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Acute Fatty Liver of Pregnancy; 10 Years' Experience in a Large Tertiary Center in Egypt

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ABSTRACT

Objective: To provide a description for the demographics, clinical presentation, maternal and perinatal outcome in patients with acute fatty liver of pregnancy (AFLP) admitted in Assiut Woman's Health Center, Egypt.

Materials and Methods: This was a retrospective study over a period of 10 years included all women who were admitted in Assiut Woman's Health Center with the diagnosis of AFLP. Data were collected from the records of patients; their symptoms, laboratory findings, clinical course, maternal and perinatal outcome were reviewed.

Results: Thirty-two women with AFLP were identified. Twenty-nine of them were diagnosed in the antepartum period, and three cases were diagnosed after delivery. There were 27 cases of maternal deaths (84.7%). Persistent nausea and vomiting was the most common initial presentation (68.8%). Moderate rise of liver transaminases was the only constant laboratory finding in all cases.

Conclusions: AFLP is a medical and obstetrical emergency. In Egypt, the disease still has a high mortality rate. Lack of awareness of many health care providers about the nature of this mysterious disease is a contributing factor. Early recognition and treatment can improve both maternal and fetal survival.

Keywords: Acute fatty liver of pregnancy, jaundice, hepatic diseases

Introduction

In pregnancy, there are many pathological conditions causing liver function tests abnormalities need to be differentiated from normal physiologic changes. Among various causes of pathological hepatic dysfunction, acute fatty liver of pregnancy (AFLP) is uncommon compared to pre-eclampsia and hemolytic anemia, elevated liver enzymes and low

platelets (HELLP) syndrome[1].

Previously named "Acute yellow atrophy of the liver," a rare and fatal complication of pregnancy, was first described by Stander and Cadden in 1934[2]. The etiology of the disease is unknown with an incidence of 1 in 10,000 to 1 in 20,000[3]. The most common presentation is malaise, nausea, vomiting and epigastric pain followed by jaundice.

Liver biopsy is diagnostic but is not always feasible especially in patients with severe coagulopathy and it rarely affects acute management[4]. Ultrasound and computed tomography have been used but the sensitivity and specificity of these imaging studies are insufficient to make a definitive diagnosis, and false negative results are common[5].

The definitive management of AFLP is rapid delivery of the fetus and supportive care. Usually jaundice, liver dysfunction, and DIC may progress for one to two days after delivery but then improve [5]. Before 1980, both the maternal and fetal mortality rates were about 85%[6]. Mortality has been reduced to less than 20% at present because of better recognition and appropriate management[7].

In this study, we reviewed the incidence and maternal mortality burden from AFLP and identified the major characteristics, different clinical presentations, laboratory investigations and perinatal outcome in the largest tertiary care hospital in Upper Egypt.

Materials and Methods

This was a retrospective study conducted in Assiut Woman's Health Center, which is a tertiary care university hospital, between first of January 2004 until 31st of December 2013. The high mortality rate from this mysterious disease at our hospital urged us to conduct this study. Our aim was to determine the demographics, clinical presentation, maternal and perinatal outcome of women diagnosed as AFLP and to review their hospital management in terms of efficacy and promptness.

Data were collected from the files of pregnant women admitted to the hospital. We anticipated the diagnosis of AFLP in our included cases according to the clinical manifestations and laboratory investigations of the Swansea diagnostic criteria[8] (Table 1).

Table 1. Swansea diagnostic criteria for diagnosis of AFLP.

