33 Acute Fatty Liver of Pregnancy, Liver Failure, and Liver Transplantation

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Bullet Points

- Acute fatty liver of pregnancy (AFLP) is an uncommon, severe liver disorder leading to liver failure in women in late pregnancy.
- AFLP is characterized by defective fatty acid oxidation and consequent maternal "energy failure" and accumulation of toxic by-products.
- A high index of suspicion leading to early diagnosis, together with early institution of management, is imperative for good maternal outcome in AFLP.
- Any women presenting with severe liver dysfunction (jaundice and coagulopathy with or without encephalopathy and/or hypoglycemia) in late pregnancy should be suspected to have AFLP and should undergo appropriate evaluation.
- Diagnosis is confirmed by "Swansea" criteria. Presumptive diagnosis does not require liver biopsy.
- Urgent institution of delivery (with adequate precautions) remains the cornerstone of therapy for AFLP. Early appropriate supportive care should be instituted in parallel.
- The characteristic finding of AFLP in liver biopsy (which should be performed after delivery) is diffuse/perivenular microvesicular hepatic steatosis.
- There is small risk of recurrence of AFLP in future pregnancies.

33.1 Introduction

Acute fatty liver of pregnancy (AFLP) is an obstetric medical emergency that can occur at any time during pregnancy and labor. The diagnostic window to urgently terminate the pregnancy means that any delay in treatment can translate into worsening maternal liver failure and risk of maternal and fetal death/severe morbidity. In this chapter we review some of the recent insights into the pathogenesis of this fascinating disease, recent improvements in diagnosis, and newer advances in treatment.

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33.2 Epidemiology

A nationwide prospective population based study conducted in the United Kingdom (UK) in 2005–2006 estimated the incidence of AFLP to be 5/100,000 pregnancies (95% confidence interval 3.8–6.5/100,000). Twin pregnancies were at high risk of being complicated by AFLP (of the 57 women with AFLP, 18% had twin pregnancies) [1].

The predominant causes of liver dysfunction during pregnancy may differ according to geographic location. A prospective study from Wales in the UK noted that pregnancy-related liver diseases (pre-eclampsia, the HELLP syndrome [see details below], intrahepatic cholestasis of pregnancy, AFLP and hyperemesis gravidarum) are the predominant cause of liver dysfunction in pregnancy [2]. In contrast, in India, liver diseases unrelated to pregnancy are the predominant cause of liver dysfunction [3] and of liver-related maternal deaths [3–5].

33.3 Pathogenesis

33.3.1 The Hibernating Bear: A Good Analogy for AFLP Pathogenesis

Our current understanding of the pathogenesis of AFLP is best depicted by the analogy of a hibernating bear, as explained below [6, 7] (Fig. 33.1).

Fig. 33.1 Switch to fats as primary energy source during hibernation in bears and during late pregnancy in women may explain pathogenesis of acute fatty liver of pregnancy

AFLP is termed a mitochondrial hepatopathy. Ultrastructural mitochondrial alterations have been demonstrated in patients with AFLP [8, 9]. Defective functioning of the mitochondria (the powerhouse of the cells) in the liver leads to energy deficiency in the liver.

Genetic predisposition: One factor predisposing to AFLP is the presence of an autosomal recessive congenital defect in utilizing stored fats.

In an initial report of a woman with consecutive pregnancies complicated by AFLP, maternal liver function rapidly improved after delivery in both pregnancies. However, both babies died by 6 months of age with fatty infiltration of several organs. The authors suspected a familial defect in fatty acid oxidation, which in turn predisposed the mother to develop AFLP [10]. Subsequent reports confirmed fetal fatty acid oxidation defects to be associated with maternal AFLP. A study that compared 50 children with fatty acid oxidation disorders versus 1250 control children (without these disorders) reported that the risk of maternal liver diseases such as AFLP was increased 20-fold among pregnant women with children who themselves had fatty acid oxidation disorders [11].

Thus, AFLP is an example of maternal mitochondrial hepatopathy that is linked to fetal fatty acid oxidation disorders. Fetal fatty acid oxidation disorders are autosomal recessively inherited. Both the pregnant woman and her husband can only be heterozygotes for the fatty acid oxidation disorder. However, if the fetus is a compound heterozygote or a homozygote for this disorder, the mother is at risk for developing AFLP during that pregnancy. On the other hand, if the fetus is a simple heterozygote or wild type, the mother will not have liver dysfunction during pregnancy.

