World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
bpgoffice@wjgnet.com
doi:10.3748/wjg.v19.i43.7630

World J Gastroenterol 2013 November 21; 19(43): 7630-7638
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

Liver diseases in pregnancy: Diseases not unique to pregnancy

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Author contributions: Almashhrawi AA wrote and revised the manuscript; Ahmed KT, Rahman RN, and Hammoud GM were involved in reviewing the literature and collecting data; and Ibdah JA conceived the topic, contributed to the writing, analyzed and edited the manuscript, and provided overall intellectual input into the design and execution of the manuscript.

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Received: June 10, 2013 Revised: August 5, 2013
Accepted: September 4, 2013
Published online: November 21, 2013

Abstract

Pregnancy is a special clinical state with several normal physiological changes that influence body organs including the liver. Liver disease can cause significant morbidity and mortality in both pregnant women and their infants. Few challenges arise in reaching an accurate diagnosis in light of such physiological changes. Laboratory test results should be carefully interpreted and the knowledge of what normal changes to expect is prudent to avoid clinical misjudgment. Other challenges entail the methods of treatment and their safety for both the mother and the baby. This review summarizes liver diseases that are not unique to pregnancy. We focus on viral hepatitis and its mode of transmission, diagnosis, effect on the pregnancy, the mother, the infant, treatment, and breast-feeding. Autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, Wilson's disease, Budd Chiari and portal vein thrombosis in pregnancy are also discussed. Pregnancy is rare in patients with cirrhosis because of the metabolic and hormonal changes associated with cirrhosis. Variceal bleeding can happen in up to 38% of cirrhotic pregnant women. Management of portal hypertension during pregnancy is discussed. Pregnancy increases the pathogenicity leading to an increase in the rate of gallstones. We discuss some of the interventions for gallstones in pregnancy if symptoms arise. Finally, we provide an overview of some of the options in managing hepatic adenomas and hepatocellular carcinoma during pregnancy.

Key words: Liver; Pregnancy; Viral hepatitis; Autoimmune; Cirrhosis; Gallstones; Adenoma

Core tip: Pregnancy is a special clinical state with several normal physiological changes that influence body organs including the liver. Liver disease can cause significant morbidity and mortality in both pregnant women and their infants. Challenges involve making the diagnosis and the methods of treatment and their safety for both the mother and the baby. This review summarizes liver diseases that are not unique to pregnancy.

Almashhrawi AA, Ahmed KT, Rahman RN, Hammoud GM, Ibdah JA. Liver diseases in pregnancy: Diseases not unique to pregnancy. *World J Gastroenterol* 2013; 19(43): 7630-7638 Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i43/7630.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i43.7630

INTRODUCTION

Although not unique to pregnancy, liver diseases reviewed here can have significant consequences on pregnant women and their infants.

Approach to the diagnosis of liver conditions in preg-

Table 1 Normal physiological alterations in liver tests in pregnancy

Test	First trimester	Second/third trimesters
Albumin	↓	↓
ALT	N	N
AST	N	N
Total bilirubin	↓	↓
Alkaline phosphatase	N	↑
GGT	N	↓
5′-nucleotidase	N	May increase in second and third trimesters
Fasting total bile acids	N	N
Prothrombin time	N	N

N: No change; ↑: Increase; ↓: Decrease; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; GGT: Gamma-glutamyl transpeptidase.

Table 2 Interpretation of hepatitis B blood tests

Test	HBsAg	Anti-HBs	Total Anti-HBc	Anti-HBc IgM	HBV DNA
Acute infection	+	-	+	+	+
Resolved infection with natural immunity	-	+	+	-	-
Immunity through vaccination	-	+	-	-	-
Chronic infection	+	-	+	-	+/-
Different possibilities[1]	-	-	+	-	-

[1]Could represent resolving acute infection, resolved infection (most likely), chronic infection with low viral load or false positive. HBsAg: Hepatitis B surface antigen; Anti-HBs: Hepatitis B surface antibody; Total anti-HBc: Total hepatitis B core antibody; Anti-HBc IgM: Hepatitis B core antibody immunoglobulin M; HBV: Hepatitis B virus.

nant women should take into consideration the physiological changes during pregnancy that allow for normal fetal development. Sex hormones such as estrogen and progesterone increase progressively during pregnancy. This increase has an influence on hepatic metabolic, synthetic, and excretory functions[1]. During late pregnancy, biliary excretion of few compounds can be reduced. Furthermore, reduction in serum protein concentrations secondary to reversible hemodilution resulting from expanding plasma volume while pregnant is reflected by alterations in some liver function tests (Table 1).

Whereas nausea and vomiting are common in early pregnancy, those should not be considered normal in the second or third trimesters and ought to be investigated[2]. Jaundice and generalized pruritus are not normal features in pregnancy. Spider nevi and palmar erythema were found up to 66% and 63% respectively by the end of normal pregnancy in one study[3]. Most of those were reversible after delivery.

Unique aspects such as the effect of the disease on pregnancy, the effect of the pregnancy on disease progression, the use of specific therapies during pregnancy, and issues related to breast-feeding are discussed.

VIRAL HEPATITIS AND PREGNANCY

Hepatitis A virus

Hepatitis A virus (HAV) is an RNA virus that transmits through fecal-oral route, usually through contaminated water or food. Overall incidence is 9.1 per 100000 in the United States and less than 1:1000 pregnancies. Clinical presentation ensues within 2-4 wk of exposure. Generally, HAV does not result in chronic infection. Acute hepatitis A starts with prodromal symptoms including anorexia, malaise, nausea and vomiting, and progresses into jaundice and elevated liver transaminases. Presence of HAV immunoglobulin M (IgM) antibodies confirms the acute infection. Management is supportive care including optimizing hydration and nutrition. Rarely acute hepatitis A can lead to fulminant hepatic failure. Inactivated HAV vaccine and immunoglobulin prophylaxis are safe in pregnancy[4]. Although vertical transmission has been reported, intrauterine transmission is rare[5-7]. Fecal-oral transmission during birth is possible. No cases of teratogenicity were reported, but maternal complications such as preterm labor were described. Susceptible woman should receive vaccination. Breast-feeding is not contraindicated in acute hepatitis A with following appropriate hygiene measures.

Hepatitis B virus

Hepatitis B virus (HBV) is a DNA virus that is highly infectious and transmits through intravenous route, sexual contact, and vertically from the mother to her fetus. It can present both as an acute or chronic infection. Pregnancy does not affect the course of infection directly. Fortunately, since universal children vaccination for hepatitis B was implemented in 1992, the numbers of vertically transmitted chronic hepatitis B cases, and its complications such as hepatocellular carcinoma have dropped[8-10]. Prenatal screening for HBV is standard of care in many countries including the United States. Those susceptible should be vaccinated. Pregnant women exposed to HBV should receive HBV immunoglobulins (HBIG) within 72 h of exposure in addition to the vaccination series. Infants with infected mothers should receive both immunoglobulins and vaccination series at the time of delivery. While acute infection can present with a viral syndrome and jaundice such as that of acute hepatitis A infection, chronic infection is usually asymptomatic and diagnosis can be made relying on serum serology testing. A summary of the tests used in hepatitis B diagnosis and their interpretation is displayed in Table 2.

