Original Article

Acute Fatty Liver Of Pregnancy: Our Experience with Six Cases

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Keywords: *Acute Fatty Liver, Pregnancy, Caesarean, Jaundice, Metabolic acidosis, Ventilatory Support, Liver Failure.*

ABSTRACT

Background: Acute Fatty Liver Of Pregnancy (AFLP) is a rare, life-threatening pregnancy associated disorder manifesting in the late trimester or early postpartum period. Early diagnosis and treatment is very important due to multi organ involvement and high mortality.

Method: Ours is a retrospective case study of AFLP in Amrita Institute of Medical Sciences &Research Centre, Kochi during the 2years of september 2013 to august 2015.Clinical presentations and management details were extracted from records.

Results: Out of 6 cases, 5 were primi and 1 mutigravida. The mean gestational age of diagnosis was 36.67 weeks. The clinical features were vomiting in 2,jaundice in 5, pruritus in 2,encephalopathy in 2.Ultrasonography were done in all the 6 cases . Fatty liver in 3, ascites in 6 and bright liver were seen in 2. Labor induction with vaginal delivery in 1 and 5 had Caesarean delivery under general anaesthesia.

The post op complications were acute renal insufficiency in 5 , liver failure in 3 , pancreatitis in 1, metabolic acidosis in 5 ,pleural effusion in 3, pulmonary edema in 5, pneumonia in 2, sepsis in 5,hypoglycemia in 3, DIC in 3 , ARDS in 3, MODS in 3, maternal mortality in 3 and perinatal mortality in 1. Ventilatory support were given in 5 and ionotropes were used in 3. Blood & blood products were given in 5. The average duration of stay in the hospital and ICU were 12.7days and 4.8 days respectively.

Conclusion: Aggressive management which includes maternal stabilization, rapid termination of pregnancy and intensive care support with multidisciplinary approach is important in reducing the complications associated with it.

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Introduction

AFLP is a rare life threatening complication which is usually seen in third trimester of pregnancy/ early post partum period. AFLP is commonly seen in primigravida, twin pregnancy and pregnancies carrying a male baby. The incidence of AFLP is 1 in 7,000 to 1 in 16,000pregnancies. [1,2]

The exact etiology of AFLP is unknown. But the most probable cause is due to hepatic damage caused by deficiency of long chain 3- hydroxy acyl co-A dehydrogenase (LCHAD) causes accumulation of toxins. Interaction between LCHAD deficient mother and fetus leads to progression to AFLP. This could also explain why the disease is so rare[3].

Materials and Methods

We reviewed the case records of AFLP diagnosed during the period. The clinical manifestations, gestational age of diagnosis and termination of pregnancy were noted. The investigations at the time of admission were used for diagnosis of AFLP, mode of termination and anesthesia, ICU care with supports were also documented. The maternal and fetal outcome were also noted.

Objectives: To study the clinical presentations, management and outcome of AFLP in Amrita Institute of Medical Sciences &Research Centre, Kochi during the 2 years of september 2013 to august 2015.

Type of study: Retrospective case study.

Results

All the 6 cases were referred to us from peripheral centres. Pregnancy was terminated by caesarean section in 3 cases from outside hospitals . The other 3 were referred as AFLP for further management . The mean age of the patients in our study was 27.3years. We had 5 primigravidas and one multigravida. There were 2 twin pregnancies. In our study of the 8 newborns 6 were males. The mean gestational age of diagnosis of was 36.67 weeks. The average diagnosis to delivery interval was 12.67 hours (3-24 hours). The clinical features were vomiting in 2,epigastric pain in 1,jaundice in 5, pruritus in 2,encephalopathy in 2 .The investigations at the time of admission are shown in the table3. The ultrasound were done in all the 6 cases. Fatty liver was diagnosed in 3 cases, ascites were found in 6 patients and bright liver were seen in 2 of these AFLP cases. Labor induction were done in one case and vaginal delivery were accomplished in that case. Caesarean delivery were done in other 5 cases. All the caesarean sections were done under general anaesthesia as all of them had coagulation abnormalities and regional anaesthesia were contraindicated. All patients had severe metabolic acidosis intra operatively and could not be extubated on table. The patients were shifted to ICU in the postoperative period and were put on mechanical ventilatory support.

In the post operative period the complications encountered were acute renal insufficiency in 5 , liver failure in 3 , pancreatitis in 1, metabolic acidosis in 5 ,pleural effusion in 3, pulmonary oedema in 5, pneumonia in 2, sepsis in 5,hypoglycemia in 3, DIC in 3 , ARDS in 3, MODS in 3, maternal mortality in 3 and perinatal mortality in 1. The ventilator support were given in 5 cases. . Inotropic support were required in 3 patients. Blood and blood product transfusions were required in 5 of the 6 cases. The mean blood products that were given are shown in table 2. The average duration of stay in the hospital and ICU were 12.7days and 4.8 days respectively.

