RESEARCH ARTICLE

Acute Fatty Liver of Pregnancy: Experience of 8 Cases from a Tertiary Hospital

Amanjot Kaur[1], Beant Singh[2], Chinky Thukral[3]

Received on: 18 December 2020; *Accepted on:* 25 June 2024; *Published on:* 23 October 2024

Abstract

Objective: The aim of the present study is to discuss the clinical presentation, laboratory findings, and maternal and fetal outcomes of patients with acute fatty liver of pregnancy (AFLP) presenting to a tertiary care institution.

Materials and methods: All pregnant patients presenting to our institution with acute liver failure from January 2019 to December 2020 were evaluated for AFLP based on Swansea criteria. The demographic, clinical, and laboratory parameters of all patients, course of pregnancy, mode of delivery, and maternal and fetal outcomes of the pregnancy were evaluated for all patients.

Results: Eight patients were identified to have AFLP during the study period. The mean age at presentation was 26 years, the mean gestational age at presentation was 33 weeks. Three patients were primigravida, two had twin pregnancies, and 40% of patients who delivered had a male fetus. All patients presented with vomiting and jaundice and the majority had abdominal pain. Leukocytosis was observed in 75%, thrombocytopenia in 37.5%, coagulopathy in 37.5%, renal failure in 50%, encephalopathy in 75%, and hypoglycemia in 100% of patients. Two patients had ultrasound findings suggestive of AFLP. Two patients had a cesarean section, three had vaginal deliveries, and three maternal deaths occurred with undelivered status. There were five maternal deaths, and out of the five delivered patients, there were two fetal deaths.

Conclusion: Acute fatty liver of pregnancy is associated with high morbidity and mortality. Adverse maternal and fetal prognosis can be prevented by diagnosis early in the course of disease, prompt termination of pregnancy, and good supportive care.

Keywords: Acute fatty liver of pregnancy, Acute fatty liver, Fatty liver, Fulminant, Gestational, Liver failure, Pregnancy complication.

Journal of South Asian Federation of Obstetrics and Gynaecology (2024): 10.5005/jp-journals-10006-2490

Introduction

Acute fatty liver of pregnancy (AFLP) is associated with significant morbidity and mortality and is a potentially life-threatening complication associated with late trimesters of pregnancy and early postpartum periods. It was first described by Sheehan in 1940.[1] Its incidence ranges from one in 7,000 to one in 20,000 pregnancies.[2] The disease has multiorgan involvement and results in a plethora of clinical and laboratory abnormalities. The present study was done to study the clinical course and the laboratory parameters of patients presenting with AFLP in a tertiary care institution. An attempt was made to correlate the clinical and laboratory parameters with the severity of the disease.

Materials and Methods

All pregnant patients presenting to our institution with acute liver failure from January 2019 to December 2020 were evaluated for AFLP. All these patients were admitted to the obstetric unit or intensive care unit of the hospital and were managed in conjunction with medical specialists and intensivists. The objective diagnosis of AFLP was based on Swansea criteria (six or more): vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, elevated serum bilirubin level (>14 µmol/L), elevated uric acid (>340 µmol/L), hypoglycemia (<4 mmol/L), leukocytosis (>11 × 10^6 cells/L), elevated transaminases (AST or ALT >42 IU/L), ascites or bright liver on ultrasound scan, elevated ammonia (>47 µmol/L), renal impairment (serum creatinine >150 µmol/L), coagulopathy (PT>14 s), and microvesicular steatosis on liver biopsy.[3] Patients with viral hepatitis, HELLP syndrome, drug-induced hepatitis, and biliary tract disease were excluded. The demographic, clinical, and laboratory parameters of all patients were recorded. The course of pregnancy, mode of delivery, and the maternal and fetal outcomes of the pregnancy were determined for all patients. In view of the study being a case series with less number of patients, numbers and percentages were used as statistical parameters. Ethical clearance was not sought in view of the observational and non-interventional nature of the study.

Results

Eight patients were identified to have AFLP during the course of the study and were 22–39 years of age. Three were primigravidas, whereas the rest were multigravidas. Two (25%) patients had twin gestation. All patients were in their third trimester, and the majority (75%) were more than 34 weeks of gestation. There were two twin pregnancies, and two patients delivered male babies (Table 1).

