Society for Maternal-Fetal Medicine (SMFM) Consult Series #56: Hepatitis C in Pregnancy: Updated Guidelines

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Condensation: This Consult reviews the current literature on hepatitis C in pregnancy and provides recommendations based on the available evidence.

Abstract:

In the United States, it is estimated that 1% to 4% of pregnant women are infected with hepatitis C virus, which carries approximately a 5% risk of transmission from mother to infant. Hepatitis C virus can be transmitted to the infant in utero or during the peripartum period, and infection during pregnancy is associated with an increased risk of adverse fetal outcomes, including fetal growth restriction and low birthweight. The purpose of this document is to discuss the current evidence, provide updated recommendations regarding screening, review treatment, and address management of hepatitis C virus during pregnancy. The following are the Society for Maternal-Fetal Medicine's recommendations: (1) Antenatal testing is not indicated in the setting of hepatitis C virus diagnosis alone (GRADE 2C); (2) we suggest screening for viral hepatitis in patients with a diagnosis of intrahepatic cholestasis of pregnancy at an early gestational age or with significant elevations of bile acids (GRADE 2C); (3) we recommend that obstetric providers screen all pregnant patients for hepatitis C virus by testing for anti-hepatitis C virus antibodies in every pregnancy (GRADE 1B); (4) we suggest that obstetric care providers screen hepatitis C virus-positive pregnant patients for other sexually transmitted infections (if not done previously), including human immunodeficiency virus, syphilis, gonorrhea, chlamydia, and hepatitis B virus (GRADE 2C); (5) we recommend vaccination against hepatitis A and B viruses (if not immune) for patients with hepatitis C virus (GRADE 1B); (6) we recommend that direct-acting antiviral regimens only be initiated in the setting of a clinical trial during pregnancy and that people who become pregnant while taking a direct-acting antiviral should be counseled in a shared decision making framework about the risks and benefits of continuation (GRADE 1C); (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 (GRADE 2C); (8) we recommend against cesarean delivery solely for the indication of hepatitis C virus (GRADE 1B); (9) we suggest that obstetric care providers avoid internal fetal monitors and early artificial rupture of membranes when managing labor in patients with hepatitis C virus 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); (10) we recommend that hepatitis C virus status not alter standard breastfeeding counseling and recommendations unless nipples are cracked or bleeding (GRADE 1A).

Key Words: antiviral therapy, HCV, Hepatitis C virus, screening, vertical transmission

Epidemiology

Worldwide, up to 8% of pregnant women are infected with hepatitis C virus (HCV).[1] In the United States, the estimated prevalence of antenatal HCV infection is 1% to 4% in single-center studies.[2] Between 2009 and 2017, the prevalence of maternal HCV increased 161% in the United States,[3] coinciding with the emergence of the opioid epidemic.[4,5] A recent national multicenter prospective cohort study from the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development Maternal-Fetal Medicine Units Network (MFMU) estimated a seroprevalence of 0.24% among all women.[6] Because of concern for the increasing prevalence of HCV in pregnancy and its implications for pregnant patients and their newborns, updated guidelines for universal screening in pregnancy have been issued by the Centers for Disease

Control and Prevention (CDC) and the US Preventative Services Task Force (USPSTF).[7,8] The Society for Maternal-Fetal Medicine (SMFM) endorses alignment with these recommendations.

The primary mode of HCV transmission is percutaneous exposure to blood from injection of illicit drugs. Other modes of transmission include vertical transmission (mother to child); sharing of contaminated devices for noninjection drug use; exposure to infected blood through occupational exposures, tattoo needles, or other means; and sexual intercourse (specifically increased in the setting of multiple partners).[9,10]

Two primary concerns related to HCV in pregnancy are addressed in this document: (1) effect of pregnancy on maternal disease progression; and (2) effect of the disease on pregnancy outcomes, including mother-to-infant transmission of HCV.

What is the natural course of HCV infection?

HCV can cause both acute and chronic hepatitis. The first 6 months after exposure to HCV is referred to as acute HCV infection. Acute HCV infection is asymptomatic in 75% of cases; when symptoms occur, they include abdominal pain, nausea, anorexia, jaundice, and malaise.[11] Without treatment, approximately 15% to 45% of infected individuals spontaneously clear HCV within 6 months of infection.[12] Those who do not clear the virus, and do not receive treatment, will develop chronic HCV infection. Chronic infection accounts for most HCV-associated morbidity and mortality. As with the acute stage of infection, chronic HCV infection is usually asymptomatic, although it can cause progressive liver damage. Without treatment, 15% to 30% of patients with chronic HCV infection develop cirrhosis within 20 years, though rates vary widely by study; 27% of those with cirrhosis develop hepatocellular carcinoma (HCC) within 10 years.[13-15] In comparison, among patients with cirrhosis treated with antiviral medications and

who achieve a sustained virological response (SVR), only 5% develop HCC within 10 years.[16] HCC is a primary cause of mortality from HCV infection,[17] with a median length of survival from diagnosis of 20 months.[18] In addition, there is a clear causal relationship between chronic HCV infection and extrahepatic diseases, including cryoglobulinemic vasculitis, lymphoma, cardiovascular diseases, insulin resistance, and type 2 diabetes mellitus.[19]

What is the impact of pregnancy on chronic hepatitis C?