Fetal fatty acid oxidation disorders linked to AFLP and other maternal liver diseases include defects in long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) [12–15], medium-chain 3-hydroxyacyl-CoA dehydrogenase [16], short-chain 3-hydroxyacyl-CoA dehydrogenase (SCHAD) [17], and carnitine palmitoyltransferase I [18]. LCHAD deficiency is the most common fetal fatty acid oxidation disorder reported in association with AFLP [11]. Raised hydroxy-

acyl carnitine levels in patients with AFLP may suggest a defect in LCHAD or mitochondrial trifunctional protein [19].

However, pregnancies without evidence of fatty acid oxidation defects in the mother and baby have also been reported to be complicated by AFLP [20]. Centers studying women with AFLP have noted that the most prevalent LCHAD mutation, G1528C, was absent in several women [21, 22]. Therefore, although fetal fatty acid oxidation defects may be causative in some pregnant women with AFLP, currently there is insufficient evidence to instigate routine screening for fatty acid oxidation defects among all babies following maternal AFLP [23].

33.4 Acquired Predisposition

Diffuse hepatic microvesicular steatosis is an uncommon cause of liver failure. Reye's syndrome, precipitated by ingestion of aspirin, is an example of hepatic microvesicular steatosis and encephalopathy associated with fatty acid oxidation disorders [24]. In children and teenagers, avoidance of aspirin has been recommended in order to prevent the occurrence of Reye's syndrome in predisposed individuals. However, aspirin is commonly prescribed for preventing complications related to pre-eclampsia during pregnancy [25]. It has been hypothesized that non-steroidal anti inflammatory drugs (NSAIDs), including aspirin, can inhibit both the LCHAD enzyme and fatty acid oxidation during pregnancy, thus predisposing to AFLP [26]. Although an association between treatment with aspirin and the occurrence of AFLP has been reported in pregnancy [17, 27], this is uncommon and may be a chance association rather than a causative one.

33.5 Placental Pathogenesis

The dramatic postpartum improvement observed in maternal liver function raises questions regarding placental involvement in AFLP pathogenesis [28]. The placenta has the same genetic composition as the fetus, and LCHAD and SCHAD enzymes are both active in the human placenta. The activity of these enzymes inversely correlates with maternal gestational age in the second and third trimesters of pregnancy [29]. A rat model of valproate-induced hepatic microvesicular steatosis showed defective mitochondrial fatty acid oxidation and increased peroxisomal and microsomal oxidation in the liver [30]. Both the placenta and the serum of AFLP mothers show oxidant and nitrosative stress (in placental mitochondria and peroxisomes and in serum) compared to controls. Mitochondrial function was affected in the placentas of AFLP mothers. Raised arachidonic acid levels were seen in the placenta and serum of AFLP mothers. Such high arachidonic acid levels have been shown to induce oxidative stress and apoptosis in mitochondria and lipid deposition in hepatocytes grown in culture [31].

33.6 Timing of AFLP Manifestation: Why Does AFLP Manifest in Late Pregnancy?

An adult bear hibernates for about 3 months of the year, during which time the bear utilizes about 4000 kcal of energy each day. During hibernation, the bear eats no food and subsists on endogenous energy (fat) stores [6]. If a hypothetical bear had a defect in metabolizing fats or utilizing fat stores for energy needs, it would be expected to become sick during hibernation due to systemic energy depletion. Such problems in this hypothetical bear may occur due either to a genetic predisposition, to an acquired cause affecting fat metabolism, or both [32].

In the well-nourished non-obstetric population, the primary energy source after each meal (the subsequent 2–4 h) is glucose. Conversely, during late pregnancy, lipids are used as the maternal energy source, while glucose and amino acids are channeled to the fetus. The pregnant woman shares carbohydrates (her primary energy source in the nonpregnant state) with the fetus during her pregnancy. This dependence on fats as the primary energy source in pregnant women increases towards the latter part of pregnancy

[7]. Thus, using the analogy of the hibernating bear described above, late pregnancy forms the setting for the clinical manifestation of AFLP among pregnant woman with defective fatty acid oxidation.