[1]Department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

[2,3]Department of Obstetrics and Gynaecology, Government Medical College, Patiala, Punjab, India

Corresponding Author: Amanjot Kaur, Department of Obstetrics and Gynaecology, Postgraduate Institute of Medical Education and Research, Chandigarh, India, Phone: +91 8437000718, e-mail: aman50055@yahoo.com

How to cite this article: Kaur A, Singh B, Thukral C. Acute Fatty Liver of Pregnancy: Experience of 8 Cases from a Tertiary Hospital. J South Asian Feder Obst Gynae 2024;16(5):546–549.

Source of support: Nil

Conflict of interest: None

Table 1: Demographic parameters and clinical outcomes of the patients

S. No.	*Age (years)*	*Gravida*	*Gestational age (weeks)*	*Pregnancy outcome*	*Maternal outcome*	*Fetal outcome*	*Sex of the baby*
1	26	G1	37	Cesarean section	Survivor	Live born	female
2	39	G4	32	Maternal mortality (undelivered)	Nonsurvivor	–	–
3	27	G4	34	Cesarean section	Survivor	Live born	Male
4	24	G3	37	Vaginal delivery (spontaneous)	Survivor	Live born	Female
5	20	G1	34	Vaginal delivery (spontaneous)	Nonsurvivor	Still born	Male
6	30	G5	30	Vaginal delivery (induced)	Nonsurvivor	Still born	Female
7	20	G2	29	Maternal mortality (undelivered)	Nonsurvivor	–	–
8	22	G1	35	Maternal mortality (undelivered)	Nonsurvivor	–	–

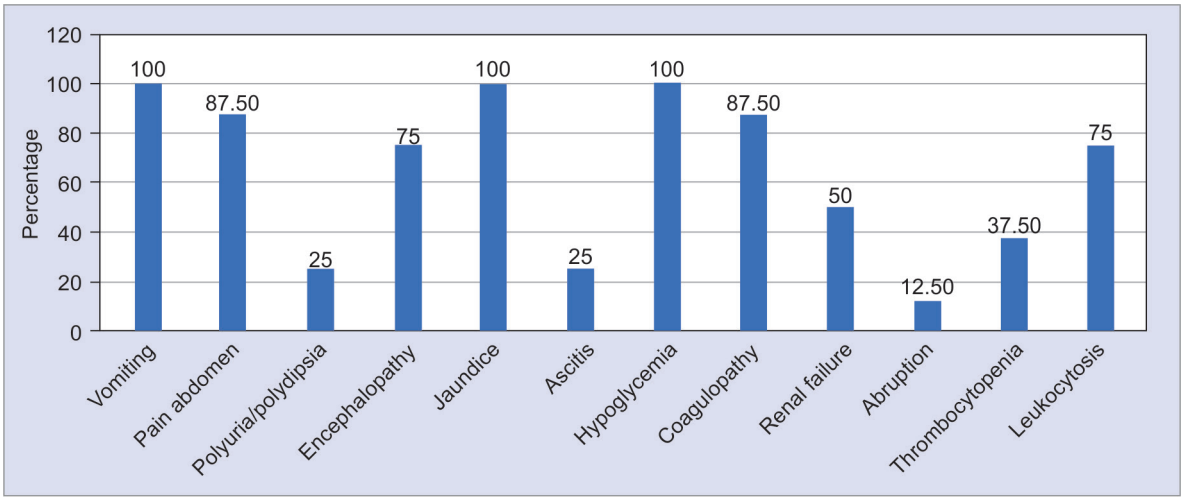

Fig. 1: Clinical presentation and complications in the patients

All patients had vomiting at presentation, and the majority had pain in the abdomen (87.5%), and encephalopathy (75%) and polyuria or polydipsia were seen in 25% of patients (Fig. 1).

Leukocytosis (>11×10^6 cells/L) was observed in 6 (75%), thrombocytopenia (<1.5 lac/microliter in 3 (37.5%), deranged coagulogram (PT > 14s) in 7 (87.5%), deranged renal functions in 6 (75%), and hypoglycemia was observed in all patients. Bilirubin and transaminases were raised in all patients. Ultrasound findings suggestive of AFLP were observed in two patients.

