APŽVALGINIAI STRAIPSNIAI

Liver diseases unique to pregnancy

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Summary. *The aim of this review article is to improve knowledge of the liver disease in pregnancy. The article summarizes the results of own experience and the recent reviews of liver disorders unique to pregnancy. Abnormalities in liver tests occur in 3% of pregnancies with causes ranging from self-limiting to rapidly fatal. In Kaunas University of Medicine Hospital, a retrospective analysis disclosed a rate of 0.52% of liver diseases in 16252 pregnant women over a 5-year period. Several liver diseases occur only during pregnancy and are considered to be associated with the pregnant state. The liver disorders unique to pregnancy have characteristic clinical features and timing of onset. Hyperemesis gravidarum occurs in the first trimester, intrahepatic cholestasis of pregnancy in the second or third trimester, preeclampsia, HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome, and acute fatty liver of pregnancy usually in the third trimester. The disorders of late pregnancy – preeclampsia, HELLP syndrome, and acute fatty liver of pregnancy – may progress to severe liver dysfunction. The correct diagnosis is critical, as any delay can result in morbidity or mortality of both the mother and fetus. Early delivery and advances in supportive management are the only available option for improving the prognosis.*

Introduction

During pregnancy, the liver synthetic and metabolic functions are affected by the increased serum estrogen and progesterone levels. Pregnancy is associated with many normal physiologic changes, which can mimic chronic liver disease: spider angiomas, palmar erythema, elevated alkaline phosphatase due to placental production, increased plasma volume, hypoalbuminemia. An increase in serum aminotransferase, bilirubin, or serum bile acid concentrations during pregnancy is always pathologic and should prompt further evaluation (1). A prospective study of 4377 deliveries found abnormal liver tests in 3% of patients (2). In Kaunas University of Medicine Hospital, Lithuania, a retrospective analysis disclosed a rate of 0.52% of liver diseases in 16 252 pregnant women over a period of 5 years (1996–2000; Kondrackienė J, unpublished data; April 8, 2003). There are liver disorders unique to pregnancy, diseases occurring coincidentally, and preexisting chronic liver diseases. The pregnancy-related liver disorders have characteristic clinical features and timing of onset, whereas diseases unassociat-

ed with pregnancy may occur at any time (Table 1) (3). While specific diseases are typically confined to a particular trimester, exceptions exist. For example, acute fatty liver of pregnancy (AFLP) usually presents in the late pregnancy but may be seen as early as 26 weeks of gestation. In addition, the diseases that occur during the third trimester may also present postpartum: HELLP (*h*emolysis, *e*levated *l*iver enzymes, and *l*ow *p*latelet count) syndrome, Budd-Chiari syndrome. The correct diagnosis is critical because prompt therapy markedly improves the outcome of pregnancy. The diagnostic algorithm should include the following questions:

1) Are there any symptoms of underlying chronic liver diseases?
2) Are there any features of biliary disease?
3) Is there any evidence of acute viral hepatitis?
4) Is there any history of drug, herbal medication, and alcohol consumption and travel?
5) Does clinical presentation fit one of the liver diseases unique to pregnancy?

Analyzing the pattern of serum liver tests abnor-

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Table 1. **Causes and trimester of liver disease in pregnancy**

Disease category	Specific disease	Trimester of pregnancy
Pregnancy-related liver disease	Hyperemesis gravidarum Intrahepatic cholestasis of pregnancy Preeclampsia HELLP syndrome Acute fatty liver of pregnancy	1 2–3 3, late 2 3, late 2, postpartum 3
Liver disease coincidental with pregnancy	Acute viral hepatitis Budd-Chiari syndrome Gallstones Drug-induced hepatitis	1–3 1–3, postpartum 1–3 1–3
Chronic liver disease	Chronic viral hepatitis Autoimmune hepatitis Liver cirrhosis Wilson's disease	1–3 1–3 1–3 1–3