Treatment should follow guidelines published by medical societies such as the American Association for the Study of Liver Disease (AASLD)[11], the European Association for the Study of the Liver[12], or the Asian Pacific Association for the Study of the Liver[13]. In the United States, we recommend referring infected pregnant women to the state's perinatal hepatitis B prevention program[14], that is CDC-funded (centers for disease control and prevention), and to liver specialists for optimizing counseling and treatment.

There are seven Food and Drug Administration (FDA)-approved medications for the treatment of hepati-

Table 3 Food and Drug Administration approved medications for hepatitis B treatment

Generic name	Trade name	Company	Approved for HBV treatment
Interferons			
Interferon α-2b, recombinant	Intron® A	Schering Corporation/ Merck and Co	1992
Perinterferon α-2a	Pegasys®	Genentech/Roche group	2005
Nucleosides/nucleotides			
Lamivudine[1]	EPIVIR-HBV®	GlaxoSmithKline	1998
Adefovir dipivoxil	HEPSERA™	Gilead Sciences	2002
Entecavir	BARACLUDE™	Bristol-Myers Squibb	2005
Telbivudine[2]	TYZEKA™	Novartis	2006
Tenofovir[2]	Viread	Gilead Sciences	2008

[1]Pregnancy risk category C, can be used in the third trimester; [2]Pregnancy risk category B. HBV: Hepatitis B virus.

tis B (Table 3) in non-pregnant patients. Interferon use is contraindicated in pregnancy. Tenofovir and Telbivudine belong to pregnancy risk category B; all others belong to category C. The choice to treat or not should be weighed in light of benefits versus risks for both the mother and her fetus. Those with higher viral load (serum HBV DNA > 10^8 copies/mL) were at higher risk for vertical transmission in one study[15]. Wen *et al*[16] showed recently that the adjusted odds ratio of transmission for each log10 copy/mL increase, is 3.49 ($P = 0.001$), with predictive rates of infection at maternal viral load levels of 7, 8, and 9-log10 copies/ml of 6.6% ($P = 0.033$), 14.6% ($P = 0.001$), and 27.7% ($P < 0.001$), respectively. Therefore, it is reasonable to treat those women or women with previous infected children, especially towards the end of pregnancy (from week 28 and up), with risk category B drugs or Lamivudine (increases birth defects if used in 1st trimester)[17,18]. In a meta-analysis, significant drop in the risk of vertical transmission was found in those who succeeded to lower HBV DNA below 10^6 copies/mL[18]. Telbivudine was used safely and with good efficacy in reducing transmission (0% *vs* 8%; $P = 0.002$) in a recent study[19].

Although cesarean section is proposed as a measure to lower the risk of transmission, particularly in women with high viral loads towards term, there is a conflicting evidence regarding choosing cesarean section versus vaginal delivery to lower the risk of vertical transmission[20,21]. Breast-feeding should be encouraged for infants receiving HBIG and vaccination[22-25]. On the other hand, no adequate evidence of the safety of breast-feeding in mothers receiving antiviral therapy is available and women on antiviral therapy with lamivudine, telbivudine or tenofovir should be discouraged from breast-feeding[26-28].

Hepatitis C virus

With prevalence around 1.6%, chronic hepatitis C infection continues to present a big public health concern in the United States. The majority of those patients, left untreated, will progress to cirrhosis with expected peak in prevalence around the year 2030, with expected medical cost exceeding $85 billion[29]. Generally, all high-risk patients should be screened for hepatitis C virus (HCV) following CDC and AASLD guidelines. Those include children born to HCV infected mothers. While there is no approved medicine to treat chronic hepatitis C in pregnant women, those should be referred to liver experts for education regarding options of treatment after delivery and preventive measures to slow the progression of the disease. HCV antibodies ELISA testing is a sensitive test and carries high positive predictive value in high-risk patients. Diagnosis can be confirmed using HCV RNA polymerase chain reaction (PCR). There are several therapies for hepatitis C that are under investigation currently. Some of those could prove safe to use in pregnancy in the future. Pregnant women with hepatitis C should be educated about the mode of transmission and how to reduce the risk, smoking cessation, alcohol abstinence, and vaccination for hepatitis A and hepatitis B. They should also be screened for hepatitis B and human immunodeficiency virus (HIV) infection. Women undergoing treatment for hepatitis C, or those with partners undergoing treatment for hepatitis C, should avoid pregnancy by using at least 2 forms of barrier contraception, for the period of treatment and 6 mo after.

Infants of hepatitis C infected- mothers were at higher risk for low birth weight, being small for gestational age, or requiring intensive care upon birth in one report[30]. The risk of vertical transmission is approximately 4%. This risk increased up to 19.4% when co-infected with HIV[31-35]. High viral load also increase the risk for vertical transmission. HCV transmission could occur through viral trancytosis across trophoblast cells mediated by HCV receptors expressed on trophoblasts or through some form of injury that influences the placental barrier[36]. Although there were few reports of increased risk of transmission with premature rupture of membrane, more than 6 h before delivery, mode of delivery was not found to change the risk of hepatitis C transmission[31,37-39]. As the new era of direct antiviral agents is evolving, treating hepatitis C during pregnancy may become an option and thus the possibility of reducing the risk of transmission[40].

Breast-feeding is considered safe when nipples are not cracked or bleeding according to CDC recommendations.

Hepatitis D virus

Hepatitis D virus (HDV) is an RNA virus that requires

hepatitis B surface antigen for replication. Anti-HDV antibodies establish the diagnosis. Although vertical transmission is possible, hepatitis D is preventable by preventing HBV transmission[41].

Hepatitis E virus

Hepatitis E virus (HEV) is an RNA virus that is usually transmitted through fecal-oral means, although transmission via infected blood products and vertical transmission has been reported[42]. It is usually a self-limiting disease in immunocompetent patients. Hepatitis E can cause significant disease in patients with chronic liver disease and can present in a chronic form leading to fibrosis in immunocompromised individuals[43]. Pregnant women in highly endemic areas are particularly at risk with up to 60% developing fulminant hepatic failure with a maternal death rate of up to 31%[44,45]. A review from Bangladesh suggests it is responsible for 9.8% of pregnancy-related deaths[46]. On the other hand, the severity of the disease was not different between pregnant and non-pregnant women in non-endemic places such as the United States and Europe. A report suggested that such variance in severity between endemic and non-endemic areas might be related to different genotypes of HEV[47]. Other studies suggested that pregnancy per se is not a poor prognostic factor for those who developed acute liver failure[48]. To a lesser extent, hepatitis E is prevalent in some western countries, particularly genotype 3.