Out of the eight patients, two had cesarean sections, three had vaginal deliveries, of which two were spontaneous and one was induced, and three patients died with pregnancy *in situ* as they presented late during the course of the disease. Five maternal deaths were observed, resulting in a mortality rate of 62.5%. Out of the five patients who delivered, three delivered live babies, while two had stillbirths (Table 1).

Discussion

Acute fatty liver of pregnancy is a rare idiopathic disease with unknown etiology and nonspecific but multiorgan clinical manifestations and is potentially fatal. These nonspecific clinical findings, clubbed with multiorgan involvement, make an early diagnosis difficult. Timely diagnosis and delivery can help to salvage both the maternal and fetal outcome.[4–6] Though anomalous mitochondrial fatty acid oxidation has been proposed as the basis of disease, a definitive etiology has still not been established.[7] Existing hypotheses attribute the disease to toxins produced due to defects in the activity of long-chain 3-hyroxyacyl coenzyme A dehydrogenase (LCHAD). It is opined that an interaction between LCHAD-deficient female and a similarly deficient fetus results in the progression of the disease.[8] Lack of specific symptoms causes difficulty in diagnosing the disease entity early in its course, delaying appropriate management. The "Swansea Criteria," which have been used for diagnostic purposes in our study, were validated in a cohort from the United Kingdom, where the incidence of AFLP was 5.0 per 1,00,000 pregnancies. The authors reported a positive predictive value of 85% and a negative predictive value of 100% for hepatic microvesicular steatosis when used for patients who underwent liver biopsy.[9] Another retrospective study done by Wang et al. on 52 patients also affirmed the usefulness of Swansea criteria in the diagnosis of AFLP.[10] Morton and Laurie, however, state that raised ammonia levels, transient diabetes insipidus, hypoglycemia, and encephalopathy strongly support AFLP but may not be present in all patients with the disease and opine that due consideration should be given to pregnancy-specific gestational values of laboratory investigations before arriving at a conclusion.[11] Goel et al. assessed the Swansea criteria against biopsy-proven hepatic microvesicular steatosis and reported a sensitivity, specificity, positive predictive value, and negative predictive value of 100, 57, 85, and 100%, respectively.[12] The majority of the patients were present in the third trimester. Commonly associated risk factors reported are primigravida patient,[13,14] multiple pregnancy,[15,16] and male fetus.[6,9] These findings can be appreciated in Table 2, which compares data from various previously published studies. However, the incidence of primigravida patients and male fetuses is lesser in our study than reported in the literature, probably because of the lesser number of patients.

Table 2: Clinical and laboratory parameters in our study in comparison to previous studies

Parameter	*Present study (n = 8)*	*Dwivedi et al. (n =7)*	*Weiwen Ynag et al. (n = 8)*	*Qiang Wei et al. (n =11)*	*Usta et al. (n = 14)*	*Lau et al. (n = 18)*	*Xiong et al. (n = 25)*	*N Cheng et al. (n = 32)*	*Gracia et al. (n = 35)*	*Zhang et al. (n = 56)*
Mean maternal age (years)	26	26		27	27.9	30	27.2	26.6	30.1	29.59
Gestational age (weeks)	33.5	36	34	36.4	34.5	36.5	35.3	35.9	36	35.86
Primigravida patients (%)	37.5%	85.7%	100%	100%	57%	61.11%	–	59.37%	40%	70%
Twin pregnancy (%)	25%	42.85%	–	18.18%	7.14%	22.22%	–	28.12%	11.42%	9%
Male fetus (%)	40%	80%	–	–	–	59%	–	57%	–	67%
Mode of delivery										
Cesarean section (%)	40%	71.4%	37.5%	91%	71.42%	72%	76%	59.37%	–	80.35%
Vaginal delivery (%)	60%	28.5%	62.5%	9%	28.57%	28%	24%	40.62%	–	19.64%
Mean bilirubin (μmol/L)	207.76	327.4	59–511.29	156.2	–	145	258.8	187.3	150.48	103.8
Mean TLC count ($\times 10^9$/L)	16.33	15.4	–	14.6	–	–	22.1	18.6	19.8	11.64
Mean blood sugar (mmoL/L)	3.15	3	–	5.4	3.38	3.611	3.5	3.47	2.49	4.03
Mean PT (s)	17.76	17	–	28.7	19.5	24.3	–	27.9		15.57
Mean SGOT (U/L)	231.8	177.5	–	134.6		208	376.4	108.3	280	262.16
Mean SGPT (U/L)	184.5	112.3	–	278.9		156	385.4	129.7	256	260.98
Mean creatinine (μmol/L)	196.40	306	–	217.5	212.21	212.21	207.3	184.7		119.84
Maternal death (% of total patients)	62.5%	14.2%	12.5%	9.1%	0%	11%	–	43.75%	11.4%	–
Fetal death (% of total births)	75%	14.2%	0%	9.1%	13.3%	18%	–	25%	12.5%	16%

