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Maternal and Fetal Outcome in Acute Fatty Liver of Pregnancy

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Abstract: ***Background: Acute fatty liver of pregnancy is an idiopathic disorder with high mortality in the third trimester. The pathogenesis is unclear but there is emerging evidence of the genetic basis of AFLP where defective mitochondrial fatty acid beta oxidation in the fetus is implicated in some cases. Prompt delivery and intensive supportive care remain as the mainstay of treatment. Methods: We performed a descriptive prospective study of 22 patients with AFLP who met the Swansea criteria between March 2022 and March 2023. We analyzed the clinical features, laboratory results, maternal and neonatal outcomes. Results: Jaundice and Hypertension (59.1%) were the most common clinical manifestations. Nausea, vomiting and upper abdominal pain were the next common (40.9%) clinical symptoms. DIC was the major contributing factor for maternal mortality (60%) and maternal morbidity (45.5%). 50% pregnant women required ICU care and 22.7% maternal mortality was seen. Pregnant women with male fetuses (77.3%) was found to have a strong association with AFLP in our study. 54.5 % were preterm babies.50% babies required NICU care and 18.2% neonatal deaths was seen. Conclusion: Early diagnosis and termination of pregnancy plays a major role in preventing maternal mortality in AFLP.***

Keywords: Acute Fatty Liver of Pregnancy, LCHAD enzyme, HELLP syndrome, DIC.

1. Introduction

Acute fatty liver of pregnancy is an idiopathic disorder with extremely high mortality in the third trimester[1, 2]. It was described by Sheehan in 1940[3]. The most common cause of acute liver failure during pregnancy is acute fatty liver-also called acute fatty metamorphosis or acute yellow atrophy[4]. Incidence probably approximates 1 in 10000 pregnancies[5].

Characteristically, AFLP include rapidly progressing hepatic dysfunction, coagulation disorders triggered by micro vesicular fatty infiltration of the liver. AFLP can occur at any age. It has no unique clinical characteristics and develops rapidly, posing threat to both mother and fetus. The pathogenesis of AFLP is unclear but there is emerging evidence of the genetic basis of AFLP where defective mitochondrial fatty acid beta oxidation in the fetus is implicated in some cases[6]. There is a strong association between AFLP and a deficiency of the enzyme long chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) in the fetus, a disorder of mitochondrial fatty acid beta oxidation[7].

It is difficult to diagnose AFLP as there are no specific symptoms and reliable examinations for AFLP. Gastrointestinal symptoms are anorexia, vomiting, abdominal pain. Ultrasound, computed tomography, magnetic resonance imaging are not reliable as the sensitivity of these tests are less[8]. More accurately, it is diagnosed with liver biopsy but biopsy can cause complications if there is coagulopathy[9]. When AFLP is diagnosed or suspected, termination of pregnancy and supportive treatment are important. Delay in diagnosis and treatment may lead to death[10].

A better understanding of AFLP and its features will help in timely diagnosis and treatment, including prompt termination of pregnancy. Prompt delivery of the infant and intensive supportive care remain as the mainstay of treatment[11]. This helps in increasing the cure rate, reduces mortality and improve pregnancy outcomes.

2. Literature Survey

A retrospective study conducted by Zhang Y et al, (n=56) at China between June 2008 and July 2013 showed that nausea and vomiting may be the most common symptoms of AFLP. Indexes of liver dysfunction and coagulation disorders should also be considered. It conclude that prompt pregnancy termination is currently the only way to control the development of AFLP, emphasizing the possible role of placenta in the pathogenesis of AFLP[12].

A retrospective study conducted by Dwivedi S et al, (n=7) at China from February 2005 to January 2013 showed that patients who are critically ill at the time of clinical presentation, develop complications or continue to deteriorate despite emergency delivery and require collaborative management in ICU. Early diagnosis, prompt delivery, adequate supportive care and a multidisciplinary approach are the key to a good outcome[13].

3. Methods

Subjects and methods:
We performed a prospective descriptive study of 22 in patients who were admitted at Vani Vilas hospital, Bangalore between March 2022 and March 2023. The diagnosis of AFLP was based on the Swansea criteria.