Vertical transmission was described up to 78.9% with infant mortality of 40%[42]. The level of viremia appears to be associated with the severity of the disease during pregnancy[49]. Despite such high mortality, current treatment remains supportive. Pregnant woman seeking travel to endemic areas should be counseled about the risk of hepatitis E, and be advised to avoid unpurified water, uncooked fruit, vegetables, and shellfish.

Hepatitis E vaccines have been developed and evaluated in trials but has not been approved for commercial use yet. Their utility is yet to be determined[50-54].

Herpes simplex virus

32 out of 137 cases of herpes simplex virus (HSV) hepatitis were pregnant women in one report, suggesting their susceptibility[55]. Although rare, HSV hepatitis carries a very high mortality (39%) if inappropriately treated[56]. Providers should have high index of suspicion in this patient group in the appropriate clinical setting; elevated liver transaminases usually 100 times upper level of normal with typically normal or mildly elevated bilirubin (anicteric hepatitis)[57-60]. Serology testing including anti-HSV IgM should be ordered. HSV PCR can be ordered as well to confirm diagnosis. Recent study has revealed that HSV DNA load correlated with liver transaminase levels and disease severity[61]. Although no strong evidence to support starting Acyclovir in patients with indeterminate acute liver failure, clinicians should consider empirical therapy with acyclovir when HSV hepatitis is suspected[59]. Liver biopsy with appropriate immunohistochemistry staining can be useful, but usually is avoided because of its invasive nature, coagulopathy and because of the potential delay in results/treatment.

AUTOIMMUNE HEPATITIS AND PREGNANCY

Autoimmune hepatitis is a disease characterized by elevated liver aminotransferases, hypergammaglobulinemia, and positive serum autoantibodies. Autoimmune hepatitis and pregnancy (AIH) is more common in females, especially those in childbearing ages. It can happen during pregnancy and may not follow consistent pattern. Normalization of liver aminotransferases has been described in patients with no treatment[62]. This normalization could be related to the immunotolerant state that predominates pregnancy. On the other hand, flare-ups have been reported during and after pregnancy[63]. Prematurity and fetal-loss were described in those patients[64]. A link was observed between antibodies to soluble liver antigen/liver-pancreas and ribonucleoprotein/Sjögren's syndrome A and adverse outcomes[65]. Inadequate disease control in the year prior to pregnancy and the absence of treatment during pregnancy were associated with unfavorable outcomes in a recent study[66].

Although the patients should be counseled about possible adverse outcomes, pregnancy appears to be safe in well-controlled AIH women[67]. Special considerations should be given to the postpartum period as flare-ups may occur frequently, and treatment should be resumed preemptively two weeks before delivery and maintained thereafter[68]. Immunosuppressive therapy with steroids and agents such as azathioprine is the mainstay for treatment of AIH. Azathioprine use during pregnancy is generally safe (despite reports of birth defects in animal models)[64].

PRIMARY BILIARY CIRRHOSIS/PRIMARY SCLEROSING CHOLANGITIS AND PREGNANCY

There is limited data about pregnancy in patients with primary biliary cirrhosis. Reports have ranged from normal course of pregnancy and good fetal outcomes to poor prognosis for both mother and fetus[69,70]. Earlier diagnosis and the use of ursodeoxycholic acid (UDCA) in treatment, which has been used safely in pregnancy, have been linked to favorable outcomes[71]. Primary sclerosing cholangitis did not appear to reduce fertility and resulted in good outcomes, in one report. UDCA was successfully used to control pruritus in this cohort[72].

WILSON'S DISEASE AND PREGNANCY

Wilson's disease is an autosomal recessive disease with

Table 4 Options for portal hypertension management in pregnancy

Esophageal varices	Nonselective β-blockers
	Endoscopic and ligation and/or sclerotherapy
	TIPS: Data on TIPS and pregnancy is limited
Ascites	Sodium (salt) restriction, diuretics
Hepatic encephalopathy	Lactulose, rifaximin

TIPS: Transjugular portosystemic shunt.

prevalence of 1:30000 to 1:50000[73]. It affects hepatic copper transport with inhibition of biliary excretion, resulting in excess circulating copper and deposition in organs such as the liver and the brain. Cases of reduced fertility and recurrent spontaneous abortions in untreated women were reported[74]. Chelation therapy using *D*-penicillamine or trientine, or the use of zinc to reduce intestinal absorption of copper, have been the mainstay therapy for Wilson's disease. Zinc has been used with minimal teratogenicity during pregnancy[75]. Although teratogenic effects of *D*-penicillamine in humans and animals, and teratogenic effects of trientine in animals were described[76,77], therapy should not be discontinued as this can result in severe hemolysis, worsening of liver function and even death. Even though zinc dosages can be maintained during pregnancy, AASLD recommends lowering *D*-penicillamine and trientine to the minimum needed (usually 25%-50% of the pre-pregnancy dose)[78], particularly towards term to aid in wound healing. Baseline dosages can be resumed postnatal. The mother should be counseled, and both the mother and her fetus should be monitored closely during pregnancy. Breastfeeding is discouraged as *D*-pencillamine can be harmful to the infant and safety has not been established with trientene and zinc.

GALLSTONES AND PREGNANCY

Physiological changes during pregnancy particularly hormonal changes lead to decrease in contractility of the gallbladder and changes in bile content, with increase in cholesterol saturation, resulting in increase in lethogenicity of the bile[79]. Incidence of gallstones is up to 12% in pregnant women[80]. Those typically remain asymptomatic. The patient can present with biliary pain, gallstone pancreatitis, or less likely acute cholecystitis. Other manifestations such as choledocholithiasis and cholangitis can also happen. Management is mostly conservative with hydration and antibiotics if indicated. In more severe cases, cholecystectomy can be indicated. Endoscopic retrograde cholangiopancreatography (ERCP) can also be used with taking precautions to minimize radiation exposure of the fetus. In general, surgical procedures are the safest in the second trimester. ERCP was reported to be associated with higher risk for preterm pregnancy and low birthweight when performed in the first trimester. Post-ERCP pancreatitis rate was higher in pregnancy than general population[81-85].