Table 1

	7 cases (Suchi et al)	6 cases (our study)
Age (mean)	26	27.3
Gestational age (mean)	36W	36.7W
Primigravida	6 (85.7%)	5(83.3%)
Multi gravida	1 (14.2%)	1(16.7%)
Mode of delivery	CS-5 (71.4%), vaginal delivery-2(28.5%)	CS -5 (83.3%) vaginal delivery -1(16.7%)
Maternal mortality	1	3
Perinatal mortality	4	1
Hypoglycaemia	4 (57.1%)	3(50%)
Acute renal insufficiency	7 (100%)	5(83.3%)
DIC	4	3
Ascitis	2	4
Liver failure	4	3
Hepatic encephalopathy	3	2
ARDS	3	3

	7 cases (Suchi et al)	6 cases (our study)
Hemorrhagic shock	3	0
Pulmonary edema	1	5
Sepsis	1	5
Metabolic acidosis	2	5
MODS	4	3
Pancreatitis	0	1
Vomiting	6	3
Epigastric pain	6	1
Jaundice	7	5
Polydipsia	4	0
Pruritis	3	2

Table 2

	N	Minimum	Maximum	Mean	Std. Deviation
ICU stay	6	0	8	4.83	2.927
Hospital stay	6	7	16	12.67	3.141
Hb	6	8.80	14.20	11.24	1.92562
Neutrophil	5	72.00	91.00	82.4	7.02140
WBC	6	12.50	26.80	19.56	5.81401
Platelet	6	40.00	331.00	156.6	100.60550
Urea	6	6.90	42.00	25.81	14.68801
S creatinine	6	.64	3.24	2.02	.98555
Ammonia	6	0.00	234.50	76.0	86.20349
PT INR	6	1.08	5.23	2.4083	1.44598
APTT	6	33.00	57.00	44.5500	10.88811
Fibrinogen	4	85.00	740.00	294.2500	300.94005
SGOT	6	55.50	404.00	261.2500	120.59260
SGPT	6	54.30	670.00	293.5333	209.90864
LDH	6	331.00	707.00	544.3333	139.45561
TBilirubin	6	2.08	12.40	8.6983	3.66722
TProtein	5	4.20	5.87	5.3780	.69478
CRP	6	3.00	207.00	67.6667	81.24941
PRBC	3	2.00	6.00	4.3333	2.08167
FFP	5	4.00	18.00	10.2000	5.58570
Cryoprecipitate	1	4.00	4.00	4.0000	
Gestational age	6	36	38	36.67	.816
Deliveryinterval	6	3	24	12.67	9.288
Glucose	6	40	95	70.83	23.676
Valid N (listwise)	0				

Discussion

The mean gestational age at which AFLP is diagnosed is 35 to 36 weeks, with a range of 28-40weeks. AFLP is commoner in primigravida and there is an association with obesity, multiple pregnancies and male foetus (ratio 3:1) [4]. AFLP is thought to be a rare variant of preeclampsia (associated in 50 to 100% of cases) [1]. It can cause multiple organ failure in case of delayed diagnosis[5].Patients often present with non specific symptoms such as anorexia, nausea, vomiting, malaise, fatigue, headache, thirst, altered mental status, abdominal pain. Signs commonly found are fever and jaundice. Abnormal laboratory findings are moderate elevations of amino transferase (300-500 u/l), bilirubin (3-25mg/dl), markedly elevated alkaline phosphatase, hypoglycemia, leukocytosis and coagulation parameters. In severe cases, patient can present with multi-system involvement such as ARF, encephalopathy, GI bleeding, pancreatitis, and coagulopathy.[6].Some of

the patients may have pulmonary oedema also. Transient diabetes insipidus is a very rare complication. AFLP also has a detrimental effect on the fetus.[7].One of the complications of AFLP is maternal metabolic acidosis secondary to impaired clearance of serum lactate by damaged hepatocytes.[8] Common complications seen are [9] renal failure (60%),hypoglycemia (53%),infection (45%),gastrointestinal hemorrhage (33%),coagulopathy (30%),severe postpartum hemorrhage,fulminate hepatic failure,stillbirth.

Gold standard for diagnosis is liver biopsy . But may not be feasible in presence of coagulopathy. The Swansea diagnostic criteria are an alternate to liver biopsy. According to the Swansea [10], criteria for diagnosis of AFLP include six or more of the following features in the absence of another explanation: vomiting, abdominal pain, polydipsia/polyuria, encephalopathy, elevated bilirubin (>14 µmol/L), leukocytosis (>11 × 10^9/L), elevated uric acid (>340 µmol/L), hypoglycemia (<4 mmol/L), ascites on ultrasound scan, increase in the level of transaminases (aspartate aminotransferase or alanine aminotransferase > 42 IU/L), renal impairment (creatinine > 150 µmol/L), elevated ammonia (>47 µmol/L), coagulopathy (prothrombin time > 14 sec or activated partial thromboplastin time > 34 sec), and microvesicular steatosis on liver biopsy.