Inclusion Criteria:
1) Age > 18 years
2) Patient willing to give informed consent

3) Patients with signs and symptoms (persistent nausea and vomiting, malaise, anorexia, epigastric pain and progressive jaundice) suggestive of AFLP[14]
4) Patients fulfilling Swansea criteria. According to Swansea criteria for the diagnosis of acute fatty liver of pregnancy, six or more of the following findings are required in the absence of another cause

Vomiting
Abdominal pain
Polydipsia/ polyuria
Encephalopathy
Elevated bilirubin > 14 pmol/l
Hypoglycemia < 4 mmol/l
Elevated urea > 340 pmol/l
Leucocytosis > 11 x 109/l
Ascites or bright liver on ultrasound scan
Elevated transaminases (AAT or ALT) > 42 IU/ l
Elevated ammonia > 47 pmol/l
Renal impairment: creatinine > 150 pmol/
Coagulopathy: prothrombintime> 14 seconds or APPT> 34 seconds
Microvascular steatosis on liver biopsy

Exclusion Criteria:
1) Patient not willing to give informed consent
2) Proven hepatic viral disease.
3) Patients with other systemic illness

Outcome measures:
1) Maternal morbidity measured in terms of
   - Acute renal failure
   - Need for blood and blood component transfusion
   - HELLP syndrome
   - Pre eclampsia
   - Disseminated intravascular coagulation
   - Need for ICU admission
   - Maternal mortality
2) Fetal outcome in terms of
   - Intrauterine growth restriction
   - Intrauterine death
   - Gender
   - Preterm delivery
   - Birth weight
   - NICU admission

Statistical Analysis:

The collected data was analysed using IBM SPSS software ver.20
- **Shapiro-Wilk test** was used to determine the normality of the data.
- Continuous variables are expressed in terms of **MEAN + Standard deviation, Median (Interquartile range).**
- Categorical variables are expressed as **frequency (n) and percentage (%)**

4. Results

22 patients were included in the study.
Mean age distribution of pregnant women included in the study was 25.2 + 4 years.

17 out of 22 women were primipara (77.2%) and 5 were multiparous women (22.8%).

The clinical features are shown in table 1.

Table 1: Clinical features of patients with AFLP

Clinical features / symptoms	n	%
Jaundice	13	59.1%
Hypertension	13	59.1%
Edema	11	50%
Hypoglycemia	10	45.5%
Haemorrhagic tendancy	10	45.5%
Nausea and vomiting	9	40.9%
Upper abdominal pain	9	40.9%
Fatigue	8	36.3 %
Pruritus	3	13.6%
Diarrhoea	2	9.1%

Clinical features are shown in Table 1. Nausea, vomiting were most common symptoms (40.9 %) along with upper abdominal pain (40.9%). Most common signs were hypertension and jaundice (59.1 %). Haemorrhagic tendancy was seen in 45.5% of the patients in the form of purpura and gum bleeding.45.5% patients were found to have hypoglycemia.

These women underwent various blood investigations which are shown in table 2.

Table 2: Laboratory findings in cases with AFLP

Laboratory parameters	Frequency	Median/ Mean + SD %
Elevated transaminases	13	59.1%
Elevated PT/APTT	10	45.5%
Elevated bilirubin	9	40.9%
Elevated creatinine	8	36.4%
Thrombocytopenia	8	36.4%
Elevated urea	3	13.6%
Hypoglycemia	76.5 - 95.75	86.91 + 12.97
Elevated ammonia	3	13.6%

59.1% of the patients had elevated transaminases in liver function tests.50% had altered renal function tests in the form of elevated creatinine (36.4%) and urea (13.6%). Coagulation disorder was indicated by elevated PT/APTT in 45.5%women.40.9% patients had elevated bilirubin levels. Thrombocytopenia was seen in 36.4% patients.13.6% patients had elevated ammonia.

Table 3: Laboratory investigations

Lab parameters	Range	Mean lab values
Elevated bilirubin	3.75 - 10.75	8.5 (Median)
Elevated urea	17.5 - 42.5	26.50 (Median)
Leucocytosis	13.75 - 25.25	20.77 + 7.84 (Median)

50% of the women had hypoglycemia (mean = 86 mg/dl). Range of bilirubin values found in these women was 3.75-10.75 mg/dl (Median = 8.5 mg/dl). Range of total leucocyte count was 13.75 - 25.25 cells/cumm (Median = 20.77 + 7 cells/cumm).

Management
As soon as the diagnosis of AFLP was made/ suspected, early termination of pregnancy was done. Comprehensive treatment was started which includes hepatoprotective drugs,

treatment for hypertension and organ dysfunction, correction of anemia, hypoproteinemia and coagulation abnormalities and assisted ventilation.