CIRRHOSIS/ PORTAL HYPERTENSION AND PREGNANCY

Pregnancy in cirrhotic women is rare, probably because of low prevalence of cirrhosis in reproductive age group (45 in 100000) and also due to amenorrhea and anovulation, likely related to metabolic and hormonal derangements[86]. The physiological increase in plasma volume during pregnancy can worsen portal hypertension, resulting in increase risk of variceal bleeding. Variceal bleeding can happen in up to 38% of cirrhotic pregnant women. This is even higher in those with known portal hypertension. Those with known varices have a 78% chance of bleeding[87]. AASLD recommends screening for esophageal varices by the second trimester, as the risk of bleeding appears to be highest at that time. Women with cirrhosis planning to become pregnant should be screened before conception by endoscopy and prophylaxis (with nonselective beta blockers) should be started as recommended by AASLD guidelines. Complications of portal hypertension in pregnancy can be as high as 50% resulting in high mortality rate of up to 18%, and higher risk for fetal loss[88]. Pregnancy should be avoided in women with previous history of variceal bleeding and liver insufficiency. Means such as early forceps delivery or vacuum extraction should be considered to prevent excessive straining during vaginal delivery. Management options of complications of portal hypertension are summarized in Table 4. All medications used during pregnancy should be checked as of which risk category they fall under according to the FDA classification before prescribing (Tables 5 and 6).

HEPATOCELLULAR ADENOMA AND PREGNANCY

The incidence of hepatocellular adenoma has increased since the introduction of oral contraceptives. There is a link between pregnancy and liver adenomas secondary to higher levels of hormones[89]. Rupture of adenomas has resulted in maternal mortality of a 44% and fetal loss of 38% in one study[90]. Adenoma rupture risk increases towards the end of pregnancy[91]. Women with adenomas > 5 cm or those with previous complications with adenomas, should avoid subsequent pregnancies. Those pregnant with smaller adenomas should be monitored closely with serial ultrasound imaging. If the lesion is progressively enlarging, or 5 cm in size or bigger, surgical resection should be considered[90]. Radiofrequency ablation is another modality that can be used in the treatment of hepatic adenomas[91-93]. Close monitoring of the lesion should continue in the postpartum period as well.

HEPATOCELLULAR CARCINOMA AND PREGNANCY

Although rare, hepatocellular carcinoma has been reported during pregnancy. Fibrolamellar variant of hepatocel-

Table 5 The Food and Drug Administration pregnancy risk categories of medicines

Pregnancy category	Definition
A	Controlled studies show no risk
B	Animal studies show no risk, and there are no human controlled studies. Or animal studies may have revealed an adverse effect that was not reproduced in human controlled studies
C	No human studies and either animal studies show an adverse effect or there are no studies available. Use if the risk is justified
D	Positive evidence of risk in human studies, only if the potential benefits outweigh the risk
X	Contraindicated in pregnancy: Risk is confirmed in animal and human studies and outweighs any advantage

Table 6 Food and Drug Administration pregnancy risk categories of some liver disease medications

Medicine	Pregnancy category	Medicine	Pregnancy category
Nadolol	C	Ribavirin	X
Propranolol	C	Telaprevir	B
Rifaximin	C	Boceprevir	B
Lactulose	B	Tenofovir	B
Furosemide	C	Entecavir	C
Spironolactone	C	Telbuvidine	B
Corticosteroids	B	Adefovir	C
Azathioprine	D	Lamuvidine	C
Cyclosporin	C	Acyclovir	B
Mycophenolate mofetil	D	Ursodeoxycholic acid	B
Tacrolimus	C	Penicillamine	D
Sirolimus	C	Trientine	C
Antithymocyte globulin	C	Zinc sulfate	C
Pegylated interferon	C (contraindicated in pregnancy)	Interferon alpha 2b	C (contraindicated in pregnancy)

lular carcinoma (HCC) was also reported[94-96]. Pregnant women with HCC can have shorter median survival than those non-pregnant. Higher levels of estrogen and immune suppression during pregnancy can play a role with HCC progression[97]. Modalities such as surgical resection and radiofrequency ablation can be used in selected patients. Limited data are available about the management of hepatocellular carcinoma in pregnancy.

HEPATIC VEIN THROMBOSIS/PORTAL VEIN THROMBOSIS AND PREGNANCY

Budd-Chiari syndrome (BCS) is rare in pregnancy but can have grave consequences for both the mother and her fetus. The physiological hypercoagulable state can contribute in BCS development in pregnancy. Other predisposing factors are factor V Leiden mutation and prothrombin gene mutations. BCS entails thrombosis of the hepatic vein resulting in passive congestion of the hepatic sinusoids leading to ischemia and portal hypertension. Low molecular weight heparin should be started if no contraindications. Extreme measures such as portacaval shunting and liver transplantation during pregnancy were reported[98,99]. Subsequent pregnancies are not absolutely contraindicated with appropriately treated disease. The mother should be counseled about the possible maternal and fetal unfavorable outcomes.

Portal vein thrombosis (PVT) is rare and can also occur during pregnancy. Local causes such as cirrhosis, intra-abdominal infections, or malignancies may predispose to PVT. Systemic disorders resulting in hypercoagulable state such as factor V Leiden mutation, anti-phospholipid syndrome, or myeloproliferative disorders should be also excluded. In acute portal vein thrombosis, anti-coagulation should be used for 3 mo at the least. Patients with chronic portal vein thrombosis should be screened for gastroesophageal varices and should be treated accordingly[100].

CONCLUSION

Pregnant women can have a variety of liver diseases with different incidences. Clinicians should be aware of the clinical presentations and be able to manage those conditions with special attention to the peculiarities in relation to the mother and her infant. In this review we have summarized several of the liver diseases that can happen during pregnancy and offered an overview of their management.

REFERENCES

1 **Van Thiel DH**, Gavaler JS. Pregnancy-associated sex steroids and their effects on the liver. *Semin Liver Dis* 1987; **7**: 1-7 [PMID: 3589711 DOI: 10.1055/s-2008-1040558]
2 **Bacq Y**, Riely C. The liver in pregnancy. In: Schiff's diseases of the liver. 9th ed. Philadelphia: Lippincott Williams and Wilkins; 2003: 1435–1457
3 **Bean WB**, Cogswell R. Vascular changes of the skin in pregnancy; vascular spiders and palmar erythema. *Surg Gynecol Obstet* 1949; **88**: 739-752 [PMID: 18130313]
4 **Magriples U**. Hepatitis in pregnancy. *Semin Perinatol* 1998; **22**: 112-117 [PMID: 9638905]
5 **Motte A**, Blanc J, Minodier P, Colson P. Acute hepatitis A in a pregnant woman at delivery. *Int J Infect Dis* 2009; **13**: e49-e51 [PMID: 18774327 DOI: 10.1016/j.ijid.2008.06.009]
6 **Selander B**, Bläckberg J, Widell A, Johansson PJ. No evidence

