

HCV in Pregnancy

Testing

Recommendation for Universal Hepatitis C Screening in Pregnancy	
RECOMMENDED	RATING 
As part of prenatal care, all pregnant persons should be tested for HCV infection with each pregnancy, ideally at the initial visit. (See Recommendations for Initial HCV Testing and Follow-Up.)	I, B

It has been estimated that up to 29,000 HCV-infected women gave birth each year from 2011 to 2014 ([Ly, 2017](#)). Additionally, there has been an increase in HCV among young adults, including women of childbearing age ([Watts, 2017](#)); ([Koneru, 2016](#)); ([Kuncio, 2016](#)). Identifying HCV infection as women engage in prenatal care would allow for appropriate assessment of liver disease status and ideally facilitate linkage to HCV care after delivery. In addition, prenatal HCV diagnosis is a prerequisite for appropriate screening and care for exposed children. Risk factor-based HCV screening has never been shown to be effective ([Kuncio, 2015](#)); ([Waruingi, 2015](#)); ([Fernandez, 2016](#)) and inconsistent screening and counseling practices have been reported among obstetricians and gynecologists ([Boaz, 2003](#)). Consequently, the US Preventative Task Force ([Owens, 2020](#)), US Centers for Disease Control ([Schillie, 2020](#)), have published recommendations for universal HCV screening of all adults, including screening during prenatal care. Recently, the American College of Obstetricians and Gynecologists have issued the Practice Advisory to test all women at the beginning of each pregnancy for HCV (<https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2021/05/routine-hepatitis-c-virus-screening-in-pregnant-individuals>). Testing at the initiation of prenatal care is considered optimal to maximize opportunities for education, referral, and appropriate testing for the exposed infant. Early identification is key as women living with HCV and their exposed infants are at significant risk for not linking to appropriate HCV evaluation or care. Women should be tested with an HCV-antibody test. If positive, this should be followed with testing for HCV RNA.

HCV-infected pregnant persons should be linked to care so that antiviral treatment can be initiated at the appropriate time (see [Testing and Linkage to Care](#) section). Recent modeling studies demonstrate that universal HCV screening in pregnancy is cost-effective and would reduce long-term morbidity with linkage to care and treatment ([Tasillo, 2019](#)). Infants of HCV-infected women should be tested and followed as described in the [HCV in Children](#) section.

The Society for Maternal-Fetal Medicine recommends several obstetrical practices in women with HCV infection, including preference for amniocentesis over chorionic villus sampling when invasive prenatal diagnostic testing is indicated, as well as avoidance of internal fetal monitoring during labor, prolonged rupture of membranes, and episiotomies ([Hughes, 2017](#)).

Whom to Treat

Recommendation Regarding HCV Treatment and Pregnancy

RECOMMENDED	RATING 
For women of reproductive age with known HCV infection, antiviral therapy is recommended before considering pregnancy, whenever practical and feasible, to reduce the risk of HCV transmission to future offspring.	I, B

Women of reproductive age with HCV should be counseled about the benefit of antiviral treatment prior to pregnancy to improve the health of the mother and eliminate the low risk of mother-to-child transmission (MTCT). People who become pregnant while on DAA therapy (with or without ribavirin) should discuss the risks versus benefits of continuing treatment with their physicians. Ribavirin is contraindicated in pregnancy due to its known teratogenicity. In addition, the risk for teratogenicity persists for up to 6 months after ribavirin cessation and applies to women taking ribavirin and female partners of men taking ribavirin. If exposed to ribavirin, they should also have their maternal and fetal outcomes reported to the ribavirin pregnancy registry (also see [Recommended Monitoring for Pregnancy-Related Issues Prior to and During Antiviral Therapy That Includes Ribavirin](#)).

There are no large-scale clinical trials evaluating the safety of direct-acting antivirals (DAAs) in pregnancy. A small study evaluating the pharmacokinetics of ledipasvir/sofosbuvir in pregnancy demonstrated 100% SVR12 and no safety concerns. Similarly, an international case series of 15 pregnant persons treated with ledipasvir/sofosbuvir reported 100% SVR12 and no early safety concerns in the women or their infants ([Yattoo, 2018](#)); ([Chappell, 2020](#)). Currently, there are no available data on the use of pangenotypic regimens during pregnancy.

Despite the lack of a recommendation, treatment can be considered during pregnancy on an individual basis after a patient-physician discussion about the potential risks and benefits.

Monitoring During Pregnancy

Recommendations for Monitoring HCV-Infected Women During Pregnancy

RECOMMENDED	RATING 
HCV RNA and routine liver function tests are recommended at initiation of prenatal care for HCV-antibody-positive pregnant persons to assess the risk of mother-to-child transmission (MTCT) and severity of liver disease.	I, B
All pregnant persons with HCV infection should receive prenatal and intrapartum care that is appropriate for their individual obstetric risk(s) as there is no currently known intervention to reduce MTCT.	I, B
In HCV-infected pregnant persons with pruritus or jaundice, there should be a high index of suspicion for intrahepatic cholestasis of pregnancy (ICP) with subsequent assessment of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and serum bile acids.	I, B
HCV-infected persons with cirrhosis should be counseled about the increased risk of adverse maternal and perinatal outcomes. Antenatal and perinatal care should be coordinated with a maternal-fetal medicine (ie, high-risk pregnancy) obstetrician.	I, B