Six or more of the following features in the absence of another explanation:
- Vomiting
- Abdominal pain
- Polydipsia/polyuria
- Encephalopathy
- High bilirubin (>14 µmol/L)
- Hypoglycemia (< 4 mmol/L)
- High uric acid (> 340 µmol/L)
- Leukocytosis (> 11 x 106/L)
- Ascites or bright liver on ultrasound scan
- High AST/ALT (> 42 IU/L)
- High ammonia (> 47 µmol/L)
- Renal impairment (creatinine >150 µmol/L)
- Coagulopathy (PT >14 s or APTT > 34 s)
- Microvesicular steatosis on liver biopsy

AST: aspartate transaminase; ALT: alanine transaminase; PT: prothrombin concentration; APTT: activated partial thromboplastin time

Results

During the period of the study, a total of 185349 pregnant women were admitted to our hospital. We found that the number of deliveries was 162903. Thirty-two cases were reported to have AFLP; twenty-seven of them (84.4%) died. Hepatic diseases were the leading cause of indirect causes of maternal mortality (9.9%) in our hospital during this period.

When we analyzed the characteristics of women with AFLP we found that nearly most of cases occurred in middle-aged women, only three cases were below 20 years. The mean age of patients was 27.3 years.

Thirty cases had the signs of AFLP during the third trimester of pregnancy, two cases occurred at 22, 24 weeks gestation, from whom one case died during pregnancy before termination. The mean gestational age at AFLP diagnosis was 35 weeks.

Over 75% of maternal deaths occurred in women with low parity. There were 16 cases of maternal deaths died within the first week after delivery. As regards the pregnancy outcome, the perinatal mortality rate was 23.8%. Only two cases delivered twins, both were living. Twenty-two women delivered male fetuses (68.8%).

As regards to initial clinical presentation of those patients, most of cases (68.8%) were presented with persistent nausea, vomiting. Other presentations include abdominal pain, jaundice, bleeding tendency, fever and disturbed conscious level (Table 2).

Revision of the laboratory results revealed that all cases had moderate rise of liver transaminases with highest-level 143 IU/L in two cases. Marked rise of direct bilirubin also is constant finding in 28 cases reaching up to 20 mg/dl in four of them. Other results showed impaired prothrombin concentration, hypoglycemia, high serum uric acid, creatinine and leukocytosis in some cases but not the majority (Table 2).

Table 2. Initial clinical presentation and laboratory results of patients with AFLP

	Frequency	%
Clinical presentation *		
Nausea, vomiting	22	68.8
Abdominal pain	19	59.4
Jaundice	19	59.4
Fever	8	28.1
Disturbed conscious level	6	18.8
Bleeding tendency	4	12.5
Abnormal laboratory investigations		
High AST (IU/L)	32	100
High ALT (IU/L)	32	100
High total bilirubin (mg/dl)	28	87.5
Impaired prothrombin concentration	14	43.75
High uric acid (µmol/L)	13	40.6
Leukocytosis	11	34.4
High creatinine (mmol/L)	9	28.1
Low blood glucose (mg/dl)	6	18.8

AST: aspartate transaminase; ALT: alanine transaminase

* One case may have more than one symptom.

There were many complications developed in patients with AFLP and contributed signifcantly in the high mortality rate from this disease. Most of patients had more than one complication either sequentially or concurrently (Table 3).

Table 3. Complications and causes of death in patients with AFLP

	Frequency	%
Complications (n=32)*		
DIC	18	56.3
Liver failure	13	40.6
Renal failure	12	37.5
Brain abscess	4	12.5
Lung abscess	4	12.5
Acute pancreatitis	3	9.4
Pelvic abcess	2	6.3
Encephalopathy	2	6.3
Causes of death (n=27)		
Cerebral hemorrhage	10	37
Intraperitoneal hemorrhage	7	25.9
Septicemia	5	18.5
Acute pancreatitis	3	11.1
Encephalopathy	2	7.5

* One case may have more than one complication.

Discussion

Jaundice during pregnancy can be attributed to many causes like cholestasis, gall bladder stones, viral hepatitis, pre-eclampsia with or without HELLP syndrome, and AFLP. Acute fatty liver of pregnancy is one of the mitochondrial cytopathies, which include Reye's syndrome and other drug-related liver diseases. Abnormality in mitochondrial β oxidation is recognized as the cause of this condition[9].

