

Liver Diseases Associated with Pregnancy

Gebeliğe Özgü Karaciğer Hastalıkları

Emel AHISHALI

Department of Gastroenterology, Dr. Lutfi Kırdar Kartal Education and Research Hospital, Istanbul, Turkey

Abstract

Pregnancy is a time of great maternal physiological and metabolic changes. Pregnancy-related liver disease is the most frequent cause of liver dysfunction in pregnancy and provides a real threat to fetal and maternal survival. Liver diseases associated with pregnancy include hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, preeclampsia and eclampsia, hemolysis (H), elevated liver enzymes (EL) and a low platelet count (LP) (HELLP) syndrome and acute fatty liver of pregnancy. A rapid diagnosis differentiating between liver disease related and unrelated to pregnancy is required in women who present with liver dysfunction during pregnancy. This review summarizes the incidence, risk factors, pathogenesis, clinical presentation, diagnosis, treatment and outcome of liver diseases unique to pregnancy. (*Marmara Medical Journal 2012;25:58-63*)

Key Words: Pregnancy, Hyperemesis gravidarum, Intrahepatic cholestasis of pregnancy, Preeclampsia and eclampsia, HELLP syndrome, Acute fatty liver of pregnancy.

Özet

Gebelik anne adayında önemli fizyolojik ve metabolik değişikliklerin olduğu bir dönemdir. Gebelerdeki karaciğer disfonksiyonunun en sık nedeni gebelikle ilişkili karaciğer hastalıklarıdır. Gebelikle ilişkili karaciğer hastalıkları fetal ve maternal sağ kalımı açık bir şekilde tehdit eder. Gebeliğe bağlı karaciğer hastalıkları hiperemesis gravidarum, gebeliğin intrahepatik kolestazi, preeklampsi ve eklampsi, hemoliz (H), karaciğer enzimlerinde yükselme (EL) ve düşük trombosit sayısı (LP) (HELLP) sendromu ve gebeliğin akut yağlı karaciğerini kapsamaktadır. Gebelikte karaciğer disfonksiyonu gelişen kadınlarda gebelikle ilişkili ve ilişkisiz karaciğer hastalıkları arasında hızlı bir ayrıcı tanı gereklidir. Bu derlemede gebeliğe özgü karaciğer hastalıklarının insidansı, risk faktörleri, patogenezi, klinik bulguları, tanısı, tedavisi ve sonuçları özetlenmiştir. (*Marmara Üniversitesi Tıp Fakültesi Dergisi 2012;25:58-63*)

Anahtar Kelimeler: Gebelik, Hiperemesis gravidarum, Gebeliğin intrahepatik kolestazi, Preeklampsi and eklampsi, HELLP sendromu, Gebeliğin akut yağlı karaciğeri.

Introduction

Various changes in the gastrointestinal system and liver occur during gestation as in other organs and systems. Normal physiological changes during gestation may mimic signs of chronic liver disease. Spider angiomas and palmar erythema may develop due to gestational hyperestrogenemia, and they disappear after the birth. Plasma volume starts to increase at the 6th week of gestation, and it is raised by approximately 50% at the 36th week of gestation. Although the erythrocyte volume is elevated slightly, the hematocrit is decreased due to hemodilution

which occurs secondary to the increased total blood volume. Cardiac output increases until the second trimester and then gradually returns to normal limits towards term. Total hepatic blood flow is not changed, but the fraction of cardiac output passing to the liver is decreased. Blood pressure is lower during gestation and if it is increased, preeclampsia or eclampsia should be considered¹.

The serum albumin level is decreased owing to hemodilution and diminished synthesis. Coagulation factors like factor VII, VIII, X and fibrinogen are increased because of enhanced hepatic synthesis. Hypercholesterolemia and hypertriglyceridemia are

considered as normal findings of gestation, since serum cholesterol and triglyceride levels may increase by 50% and 30%, respectively. Prothrombin time (PT) and activated partial thromboplastin time (APTT) are not changed²⁻⁴. Normal values of liver function tests during gestation are shown in Table I.

Among the liver diseases associated with pregnancy are hyperemesis gravidarum, intrahepatic cholestasis of pregnancy, preeclampsia and eclampsia, acute fatty liver of pregnancy and hemolysis (H), elevated liver enzymes (EL) and low platelets (LP) (HELLP) syndrome. This review outlines the incidence, risk factors, pathogenesis, clinical presentation, diagnosis, treatment and outcome of liver diseases associated with pregnancy.