Typically, during the initial phase of the disease, the patients present with nausea, vomiting, sudden onset abdominal pain, and malaise during the third trimester of pregnancy.[17] According to Reyes et al., these symptoms are seen in 60–80% of cases.[18] The findings in our study (Fig. 1) corroborate with the literature. The onset of symptoms may be insidious in some cases. Subsequently, the disease generally follows a torrential course. Patients develop acute liver failure, renal insufficiency, encephalopathy of various grades, coagulopathy secondary to liver failure and consequent hemorrhagic complications, secondary infections, and adult respiratory distress syndrome (Fig. 1).

Laboratory findings include raised serum bilirubin levels, transaminases, renal functions, leukocytosis, deranged coagulation profile, hypoglycemia, and hyperammonemia. Table 2 compares mean laboratory parameters in our study with previously published studies, and the values are comparable. Notably, all our patients had negative serology for viral hepatitis. Ultrasonography and computed tomography are the imaging modalities frequently used for diagnosis, but the sensitivity and specificity of these are insufficient to provide a definitive diagnosis of AFLP.[19] The typical findings on imaging are ascites and bright echotexture of the liver. However, these findings should be interpreted along with the clinical and laboratory parameters to arrive at the diagnosis. Two of our patients exhibited these findings on ultrasonography. Liver biopsy is considered the gold standard for diagnosis but is generally contraindicated due to a grossly deranged coagulogram.[20] For the same reason, liver biopsy was not done in our patients.

A combination of analysis of serological, biochemical, and hematological findings and imaging helps to provide a diagnosis. There is a marked association with hyperbilirubinemia, increased prothrombin time, and hypoglycemia.[21] In our study, all our patients had hyperbilirubinemia and hypoglycemia, and 87.5% had increased prothrombin time. Other associated complications observed in our study were coagulopathy (87.5%), abruption (one patient), encephalopathy (75%), and renal failure (50%) (Fig. 1).

Patients should preferably be admitted to an obstetric high-dependency unit or intensive care unit and regularly monitored for clinical status and laboratory parameters, especially the liver function tests, coagulation profile, and blood sugar levels. Close attention should be paid to the fluid status, as aggressive fluid replacement in settings of low oncotic pressure may lead to pulmonary edema. Development of encephalopathy, especially in advanced stages, is invariably associated with worse outcomes. Termination of pregnancy is the definitive treatment of AFLP. Vaginal delivery following induction of labor is the method of choice. However, a cesarean section may be the preferred method in cases where there is a rapid deterioration in clinical status and laboratory parameters or if the obstetric parameters are indicative of a cesarean section as the preferred mode of delivery. Delivery by any method helps in the improvement in the clinical condition, and it is prudent to take an early decision for pregnancy termination as soon as the diagnosis is confirmed before encephalopathy or coagulopathy sets in. Once the coagulopathy sets in, vaginal delivery is a safer option. If a cesarean section needs to be done in these settings, general anesthesia should be preferred over spinal anesthesia to prevent hemorrhagic complications. Judicious use of blood products is imperative. One must also be prepared for uterine artery embolization and peripartum hysterectomy if required. A delay in diagnosis and pregnancy termination results in rapid clinical deterioration. Those delivering late in the course of the disease remain at high risk for the development of liver failure-related complications like hemorrhage from various sites, gastrointestinal bleeding, sepsis, renal failure, hypoglycemia, and encephalopathy. If the interval between occurrence of AFLP and pregnancy termination is less than 1 week, the survival rate is almost 100%, and if this interval is 2 weeks, the peripartum maternal mortality rate increases to 30%.[22,23] Most of our patients presented late in the course of the disease in view of ours being a referral center, and thus the maternal and fetal mortality rate in our study was much higher than other recent studies. Early referral