Recommendations for Monitoring HCV-Infected Women During Pregnancy

Pregnancy Impact on HCV Infection

Pregnancy itself does not appear to negatively affect chronic HCV infection. In general, serum ALT levels decrease during the first and third trimesters of pregnancy and increase after delivery. HCV RNA levels rise during the first and third trimesters, reaching a peak during the third trimester, and decrease postpartum ([Conte, 2000](#)); ([Gervais, 2000](#)). These effects are likely due to the immunosuppressive effects of pregnancy and increased maternal plasma volume. HCV-infected pregnant persons have a higher incidence of intrahepatic cholestasis of pregnancy (ICP) (pooled OR 20.40 [95% CI, 9.39-44.33, $I^2=55\%$]) based on a meta-analysis of 3 studies when compared to noninfected pregnant persons ([Wijarnpreecha, 2017](#)). ICP is associated with an increased rate of adverse maternal and fetal outcomes; all patients with this syndrome should be immediately referred to a high-risk obstetrical specialist for monitoring and treatment.

HCV Infection Impact on Pregnancy and Perinatal Outcomes

Although some studies show an increased risk of adverse perinatal outcomes (eg, preterm delivery, low birth weight infants, and congenital anomalies) with maternal HCV infection, these risks are confounded by comorbid conditions, such as substance use ([Connell, 2011](#)). However, pregnant persons with cirrhosis are at increased risk for poor maternal outcomes (ie, preeclampsia, cesarean section, hemorrhagic complication, and death) and neonatal outcomes (ie, preterm delivery, low birth weight, and neonatal death) ([Puljic, 2016](#)); ([Tan, 2008](#)). Women with cirrhosis should be counseled about these increased risks and care should be coordinated with specialists in maternal-fetal medicine.

Hepatitis C MTCT occurs at an overall rate of 5% to 15% ([Jhaveri, 2015](#)); ([Shebl, 2009](#)); ([Mast, 2005](#)); ([Ceci, 2001](#)), with the number that progress to chronic infection being 3% to 5%. No specific risk factor predicts transmission and no specific intervention (eg, antiviral, mode of delivery, or others) has been demonstrated to reduce HCV transmission—except for suppression of HIV replication in women with HIV/HCV coinfection ([Checa Cabot, 2013](#)). Given the potential associated risk of MTCT, it is advisable to avoid invasive procedures (eg, fetal scalp monitors and forceps delivery).

The neuropsychiatric and systemic side effects of interferon-based agents and the pregnancy category X rating of ribavirin made studies involving these drugs to interrupt MTCT untenable for safety reasons. It is important to note that DAAs have not been formally studied as a way to interrupt MTCT. DAAs have not demonstrated significant toxicity in animal studies, and antiviral medication use has become the standard of care for people with HIV and hepatitis B infection. Therefore, it is realistic to think that DAAs could be used in the future to interrupt MTCT. However, with a low transmission rate, improved methods to identify mothers who are likely to transmit are needed to reduce the number needed to treat below 20 to prevent 1 transmission event. DAA therapy is not recommended during pregnancy to reduce MTCT due to the current lack of safety and efficacy data.

Postpartum Issues

Recommendations Regarding Breastfeeding and Postpartum Care for HCV-Infected Women

RECOMMENDED	RATING 
Breastfeeding is not contraindicated in women with HCV infection, except when the mother has cracked, damaged, or bleeding nipples, or in the context of HIV coinfection.	I, B
Women with HCV infection should have their HCV RNA reevaluated after delivery to assess for spontaneous clearance.	I, B

Recommendations Regarding Breastfeeding and Postpartum Care for HCV-Infected Women

HCV and Breastfeeding

Breastfeeding is not a risk for HCV MTCT ([CDC, 1998](#)) with studies showing similar rates of maternal infection in breast-fed and bottle-fed infants ([Resti, 1998](#)). However, given the associated risks of HCV transmission with blood exposure and HIV transmission with breastfeeding, it is recommended that HCV-infected women who breastfeed abstain from doing so while their nipples are cracked, damaged, or bleeding, and in the context of HIV/HCV coinfection.

Spontaneous Clearance in the Postpartum Period

HCV RNA levels can fluctuate during pregnancy and the postpartum period. The most frequently observed pattern is a steady rise in HCV RNA levels during pregnancy followed by a slight or significant drop (>3 to $4 \log_{10}$) in the postpartum period ([Lin, 2000](#)). This is most likely due to the release of tolerance in HCV-specific T lymphocyte responses that develop during pregnancy ([Honegger, 2013](#)). Spontaneous clearance of HCV can occur in the postpartum period. Previous studies with small numbers of patients demonstrated that up to 10% of postpartum women became HCV RNA undetectable ([Honegger, 2013](#)); ([Hattori, 2003](#)); ([Lin, 2000](#)). A recent study from Egypt demonstrated a 25% rate of spontaneous resolution that was strongly associated with the favorable IL28B allele ([Hashem, 2017](#)).

Given these findings, women should have their HCV RNA re-evaluated after delivery. In that time, HCV RNA could become undetectable or rebound to prepregnancy levels. The possibility of spontaneous viral clearance should be considered for any woman who is being assessed for DAA treatment in the postpartum period.

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