Hyperemesis Gravidarum

Hyperemesis gravidarum (HG) is generally encountered in 0.3-2% of all pregnancies in the first trimester before the 10th week of gestation, and nearly half of the patients require hospitalization. It is characterized by intractable nausea and vomiting leading to dehydration, fluid-electrolyte imbalance, body weight loss of more than 5% and ketonuria. Generally it starts at the 4th-10th week, and alleviates by 16th-18th week. However, it may persist until the third trimester in 15-20% of patients, and until parturition in 5-10% of patients^{1,5}.

The pathogenesis is not clearly known, but it is believed to be multifactorial with possibly endocrine, immunological and psychological factors playing roles in the etiology^{1,5}. Human chorionic gonadotropin (hCG) is a strong stimulator of the secretions of the gastrointestinal system and it resembles thyroid stimulating hormone. Its increase leads to hyperthyroidism, so that severe and elongated vomiting is observed. hCG production reaches its peak at the 12th-14th week of gestation, which coincides with the initiation of nausea and vomiting⁶⁻⁸. Progesterone can lead to decrease in the motility of the gastrointestinal system during gestation. It is known that elevations in estrogen and estradiol cause nausea and vomiting in pregnant women⁶. T cell mediated immune reactivation, immunoglobulins and the complement system are also considered to play an important role in HG etiology⁵. Among the risk factors that have been reported to be associated with HG development are a young maternal age, a multiple pregnancy,

molar pregnancy, nulliparity, a female fetus, hyperthyroidism, psychiatric illness, presence of family history, specific nutrient deficiencies and chronic infection of helicobacter pylori^{1,9-11}.

Liver function tests are lowered in 50-67% of cases. Transaminases, especially aspartate aminotransferase (AST), are increased 2-4 fold, but they may also be increased up to 10-20 fold. Jaundice is not common and serum bilirubin levels are generally below 4 mg/dl. Among the other biochemical disorders are increased serum urea and creatinine, hypophosphatemia, hypomagnesemia and hypokalemia¹⁰⁻¹². Complications are rare in HG, but retinal hemorrhage, Wernicke's encephalopathy, esophageal tear or rupture, pneumothorax and splenic avulsion may be encountered^{1,10}.

Diagnosis is mainly based on clinical findings; it is diagnosed by the typical initiation of the symptoms at 4th-10th weeks of gestation and by ruling out other diseases like gastroenteritis, viral hepatitis, pancreatitis, cholelithiasis, peptic ulcer, genitourinary system diseases, metabolic disorders, diabetes, porphyria, neurological diseases, drug toxicity and psychological problems. Liver biopsy, though unnecessary may reveal nonspecific changes including mild steatosis and cholestasis^{1,4,13}.

Treatment is symptomatic with intravenous fluids and measures to prevent vomiting. Antiemetics like ondansetron, metoclopramid, phenothiazines and droperidol are known to be safe to use. Ondansetron is the most widely used and effective antiemetic. Metoclopramid, pyridoxine, antihistaminics and anticholinergics may also be used in the treatment. Daily ginger supplementation (1 g/day) has been shown to be useful in HG without causing teratogenic effects. Severe dehydration or ketonuria requires hospitalization with intravenous fluid and electrolyte replacement therapy. Thiamin should be given in order to prevent Wernicke's encephalopathy. Occasionally oral or enteral nutrition is not tolerated, and total parenteral nutrition may be indicated. Corticosteroids are used in treatment of refractory HG cases. The guidelines of the "The Royal College of Obstetricians and Gynecologists" recommend prophylaxis with low molecular weight heparin in cases of immobility and dehydration^{6,7,9,14}. It has also been reported that non-pharmacological treatments like hypnosis and acupuncture are also effective^{7,9,15,16}.

HG generally self-recovers near the 20th week of gestation independently of treatment. HG may cause fetal growth

Table I. Liver function tests in normal pregnancy³

	Non-pregnant	1 st trimester	2 nd trimester	3 rd trimester
AST (IU/L)	7-40	10-28	10-29	11-30
ALT (IU/L)	0-40	6-32	6-32	6-32
Bilirubin (mg/dl)	0-0.99	0.2-0.93	0.17-0.76	0.17-0.81
GGT (IU/L)	11-50	5-37	5-43	3-41
ALP (IU/L)	30-130	32-100	43-135	133-418
Bile acids (µmol/L)	5-10		5.3-5.7	5.6-6.5

AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; ALP, alkaline phosphatase.

retardation and death in developing countries or in those with limited public health preventive services. Fetal complications arise mainly due to the low body weight of the pregnant woman. In developed countries, fetal or maternal complications are very rare. Abnormalities in liver function tests are improved by rehydration treatment^{1,4,10}.