of patients presenting with hyperbilirubinemia to higher centers is of outmost importance.

There is no specific diagnostic test or clinical manifestation for early diagnosis of AFLP. The key to reaching the diagnosis hinges on the clinician's ability to differentiate from disorders having similar presentations like severe viral hepatitis, gastroenteritis, sepsis, and hemolysis, elevated liver transaminases, and low platelet counts syndrome. Once these differentials are ruled out, a patient should be managed as AFLP, and delivery should be hastened. Failure to do so in an expedited manner may result in disastrous consequences.

The existing data suggests that the disease is totally reversible.[24] However, recurrences have been reported even if testing for LCHAD deficiency mutation is negative. Due to the rarity of the disease, more studies are required to study the genetics, etiopathogenesis, and postpartum behavior of the disease. Artificial liver support systems, plasma exchange treatment and liver transplants have been described in disease management.

A major shortcoming of the present study is that the number of patients was small, and the results and mortality data are difficult to extrapolate to the entire population. Prospective studies of longer duration will help in further elucidation of the natural history of the disease and its subsequent management. Supportive treatment and close observation should continue in the postpartum period. Contraceptives and other drugs should be prescribed with caution.

Conclusion

Acute fatty liver of pregnancy is a life-threatening complication of pregnancy presenting with acute liver failure and can be diagnosed on the basis of the noninvasive "Swansea Criteria" relatively early in the course of the disease. It presents generally in the third trimester of pregnancy with non-specific symptoms like nausea, vomiting, abdominal pain, and jaundice. It has a fulminant clinical course and causes acute liver decompensation and is associated with complications like encephalopathy of various grades, hypoglycemia, coagulopathy, and renal failure. Timely referral to higher and well-equipped centers and early termination of pregnancy by any means, along with good supportive management, prevent maternal mortality and perinatal mortality and morbidity.

