

Society for Maternal-Fetal Medicine consult series #56: Hepatitis C in pregnancy: updated guidelines

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Introduction

In the United States, the estimated prevalence of antenatal hepatitis C virus (HCV) infection is 1% to 4% in single-center studies.¹ A national multicenter prospective cohort study estimated an HCV antibody seroprevalence of 0.24% among an obstetric population screened between 2012 and 2015.² The primary mode of HCV transmission is percutaneous exposure to blood from injection of illicit drugs. Other modes of transmission include sharing of contaminated devices for noninjection drug use, exposure to infected blood, and sexual intercourse.^{3,4} Vertical transmission is the leading cause of HCV infection in children.⁵

HCV can cause both acute and chronic hepatitis. The first 6 months after exposure to HCV constitute the acute stage of infection.⁶ For the 25% of cases that are symptomatic, symptoms include abdominal pain, nausea, anorexia, jaundice, and malaise.⁷ Those

who do not clear the virus and do not receive treatment will develop chronic HCV infection.⁸ As with the acute stage of infection, chronic HCV infection is usually asymptomatic. Chronic infection accounts for most HCV-associated morbidity and mortality.

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HCV infection is associated with higher rates of gestational diabetes, preterm birth, and low birth weight.⁹⁻¹³ However, these associations are often complicated by confounding factors such as maternal age, race, substance use, and prenatal care usage.^{14,15} **Antenatal testing is not indicated in the setting of HCV diagnosis alone (grade 2C).**

Intrahepatic cholestasis of pregnancy (ICP) is more prevalent in patients with

chronic HCV infection than in uninfected patients.^{16,17} **We suggest screening for viral hepatitis in patients with a diagnosis of ICP at an early gestational age or with significant elevations of bile acids (grade 2C).** We empirically suggest that this screening be performed if the diagnosis of ICP is made at less than 24 weeks of gestation or if bile acids are greater than or equal to 100 $\mu\text{mol/L}$.

Screening

Screening recommendations are changing to be more inclusive because of an increase in the prevalence of HCV infection among women of reproductive age and emerging data suggesting that the majority of neonates are not identified with the current risk-based screening strategies.¹⁸⁻²⁰ A recent cost-analysis model demonstrated that universal prenatal HCV screening improved health outcomes of people with HCV infection and identification of neonates with infection and was cost-effective, even



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in areas with very low prevalence.²¹ The Centers for Disease Control and Prevention (CDC) now recommends universal screening for HCV during pregnancy.²² The United States Preventive Services Task Force (USPSTF) also recommends screening in all individuals ages 18 to 79 and specifically notes that pregnant women should be screened but does not recommend a frequency.²³ Early identification of HCV-positive patients during pregnancy can potentially facilitate more efficient linkage to care and treatment in the postpartum period, because none of the antiviral therapies recommended for HCV infection are approved for use during pregnancy. **We recommend that obstetric providers screen all pregnant patients for HCV by testing for anti-HCV antibodies in every pregnancy (grade 1B).** Screening in the first trimester would theoretically identify the most patients at the earliest opportunity.

Diagnosis of HCV infection depends on detection of anti-HCV antibodies and HCV RNA. Anti-HCV antibodies usually develop 2 to 6 months after exposure, during the acute phase of infection, and persist throughout life.²⁴ HCV viremia or the presence of HCV RNA indicate active infection and can be detected 1 to 3 weeks after exposure.^{25,26}

Treatment and outcomes

The Box presents recommended labs for confirmed active HCV infection in pregnancy. Considering common risk factors, **we suggest that obstetric care providers screen HCV-positive pregnant patients for other sexually transmitted infections (if not done previously), including HIV, syphilis, gonorrhea, chlamydia, and hepatitis B virus (HBV) (grade 2C).** Pregnant patients with HCV should be screened

for immunity to hepatitis A virus (HAV). **We recommend vaccination against HAV and HBV (if not immune) for patients with HCV (grade 1B).**

Among nonpregnant women, direct-acting antiviral (DAA) regimens are first-line treatments.³ Currently, none of the antiviral therapies recommended for HCV infection are approved for use during pregnancy.²⁷ Until more data exist, if a patient becomes pregnant while taking one of the DAA therapies, animal data do not suggest teratogenic risk but patients should be counseled that human data are lacking.^{28,29} In these scenarios, shared decision-making regarding risks and benefits of cessation versus continuation should occur. **We recommend that DAA regimens should be initiated only in the setting of a clinical trial during pregnancy and that individuals who become pregnant while taking a DAA should be counseled in a shared decision-making framework about the risks and benefits of continuation (grade 1C).** Referral to a hepatologist or infectious disease specialist during pregnancy for patients with HCV may be considered to expedite therapy following pregnancy.