Intrahepatic Cholestasis of Pregnancy

Intrahepatic cholestasis of pregnancy (ICP) is a cholestatic liver disease, that recovers after the birth. Its incidence is between 1/1000 and 1/10000 pregnancies. Its prevalence varies according to ethnic background and geographic region with the highest rates found in South America (4-6.5%) and the lowest in Scandinavia (1-2%). Once ICP develops in a patient, the probability of recurrence in subsequent pregnancies is as high as 40-70%. The ICP development rate is higher in cases of multiple pregnancies after in vitro fertilization treatment and cholestasis due to oral contraceptives. Moreover, a maternal age above 35 years, a history of cholelithiasis in the mother or in her family, and the presence of hepatitis C have been reported as risk factors in the development of ICP^{17,18}.

The reasons for the development of ICP are not well-known. It is believed to be multifactorial with possible genetic, endocrine and environmental factors playing roles in the pathogenesis. ICP is related to a biliary transport defect in canalicular membrane and mutations of genes coding for biliary transport proteins play an important role in the pathogenesis. Elevation of circulating sex hormones are also reported to cause cholestasis by lowering the expression and/or function of canalicular transport proteins^{19,20}. Regional differences in the prevalence of the disease also suggest a possible relationship with nutritional habits. On the other hand, owing to the increased intestinal permeability in the pregnant the absorption of bacterial endotoxins is increased which in turn stimulates Kupffer cells to secrete proinflammatory cytokines leading to liver damage¹⁷⁻²¹.

ICP develops in the second half of gestation and increased serum bile acids and itching are among its typical features. Although it is considered that itching results from accumulation of bile acids in the skin, no correlation has been detected between the degree of itching and serum bile acid levels. Itching develops in 80% of pregnant women after the 30th week of gestation. It worsens at night and causes insomnia leading to fatigue and tiredness during the day. Jaundice develops in 10-20% of patients 1-4 weeks after itching, and mild nausea may also accompany this. General signs of cholestasis like loss of appetite and steatorrhea may develop and weight loss and deficiencies of fat soluble vitamins may be encountered¹⁷⁻¹⁹.

In a normal pregnancy, there is a minimal increase in serum total bile acids. However, in ICP, cholic acid (CA) and chenodeoxycholic acid (CDCA) levels increase up to 10-100 fold. Serum alanine aminotransferase (ALT) and aspartate aminotransferase level are increased by 2-10 folds in 80% of ICP cases. Bilirubin is normal or

slightly increased, and does not generally exceed 5 mg/dl. γ -glutamyl transferase (GGT) is normal or increased 2-4 fold, and the ABCB4 gene mutation is considered to be responsible in cases with high GGT. Five to 10 fold increases in alkaline phosphatase (ALP) are observed probably by contribution of placental ALP. Serum 5'-nucleotidase is also increased¹⁷⁻¹⁹.

A diagnosis is made by excluding other liver diseases related to gestation, chronic liver diseases and certain disorders resulting in intra- and extrahepatic cholestasis in a pregnant woman with itching, increased bile acids and abnormal liver function tests. A liver biopsy is not indicated for diagnosis. Follow-up of the patient twice a week and, if required, hospitalization is recommended. The aim is to induce labor once the 37th week of gestation is completed.

Ursodeoxycholic acid (UDCA), rifampicin (600mg/day) and dexamethasone (12mg/day) are used in the medical treatment. UDCA (1g/day-15mg/kg/day) decreases itching. The CA/CDCA ratio can be normalized by altering the composition of the bile acid pool and this improves biochemical findings of cholestasis¹⁷⁻¹⁹.

The outcome of a pregnancy with ICP is benign. Itching is usually relieved within hours after the delivery but may persist for two days. Abnormal biochemical tests generally are normal within 2-4 weeks, but occasionally may last for 8 weeks. Among the fetal complications are preterm delivery, intrapartum fetal distress, meconium stained amniotic fluid and intrauterine death. Perinatal mortality rate ranges between 3.5-11%¹⁷⁻¹⁹.