HELLP – hemolysis, elevated liver enzymes, low platelet count.
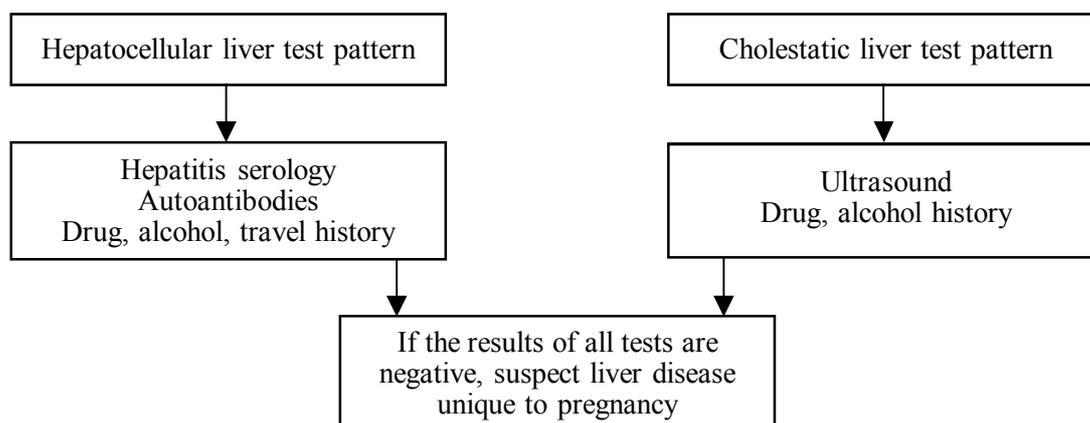
Fig. **Algorithm of abnormal liver tests**

malities is also helpful in making the diagnosis (Fig.).

Hyperemesis gravidarum

Hyperemesis gravidarum (HG) is characterized by intractable nausea and vomiting usually resolving by week 16–18 of gestation. Mild nausea with or without vomiting occurs in 50 to 90% of all pregnancies (4). HG may be considered the severe end of the spectrum of symptoms; however, there is no clear demarcation between common pregnancy-related morning sickness and the infrequent pathologic form (5). One definition of hyperemesis that has been proposed is persistent vomiting accompanied by weight loss exceeding 5% of prepregnancy body weight and ketonuria unrelated to other causes. The prevalence of HG varies from as low as 3 cases per 1000 pregnancies to as high as 1 per 100 (6).

Etiology

Hyperemesis has been attributed to a number of factors, but the etiology remains uncertain. Psychologic, hormonal, and genetic factors, abnormal gastric motility, specific nutrient deficiencies, alterations in lipid levels, changes in the autonomic nervous system may be involved in the pathogenesis of HG (7, 8). None is consistently associated with or highly predictive of the disease.

Clinical features

HG has its onset in early pregnancy and resolves by 16–18 weeks of gestation. However, symptoms continue until the third trimester in 15 to 20% of patients and until delivery in 5%. Symptoms range from mild to severe. Patients may present with weight loss exceeding 5% of their body weight, dehydration, ke-

tosis, and electrolyte derangements, such as hypokalemia and metabolic alkalosis. Rarely HG may lead to serious complications, including Wernicke encephalopathy (from deficiency of vitamin B1), sequelae of malnutrition (immunosuppression, poor wound healing), and spontaneous esophageal rupture (9, 10). Mild hyperthyroidism may be associated with HG, perhaps due to high serum concentrations of human chorionic gonadotropin, which may have more thyroid-stimulating activity in pregnant women (11).

Abnormal liver enzyme values occur in approximately 50% of patients who are hospitalized with HG. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values can rise to 200 U/L. Mild hyperbilirubinemia also can occur. Serum amylase and lipase may increase, but their origin is from salivary glands. The severity of these abnormalities in liver tests correlates with the severity of vomiting (8). Abnormalities resolve promptly upon resolution of the vomiting. Liver biopsy shows necrosis with cell dropout, steatosis, centrilobular vacuolization, and rare bile plugs.

Differential diagnosis

HG is generally a diagnosis of exclusion. Other conditions unrelated to pregnancy that can cause persistent nausea and vomiting include gastrointestinal disorders (gastroenteritis, hepatitis, pancreatitis, cholelithiasis), genitourinary tract disorders, metabolic (*e.g.*, diabetes, porphyria) and neurologic diseases (*e.g.*, migraine, tumor, vestibular lesions), drug toxicity, and psychological problems. Serum aminotransferase elevation is usually lower in hyperemesis than in viral hepatitis. Similarly, serum amylase levels are usually elevated to a lesser degree than in patients with acute pancreatitis and are of salivary rather than pancreatic origin.