Methods to reduce vertical transmission

Amniocentesis does not appear to increase the risk of vertical transmission, although this conclusion is based on small sample sizes and limited data that have not addressed the potential impact of viral load.³⁰ No studies have been published on the risk of vertical transmission of HCV with other prenatal testing modalities, including chorionic villus sampling. **We suggest that if prenatal diagnostic testing is requested, patients be counseled**

Box. Recommended Labs for Confirmed Active HCV Infection in Pregnancy

- Liver function tests (AST, ALT, bilirubin)
- Albumin
- Platelet count
- Prothrombin time
- Quantitative HCV RNA
- HCV genotype (if not previously obtained)
- STI screening (HIV, syphilis, gonorrhea, chlamydia, and HBV)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HCV, hepatitis C virus; STI, sexually transmitted infection.

that data regarding the risk of vertical transmission are reassuring but limited (grade 2C). When the need or desire for diagnostic testing arises in patients with HCV, shared decision-making regarding the limited data should occur.

Vaginal delivery has not been shown to be a risk factor for vertical transmission of HCV.^{31,32} Because all published studies on the mode of delivery and the risk of vertical transmission of HCV are observational, and most did not assess viral load at the time of delivery, these results should be interpreted cautiously.³³ **We recommend against cesarean delivery solely for the indication of HCV (grade 1B).**

Several factors in labor management may be associated with an increased risk of vertical transmission of HCV, namely prolonged rupture of membranes, internal fetal monitoring, and episiotomy.³⁴⁻³⁷ **We suggest that obstetric care providers avoid internal fetal monitors and early artificial rupture of membranes when managing labor in patients with HCV, unless necessary**

in the course of management (ie, when unable to trace the fetal heart rate with external monitors and the alternative is proceeding with cesarean delivery) (grade 2B).

Expectant management of ruptured membranes should be avoided at term. Usual obstetric management for preterm premature rupture of the membranes should not be altered because of maternal HCV infection. It is unclear whether a patient with a positive HCV antibody and a negative viral load should be managed in labor in the same fashion as one with a detectable viral load. We suggest that if the confirmatory HCV antibody test result were negative that the result be considered a false positive; thus, the additional precautions suggested above are likely unnecessary. However, if the confirmatory test result is positive or if the test was not performed, then until further data are available, it may be safest in labor to follow the same suggestions as in a patient with a positive viral load because of the theoretical possibility of intermittent viral shedding.

Postnatal care related to HCV

Breastfeeding does not appear to affect the risk of vertical transmission of HCV.³¹

We recommend that HCV status not alter standard breastfeeding counseling and recommendations unless nipples are cracked or bleeding (grade 1A). In patients with cracked or bleeding nipples, breast milk should be expressed and discarded. ■

FOR REFERENCES VISIT

contemporaryobgyn.net/HCP-guidelines

Summary of Recommendations

Number	Recommendations	Grade
1	Antenatal testing is not indicated in the setting of HCV diagnosis alone.	2C Weak recommendation, low-quality evidence
2	We suggest screening for viral hepatitis in patients with a diagnosis of ICP at an early gestational age or with significant elevation of bile acids.	2C Weak recommendation, low-quality evidence
3	We recommend that obstetric providers screen all pregnant patients for HCV by testing for anti-HCV antibodies in every pregnancy.	1B Strong recommendation, moderate-quality evidence
4	We suggest that obstetric care providers screen HCV-positive pregnant patients for other sexually transmitted infections (if not done previously), including HIV, syphilis, gonorrhea, chlamydia, and HBV.	2C Weak recommendation, low-quality evidence
5	We recommend vaccination against HAV and HBV (if not immune) for patients with HCV.	1B Strong recommendation, moderate-quality evidence
6	We recommend that DAA regimens only be initiated in the setting of a clinical trial during pregnancy and that individuals who become pregnant while taking a DAA be counseled in a shared decision-making framework about the risks and benefits of continuation.	1C Strong recommendation, low-quality evidence
7	We suggest that if prenatal diagnostic testing is requested, patients are counseled that data regarding the risk of vertical transmission are reassuring but limited.	2C Weak recommendation, low-quality evidence
8	We recommend against cesarean delivery solely for the indication of HCV.	1B Strong recommendation, moderate-quality evidence
9	We suggest that obstetric care providers avoid internal fetal monitors and early artificial rupture of membranes when managing labor in patients with HCV, unless necessary in the course of management (ie, when unable to trace the fetal heart rate with external monitors and the alternative is proceeding with cesarean delivery).	2B Weak recommendation, moderate-quality evidence
10	We recommend that HCV status not alter standard breastfeeding counseling and recommendations unless nipples are cracked or bleeding.	1A Strong recommendation, high-quality evidence

DAA, direct-acting antiviral; HBV, hepatitis B virus; HCV, hepatitis C virus; ICP, intrahepatic cholestasis of pregnancy.