33.7 Manifestations

The typical presentation of AFLP is a previously healthy woman presenting in the third trimester of pregnancy with a general description of "feeling unwell" and vomiting for the past 4 h. However, some pregnant women may present with signs and symptoms that overlap with pre-eclampsia (hypertension, pedal edema, proteinuria) together with liver dysfunction or hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Liver function tests may show a mild-to-moderate rise in AST and ALT. Coagulopathy (prolongation of prothrombin time) is seen in almost all these patients. Hypoglycemia and encephalopathy are more rarely seen, as these are late manifestations of severe liver failure.

33.8 Diagnosis

A high index of suspicion is key in making an early diagnosis of AFLP. For a pregnant woman suspected to have AFLP, it is vital to rapidly exclude other potential causes of liver disease, as urgent termination of pregnancy may be required. Any woman with acute liver failure in late pregnancy (third or late second trimester) should therefore be suspected to be suffering from AFLP. Rapid diagnosis of AFLP and urgent termination of pregnancy have improved maternal survival. A recent UK study of 57 women with AFLP reported a case fatality rate of 1.8% and a perinatal mortality rate of 104/1000 births [1].

Once suspicion of AFLP has been raised, it is imperative to rapidly rule out common alternative differential diagnoses. The differential diagnoses to consider are either pregnancy-related liver disorders (HELLP syndrome and pre-eclamptic liver dysfunction) or other illnesses causing acute liver failure unrelated to pregnancy (e.g., acute viral hepatitis or drug-induced hepatitis). Since the infectious causes of acute liver failure that may mimic AFLP are varied (e.g. malaria, dengue, scrub typhus, viral hepatitis), diagnostic testing should be individualized, taking into consideration the epidemiology of the specific locale. Peripheral smear examination for the malaria parasite and serology for acute viral hepatitis A, B, and E are examples of tests that should be considered for diagnosing hepatic illnesses unrelated to pregnancy.

HELLP syndrome (presence of hemolysis-raised lactate dehydrogenase, elevation in aspartate aminotransferase, and thrombocytopenia) and pre-eclampsia (hypertension and proteinuria after 20 weeks of pregnancy) also constitute differential diagnoses. Although in theory these conditions should be simple to diagnose if the signs and symptoms are acknowledged, AFLP patients can often also be misclassified as suffering from HELLP syndrome or pre-eclamptic liver dysfunction. It is therefore difficult to differentiate between these disorders in an emergency setting.

The Swansea clinical criteria for diagnosing AFLP are comprised of 14 criteria including symptoms, laboratory parameters, and radiology and liver biopsy findings [2]. However, most pregnant women with AFLP have coagulopathy and thrombocytopenia (often severe), making it risky to perform a liver biopsy. In addition, the time taken to organize, obtain, and interpret a liver biopsy will delay initiation of management in these critically ill patients. Thus, although a liver biopsy showing microvesicular steatosis is the "gold standard" for diagnosis of AFLP, it is neither warranted nor necessary in the antepartum state. The authors of this chapter have studied the accuracy of the Swansea clinical criteria to predict diffuse hepatic microvesicular steatosis in pregnant women suspected to have AFLP who did undergo liver biopsy (postpartum or postmortem) [32]. Due to coexistent coagulopathy, most of the liver biopsies were performed via the transjugular route. Among 24 pregnant women with suspected AFLP, the negative predictive value for ruling out the presence of diffuse/perivenular microvesicular steatosis of the

liver was 100% using the Swansea clinical criteria [33]. Thus, these clinical criteria are appropriate for diagnosing AFLP in pregnant women. Based on these data, simplified criteria for diagnosing AFLP are proposed. These include (1) the setting of late pregnancy (third or late second trimester of pregnancy); (2) acute liver failure, jaundice with coagulopathy with/without hypoglycemia with/without encephalopathy; and (3) no other explanation for liver failure [34]. Once these simplified criteria are met, the woman should be considered suspect for AFLP and therefore at risk for rapid deterioration. Appropriate management should be rapidly initiated, preferably in an intensive care/high-dependency setting. Supporting this conservative approach is the fact that regardless of whether the cause of liver failure is AFLP, HELLP syndrome, or pre-eclamptic liver dysfunction, the management of liver dysfunction in all three conditions is essentially similar.