Treatment

Treatment is symptomatic. Hospitalization, as well as replenishment of fluids and electrolytes, may contribute to palliation of symptoms. Dietary management generally consists of frequent high-carbohydrate, low-fat, and small meals. Fluids are better tolerated if cold, clear, and carbonated and if taken in small amounts between meals. Enteral nutrition should be initiated in women who cannot maintain their weight because of vomiting (12). No medication is currently approved by the United States Food and Drug Administration for treatment of HG. Thus, a reasonable approach is to begin therapy with agents that have minimal maternal side effects. In a systematic review, seven ran-

domized controlled trials testing different methods of treatment in HG were identified, including corticosteroids, ginger root extract, intravenous diazepam, and acupuncture (12). No treatments were shown to be beneficial. Two trials have suggested that pyridoxine (vitamin B6) is effective in reducing the severity of nausea, but there is no evidence of an effect on vomiting (12). Pyridoxine (10 to 25 mg orally TID) may help women with mild to moderate nausea and minimal vomiting. Antiemetics, including promethazine (12.5 to 25 mg Q4h PO, IM, or PR), metoclopramide (5 to 10 mg Q8h IV or PO), ondansetron (8 mg Q12h IM or PO), prochlorperazine (5 to 10 mg Q3 to 4h IM or PO or 25 mg BID PR), or a combination of droperidol and diphenhydramine, may benefit selected patients. The safety of antihistamines was affirmed in a meta-analysis that examined the association between antihistamine use and major malformations (13). The role of corticosteroids for hyperemesis is unsettled. There may be a slightly increased risk of oral clefts when the drugs are administered before 10 weeks of gestation (14). A recent randomized, placebo-controlled trial involving 126 women revealed that corticosteroids had no adverse effect on pregnancy and neonatal outcome, but also no beneficial effect on the course of hyperemesis (15). Patients with prolonged vomiting should receive thiamine supplementation to prevent Wernicke's encephalopathy. Oral tablets (1.5 mg daily) can be given if tolerated. Other options are P6 acupuncture or acupressure wristbands and powdered ginger (1 g daily). A Cochrane-type review did not find P6 acupuncture or acupressure to be clearly effective (12). Although ginger has been shown to be more effective than placebo and equivalent to vitamin B6, its safety in pregnancy has not been firmly established (16). Hypnosis has been reported to be helpful in selected patients (17).

Prognosis

Pregnancy outcome is favorable and does not differ from the general population.

Intrahepatic cholestasis of pregnancy

Intrahepatic cholestasis of pregnancy (ICP) is the most common liver disorder unique to pregnancy. In many areas of the world, ICP is a rare disease occurring at a rate of 1 in 1000 to 10 000 pregnancies (18). However, the incidence of ICP is markedly higher in Sweden and other Scandinavian countries (up to 2% of deliveries in 1950–1960) and even more in Chile (up to 14% of deliveries in 1960–1970) (18). In Lithuania, a retrospective analysis disclosed a rate of 0.4%

of ICP in 16 252 pregnant women (1996–2000; Kondrackienė J, unpublished data).

Etiology and pathogenesis

The cause of ICP is still under discussion. The pathogenesis can be related to abnormalities in the metabolism and disposition of sex hormones and/or bile acids, determined by a genetic predisposition and environmental factors (19). There is increasing evidence that genetically determined dysfunction in the canalicular bile salt export pump (BSEP, ABCB11) and multidrug resistance protein 3 (MDR3, ABCB4) might be risk factors for development of ICP (19). Hormonal factors may trigger the transient decompensation of the heterozygous state for a MDR3 gene defect during pregnancy, leading to ICP (20).

Clinical features

ICP is characterized by pruritus starting in the second or third trimester of pregnancy and disappearing after delivery. It is often generalized but predominates on the palms and the soles of the feet, and is worse at night (21). Physical examination may show excoriations due to scratching. Jaundice occurs in 10 to 20% of cases, typically within 4 weeks of the onset of itching.

Serum total bile acid concentrations increase in ICP and may be the first or only laboratory abnormality. The concentration of serum cholic acid increases more than concentration of chenodeoxycholic acid, resulting in a marked elevation of the cholic/chenodeoxycholic acid ratio compared to pregnant women without ICP (21). Serum aminotransferase levels are elevated and may reach values greater than 1000 U/L, making distinction from viral hepatitis important (22). Total bilirubin concentration is increased (up to 100 μmol/L). Surprisingly, the level of serum gamma glutamyltranspeptidase is normal or modestly elevated. Alkaline phosphatase is of poor diagnostic value due to placental production. The prothrombin time is usually normal. When present, prolonged prothrombin times reflect vitamin K deficiency due to cholestasis or to the use of bile acid sequestrants (such as cholestyramine) rather than liver dysfunction. Liver biopsy is rarely necessary for the diagnosis. Histology is characterized by cholestasis without inflammation. Bile plugs in hepatocytes and canaliculi predominate in zone 3 (21).

