequency N (%) or Mean ± SD
I	Demography	
	Maternal age (years)	28.3 ± 6.8
	Gestational age at diagnosis (week)	36.05 ± 2.32
	Primigravida	22 (61.1%)
II	Symptoms at admission	
	Malaise	25 (69.4%)
	Nausea/Vomiting	28 (77.8%)
	Pruritus	5 (13.9%)
	Icterus	36 (100%)
	Abdominal pain	12 (33.3%)
	Oliguria	05 (13.9%)
	Preeclampsia	23 (63.8%)
III	Laboratory parameters	
	Hematological	
	Hemoglobin (g/l)	9.83 ± 2.61
	Total leucocyte count (X 10 ⁹ /l)	16.9 ± 8.2
	Platelet count (X 10 ⁹ /l)	128.4 ± 86.1
	Liver function test	
	S. Bilirubin (mg/dl)	10.8 ± 5.9
	AST* (U/L)	162.42 ± 148.31
	ALT** (U/L)	142.28 ± 128.21
	S. Creatinine (mg/dl)	1.21 ± 0.82
	Prothrombin time (seconds)	28.4 ± 11.6
	Fibrinogen (mg/dl)	152 ± 38
	Others	
	Blood glucose (mg/dl)	72.42 ± 68.4
	Swansea criteria 6 and above	28 (77.8%)
	MELD^ score	27.82 ± 8.12

Table 1: Description of demographic, clinical symptoms and laboratory parameters of 36 women with AFLP.

*AST: Aspartate Amino Transferase; ** ALT: Alanine Amino Transferase; ^ MELD: Model for End Stage Liver Disease.

common adverse maternal outcome was coagulopathy followed by postpartum hemorrhage (DIC) and acute kidney injury (AKI). The maternal mortality rate was 38.9%. Though all the women received transfusions in the peripartum period, 69.2% of women received

S. NO	Clinical outcome	Frequency, n (%)
I	Maternal outcome	
1	Disseminated intravascular coagulation	19 (52.8%)
2	Postpartum hemorrhage	17 (47.2%)
3	Acute Kidney injury	17 (47.2%)
4	ARDS*	11 (30.6%)
5	Encephalopathy	13 (36.1%)
6	MODS^	07 (19.4%)
7	Maternal death	14 (38.9%)
II	Perinatal outcome	
1	Birth weight <2000grams	21 (58.3%).
2	Intrauterine fetal demise	16 (44.4%)
3	Admission to NICU#	12 (33.3%)
4	Neonatal death	2 (5.6%)

Table 2: Maternal and fetal outcome among 36 women diagnosed with AFLP.

*ARDS: Acute Respiratory Distress Syndrome; ^MODS: Multi Organ Dysfunction Syndrome; #NICU: Neonatal Intensive Care Unit.

massive transfusion around delivery and in the postpartum period. A total of 22 women underwent caesarean section (61.1%) and five of them were in advanced labour at the time of referral. The most common adverse perinatal outcome was intrauterine fetal demise (IUID). The sex of the fetus was male in 24 babies (66.7%). The perinatal mortality rate was 50%.

Discussion and Conclusion

AFLP, characterized by fatty infiltration of liver is a rare life threatening obstetric emergency usually occurs in the last trimester and early postpartum period [1,2,8,9]. The condition is characterized by micro vesicular fatty infiltration and will get worsened from the time of diagnosis. Though the exact reason for its occurrence is not very clear, there is controversial association with fetuses carrying long and medium chain enzymes involved in fatty acid oxidation. The clinical spectrum and histological features of AFLP closely mimics Reye’s syndrome, sodium valproate toxicity and Jamaican morning sickness syndrome [10]. As described in literature, all the women in our case series presented in third trimester. Though AFLP closely mimics HELLP syndrome at admission,

the clinical and laboratory features of each may be different and it helps to identify the correct spectrum of P-sLD after evaluation [11,12]. The Swansea criteria of 6 and above was present in 77.8% of women in our case series which is similar to 60-90% of women in various case series. The histopathological diagnosis is not mandatory for the diagnosis of AFLP in clinical practice, and Swansea criteria is a good screening tool with 100% negative predictive value for micro vesicular fatty infiltration [13]. It is not uncommon to have a Swansea criteria of more than 6 in women with HELLP syndrome, presence of coagulopathy in almost all situations and low anti thrombin III levels will give a hint towards AFLP.