Acute fatty liver of pregnancy usually occurs in the latter part of the third trimester but can be seen as early as 26 weeks of gestation[10], this was clear in our study where 27 cases occurred between 33 – 37 weeks while only 2 cases occurred as early as 22, 24 weeks of gestation. AFLP is commonly reported in primiparous women over the age of thirty. In our study, 30% of cases were primpara, but the disease was more common in women aged 20-29 years. Those constitute 50% of the studied cases. On the contorary, Zhou and colleagues stated that AFLP occurs in 75% of cases in primiparas[11].

The signs and symptoms at initial presentation may vary, making the diagnosis of this disease difficult, or there might be delay in diagnosis. In our study where most of cases were diagnosed after 2 – 3 days from initial symptoms, taking false medications for symptomatic relief but the striking sign was jaundice which alarmed health care personnel in discrete hospitals to refer such cases to our tertiary care center. The delay of diagnosis and termination of pregnancy, which is crucial for their life saving contributed significantly in the rise of maternal deaths of such cases. Most of cases had terminated their pregnancy after 3–5 days from onset of clinical manifestations; this was attributed to their ignorance to the dangerous signs during pregnancy, delay in their referral from discrete

cities, lack of experience of health care providers in primary hospitals about nature of the disease and how it is crucial to rapidly terminate the pregnancy for saving mother's life. Poverty and illiteracy are contributing factors in our locality.

The most striking feature of this syndrome is a high level of bilirubin associated with moderate increases of transaminases; the platelet count may be decreased with or without other signs of disseminated intravascular coagulation (DIC)[12]. This coinciding clearly with our results that shown that all the patients had a rise of hepatic transaminases, and 28 of them had higher level of bilirubin also.

DIC can be present in about 80–100% of patients with AFLP[13]; the main cause of the coagulopathy leading to DIC in patients with AFLP is the severe hepatic dysfunction. In our study, 17 cases (62.9%) were died from coagulopathy leading to cerebral hemorrhage or fatal intraperitoneal hemorrhage. This was coincided with the study of Dwivedi and Runmei in China who found that DIC occurred in 57.1% of patients[14].

Plasmapharesis (Plasma exchange) could significantly decrease rate of maternal mortality and morbidity in AFLP[15]. The only five saved women who were improved from the disease in our study received repeated settings of plasmapharesis that was contributed definitely in their improvement. The problem in our locality was the high cost of plasmapharesis sessions and the lack of continuous availability of plasmapharesis requirements.

There was a great association between AFLP and severe pyogenic infections of major body systems. Those septic complications usually appeared late in the course of the disease during the period of recovery from initial symptoms and improvement of laboratory results, so broad spectrum antibiotics should be given for all patients diagnosed as AFLP early in the course of the disease. In our study, there were six cases suffered from pyogenic infections in different body areas.

In addition, all patients with AFLP should undergo serial screening of serum lipase and amylase for several days. Pancreatitis is a potentially lethal complication of AFLP[16]. Finally, the presence of AFLP is not an indication for delivery by Cesarean section because of the risks of bleeding complications in the presence of coagulopathy[17].

Prompt delivery is life saving in women with AFLP. After delivery, women can develop cholestatic jaundice for a long period up to 4 weeks. Liver transplantation may be needed in cases of severe hepatic encephalopathy, liver rupture, and in case of failure of recovery of liver function.

Conclusion

In conclusion, AFLP is a medical and obstetrical emergency. In developing countries like Egypt, the disease still has a high mortality rate. Lack of awareness of many health care providers about the nature of this mysterious disease is a contributing factor. Early recognition and treatment can improve both maternal and fetal survival. Such cases should be rapidly referred and managed in tertiary care centers equipped with Intensive care units and blood banks.

Conflict of Interest

The authors declare that they have no conflict of interest.

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