Differential diagnosis

The cardinal feature of ICP (pruritus) helps to distinguish it from other types of pregnancy-related liver disease that can share similar laboratory features (such as early HELLP syndrome or preeclampsia). The main differential diagnoses of pruritus of ICP without icterus are skin diseases, allergic reactions, abdominal striae. In patients with high transaminase levels, acute viral hepatitis, choledocholithiasis, and toxic hepatitis are to be excluded.

Treatment

Until now, optimal treatment of ICP is still under debate. Treatment of ICP focuses on reducing symptoms and preventing maternal and fetal complications. Several drugs have been studied, but they just relieved symptoms. Antihistamines, benzodiazepines, phenobarbital, dexamethasone, epomediol, S-adenosyl-L-methionine, and cholestyramine have been used without clear evidence of efficacy. Cholestyramine has been used for reducing pruritus. Observational studies suggest that cholestyramine may be associated with improved maternal morbidity without a documented improvement in fetal outcome (23). Cholestyramine may worsen the malabsorption of fat-soluble vitamins, especially vitamin K. A case report of severe fetal intracranial hemorrhage during treatment of ICP with cholestyramine has raised the possibility that severe maternal vitamin K deficiency may lead to fetal vitamin K deficiency and coagulopathy (24). Recently, the most promising treatment is the synthetic bile acid ursodeoxycholic acid (UDCA). Improvement in maternal and fetal morbidity was suggested in eight clinical trials and several observational studies, although these studies were small and in some aspects inconsistent (23). The largest trial was conducted in Kaunas University of Medicine Hospital. A total of 84 symptomatic patients were randomly given UDCA (8–10 mg/kg body weight per day) or cholestyramine (8 g/day for 14 days). The results of the study showed a significant improvement in severity of pruritus, aminotransferase activities, and serum bile acid concentrations and a more favorable outcome of pregnancy and absence of adverse events after treatment with moderate dose of UDCA. In contrast, cholestyramine alleviated pruritus only mildly and caused side effects (nausea and vomiting) (25).

Prognosis

Maternal prognosis is favorable. Affected women generally have no hepatic sequelae. Cholestasis recurs during subsequent pregnancies in 60 to 70% of cases. The administration of oral contraceptives to women with a history of ICP rarely results in recurrent cholestasis. In contrast, ICP may have serious conse-

quences for the fetus. Clinical studies show that the disease is a strong risk factor for premature deliveries in 19 to 60% (26), stillbirths in 1 to 2 % (27), and fetal distress in 22 to 33% of cases (28). The cause is unknown. There is no ideal method for fetal surveillance in ICP. Measurement of the serum total bile acid concentration has also been suggested for fetal assessment in ICP. In a study from Sweden, the probability of fetal complications (defined as preterm delivery, asphyxial events, meconium staining of amniotic fluid, placenta, and membranes) was directly related to the concentration of bile acids even after controlling for other risk factors. Fetal complications were not observed until bile acid levels were 40 µmol/L (29). The research group from Kaunas University of Medicine has found that early onset of pruritus, along with markedly elevation of bile acid levels, may predict premature delivery (30).

The best approach is early delivery, the timing of which should be guided by the patient's symptoms (mostly pruritus), the gestational age, and whether the cervix is favorable. In most patients, delivery should be accomplished by 38 weeks. However, when cholestasis is severe (such as when patients are jaundiced), delivery should be considered at 36 weeks gestation if lung maturity is achieved or as soon thereafter as fetal lung maturity is established.

Preeclampsia

Hypertensive disorders complicate 12 to 22% of pregnancies. Preeclampsia occurs in approximately 3 to 14% of all pregnancies worldwide (31). Preeclampsia refers to the new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.