of intrauterine transmission of hepatitis A virus from a mother to a premature infant. *Acta Paediatr* 2009; **98**: 1603-1606 [PMID: 19558626 DOI: 10.1111/j.1651-2227.2009.01402.x]
7 **Renge RL**, Dani VS, Chitambar SD, Arankalle VA. Vertical transmission of hepatitis A. *Indian J Pediatr* 2002; **69**: 535-536 [PMID: 12139145]
8 **Beasley RP**. Rocks along the road to the control of HBV and HCC. *Ann Epidemiol* 2009; **19**: 231-234 [PMID: 19344859 DOI: 10.1016/j.annepidem.2009.01.017]
9 **Ni YH**, Chen DS. Hepatitis B vaccination in children: the Taiwan experience. *Pathol Biol* (Paris) 2010; **58**: 296-300 [PMID: 20116181 DOI: 10.1016/j.patbio.2009.11.002]
10 **Tajiri H**, Tanaka H, Brooks S, Takano T. Reduction of hepatocellular carcinoma in childhood after introduction of selective vaccination against hepatitis B virus for infants born to HBV carrier mothers. *Cancer Causes Control* 2011; **22**: 523-527 [PMID: 21191808 DOI: 10.1007/s10552-010-9721-4]
11 **Lok AS**, McMahon BJ. Chronic hepatitis B: update 2009. *Hepatology* 2009; **50**: 661-662 [PMID: 19714720 DOI: 10.1002/hep.23190]
12 **European Association For The Study Of The Liver**. EASL clinical practice guidelines: Management of chronic hepatitis B virus infection. *J Hepatol* 2012; **57**: 167-185 [PMID: 22436845]
13 **Liaw YF**, Leung N, Guan R, Lau GK, Merican I, McCaughan G, Gane E, Kao JH, Omata M. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2005 update. *Liver Int* 2005; **25**: 472-489 [PMID: 15910483]
14 State perinatal hepatitis B prevention program (PHBPP). Available from: URL: http: //www.cdc.gov/hepatitis/Partners/PeriHepBCoord.htm
15 **Wiseman E**, Fraser MA, Holden S, Glass A, Kidson BL, Heron LG, Maley MW, Ayres A, Locarnini SA, Levy MT. Perinatal transmission of hepatitis B virus: an Australian experience. *Med J Aust* 2009; **190**: 489-492 [PMID: 19413519]
16 **Wen WH**, Chang MH, Zhao LL, Ni YH, Hsu HY, Wu JF, Chen PJ, Chen DS, Chen HL. Mother-to-infant transmission of hepatitis B virus infection: significance of maternal viral load and strategies for intervention. *J Hepatol* 2013; **59**: 24-30 [PMID: 23485519 DOI: 10.1016/j.jhep.2013.02.015]
17 **Xu WM**, Cui YT, Wang L, Yang H, Liang ZQ, Li XM, Zhang SL, Qiao FY, Campbell F, Chang CN, Gardner S, Atkins M. Lamivudine in late pregnancy to prevent perinatal transmission of hepatitis B virus infection: a multicentre, randomized, double-blind, placebo-controlled study. *J Viral Hepat* 2009; **16**: 94-103 [PMID: 19175878 DOI: 10.1111/j.1365-2893.2008.01056.x]
18 **Han L**, Zhang HW, Xie JX, Zhang Q, Wang HY, Cao GW. A meta-analysis of lamivudine for interruption of mother-to-child transmission of hepatitis B virus. *World J Gastroenterol* 2011; **17**: 4321-4333 [PMID: 22090789 DOI: 10.3748/wjg.v17.i38.4321]
19 **Han GR**, Cao MK, Zhao W, Jiang HX, Wang CM, Bai SF, Yue X, Wang GJ, Tang X, Fang ZX. A prospective and open-label study for the efficacy and safety of telbivudine in pregnancy for the prevention of perinatal transmission of hepatitis B virus infection. *J Hepatol* 2011; **55**: 1215-1221 [PMID: 21703206 DOI: 10.1016/j.jhep.2011.02.032]
20 **Wang J**, Zhu Q, Zhang X. Effect of delivery mode on maternal-infant transmission of hepatitis B virus by immunoprophylaxis. *Chin Med J* (Engl) 2002; **115**: 1510-1512 [PMID: 12490098]
21 **Lee SD**, Lo KJ, Tsai YT, Wu JC, Wu TC, Yang ZL, Ng HT. Role of caesarean section in prevention of mother-infant transmission of hepatitis B virus. *Lancet* 1988; **2**: 833-834 [PMID: 2902274]
22 **Jhaveri R**, Murray N. An omission in the AASLD Practice Guidelines on Chronic Hepatitis B. *Hepatology* 2007; **46**: 280; author reply 280 [PMID: 17596892 DOI: 10.1002/hep.21756]
23 **Hill JB**, Sheffield JS, Kim MJ, Alexander JM, Sercely B, Wendel GD. Risk of hepatitis B transmission in breast-fed infants of chronic hepatitis B carriers. *Obstet Gynecol* 2002; **99**: 1049-1052 [PMID: 12052598]
24 **Zheng Y**, Lu Y, Ye Q, Xia Y, Zhou Y, Yao Q, Wei S. Should chronic hepatitis B mothers breastfeed? a meta analysis. *BMC Public Health* 2011; **11**: 502 [PMID: 21708016 DOI: 10.1186/1471-2458-11-502]
25 **Bzowej NH**. Hepatitis B Therapy in Pregnancy. *Curr Hepat Rep* 2010; **9**: 197-204 [PMID: 20949113 DOI: 10.1007/s11901-010-0059-x]
26 **Novartis Pharmaceuticals Corporation**. Telbivudine [Package insert]. Available from: URL: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/022011s013lbl.pdf
27 **Gilead Sciences, Inc**. Viread [Package insert]. Available from: URL: http://www.accessdata.fda.gov/drugsatfda_docs/label/2012/021356s042,022577s002lbl.pdf
28 **GlaxoSmithKline**. EPIVIR-HBV (lamivudine) Tablets EPIVIR-HBV (lamivudine) Oral Solution [Package insert]. Available from: URL: http://www.accessdata.fda.gov/drugsatfda_docs/label/2001/21004s2lbl.pdf
29 **Pyenson B**, Fitch K, Iwasaki K. Consequences of hepatitis c virus (HCV) costs of a baby boomer epidemic, 2009. Available from: URL: http://www.natap.org/2009/HCV/051809_01.htm
30 **Pergam SA**, Wang CC, Gardella CM, Sandison TG, Phipps WT, Hawes SE. Pregnancy complications associated with hepatitis C: data from a 2003-2005 Washington state birth cohort. *Am J Obstet Gynecol* 2008; **199**: 38.e1-38.e9 [PMID: 18486089 DOI: 10.1016/j.ajog.2008.03.052]
31 **Mast EE**, Hwang LY, Seto DS, Nolte FS, Nainan OV, Wurtzel H, Alter MJ. Risk factors for perinatal transmission of hepatitis C virus (HCV) and the natural history of HCV infection acquired in infancy. *J Infect Dis* 2005; **192**: 1880-1889 [PMID: 16267758 DOI: 10.1086/497701]
32 **Polywka S**, Pembrey L, Tovo PA, Newell ML. Accuracy of HCV-RNA PCR tests for diagnosis or exclusion of vertically acquired HCV infection. *J Med Virol* 2006; **78**: 305-310 [PMID: 16372293 DOI: 10.1002/jmv.20540]
33 **Gibb DM**, Goodall RL, Dunn DT, Healy M, Neave P, Cafferkey M, Butler K. Mother-to-child transmission of hepatitis C virus: evidence for preventable peripartum transmission. *Lancet* 2000; **356**: 904-907 [PMID: 11036896]
34 **Polis CB**, Shah SN, Johnson KE, Gupta A. Impact of maternal HIV coinfection on the vertical transmission of hepatitis C virus: a meta-analysis. *Clin Infect Dis* 2007; **44**: 1123-1131 [PMID: 17366462 DOI: 10.1086/512815]
35 **Mariné-Barjoan E**, Berrébi A, Giordanengo V, Favre SF, Haas H, Moreigne M, Izopet J, Tricoire J, Tran A, Pradier C, Bongain A. HCV/HIV co-infection, HCV viral load and mode of delivery: risk factors for mother-to-child transmission of hepatitis C virus? *AIDS* 2007; **21**: 1811-1815 [PMID: 17690581 DOI: 10.1097/qad.0b013e3282703810]
36 **Le Campion A**, Larouche A, Fauteux-Daniel S, Soudeyns H. Pathogenesis of hepatitis C during pregnancy and childhood. *Viruses* 2012; **4**: 3531-3550 [PMID: 23223189 DOI: 10.3390/v4123531]
37 **Thomas SL**, Newell ML, Peckham CS, Ades AE, Hall AJ. A review of hepatitis C virus (HCV) vertical transmission: risks of transmission to infants born to mothers with and without HCV viraemia or human immunodeficiency virus infection. *Int J Epidemiol* 1998; **27**: 108-117 [PMID: 9563703]
38 **Ghamar Chehreh ME**, Tabatabaei SV, Khazanehdari S, Alavian SM. Effect of cesarean section on the risk of perinatal transmission of hepatitis C virus from HCV-RNA+/HIV- mothers: a meta-analysis. *Arch Gynecol Obstet* 2011; **283**: 255-260 [PMID: 20652289 DOI: 10.1007/s00404-010-1588-9]
39 **Cottrell EB**, Chou R, Wasson N, Rahman B, Guise JM. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013; **158**: 109-113 [PMID:

23437438]
40 **Prasad MR**, Honegger JR. Hepatitis C virus in pregnancy. *Am J Perinatol* 2013; **30**: 149-159 [PMID: 23389935 DOI: 10.1055/s-0033-1334459]
41 **Dinsmoor MJ**. Hepatitis in the obstetric patient. *Infect Dis Clin North Am* 1997; **11**: 77-91 [PMID: 9067785]
42 **Khuroo MS**, Kamili S, Khuroo MS. Clinical course and duration of viremia in vertically transmitted hepatitis E virus (HEV) infection in babies born to HEV-infected mothers. *J Viral Hepat* 2009; **16**: 519-523 [PMID: 19228284 DOI: 10.1111/j.1365-2893.2009.01101.x]
43 **Sclair SN**, Schiff ER. An update on the hepatitis E virus. *Curr Gastroenterol Rep* 2013; **15**: 304 [PMID: 23314803 DOI: 10.1007/s11894-012-0304-2]
44 **Khuroo MS**, Kamili S. Aetiology, clinical course and outcome of sporadic acute viral hepatitis in pregnancy. *J Viral Hepat* 2003; **10**: 61-69 [PMID: 12558914]
45 **Boccia D**, Guthmann JP, Klovstad H, Hamid N, Tatay M, Ciglenecki I, Nizou JY, Nicand E, Guerin PJ. High mortality associated with an outbreak of hepatitis E among displaced persons in Darfur, Sudan. *Clin Infect Dis* 2006; **42**: 1679-1684 [PMID: 16705571 DOI: 10.1086/504322]
46 **Labrique AB**, Sikder SS, Krain LJ, West KP, Christian P, Rashid M, Nelson KE. Hepatitis E, a vaccine-preventable cause of maternal deaths. *Emerg Infect Dis* 2012; **18**: 1401-1404 [PMID: 22931753 DOI: 10.3201/eid1809.120241]
47 **Renou C**, Pariente A, Nicand E, Pavio N. Pathogenesis of Hepatitis E in pregnancy. *Liver Int* 2008; **28**: 1465; author reply 1466 [PMID: 19055645 DOI: 10.1111/j.1478-3231.2008.01885.x]
48 **Bhatia V**, Singhal A, Panda SK, Acharya SK. A 20-year single-center experience with acute liver failure during pregnancy: is the prognosis really worse? *Hepatology* 2008; **48**: 1577-1585 [PMID: 18925633 DOI: 10.1002/hep.22493]
49 **Borkakoti J**, Hazam RK, Mohammad A, Kumar A, Kar P. Does high viral load of hepatitis E virus influence the severity and prognosis of acute liver failure during pregnancy? *J Med Virol* 2013; **85**: 620-626 [PMID: 23280991 DOI: 10.1002/jmv.23508]
50 **Shrestha MP**, Scott RM, Joshi DM, Mammen MP, Thapa GB, Thapa N, Myint KS, Fourneau M, Kuschner RA, Shrestha SK, David MP, Seriwatana J, Vaughn DW, Safary A, Endy TP, Innis BL. Safety and efficacy of a recombinant hepatitis E vaccine. *N Engl J Med* 2007; **356**: 895-903 [PMID: 17329696 DOI: 10.1056/nejmoa061847]
51 **Krawczynski K**. Hepatitis E vaccine--ready for prime time? *N Engl J Med* 2007; **356**: 949-951 [PMID: 17329703 DOI: 10.1056/nejme068311]
52 **Zhu FC**, Zhang J, Zhang XF, Zhou C, Wang ZZ, Huang SJ, Wang H, Yang CL, Jiang HM, Cai JP, Wang YJ, Ai X, Hu YM, Tang Q, Yao X, Yan Q, Xian YL, Wu T, Li YM, Miao J, Ng MH, Shih JW, Xia NS. Efficacy and safety of a recombinant hepatitis E vaccine in healthy adults: a large-scale, randomised, double-blind placebo-controlled, phase 3 trial. *Lancet* 2010; **376**: 895-902 [PMID: 20728932 DOI: 10.1016/s0140-6736(10)61030-6]
53 **Aggarwal R**. Hepatitis E: Historical, contemporary and future perspectives. *J Gastroenterol Hepatol* 2011; **26** Suppl 1: 72-82 [PMID: 21199517 DOI: 10.1111/j.1440-1746.2010.06540.x]
54 **Kamili S**. Toward the development of a hepatitis E vaccine. *Virus Res* 2011; **161**: 93-100 [PMID: 21620908 DOI: 10.1016/j.virusres.2011.05.008]
55 **Norvell JP**, Blei AT, Jovanovic BD, Levitsky J. Herpes simplex virus hepatitis: an analysis of the published literature and institutional cases. *Liver Transpl* 2007; **13**: 1428-1434 [PMID: 17902129 DOI: 10.1002/lt.21250]
56 **Kang AH**, Graves CR. Herpes simplex hepatitis in pregnancy: a case report and review of the literature. *Obstet Gynecol Surv* 1999; **54**: 463-468 [PMID: 10394584]