Orcid

Amanjot Kaur https://orcid.org/0000-0003-4452-3455

References

1. Sheehan HL. The pathology of acute yellow atrophy and delayed chloroform poisoning. J Obstet Gynaecol Br Emp 1940;47:49–62. DOI: 10.1111/j.1471-0528.1940.tb14731.x.
2. Watson WJ, Seeds JW. Acute fatty liver of pregnancy. Obstet Gynecol Surv 1990;45:585–591. DOI: 10.1097/00006254-199009000-00004.
3. Ch'ng CL, Morgan M, Hainsworth I, et al. Prospective study of liver dysfunction in pregnancy in Southwest Wales. Gut 2002;51:876–880. DOI: 10.1136/gut.51.6.876.
4. Liu G, Shang X, Yuan B, et al. Acute fatty liver of pregnancy: Analysis on the diagnosis and treatment of 15 cases. J Reprod Med 2016;61: 282–286. PMID: 27424373.
5. Mellouli MM, Amara FB, Maghrebi H, et al. Acute fatty liver of pregnancy over a 10-year period at a Tunisian tertiary care center. Int J Gynaecol Obstet 2012;117:88–89. DOI: 10.1016/j.ijgo.2011.11.012.
6. Cheng N, Xiang T, Wu X, et al. Acute fatty liver of pregnancy: A retrospective study of 32 cases in South China. J Matern Fetal Neonatal Med 2014;27:1693–1697. DOI: 10.3109/14767058.2013.871704.
7. Treem W. Beta oxidation defects. Clin Liv Dis 1999;3:50–67. DOI: 10.1016/S1089-3261(05)70053-2.
8. Bellig LL. Maternal acute fatty liver of pregnancy and the associated risk for long-chain 3-hydroxyacyl-coenzyme a dehydrogenase (LCHAD) deficiency in infants. Adv Neonatal Care 2004;4(1):26–32. DOI: 10.1016/j.adnc.2003.12.001.
9. Treem WR, Shoup ME, Hale DE, et al. Acute fatty liver of pregnancy, hemolysis, elevated liver enzymes, and low platelets syndrome, and long chain 3hydroxyacylcoenzyme A dehydrogenase deficiency. Am J Gastroenterol 1996;91:2293–2300. PMID: 8931405.
10. Wang S, Li SL, Cao YX, et al. Noninvasive Swansea criteria are valuable alternatives for diagnosing acute fatty liver of pregnancy in a Chinese population. J Matern Fetal Neonatal Med 2017;30(24):2951–2955. DOI: 10.1080/14767058.2016.1269316.
11. Morton A, Laurie J. Physiological changes of pregnancy and the Swansea criteria in diagnosing acute fatty liver of pregnancy. Obstet Med 2018;11(3):126–131. DOI:10.1177/1753495X18759353.
12. Goel A, Ramakrishna B, Zachariah U, et al. How accurate are the Swansea criteria to diagnose acute fatty liver of pregnancy in predicting hepatic microvesicular steatosis? Gut 2011;60:138–139. DOI: 10.1136/gut.2009.198465.
13. Holzman RS, Riley LE, Aron E, et al. Perioperative care of a patient with acute fatty liver of pregnancy. Anesth Analg 2001;92:1268–1270. DOI: 10.1097/00000539-200105000-00036.
14. Zhou G, Zhang X, Ge S. Retrospective analysis of acute fatty liver of pregnancy: Twentyeight cases and discussion of anesthesia. Gynecol Obstet Invest 2013;76:83–89. DOI: 10.1159/000351565.
15. Vigilde Gracia P, MontufarRueda C. Acute fatty liver of pregnancy: Diagnosis, treatment, and outcome based on 35 consecutive cases. J Matern Fetal Neonatal Med 2011;24:1143–1146. DOI: 10.3109/14767058.2010.531325.
16. Rajasri AG, Srestha R, Mitchell J. Acute fatty liver of pregnancy (AFLP) –An overview. J Obstet Gynaecol 2007;27:237–240. DOI: 10.1080/01443610701194705.
17. Knight M, Nelson-Piercy C, Kurinczuk JJ, et al. A prospective national study of acute fatty liver of pregnancy in the UK. Gut 2008;57:951–956. DOI: 10.1136/gut.2008.148676.
18. Reyes H. Acute fatty liver of pregnancy: A cryptic disease threatening mother and child. Clin Liv Dis 1999;3:70–81. DOI: 10.1016/S1089-3261(05)70054-4.
19. Y Bacq. Liver diseases unique to pregnancy: A 2010 update. Clin Res Hepatol Gastroenterol 2011;35(3):182–193. DOI: 10.1016/j.clinre.2010.11.011.
20. Vigil-De GP, Lavergne JA. Acute fatty liver of pregnancy. Int J Gynaecol Obstet 2001;72:193–195. DOI: 10.1016/s0020-7292(00)00370-2.
21. Mjahed K, Charra B, Hamoudi D, et al. Acute fatty liver of pregnancy. Arch Gynecol Obstet 2006;274:349–353. DOI: 10.1007/s00404-006-0203-6.
22. Reyes H, Sandoval L, Wainstein A et al. Acute fatty liver of pregnancy: A clinical study of 12 episodes in 11 patients. Gut 1994;35:101–106. DOI: 10.1136/gut.35.1.101.
23. Schorr-Losnich B, Lebovics E, Dworkin B, et al. Liver diseases unique to pregnancy. Am J Gastroenterol 1991;86:659–670. PMID: 2038986.
24. Barber MA, Eguiluz I, Martín A, et al. Acute fatty liver of pregnancy: Analysis of five consecutive cases from a tertiary centre. J Obstet Gynaecol 2010;30(3):241–243. DOI: 10.3109/01443610903452765.