33.9 Management of AFLP (Fig. 33.2)

The managment of any woman presenting with jaundice in late pregnancy should be guided by the option that AFLP is the underlying disease.

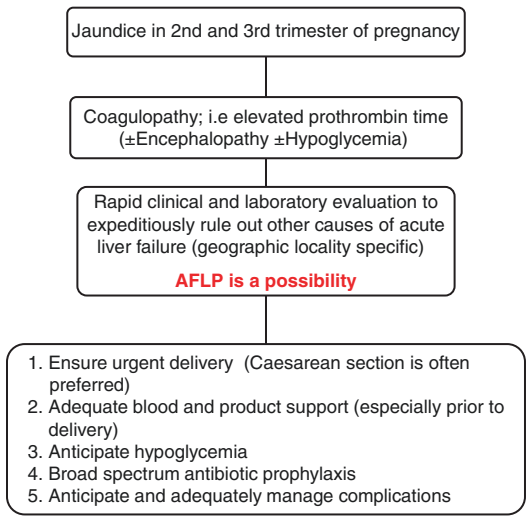

Fig. 33.2 Management algorithm for any woman presenting with jaundice in late pregnancy

The recommended management therefore includes the following steps:

1. Consider AFLP in the differential diagnosis. Quickly rule out alternative diagnoses which may present similarly, using suitable diagnostics as described above.
2. Ensure the availability of a multidisciplinary team, as more than one medical discipline is needed to manage pregnant women with AFLP. Some of these women are likely to need intensive care therapy and may require referral to a specialist liver unit.
3. Absence of specific symptomatology and paucity of laboratory indices make early diagnosis of AFLP difficult, and the mother can be sicker than expected. These patients can potentially develop multi-organ failure with or without sepsis and are likely to need aggressive management including ventilation, hemodynamic support, and dialysis. There should be a low threshold to admitting these mothers to high-dependency or intensive care units for close monitoring. Mothers can also be admitted to the ICU for stabilization and rapid treatment of coagulation abnormalities prior to termination of pregnancy.
4. Urgent delivery is the mainstay of current treatment. It is highly recommended that the patient undergo delivery as soon as feasible (see also the discussion below). AFLP can rapidly worsen (within hours), and there are no reports to date of any AFLP patient surviving without delivery.
5. The pregnant woman with AFLP needs appropriate management of the various complications likely to arise as a result of the disease. The standard recommendations for management of acute liver failure complications (e.g., mannitol for cerebral edema, etc.) remain the same and should be instituted as and when required. See below for greater detail on treatment of complications.
6. Following delivery, the neonate may need to be observed and treated in a neonatal intensive care or high-dependency care unit. We have proposed a management algorithm for patients with suspected AFLP (Fig. 33.2) [5].

33.10 Delivery Considerations

AFLP is a rapidly progressing illness. Poor maternal and fetal outcomes are to be expected if interventions are not performed early. As mentioned previously, in all cases of AFLP, it is of paramount importance to terminate the pregnancy at the earliest possible time. The medical team may be daunted by the prospect of undertaking cesarean delivery in a pregnant woman with AFLP in acute liver failure and coagulopathy, hence the importance of rapid workup and decision-making. As the disease is characterized by temporary shutdown of the liver mitochondria, opting for vaginal delivery in a pregnant women with AFLP can be considered equivalent to making a person who is in systemic energy deficiency run a marathon and should be expected to aggravate the systemic energy deficiency, leading to even more rapid patient deterioration.

A meta-analysis of 78 cohort and 2 case-control studies compared outcomes of cesarean versus vaginal delivery in pregnant women with AFLP. Maternal mortality was reduced 44% with cesarean delivery (relative risk [RR], 0.56 [0.41–0.76]) compared to vaginal delivery, as was the perinatal mortality rate (RR, 0.52 [0.38–0.71]). Maternal morbidity, including complications of liver failure (ascites, encephalopathy, etc.), renal failure, multiple organ failure, infection, or hemorrhage, was not significantly different in women who had cesarean versus vaginal delivery. Neonatal mortality rates (within 1 month after delivery) were unaffected by type of delivery (cesarean versus vaginal) (pooled RR, 0.93 [0.55–1.58]); Table 33.1 [35].