The etiology of this condition is unknown, but it seems that uteroplacental ischemia plays a major role. Placental ischemia causes activation of the endothelium. All of the clinical features of preeclampsia can be explained as maternal responses to generalized endothelial dysfunction (32). Disturbed endothelial control of vascular tone causes hypertension, increased vascular permeability results in edema and proteinuria, and abnormal endothelial expression of procoagulants leads to coagulopathy. These changes also cause ischemia of target organs, such as the brain, liver, kidney, and placenta. Fibrin deposition, periportal hemorrhage, ischemic lesions, and microvesicular fat deposition are histologic findings observed in the livers of preeclamptic women (33). The clinical manifestations of liver involvement are right upper quadrant or epigastric pain, elevated liver enzymes, and in severe cases, subcapsular hemorrhage or hepatic rupture. HELLP syndrome develops in 10 to 20% of women with severe preeclampsia.

HELLP syndrome

HELLP syndrome occurs in approximately 1 per 1000 pregnancies. The majority of cases are diagnosed between 28 and 36 weeks of gestation (34). The disease presents prior to delivery in 70%, postpartum in 30% of cases, usually within 48 h, but occasionally as long as 7 days after delivery. The HELLP syndrome probably represents a severe form of preeclampsia, but this relationship remains controversial.

Clinical features

The clinical presentation of HELLP syndrome varies. Although some patients have no symptoms, most complain of abdominal pain and tenderness (34). The pain is located in the midepigastrium, right upper quadrant, or below the sternum. Many patients also have nausea, vomiting, and malaise. Jaundice is evident in less than 5%. Bleeding related to thrombocytopenia is an uncommon presentation. Hypertension and proteinuria are present in approximately 85% of cases, pulmonary edema in 6%, ascites in 8%, and acute renal failure, usually occurring in the setting of disseminated intravascular coagulation (DIC), in 20% (34).

The diagnosis of HELLP syndrome is based on the presence of the laboratory abnormalities comprising its name: microangiopathic hemolytic anemia with characteristic schistocytes on blood smear, an elevated indirect bilirubin and a low serum haptoglobin concentration, serum LDH >600 U/L or total bilirubin >1.2 mg/dL, AST >70 U/L, platelet count <100 000 cells/µL (34). Women who do not meet all of the above laboratory abnormalities are considered to have partial HELLP syndrome. A liver biopsy is rarely necessary to establish the diagnosis and may be hazardous to perform because of the coagulopathy that may be present. It typically shows periportal hemorrhage and fibrin deposition (35). There is little correlation between the histologic findings and clinical presentation.

Differential diagnosis

The differential diagnosis includes AFLP or, because of similar symptoms or laboratory findings, gastroenteritis, hepatitis, appendicitis, gallbladder disease, idiopathic thrombocytopenic purpura, hemolytic-uremic syndrome, or thrombotic thrombocytopenic purpura. Marked elevations in serum amino-

transferases (usually 1000 to 2000 IU/L or higher) are not typical of HELLP syndrome; when they occur, they may indicate hepatic infarction or subcapsular hematoma rather than viral hepatitis. HELLP syndrome may be difficult to distinguish clinically from AFTP. Prolongation of the prothrombin and activated partial thromboplastin times, low glucose concentration, and elevated creatinine concentration are more common in women with acute fatty liver than HELLP syndrome (36).

Patients with HELLP syndrome may develop a hematoma beneath Glisson's capsule (34). Patients who develop a hematoma typically have abdominal pain and many have thrombocytopenia (with platelet count that may be below 20 000/μL), shoulder pain, nausea, and vomiting. If hepatic rupture occurs, swelling of the abdomen from hemoperitoneum and shock rapidly ensue. The aminotransferases are usually modestly elevated, but values of 4000 to 5000 U/L can occasionally be seen. Body imaging using CT or MRI is more dependable than ultrasonography in detecting these lesions (37). The management of a contained hematoma is to support the patient with volume replacement and blood transfusion, as needed, with consideration of percutaneous embolization of the hepatic arteries (38). If rupture has occurred, patients are best managed by a team experienced in liver trauma surgery (39). Operative management includes packing, drainage, hepatic artery ligation, and/or resection of affected areas of the liver. When the hemorrhage could not be contained, liver transplantation has been reported (40).