Data regarding the impact of pregnancy on chronic HCV are mixed and inconclusive. Multiple studies have found that serum levels of alanine aminotransferase (ALT) typically decrease during the second and third trimesters of pregnancies complicated by HCV infection and then return to pre-pregnancy levels after delivery.[20-23] In contrast, serum levels of HCV RNA may increase in infected patients during the second and third trimesters of pregnancy. A case-control study of 26 HCV-infected pregnant women compared with 12 HCV-infected nonpregnant women demonstrated a statistically significant increase in HCV RNA among the pregnant women during the second and third trimesters.[21] In contrast, in an observational study of 65 HCV-positive women followed through pregnancy and postpartum, there were no changes in the viral load.[23] It is biologically plausible that HCV RNA levels could increase during pregnancy due to a relative alteration of the maternal immune response. Because hepatocellular damage caused by chronic HCV infection may be immune-mediated rather than directly caused by viral cytotoxicity, alterations of the maternal immune response in pregnancy may reduce the amount of hepatocellular damage caused by HCV, which may account for the observed decrease in ALT levels.[21]

Histological evidence of the effects of pregnancy on HCV infection is also inconclusive. Some data suggest that pregnancy may be associated with a decrease in HCV-mediated hepatic injury. Di Martino et al showed a beneficial effect of pregnancy on the progression of fibrosis, as determined by liver biopsy, in a retrospective cohort study of 157 pregnant women with chronic HCV infection.[24] Specifically, they found that a history of pregnancy was independently associated with a lower likelihood of fibrosis progression.[24] In contrast, a small case-control study by Fontaine et al compared liver biopsy samples from 12 HCV-positive women obtained before and after delivery, with samples from 12 nonpregnant HCV-positive women as controls.[25] The mean period between initial and final biopsies was 4 years. During this time, 83% of pregnant patients showed deterioration in their necroinflammatory score, and 42% showed deterioration in their fibrosis score. In comparison, the rates for controls were 25% and 8%, respectively.[25] These conflicting data highlight a need for additional study of the progression of fibrosis during pregnancy.

What is the impact of HCV on obstetric and neonatal outcomes?

Although HCV infection is associated with both adverse maternal and neonatal outcomes, many confounding comorbidities in the pregnant population often complicate these associations. A population-based, retrospective cohort study from Washington state compared 506 HCV-positive pregnant women with 2022 HCV-negative pregnant controls. In multivariable analysis, after controlling for maternal age, race, tobacco use, alcohol use, drug use, and prenatal care usage, it was found that infection with HCV was associated with small-for-gestational-age birth weight, low birth weight less than 2500 g, admission to the neonatal intensive care unit, and need for assisted ventilation.[26] Another population-based retrospective cohort study of all births in

Florida compared 988 HCV-positive women with 1,669,370 controls. In multivariate analysis, after adjusting for maternal age, marital status, educational level, maternal race/ethnicity, tobacco use during pregnancy, drug abuse during pregnancy, and parity, it was found that HCV infection was associated with poor birth outcomes, including preterm birth and low birth weight.[27] A recent systematic review and meta-analysis, including these 2 studies and 5 others, reported that maternal HCV infection was associated with fetal growth restriction and low birth weight (Figure 1).[28] Based on these findings, **antenatal testing is not indicated in the setting of HCV diagnosis alone (GRADE 2C).**

The studies mentioned above by Pergam et al and Connell et al, along with a population-based cohort study using the Nationwide Inpatient Sample, report higher rates of gestational diabetes in HCV-infected women compared with uninfected women.[26,27,29] However, in the Pergam et al study, this association was limited to women with excessive weight gain during pregnancy.[26] In another population-based, retrospective cohort study, Salemi et al found that maternal HCV-infection was associated with infant feeding difficulties and other adverse neonatal outcomes, including cephalohematoma, brachial plexus injury, fetal distress, intraventricular hemorrhage, and neonatal seizures.[30]

Intrahepatic cholestasis of pregnancy (ICP) is also more prevalent in patients with chronic HCV infection than in uninfected patients.[31,32] The incidence of ICP in the general obstetric population is 0.2% to 2.5%, while the odds of developing ICP are 20-fold higher in HCV-infected pregnant women.[33] Given the increased risk of stillbirth associated with ICP, recognizing and diagnosing ICP in any pregnant woman is important. However, it is unclear if ICP is more severe or associated with higher rates of stillbirth in the setting of HCV. **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 μmol/L.