57 **Peters DJ**, Greene WH, Ruggiero F, McGarrity TJ. Herpes simplex-induced fulminant hepatitis in adults: a call for empiric therapy. *Dig Dis Sci* 2000; **45**: 2399-2404 [PMID: 11258565]
58 **Riediger C**, Sauer P, Matevossian E, Müller MW, Büchler P, Friess H. Herpes simplex virus sepsis and acute liver failure. *Clin Transplant* 2009; **23** Suppl 21: 37-41 [PMID: 19930315 DOI: 10.1111/j.1399-0012.2009.01108.x]
59 **Navaneethan U**, Lancaster E, Venkatesh PG, Wang J, Neff GW. Herpes simplex virus hepatitis - it's high time we consider empiric treatment. *J Gastrointestin Liver Dis* 2011; **20**: 93-96 [PMID: 21451806]
60 **Levitsky J**, Duddempudi AT, Lakeman FD, Whitley RJ, Luby JP, Lee WM, Fontana RJ, Blei AT, Ison MG. Detection and diagnosis of herpes simplex virus infection in adults with acute liver failure. *Liver Transpl* 2008; **14**: 1498-1504 [PMID: 18825709 DOI: 10.1002/lt.21567]
61 **Beersma MF**, Verjans GM, Metselaar HJ, Osterhaus AD, Berrington WR, van Doornum GJ. Quantification of viral DNA and liver enzymes in plasma improves early diagnosis and management of herpes simplex virus hepatitis. *J Viral Hepat* 2011; **18**: e160-e166 [PMID: 20704650 DOI: 10.1111/j.1365-2893.2010.01352.x]
62 **Buchel E**, Van Steenbergen W, Nevens F, Fevery J. Improvement of autoimmune hepatitis during pregnancy followed by flare-up after delivery. *Am J Gastroenterol* 2002; **97**: 3160-3165 [PMID: 12492204 DOI: 10.1111/j.1572-0241.2002.07124.x]
63 **Candia L**, Marquez J, Espinoza LR. Autoimmune hepatitis and pregnancy: a rheumatologist's dilemma. *Semin Arthritis Rheum* 2005; **35**: 49-56 [PMID: 16084224 DOI: 10.1016/j.semarthrit.2005.03.002]
64 **Heneghan MA**, Norris SM, O'Grady JG, Harrison PM, McFarlane IG. Management and outcome of pregnancy in autoimmune hepatitis. *Gut* 2001; **48**: 97-102 [PMID: 11115829]
65 **Schramm C**, Herkel J, Beuers U, Kanzler S, Galle PR, Lohse AW. Pregnancy in autoimmune hepatitis: outcome and risk factors. *Am J Gastroenterol* 2006; **101**: 556-560 [PMID: 16464221 DOI: 10.1111/j.1572-0241.2006.00479.x]
66 **Westbrook RH**, Yeoman AD, Kriese S, Heneghan MA. Outcomes of pregnancy in women with autoimmune hepatitis. *J Autoimmun* 2012; **38**: J239-J244 [PMID: 22261501 DOI: 10.1016/j.jaut.2011.12.002]
67 **Terrabuio DR**, Abrantes-Lemos CP, Carrilho FJ, Cançado EL. Follow-up of pregnant women with autoimmune hepatitis: the disease behavior along with maternal and fetal outcomes. *J Clin Gastroenterol* 2009; **43**: 350-356 [PMID: 19077726 DOI: 10.1097/mcg.0b013e318176b8c5]
68 **Manns MP**, Czaja AJ, Gorham JD, Krawitt EL, Mieli-Vergani G, Vergani D, Vierling JM. Diagnosis and management of autoimmune hepatitis. *Hepatology* 2010; **51**: 2193-2213 [PMID: 20513004 DOI: 10.1002/hep.23584]
69 **Goh SK**, Gull SE, Alexander GJ. Pregnancy in primary biliary cirrhosis complicated by portal hypertension: report of a case and review of the literature. *BJOG* 2001; **108**: 760-762 [PMID: 11467706]
70 **Olsson R**, Lööf L, Wallerstedt S. Pregnancy in patients with primary biliary cirrhosis--a case for dissuasion? The Swedish Internal Medicine Liver Club. *Liver* 1993; **13**: 316-318 [PMID: 8295495]
71 **Lindor KD**, Gershwin ME, Poupon R, Kaplan M, Bergasa NV, Heathcote EJ. Primary biliary cirrhosis. *Hepatology* 2009; **50**: 291-308 [PMID: 19554543 DOI: 10.1002/hep.22906]
72 **Wellge BE**, Sterneck M, Teufel A, Rust C, Franke A, Schreiber S, Berg T, Günther R, Kreisel W, Zu Eulenburg C, Braun F, Beuers U, Galle PR, Lohse AW, Schramm C. Pregnancy in primary sclerosing cholangitis. *Gut* 2011; **60**: 1117-1121 [PMID: 21339205 DOI: 10.1136/gut.2010.228924]
73 **Lee NM**, Brady CW. Liver disease in pregnancy. *World J Gastroenterol* 2009; **15**: 897-906 [PMID: 19248187]
74 **Sinha S**, Taly AB, Prashanth LK, Arunodaya GR, Swamy HS. Successful pregnancies and abortions in symptomatic