Table 33.1 The outcomes of cesarean versus vaginal delivery in pregnant women with AFLP—based on data from Wang et al. [35]

	Total number of studies	Total number of women included	Pooled unadjusted relative risk (95% CI)
Maternal death	39	517	0.56 (0.41–0.76)
Perinatal death	31	402	0.52 (0.38–0.71)
Neonatal death	19	263	0.93 (0.55–1.58)

Preparations for cesarean delivery in a pregnant woman with AFLP should parallel those for liver transplantation in a patient with acute liver failure. This requires a multidisciplinary and comprehensive approach.

Antibiotic coverage—Following diagnosis, blood should be sampled for cultures. and broad-spectrum prophylactic intravenous antibiotics, especially those covering gram-negative organisms, should be administered.

Correction of coagulation abnormalities—Sufficient blood products need to be prepared, and coagulation abnormalities should be corrected prior to delivery. As it is very difficult to fully normalize coagulation parameters, fresh frozen plasma and cryoprecipitate may be administered based on patient weight while preparing for an urgent delivery. Repeated coagulation parameter testing should not delay delivery.

Preparation for massive hemorrhage—Among six pregnant women with AFLP who underwent urgent termination of pregnancy, the median (range) of packed red cell units transfused was 6.5 (1–27) and of other blood products was 60 units (24–108). All but one woman underwent cesarean delivery, and two also underwent prophylactic bilateral uterine artery ligation. One woman required hysterectomy 2 days after delivery to control postpartum hemorrhage [36].

As massive transfusion is likely during cesarean delivery in these women, preparations should include preparation of an adequate amount of blood products, calcium and magnesium, as well as those items required for correction of hypothermia. Disseminated intravascular coagulation may occur with massive transfusion. In the presence of liver dysfunction, these mothers are also prone to citrate toxicity due to blood transfusions, leading to or exacerbating metabolic acidosis, hypocalcemia, and hypomagnesemia; these can lead to myocardial depression and cardiac arrhythmias. High levels of lactate can also chelate calcium which worsens hypocalcemia. Large-volume rapid transfusion can lead to hypothermia and dilutional coagulopathy. In addition to blood product supplementation, the correction of hypothermia, metabolic acidosis, and hypocalcemia are important cornerstones in the management of coagulopathy.

The use of viscoelastic global assessment of clotting parameters (e.g., thromboelastography) has not been well studied in pregnant women with AFLP but can guide transfusion policy intraoperatively. Postdelivery blood product support is limited to women with active bleeding or those who require additional invasive procedures.

Factor VIIa is a universal procoagulant manufactured using recombinant technology which has been used in various clinical settings. Although its use in postpartum hemorrhage is currently off-label due to reports of an increased risk of thromboembolic complications, it is still being used in some countries to control massive obstetric hemorrhage [37]. This practice is yielding a growing body of literature on the topic. One study demonstrated a significant reduction in blood and blood product requirements among postpartum women with AFLP with no thromboembolic complications, provided that the dose used was less than half that recommended (<45 μg/kg instead of 90 μg/kg) [36]. This short-acting procoagulant may therefore be considered in AFLP patients and is increasingly being used to control postpartum hemorrhage in this population [38].

33.10.1 Intensive Care Treatment

The complications of AFLP may be life-threatening, and many of the complications observed in pregnant women with AFLP require intensive care treatment and monitoring. Some of those most commonly seen are hereby described.

Hemorrhagic complications—Coagulopathy due to liver dysfunction and disseminated coagulopathy can lead to life-threatening hemorrhage before, during, and after delivery. Severe peri- and postpartum hemorrhage, intra-abdominal bleeding, and gastrointestinal bleeding have all been described [39, 40]. Coagulopathy should therefore be monitored using prothrombin time, international normalized ratio (INR), activated partial thromboplastin time, fibrinogen, and fibrin degradation products; abnormalities should be corrected if necessary. As noted above, thromboelastography may be used to guide blood product supplementation.