The maternal mortality rate in the present study was 38.9% which is higher than reported in recent literatures (<10%) [1-3,6-8]. One third of women in our case series had coagulopathy and AKI at the time of admission. One third of women had developed hepatic encephalopathy in our case series; in addition, sepsis and multi organ dysfunction (MODS) were responsible for more than 50% of maternal deaths. Early diagnosis and timely delivery are the keys in the successful management of AFLP the time interval between symptom onset and admission in our center was >4 days in 24 women (66.7%). The perinatal mortality described in literature varies between 8-23% and it is 50% in our case series [2,4,6,8]. Late presentation after symptom onset, coexisting preeclampsia might have contributed to high perinatal mortality and majority had occurred in-utero. In general, the perinatal outcome is better if it occurs after 34 weeks rather earlier gestational ages. There are case reports of AFLP occurring before 28 weeks of gestation and rarely for the first time in the postpartum period. The complications like encephalopathy, sepsis and MODS made them stay in intensive care unit (ICU) for a longer time. One of the women who had encephalopathy was referred to liver transplant unit after an ICU stay of 16 days. AFLP can mimic conditions like thrombotic microangiopathy, sepsis, leptospirosis and other conditions predispose to fulminant hepatitis in pregnancy.

We don't have follow-up of neonates after delivery. Two of them succumbed in the postnatal period. It is recommended that neonates born to mothers with AFLP should be screened for long-chain-3 hydroxyacyl-CoA-dehydrogenase (LCHAD) gene mutation in the offspring to avoid development of metabolic disturbances. There are studies looked at usefulness of Swansea criteria score, MELD (model for end stage liver disease) score in predicting adverse outcome in women with AFLP. The usefulness of Swansea

criteria for predicting adverse outcome is controversial and studies have shown MELD score has good area under curve for predicting adverse maternal and perinatal outcome [14]. The score was found to high among non-survivors. The coagulopathy is almost universal in women with AFLP and development of acute kidney injury increases the chances of adverse outcome.

The present study is one of the largest collection of women AFLP from a developing countries is the major merit of the study. In addition, the clinical presentation, laboratory parameters and outcomes are described in detail. All the case records of women with P-SLD have been screened to identify the women with AFLP. However, it is not without any limitations. The present study was a case-record based retrospective study from a single center. There were 4 women with jaundice in whom the cause was not identifiable which could be lack of time for work up or late presentation. Though the final diagnosis after thorough assessment was used to classify AFLP, the mere coexistence more number of women with preeclampsia in our study would still probably misclassified some of the women with HELLP syndrome as AFLP. It was not routine to do anti thrombin III in our setup. We don't have follow-up of neonates born to women with AFLP. We need more number studies to identify the factors associated with adverse outcome despite multidisciplinary care and the role of caesarean section on maternal and perinatal outcome.

In conclusion, the occurrence of AFLP is rare in pregnant women. All the women developed AFLP after 32 weeks and it is associated with significant adverse maternal and perinatal outcome in our setup. Early diagnosis, timely referral from peripheral health centers and appropriate multidisciplinary care with the aim to deliver within 24 hours of admission are essential to improve the outcome in women with AFLP.

Conflict of Interest

The authors declare no competing interest.

Funding

Not applicable.

Availability of Data and Materials

The data that support the findings of the study are available from the corresponding author upon request.

Ethical Concerns

The primary study on pregnancy specific liver diseases was approved from institute ethical and scientific committee (JIP/IEC/2016/28/952). For the year 2019, informed consent was taken.

Disclosure of Interest

The authors declare no financial or non-financial conflict of interest.

Author Contributions

SR, TN, LC designed and performed the research. SR, TN, ST analyzed the data. TN, SR and LC wrote the initial manuscript. SR, TN, ST, SR and LC revised the final manuscript.

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