Table 4: Hospital management in cases with AFLP

Pregnancy outcome		
Parameters	n	%
Gestational age at delivery (weeks)	32.6	
Vaginal delivery	14	63.6 %
Cesarean section	8	36.3 %

Table 4 shows hospital management of patients with AFLP. Mean gestational age at delivery was 32.6 weeks.14 women had vaginal delivery (63.6%) and 8 of the patients underwent cesarean section (36.3%).

Table 5: Maternal treatment

Parameters	n	%
Hepatoprotective drugs	16	72.7 %
ICU care	11	50.0 %
Blood transfusion	10	45.5 %
Platelet transfusion	8	36.3 %
Assisted ventilation	6	27.2 %
Blood components transfusion	4	18.1 %

Table 5 shows treatment given to women with AFLP.16 patients (72.7%) received hepatoprotective drugs. .11 out of 22 i. e 50% required ICU care out of whom 6 required assisted ventilation.10 women (45.5%) required blood transfusion.8 women (36.3%) required platelet transfusion.4 women (18.1%) required transfusion of blood components. Maternal complications are depicted in table 6.

Table 6: Maternal complications

Complications	n	%
DIC	10	45.5 %
Acute renal failure	8	36.4 %
HELLP syndrome	8	36.4%
Hypoproteinemia	7	31.8 %
Pre eclampsia	6	27.2 %
Maternal death	5	22.7 %
Hemorrhage	4	18.1 %
MODS	2	9.09 %
Gestational diabetes mellitus	1	4.54 %

Majority of the women had DIC (45.5%) followed by acute renal failure (36.4%). HELLP syndrome was seen in 8 patients (36.4%). Hypoproteinemia was seen in 31.8% patients.2 (9.09%) had MODS. Maternal death was seen in 5 women (22.7%).

Table 7: Perinatal outcome

Complications	n	%
Gestational age		
< 33 + 6 weeks	3	13.6 %
34 - 36 + 6 weeks	9	40.9 %
37 - 40 weeks	5	22.7 %
Birth weight	1.75 - 2.25	2.21 + 0.71
Neonatal death	4	18.2 %
NICU care	11	50 %
Gender		
Male	17	77.3 %
Female	5	22.7 %

Most babies were born preterm (54.5%). Mean birth weight was 2.21 kg.50 % babies needed NICU care.77.3 % of the babies were male. There were 4 neonatal deaths which were mainly due to prematurity and low birth weight.

5. Discussion

AFLP is one of the major cause for high maternal and fetal mortality. Hence it has gained major obstetric significance. The etiology and pathogenesis of AFLP are not clearly known and it lacks specific signs and symptoms making early diagnosis and treatment difficult. Currently there are few diagnostic criteria for AFLP, Swansea criteria being the most commonly used.

Nausea, vomiting were most common symptoms (40.9 %) along with upper abdominal pain (40.9%) in our study in comparable to Zhang et al where 64% patients had nausea and vomiting and 61% had upper abdominal pain. Most common clinical manifestation in our study were hypertension and jaundice (59.1 %) as compared to study by Zhang et al where hypertension was seen in 55% patients and jaundice was seen in 45 % patients. In the study by Zhang et al, main maternal complications were hypoproteinemia (75%), coagulopathy (54%) and acute renal failure (39%) which is comparable to our study where coagulopathy was seen in 45.5%, ascites (40.9%), acute renal failure was seen in 36.4%, hypoproteinemia (31.8%). In our study, there were 5 maternal deaths which is comparable to the study by Zhang et al where there were 4 maternal deaths. In our study, out of 5 maternal deaths, 2 patients had MODS, one patient had HELLP, 3 patients had DIC.
In our study, among neonatal outcome, 50% babies required NICU care. 54.5% babies were born preterm out of which 4 had neonatal death.77% of the mothers had male babies.

6. Conclusion

Nausea, vomiting and upper abdominal pain were the common symptoms of AFLP. Deranged liver function, hypoglycemia, elevated PT/ APTT along with MODS were risk factors for fatal complications for patients with AFLP. Perinatal mortality was seen in association with prematurity, low birth weight and male babies. Early diagnosis and termination of pregnancy will help in reducing maternal and fetal outcome in AFLP.

7. Future Scope

Further studies are required to identify the risk factors in pregnant women who may develop AFLP.

8. Limitation of the Study

In view of the low incidence of the condition, a longer duration study might help for better understanding and analysis.

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