Similar to the peripartum scenario, should hemorrhage occur, a massive transfusion protocol may need to be activated as a large amount of both blood and blood products may be required. Pancreatitis complicating AFLP may present as hemorrhagic pancreatitis secondary to the coagulopathy [40]. Serum amylase and lipase should therefore be monitored. In general, diagnosis may be difficult in women with altered sensorium.

Hemodynamic instability—Shock may be caused by hypovolemia, bleeding, loss of intravascular volume due to hypoalbuminemia, myocardial depression secondary to metabolic acidosis, electrolyte abnormalities (e.g., hyperkalemia), or sepsis. The use of bedside ultrasonography and echocardiography will help in guiding fluid and inotropic therapy. The choice of resuscitation fluids should be guided by the characteristics of the individual case. Of note, excessive crystalloid use in the presence of hypoalbuminemia (which lowers plasma oncotic pressure) can worsen ascites and peripheral edema and can precipitate or worsen respiratory failure. Albumin may therefore be a better choice for volume resuscitation in these pregnant women.

Renal failure—Renal failure is common in AFLP and can be secondary to shock, hepatorenal syndrome (altered flow dynamics), sepsis, hyperuricemia, and abdominal compartment syndrome [41]. Abdominal compartment syndrome is caused by ascites secondary to hypoproteinemia with low plasma oncotic pressure and portal hypertension. Abdominal paracentesis may be necessary to decrease intra-abdominal pressure. Treatment of renal failure is targeted at the etiology. Renal replacement therapy may also be required (see also Chap. 31). However, renal replacement therapy can be complicated by the presence of coagulopathy. Therefore, decisions regarding access port insertion should be individualized. Continuous renal replacement therapy (CRRT) (see Chap. 31) may provide a more favorable hemodynamic profile and better fluid balance. Intermittent therapies [slow low efficiency dialysis (SLED) or extended daily dialysis (EDD)] are alternatives to consider if cost is a constraining factor. Given the coagulation abnormalities accompanying AFLP, citrate is preferred

for anticoagulation. However, citrate intoxication should be anticipated.

Metabolic complications—The metabolic complications seen with AFLP stem from both the liver failure itself and from the treatment. Metabolic complications include metabolic acidosis, lactic acidosis, and hypoglycemia. Metabolic acidosis may need renal replacement therapy (RRT). Lactic acidosis may not respond to RRT and usually settles once the liver dysfunction improves. Supplementation of thiamine should be considered in these patients. Hypoglycemia is frequent, demanding close monitoring and glucose supplementation as required.

Electrolyte imbalance can be life-threatening. Common electrolyte imbalances are hyperkalemia, hypocalcemia, and hypomagnesemia. The causes of hyperkalemia include metabolic acidosis, renal failure, and multiple blood transfusions. Medical management with beta-2 agonists and glucose insulin infusions may be attempted, but RRT may have to be instituted. Sodium levels as well need to be monitored closely as they can complicate encephalopathy.

Encephalopathy is a common metabolic complication of any liver disease. Encephalopathy may require airway protection with endotracheal intubation. Ventilation should be used to control intracranial pressure (via arterial carbon dioxide pressures) and prevent hypoxemia. The cerebral edema associated with hyperammonemia should be treated with routine measures (see chapter Bilotta). As ammonia is highly diffusible and its clearance is dependent on flow, high-flow CRRT and intermittent hemodialysis can also be used to decrease ammonia levels in extreme cases.

Infection and sepsis—Like other types of liver failure, AFLP is accompanied by immune suppression. Secondary infections may occur, and even fungal infections have been described [42]. Pregnant women with AFLP can develop sepsis and septic shock [43, 44]. Given the pre-existing predisposition to multi-organ dysfunction in AFLP, diagnosis should be prompt, and appropriate antibiotic therapy should rapidly be instituted to prevent additional deterioration.

Nutrition—Provision of nutrition is important in these mothers. Enteral feeding should include a minimal amount of proteins (to prevent the accompanying rise in ammonia levels). If parenteral nutrition is required, aromatic amino acids should be avoided, and branched chain amino acids should instead be provided for the same reason.