Treatment

The cornerstone of therapy is delivery (41). Delivery is indicated for pregnancies 34 weeks of gestation, nonreassuring tests of fetal status (*e.g.*, biophysical profile, fetal heart rate testing), or presence of severe maternal disease: multiorgan dysfunction, DIC, liver infarction or hemorrhage, renal failure, or abruptio placenta (41). Many patients will have a normal vaginal delivery following the induction of labor. However, cesarean delivery can be considered in very preterm gestations (under 30 to 32 weeks) when the cervix is unfavorable. In pregnancies <34 weeks of gestation in whom the mother and fetus are stable, corticosteroids to enhance fetal lung maturation should be given. Magnesium sulfate is often given to prevent convulsions (6 g intravenously followed by 2 g per hour as a continuous infusion). Severe hypertension should be controlled with labetalol, hydralazine, nifedipine, or in severe cases, with sodium nitro-prusside (42). The significance of corticosteroids, other than for acceleration of fetal lung maturity, remains controversial. The optimum choice and dose of corticosteroids have not been determined, although high-dose dexamethasone (10 mg IV Q12 hours until clinical improvement) appears effective and preferable to intramuscular betamethasone (43, 44).

Prognosis

The outcome of mothers with HELLP syndrome is generally good. With treatment, maternal mortality is about 1%. Maternal complications and gestational age at delivery are strongly associated with fetal prognosis. Fetal complications may include prematurity (70%). The overall perinatal mortality is 7 to 20%, primarily related to extreme prematurity in association with abruptio placenta or growth restriction (41). However, surviving babies do not have an increased risk of liver disease or thrombocytopenia and have an outcome similar to babies of a similar gestational age. Recurrence in subsequent pregnancies is 2–6%.

Acute fatty liver of pregnancy

AFLP was first described in 1940 and was initially thought to be exceedingly rare and universally fatal. The prevalence is estimated to be 1 per 16000 cases to 1 per 7000. AFLP occurs in the second half of pregnancy, usually close to term. However, some patients may present and be diagnosed after delivery (45).

Etiology

Recently, an association between AFLP and one of the inherited defects in mitochondrial beta-oxidation of fatty acids, long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency, was suggested (46). This enzyme is one of the four enzymes, which break down long-chain fatty acids in the liver. The accumulation of long-chain 3-hydroxyacyl metabolites produced by the fetus or placenta is toxic to the liver and may be the cause of the liver disease. The most common mutation is E474Q. Testing for the known genetic variants of this LCHAD is available and should be performed in affected women, their infants, and fathers. Infants with LCHAD deficiency are at risk to develop fatal nonketotic hypoglycemia, imitating Reye's syndrome or defects in urea cycle function (46). In addition, some forms of LCHAD deficiency are associated with neonatal dilated cardiomyopathy or progressive neuromyopathy (36). These babies should be managed with foods with medium-chain fatty acids, low-fat diet and followed-up for sequela.

Clinical features

Spectrum of clinical involvement is broad, ranging from asymptomatic elevations in aminotransferases to fulminant hepatic failure. AFLP may present with malaise, fatigue, anorexia, nausea, vomiting, headache, abdominal pain, and jaundice. Within 1–2 weeks of onset of symptoms, the disease may rapidly worsen. Patients then develop acute liver failure, including hepatic encephalopathy, ascites, edema, and renal insufficiency. Over one-half of patients have preeclampsia (47). Extrahepatic complications include infection, intraabdominal bleeding, transient polyuria, and polydipsia due to central diabetes insipidus, acute renal failure, pancreatitis, severe hypoglycemia. Women with AFLP have abnormal liver tests, with the serum aminotransferase elevations ranging from modest values up to 1000 IU/L. The white blood cell count may be higher than is usually seen in pregnancy. The platelet count is normal unless the patient has progressed to DIC, which is associated with marked reduction in antithrombin III. Severely affected patients also have elevations in serum ammonia and hypoglycemia. In cases of diagnostic uncertainty, liver biopsy is indicated. Using special stains (oil red O on frozen section or electron microscopy), the typical microvesicular fatty infiltration, pericentral pallor with lobular disarray and vacuolization of the centrizonal hepatocytes can be seen (48).

Differential diagnosis

The differential diagnosis includes acute viral hepatitis, especially hepatitis E in endemic areas, or herpes simplex, drug-induced hepatitis, HELLP syndrome, biliary tract disorders. Some features of AFLP may overlap with HELLP syndrome, but in AFLP, the degree of hepatic impairment is much more significant, overt failure in terms of hypoglycemia, and marked coagulopathy being evident (Table 2).