Preeclampsia and Eclampsia

Preeclampsia is a multi-system disease involving mainly the urinary system, central nervous system and liver. Preeclampsia is defined as hypertension (HT; systolic blood pressure \geq 140 mm Hg or diastolic blood pressure \geq 90 mm Hg) and proteinuria (300 mg or greater in a 24-h urine specimen) which develops at the 20th week of gestation and/or within 48 hours postpartum and progresses to eclampsia by the onset of epileptic seizures. Although eclampsia typically occurs after the onset of hypertension and proteinuria, 20% of women who develop eclampsia do not have proteinuria^{22,23}. Eclampsia is encountered in 5-10% of all pregnancies. Among the risk factors for preeclampsia are maternal age (<16 years and > 45 years), primigravidity, presence of hypertension before gestation, a multiple pregnancy, molar pregnancy, obesity, a history of preeclampsia in previous pregnancies and a positive family history^{4,10}.

The placenta rather than the fetus is central to the pathogenesis of preeclampsia owing to the observations of an increased prevalence of preeclampsia in the setting of molar pregnancies and the resolution of the symptoms upon placental removal at delivery²². The pathophysiological mechanisms leading to preeclampsia remain to be elucidated, although defective placentation, with abnormal development of placental vasculature and hypoxic insult are reported to be important in the early development of the disease. Endothelial dysfunction due to vasoconstriction, activation of the coagulation cascade, metabolic changes and increased inflammatory response with a shift in the

balance of vasoactive mediators favoring vasoconstriction are thought to play important roles in the pathogenesis^{4,10,22,23}. Histological findings of severe preeclampsia include acute atherosclerosis with multiple infarcts, sclerotic, narrowed arteries and arterioles, deposition of fibrin and thrombosis. In addition, hepatic arterial vasospasm and fibrin accumulation in portal and periportal areas account for the development of liver damage leading to lobular ischemia and hepatitis necrosis¹⁰.

A wide spectrum of clinical manifestations are observed during the course of preeclampsia including hypertension and proteinuria, persistent severe headache, visual disturbances, hyperreflexia with brisk tendon reflexes, vomiting, epigastric pain or tenderness, sudden onset of severe edema in the hands, face, or feet, pulmonary edema, oliguria from acute renal failure and grand mal seizures. The diagnosis is easy when hypertension and proteinuria typically starts after 20 weeks of gestation. However, the diagnosis may be difficult in atypical cases without typical signs and up to 20% of women with atypical preeclampsia have slight or no proteinuria. The degree of proteinuria in preeclampsia may vary from minimal to nephrotic; however, the amount of proteinuria does not seem to affect maternal or fetal outcomes²².

Laboratory tests reveal proteinuria, signs of microangiopathic anemia, and hyperuricemia. Transaminases are increased by 2-5 fold in 20-30% of patients sometimes reaching levels up to 10-20 folds. The increase in ALP occurs due to the pregnancy. Direct bilirubin, PT and albumin levels are generally normal, whereas indirect bilirubin is slightly increased and does not exceed 5mg/dl^{4,10}.

The only efficient treatment of preeclampsia is the delivery of the child. Dietary supplementation with at least 1 g of calcium a day reduces the relative risk of preeclampsia, with the effect observed predominantly in high risk women and those with low dietary calcium. Antiplatelet drugs, primarily low dose aspirin, reduce the relative risk of preeclampsia and of stillbirth or neonatal death^{8,10,24}.

Antihypertensive drugs such as hydralazine, labetalol and nifedipine are used in the treatment of severe hypertension in preeclampsia while methyldopa is recommended for mild to moderate hypertension^{24,25}. Prophylaxis against convulsions with intravenous magnesium sulfate administrations should be considered in patients with severe preeclampsia^{26,27}.

In general, mild preeclampsia which develops after the 34th week of gestation has better maternal and fetal outcomes, but if the onset of the disease is before the 33rd week the outcomes are poor. Maternal mortality is rare in developed countries, however, mortality rates reaching up to 15-20% are recorded in developing countries. Fetal mortality has a lower rate and occurs in 1-2% of deliveries^{5,8}. Among the neonatal morbidities are abruptio placenta, preterm birth and intrauterine growth retardation, while hypertensive crisis, renal failure, pulmonary edema and cerebrovascular events account for maternal morbidities. Women with preeclampsia are subject to increased risk of future development of cardiovascular disease including hypertension, which stresses the need for aggressive screening and treatment^{5,8,10,24}.