and asymptomatic Wilson's disease. *J Neurol Sci* 2004; **217**: 37-40 [PMID: 14675607]
75 **Brewer GJ**, Johnson VD, Dick RD, Hedera P, Fink JK, Kluin KJ. Treatment of Wilson's disease with zinc. XVII: treatment during pregnancy. *Hepatology* 2000; **31**: 364-370 [PMID: 10655259 DOI: 10.1002/hep.510310216]
76 **Solomon L**, Abrams G, Dinner M, Berman L. Neonatal abnormalities associated with D-penicillamine treatment during pregnancy. *N Engl J Med* 1977; **296**: 54-55 [PMID: 830278]
77 **Tanaka H**, Yamanouchi M, Imai S, Hayashi Y. Low copper and brain abnormalities in fetus from triethylene tetramine dihydrochloride-treated pregnant mouse. *J Nutr Sci Vitaminol* (Tokyo) 1992; **38**: 545-554 [PMID: 1304599]
78 **Roberts EA**, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. *Hepatology* 2008; **47**: 2089-2111 [PMID: 18506894 DOI: 10.1002/hep.22261]
79 **Scott LD**. Gallstone disease and pancreatitis in pregnancy. *Gastroenterol Clin North Am* 1992; **21**: 803-815 [PMID: 1478736]
80 **Everson GT**. Gastrointestinal motility in pregnancy. *Gastroenterol Clin North Am* 1992; **21**: 751-776 [PMID: 1478733]
81 **Cosenza CA**, Saffari B, Jabbour N, Stain SC, Garry D, Parekh D, Selby RR. Surgical management of biliary gallstone disease during pregnancy. *Am J Surg* 1999; **178**: 545-548 [PMID: 10670869]
82 **Al-Fozan H**, Tulandi T. Safety and risks of laparoscopy in pregnancy. *Curr Opin Obstet Gynecol* 2002; **14**: 375-379 [PMID: 12151826]
83 **Jelin EB**, Smink DS, Vernon AH, Brooks DC. Management of biliary tract disease during pregnancy: a decision analysis. *Surg Endosc* 2008; **22**: 54-60 [PMID: 17713817 DOI: 10.1007/s00464-007-9220-1]
84 **Kahaleh M**, Hartwell GD, Arseneau KO, Pajewski TN, Mullick T, Isin G, Agarwal S, Yeaton P. Safety and efficacy of ERCP in pregnancy. *Gastrointest Endosc* 2004; **60**: 287-292 [PMID: 15278066]
85 **Tang SJ**, Mayo MJ, Rodriguez-Frias E, Armstrong L, Tang L, Sreenarasimhaiah J, Lara LF, Rockey DC. Safety and utility of ERCP during pregnancy. *Gastrointest Endosc* 2009; **69**: 453-461 [PMID: 19136111 DOI: 10.1016/j.gie.2008.05.024]
86 **Russell MA**, Craigo SD. Cirrhosis and portal hypertension in pregnancy. *Semin Perinatol* 1998; **22**: 156-165 [PMID: 9638910]
87 **Tan J**, Surti B, Saab S. Pregnancy and cirrhosis. *Liver Transpl* 2008; **14**: 1081-1091 [PMID: 18668664 DOI: 10.1002/lt.21572]
88 **Sandhu BS**, Sanyal AJ. Pregnancy and liver disease. *Gastroenterol Clin North Am* 2003; **32**: 407-436, ix [PMID: 12635424]
89 **Terkivatan T**, de Wilt JH, de Man RA, Ijzermans JN. Management of hepatocellular adenoma during pregnancy. *Liver* 2000; **20**: 186-187 [PMID: 10847490]
90 **Cobey FC**, Salem RR. A review of liver masses in pregnancy and a proposed algorithm for their diagnosis and management. *Am J Surg* 2004; **187**: 181-191 [PMID: 14769302 DOI: 10.1016/j.amjsurg.2003.11.016]
91 **Noels JE**, van Aalten SM, van der Windt DJ, Kok NF, de Man RA, Terkivatan T, Ijzermans JN. Management of hepatocellular adenoma during pregnancy. *J Hepatol* 2011; **54**: 553-558 [PMID: 21094555 DOI: 10.1016/j.jhep.2010.07.022]
92 **Hill MA**, Albert T, Zieske A, Levine EA. Successful resection of multifocal hepatic adenoma during pregnancy. *South Med J* 1997; **90**: 357-361 [PMID: 9076315]
93 **Fujita S**, Kushihata F, Herrmann GE, Mergo PJ, Liu C, Nelson D, Fujikawa T, Hemming AW. Combined hepatic resection and radiofrequency ablation for multiple hepatic adenomas. *J Gastroenterol Hepatol* 2006; **21**: 1351-1354 [PMID: 16872326 DOI: 10.1111/j.1440-1746.2006.03184.x]
94 **Louie-Johnsun MW**, Hewitt PM, Perera DS, Morris DL. Fibrolamellar hepatocellular carcinoma in pregnancy. *HPB* (Oxford) 2003; **5**: 191-193 [PMID: 18332985 DOI: 10.1080/13651820310015310]
95 **Gemer O**, Segal S, Zohav E. Pregnancy in a patient with fibrolamellar hepatocellular carcinoma. *Arch Gynecol Obstet* 1994; **255**: 211-212 [PMID: 7695368]
96 **Ang CS**, Do RK, Shamseddine A, O'Reilly EM, Haydar A, Al-Olayan A, Faraj W, Boulos F, Naghy M, Makanjoula D, Farran H, Sibai H, Wehbe D, Kelsen DP, Abou-Alfa GK. A young woman with liver cancer. *Gastrointest Cancer Res* 2013; **6**: 17-21 [PMID: 23505574]
97 **Lau WY**, Leung WT, Ho S, Lam SK, Li CY, Johnson PJ, Williams R, Li AK. Hepatocellular carcinoma during pregnancy and its comparison with other pregnancy-associated malignancies. *Cancer* 1995; **75**: 2669-2676 [PMID: 7743468]
98 **Grant WJ**, McCashland T, Botha JF, Shaw BW, Sudan DL, Mejia A, Iyer K, Langnas AN. Acute Budd-Chiari syndrome during pregnancy: surgical treatment and orthotopic liver transplantation with successful completion of the pregnancy. *Liver Transpl* 2003; **9**: 976-979 [PMID: 12942460 DOI: 10.1053/jlts.2003.50134]
99 **Fickert P**, Ramschak H, Kenner L, Hoefler G, Hinterleitner TA, Petritsch W, Klimpfinger M, Krejs GJ, Stauber RE. Acute Budd-Chiari syndrome with fulminant hepatic failure in a pregnant woman with factor V Leiden mutation. *Gastroenterology* 1996; **111**: 1670-1673 [PMID: 8942748]
100 **DeLeve LD**, Valla DC, Garcia-Tsao G. Vascular disorders of the liver. *Hepatology* 2009; **49**: 1729-1764 [PMID: 19399912 DOI: 10.1002/hep.22772]

P- Reviewers: Devarbhavi H, Invernizzi P, Morales-Gonzalez JA, Rigato I **S- Editor:** Gou SX **L- Editor:** A **E- Editor:** Wang CH

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ISSN 1007-9327
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