Treatment

The treatment of AFLP is delivery after maternal stabilization. The prothrombin time usually starts to normalize shortly thereafter, although in severe cases, there may be many more days of illness requiring maximal supportive management in an intensive care unit, including mechanical ventilation because of coma, dialysis for acute renal failure, parenteral nutrition because of associated pancreatitis, or even surgery to treat bleeding from a preceding cesarean section. Maternal stabilization requires glucose infusion and reversal of coagulopathy (*e.g.*, administration of fresh frozen plasma, cryoprecipitate, packed red blood cells, and, rarely, platelets), as needed. Lethargic patients should have their blood ammonia concentration evaluated and receive lactulose therapy if it is elevated. Occasional patients with AFLP have undergone liver transplantation, but this should not be needed with early diagnosis and prompt delivery (49).

Prognosis

Most severely ill patients recover and have no sequelae of the liver disease itself (45). The maternal mortality rate was very high until 1970 (92%). The maternal prognosis is currently greatly improved. With early delivery and advances in supportive management, maternal mortality is now 10–12% and fetal mortality is 9–20% (33, 50). Recurrence in subsequent pregnancies is uncommon. Affected women should be warned of this possibility and tested, along with their newborn infants who may be affected, for LCHAD (46).

Table 2. **Diagnostic differences between AFLP and HELLP**

Symptom	AFLP	HELLP
Parity	Nulliparous, twins	Multiparous, older
Jaundice	Common	Uncommon
Ammonia	High	Normal
Encephalopathy	+	–
Platelets	Low – normal	Low
Prothrombin time	Prolonged	Normal
APTT	Prolonged	Normal
Fibrinogen	Low	Normal or increased
Glucose	Low	Normal

HELLP – hemolysis, elevated liver enzymes, low platelet count,
AFLP – acute fatty liver of pregnancy, APTT – activated partial thromboplastin time.

Summary

An increase in serum aminotransferase, bilirubin, or serum bile acid concentrations during pregnancy is always pathologic and requires evaluation since the underlying liver disease may be severe and result in an increased risk to the mother and fetus. Although liver diseases unique to pregnancy are uncommon, they should always be suspected because of potential for acute liver failure. Gestational age is the best guide to differential diagnosis of pregnancy-related liver disease. Drug therapy is often required, and clinicians need to be familiar with which drugs are safe and which can be dangerous during pregnancy. ICP is the most common pregnancy-related liver disorder. UDCA is the first-line therapy for ICP. Early diagnosis of HELLP syndrome and AFLP, and prompt delivery with supportive therapy are the only available option for improving maternal and perinatal outcome.

Kepenų ligos, būdingos tik nėštumui

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Santrauka. Apžvalginio straipsnio tikslas – supažindinti su kepenų ligomis, būdingomis tik nėštumui. Straipsnyje apibendrinami autorių atliktų tyrimų duomenys, šių ligų diagnostikos ir gydymo ypatybių naujausios literatūros apžvalga. Kepenų pažeidimo požymių turi apie 3 proc. nėščiųjų. Retrospektyviosios analizės duomenimis, iš 16252 nėščiųjų, gimdžiusių Kauno medicinos universiteto klinikose 1996–2000 m., kepenų ligomis sirgo 0,52 proc. pacienčių. Nėščiajai gali pasireikšti tik nėštumui būdingos, specifinės kepenų ligos. Specifinės kepenų ligos turi tik joms būdingus klinikinius simptomus, kurie pasireiškia tam tikru nėštumo laikotarpiu: užsitęsęs nėščiųjų vėmimas (*hyperemesis gravidarum*) paprastai būna pirmuosius nėštumo mėnesius, intrahepatinė nėščiųjų cholestazė – 4–6 ar 7–9 nėštumo mėnesiais. Antroje nėštumo pusėje, dažniau 7–9 nėštumo mėnesiais, galimos sunkios kepenų ligos ir jų komplikacijos: ūminė riebalinė hepatozė, preeklampsija, HELLP sindromas (hemolizė, kepenų fermentų aktyvumo padidėjimas, trombocitopenija). Siekiant pagerinti nėštumo baigtį, labai svarbu greitai ir tiksliai nustatyti diagnozę. Pastaraisiais metais motinos ir vaisiaus mirštamumas žymiai sumažėjo, nes šios ligos anksti diagnozuojamos ir laiku skatinamas gimdymas.

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