HELLP Syndrome

This syndrome is a serious complication in pregnancy characterized by hemolysis, elevated liver enzymes and a low platelet count and hence the term HELLP was coined as the acronym for these features. It has long been known that preeclampsia may be associated with hemolysis, elevated liver enzymes and thrombocytopenia. Although HELLP was first regarded as an entity separated from severe preeclampsia, the syndrome is currently regarded as a variant of severe preeclampsia or a complication²⁵⁻²⁷. The HELLP syndrome is encountered in about 0.1 to 0.9% of all pregnancies and in 10 to 20% of cases with severe preeclampsia^{3,15,28}. The HELLP syndrome develops generally in the second and third trimesters. In approximately 30% of cases, the onset is in the postpartum period mostly in the first 48 hours after delivery and sometimes this process may extend up to the 7th day after delivery^{1,10}. Risk factors for the HELLP syndrome are advanced maternal age (>40), white race, multiparity, previous histories of preeclampsia^{4,10}.

Abnormal placental development, complement and coagulation cascade activation, vasoconstriction, thrombocyte aggregation, abnormal concentration of vascular growth factors and changes in thromboxane-prostacyclin ratio have been suggested as playing a role in the pathogenesis¹⁰.

Patients with the HELLP syndrome typically present with right upper abdominal quadrant or epigastric pain, nausea and vomiting. The upper abdominal pain may be fluctuating and colic-like. A history of malaise some days before the onset of the disease are reported by many patients. Non-specific viral syndrome-like symptoms, headache, visual disturbances and subtle signs of preeclampsia are also among the less common symptoms of the syndrome^{25,26}.

The presence of three laboratory findings, signs of hemolysis, increased levels of serum transaminases and thrombocytopenia are diagnostic for the complete form of the HELLP syndrome, while a partial or incomplete syndrome presents only one or two elements of the triad. There are two major classification systems in the diagnosis of the HELLP syndrome, as shown in Table II^{4,10,26}. The PT is normal unless albumin and direct bilirubin levels change and disseminated intravascular coagulation (DIC) develops^{5,10}.

During the clinical course of the HELLP syndrome, maternal and fetal conditions deteriorate progressively and sometimes suddenly. Therefore, prompt hospitalization and observation in a labor and delivery unit is mandatory in patients with the suspected diagnosis. Assessment and stabilization of the maternal condition, particularly coagulation abnormalities are of utmost importance and referral to a tertiary care center should be considered in patients remote from term²⁷.

Blood pressure control and seizure prophylaxis are important in the treatment, but the definitive treatment is delivery. Intravenous magnesium sulfate treatment as a prophylaxis against convulsions should also be performed along with antihypertensive medications as in patients with severe preeclampsia^{25,27}. Delivery

Table II. Classification systems in the HELLP syndrome²⁶.

HELLP class	Tennessee Classification	Mississippi Classification
1	Platelets $\leq 100 \times 10^9/L$ AST ≥ 70 IU/L LDH ≥ 600 IU/L	Platelets $\leq 50 \times 10^9/L$ AST or ALT ≥ 70 IU/L LDH ≥ 600 IU/L
2		Platelets $\leq 100 \times 10^9/L$ - $\geq 50 \times 10^9/L$ AST or ALT ≥ 70 IU/L LDH ≥ 600 IU/L
3		Platelets $\leq 150 \times 10^9/L$ - $\geq 100 \times 10^9/L$ AST or ALT ≥ 40 IU/L LDH ≥ 600 IU/L

AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase

Table III. Swansea criteria³

Six or more of the following features in the absence of another explanation:

Vomiting
Abdominal pain
Polydipsia/polyuria
Encephalopathy
Elevated bilirubin (>0.81 mg/dL)
Hypoglycaemia (<72 mg/dL)
Elevated uric acid (>5.71 mg/dL)
Leukocytosis ($>11 \times 10^6/L$)
Ascites or bright liver on ultrasound scan
Elevated transaminases (>42 IU/L)
Elevated ammonia (>47 $\mu\text{mol/L}$)
Renal impairment (creatinine >1.69 mg/dL)
Coagulopathy (prothrombin time >14 s or activated partial thromboplastin time >34 s)
Microvesicular steatosis on liver biopsy

should be performed if gestation is >34 week in the presence of severe complications or if these are any signs of multiorgan dysfunction. If gestation is between 27-34th weeks, delivery may be postponed for 24-48 hours by administering corticosteroids for pulmonary maturation^{5,10,25,27}. Postpartum management including anti-seizure prophylaxis is almost identical to that performed before the delivery. In this period a more aggressive antihypertensive approach may be appropriate in the absence of the risk of the compromising the uteroplacental circulation²⁵.