AFLP is an obstetric emergency, hence delivery is the definitive treatment of AFLP. Close continuous monitoring after delivery is vital as it can complicate severe postpartum hemorrhage and multi-organ failure even after delivery. Clinical condition may deteriorate rapidly. Severely ill patients require care in ITU and multi-organ failure may need assisted ventilation and dialysis. Aggressive correction of coagulation abnormalities are the mainstay of treatment. Disseminated intra-vascular coagulation may be a severe and potential fatal complication of AFLP. These patients may have profoundly low anti-thrombin III levels, hypofibrinogenaemia and prolonged prothrombin time and APTT levels. Hypoglycemia should be treated aggressively before and after delivery[5]

Early diagnosis, prompt delivery and intensive supportive care are the corner stones in the management of AFLP. If the patients are at high risk for multisystem organ failure and death, admission to the intensive care unit is generally recommended. Maternal stabilization should be achieved before delivery, which includes airway management, treatment of hypotension, correction of hypoglycemia, electrolyte and coagulation abnormalities.

Once the mother is stabilized , delivery of the fetus by vaginal or cesarean is accomplished within 24 hours or before. In the postpartum recovery period, AFLP are at high risk of bleeding as a result of coagulopathy. Rarely patients develop pancreatitis, which can be severe . Pancreatits generally becomes apparent only with the development of hepatic and renal dysfunction[11]. Pseudocysts with secondary infections or hemorrhagic pancreatitis with retroperitoneal bleeding can develop. Hence it is worth while to do a serial screening of serum amylase and lipase after the onset of hepatic dysfunction. Imaging with CT/MRI may be useful in assessing the development of pseudocyts or hemorrhagic pancreatitis. Pereira et al [12] recommended that liver transplantation should be reserved for patients with hepatic encephalopathy, severe metabolic acidosis, worsening coagulopathy or liver rupture complicated by hepatic necrosis as indicated by CT scan.

The lab values were normalized within 7-10 days after delivery in a series. Recurrence of AFLP in subsequent pregnancies can occur. Although the theoretical recurrence risk in subsequent pregnancies is 25% with a mother carrying a homozygous mutant or compound heterozygous fetuses, it is uncommon and only a few cases have been documented [1]. Therefore, affected women should still be informed, counselled and tested, along with their infants who may be affected, for LCHAD deficiency. If the patient decides to be pregnant again, she should be closely monitored for any of the early signs of acute fatty liver. In our case we had 3 maternal and 1 fetal mortality .

Conclusion

AFLP, a rare pregnancy related conditon with multi-organ failure and increased maternal and neonatal mortality. Aggressive management which includes maternal stabilization, rapid termination of pregnancy and intensive care support with multidisciplinary approach is important in reducing the complications associated with it.

Acknowledgements

None

Funding

None

Competing Interests

Not Declared

Reference

1. Knox TA, Olans LB. Liver disease in pregnancy. N Engl J Med. 1996;335: 569–76.
2. Riely CA. Acute fatty liver of pregnancy. Semin Liver Dis. 1987;7:47–54.
3. Suchi Dwivedi, Ma Runmei. Retrospective Study of Seven Cases with Acute Fatty Liver of Pregnancy ISRN Obstetrics and Gynecology Volume 2013 (2013) .

4. Gregory TL. Hughes S. Coleman MA. De Silva. A. 2007. Acute fatty liver of pregnancy; three cases and discussion of analgesia and anesthesia. International Journal of Obstetric Anesthesia.16 (2):175-9.
5. P Sinha, P Kyle, P Gubbala. Acute Fatty Liver of Pregnancy - A Review:. The Internet Journal of Gynecology and Obstetrics. 2009 Volume 13 Number 1
6. Hin Hin Ko,Yoshida. Acute fatty liver of pregnancy Can J Gastroenterol. 2006 Jan; 20(1): 25–3.
7. Woll PJ, Record CO. Lactate elimination in man: Effects of lactate concentration and hepatic dysfunction. Eur J Clin Invest. 1979;9:397–404.
8. Werner CJ, Zoller DP, Baskin WN, Eichmann RE. Acute fatty liver of pregnancy associated with maternal and fetal metabolic acidosis. J Fam Pract. 1988;26:198–9.
9. Yucesoy G, Ozkan SO, Bodur H, Cakiroglu Y, Caliskan E, Ozeren S. Acute fatty liver of pregnancy complicated with disseminated intravascular coagulation and haemorrhage: a case report. International Journal of Clinical Practice. 2005. Supplement (147):82-4.
10. D. Joshi, A. James, A. Quaglia, R. H. Westbrook, and M. A. Heneghan, "Liver disease in pregnancy," The Lancet, vol. 375, no. 9714, pp. 594–605, 2010.
11. Moldenhauer JS, O'brien JM, Barton JR, Sibai B. Acute fatty liver of pregnancy associated with pancreatitis: A life-threatening complication. Am J Obstet Gynecol. 2004;190:502–5.
12. Pereira SP, O'Donohue J, Wendon J, Williams R. Maternal and perinatal outcome in severe pregnancy-related liver disease. Hepatology. 1997;26:1258–62.