Direct treatment of AFLP with plasma exchange—Plasma exchange has been described in women with AFLP after delivery as an adjunct to treatment of multi-organ failure. Case reports suggest that plasma exchange is safe and effective in these women [45–49]. A retrospective analysis of 22 AFLP patients demonstrated a 19% versus 83% survival rate in 16 AFLP patients with standard medical therapy versus 6 AFLP patients with plasma exchange and perfusion as added therapy. The authors suggested that early initiation of plasma exchange and perfusion had a role in halting or reversing the progression of AFLP [50]. As AFLP is uncommon, randomized controlled trials on plasma exchange in this population do not exist, and most case series are rather small. It is difficult to derive meaningful conclusions from the existing literature; hence, plasma exchange currently remains a salvage treatment at most.

Liver rupture and liver transplant—Rupture of liver can be a fatal complication of AFLP and has been described in several cases [41].

There are very few reports of liver transplantation in AFLP [51–53]. Hence, specific listing criteria/indications for liver transplantation for AFLP have not been defined. Women undergoing liver transplantation were usually those in whom the diagnosis and treatment of AFLP were delayed. In this medical emergency, a delay of a few hours can translate to worsening maternal liver failure and its attendant complications. In a report of four AFLP patients who had liver transplantation, the King's College criteria for liver transplantation (used for any patient with acute liver failure) were considered inadequate for predicting the need for liver transplantation in AFLP [53]. The authors noted that the combination of hyperlactatemia and encephalopathy was a better predictor of the need for liver transplantation [53]. Auxiliary liver transplantation may be considered in AFLP patients [52].

33.11 Outcomes: Maternal and Fetal

Maternal Outcomes—Pregnant women with AFLP are expected to show rapid improvement (often within a few days) after delivery. Liver function tends to revert back to normal in most of these women [54]. In addition to delays in delivery, the severity of liver failure (high serum bilirubin, prolonged prothrombin time) and high serum creatinine determine the prognosis in these women [55–57]. With rapid diagnosis and urgent delivery, the authors of this chapter have noted a steady decline in the contribution of AFLP (and other pregnancy-related liver disorders) to maternal mortality in their practice [5]. Similar results have been replicated across various studies [1, 58], and the maternal mortality due to pregnancy-related severe liver disorders (including AFLP) is now expected to be <10% [23].

Increased awareness of AFLP among obstetricians as well as emergency/acute medicine physicians has led to early recognition of AFLP at medical centers with subsequently improving maternal outcomes. A woman suspected to have AFLP is categorized as "high risk." This leads to institution of a management protocol derived in consultation with the different specialties involved. In an audit of the treatment of woman with biopsy-proven AFLP (n = 17), nine underwent cesarean delivery, and most (n = 12) women delivered within 24 h of hospital admission. The median delay between the onset of symptoms to delivery was 5 days. With this active management, only two (12%) mothers died. The average length of stay in hospital in these women was 11 ± 4 days, and 18 ± 15 blood products were required per patient. The 15 women who survived showed a steady improvement in liver dysfunction with a normalization in coagulopathy in the majority by the 10th day postpartum (authors' unpublished data).

Fetal Outcomes—Stillbirths and abortion are more common in mothers with AFLP [23]. Fetal outcomes remain dismal, despite the steady improvement in maternal outcome. Ensuring an adequate supply of glucose to the fetus by providing sufficient and appropriate nutrition to the mother is currently the only suggestion that may be made to positively affect fetal outcome.

The neonatal presentation of fatty acid oxidation disorders includes hypoketotic hypoglycemia [14], hepatic failure, metabolic acidosis, and cardiomyopathy. Later presentations include episodic myopathy, neuropathy, retinopathy, and arrhythmias. Growth restriction and premature births occur in babies with fatty acid oxidation defects delivered by mothers who had AFLP [59].

33.12 Conclusion

Acute fatty liver of pregnancy (AFLP) is an uncommon, severe liver disorder leading to liver failure in women in late pregnancy. Increasingly, it is being recognized as an important preventable cause of maternal death.

Better understanding of pathogenesis, early diagnosis followed by rapid delivery of the fetus, and better supportive multi-disciplinary intensive management have led to improvement in maternal mortality secondary to AFLP.

Ensuring an adequate supply of glucose to the mother, and hence to the fetus, may improve the hitherto dismal fetal outcome.

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