Maternal and perinatal mortality rates are reported to be 1-3.5% and 7-22%, respectively, although markedly higher maternal mortality rates (24%) and perinatal mortality rates (34%) are also recorded³. Among the maternal complications are DIC (21%), abruptio placenta (16%), acute renal failure (7.7%), pulmonary edema (6%), subcapsular hematoma in the liver (0.9%) and retinal detachment (0.9%). Prematurity or intrauterine growth retardation is observed in 33% of pregnancies^{3,10,11}.

Acute Fatty Liver of Pregnancy

Acute fatty liver of pregnancy (AFLP) rarely occurs in the third trimester of gestation with an incidence of 1/10000-1/15000, but causes high maternal and fetal mortality rates. AFLP is seen in pregnant women of all ages and ethnic backgrounds and geographical area does not seem to affect the prevalence of the disease. It can be encountered in primiparous and multiparous pregnant women, particularly those with a preeclampsia history^{8,10,11}.

Mitochondrial dysfunction, particularly deficiencies of fatty acid beta oxidation enzymes in fetal liver are suspected to play a role in the pathogenesis. The most frequently deficient enzyme in this disorder is the long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD)^{1,5,10}. LCHAD is a component of the enzyme complex known as mitochondrial trifunctional protein (MTP). G1528C and E474Q mutations of MTP are known to cause LCHAD deficiencies²⁸. In the fetuses that are homozygous for these mutations, fetal fatty acids accumulate and eventually pass into the maternal circulation of the heterozygous mother. Long chain fatty acids from the fetus and the subsequently produced triglycerides can cause overloading of the fat stores and functional deterioration in the maternal liver^{5,8,10,28}. The onset of AFLP is generally between 30th and 38th weeks of gestation. The most commonly encountered symptoms are loss of appetite, nausea, vomiting and right upper quadrant pain, and in advanced phases acute liver insufficiency signs may develop. Approximately 50% of patients present clinical signs of preeclampsia¹⁰.

Laboratory findings include a moderate increase in serum transaminases, particularly ALT, however, severely elevated serum transaminases may also be encountered. Total bilirubin is generally mildly increased (<5 mg/dl), and hypoglycemia develops approximately in 40% of the patients⁵. Plasma ammonium levels may also increase. Laboratory findings of normocytic anemia, coagulopathy in the presence or absence of DIC and acute renal failure along with mild leukocytosis, normal platelet counts or thrombocytopenia, hypoalbuminemia and increased amylase and lipase levels may also be seen^{10,29-31}.

Ultrasound and computerized tomography are the most common non-invasive methods used in the early diagnosis of AFLP.

Ultrasound is the diagnostic tool of choice in liver screening owing to its convenience and safety. Although liver biopsy is considered as the gold standard for confirming a diagnosis of fatty liver, its clinical use should be avoided in cases complicated by DIC³⁰. The presence of more than 5 Swansea criteria represents a validated method for supporting the clinical diagnosis of AFLP (Table III)³.

Diagnosis and treatment of AFLP is a medical and gynecological emergency. Terminating the pregnancy with appropriate timing is the main target of the treatment³⁰. Early diagnosis and treatment of AFLP decrease maternal and fetal mortality and morbidities. Pregnancy should be monitored under intensive care conditions from the time of diagnosis. Increased transaminases and encephalopathy recover generally in 72 hours after the delivery; this interval may be elongated up to 1-4 weeks. Rarely liver transplantation is required as a result of acute liver failure^{1,5,10}. Artificial liver support systems, such as the molecular absorbents recirculating system and plasma exchange may also be used in cases of acute liver failure³⁰.

Maternal and fetal mortality ranges between 3-12% and 15-66%, respectively. Cardiomyopathy, hypoglycemia, sudden death and rarely liver failure may develop in the newborn with LCHAD deficiency. Myopathy, neuropathy, retinopathy and cardiac arrhythmias can also be seen as late complications. If the mother carries the LCHAD mutation, the probability of AFLP recurrence is 20-70%. Therefore, the subsequent pregnancies are recommended to be followed up at a tertiary healthcare service unit^{5,10,29}.

Clinical findings of AFLP are generally alleviated after delivery and the pathological alterations recover within months. Close monitoring and supportive treatment are also essential after delivery. Potentially hepatotoxic drugs such as contraceptives should be avoided. The prognosis is mostly good following active treatment³⁰.

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