As of 2021, a multicenter, prospective observational cohort study is in progress to evaluate pregnancy outcomes of patients with HCV; it is anticipated that this study will answer many unresolved questions regarding HCV in pregnancy. Outcomes being studied include vertical transmission, preterm delivery, gestational diabetes, preeclampsia, cholestasis, and infant birth weight (Clinicaltrials.gov: NCT01959321).[34]

What is the rate of vertical transmission of HCV?

Vertical transmission refers to viral transmission from mother to infant during pregnancy, delivery, or the neonatal period. At present, vertical transmission of HCV is the leading cause of HCV infection in children.[35] One-third to one-half of mother-to-child transmission of HCV appears to occur in-utero prior to the last month of pregnancy; the remaining cases of transmission are thought to occur either in the last month of pregnancy or during delivery.[36] Historically, a major risk factor for vertical transmission of HCV has been maternal coinfection with HIV. In 2014, Benova et al published a meta-analysis examining rates of vertical transmission of HCV stratified by whether women were coinfected with HIV. Pooling the results of 17 studies of women with chronic HCV infection who were HIV-negative, the risk of vertical transmission was 5.8%. In contrast, based on the results of 8 studies, the risk of vertical transmission in HIV-positive women was almost doubled at 10.8%. [37] The increased risk of vertical transmission in HIV-positive pregnant patients may be due to increased HCV viral load resulting from HIV-mediated immunosuppression. [37] However, now that the use of combined

active antiretroviral therapy in pregnant patients with HIV is common in developed countries, the risk of vertical transmission of HCV in coinfected patients appears to be lower (4% to 8.5%).[38,39]

Vertical transmission of HCV is thought to be a risk only for patients with detectable HCV RNA during pregnancy. The meta-analysis by Benova et al included 15 studies with a total of 473 children born to women who were HCV-antibody-positive yet RNA-negative. Only 1 of the 473 children was diagnosed with vertically acquired HCV infection.[37] However, vertical transmission from HCV RNA-negative patients has been reported by others,[40] which may reflect either insensitive methods for detecting HCV RNA or intermittent HCV RNA positivity in these patients.[41] In addition, whether the level of HCV viremia correlates with the risk of transmission has yet to be determined. Several studies have shown that higher viral loads correlate with an increased risk of transmission,[41-43] whereas other studies have failed to find this correlation.[20,44] Importantly, these studies involved small numbers (3% to 5%) of vertically infected infants born to patients who were HCV-RNA positive or with anti-HCV antibodies. Further data will be critical in assessing the frequency of vertical transmission from HCV RNA-negative patients.

Screening

Who should be screened for HCV during pregnancy?

Because the prevalence of HCV infection among women of childbearing age has increased 161% in the last decade, and because risk-based screening misses almost 50% of HCV cases, screening recommendations are changing to be more inclusive.[3,45] Similarly, emerging data suggest that 85% to 90% of neonates with HCV are not identified with the current strategies, thus impacting the ability to treat these infants.[46] Importantly, a recent cost-analysis model demonstrated that universal prenatal HCV screening improved health outcomes of women with HCV infection and

identification of neonates with infection and was cost-effective, even in areas with very low prevalence.[47] In light of these data, the CDC now recommends universal screening for HCV during pregnancy.[8] Similarly, the USPSTF also recommends screening in all persons aged 18 to 79 due to the rising prevalence.[7] The USPSTF specifically notes that pregnant individuals should be screened but does not recommend a screening frequency due to a paucity of data on which to base such recommendations. Early identification of patients who are HCV positive during pregnancy can potentially facilitate more efficient linkage to care and treatment in the postpartum period, as none of the antiviral therapies recommended for HCV infection are approved for use during pregnancy. The postpartum period is a critical time for patients to access curative therapy. In alignment with the recommendations from the CDC and the USPSTF and based on the data mentioned above, **we recommend that obstetric providers screen all pregnant patients for HCV by testing for anti-HCV antibodies in every pregnancy (GRADE 1B).** The timing of when to screen during pregnancy is somewhat arbitrary; screening in the first trimester would theoretically bring the most patients to attention at the earliest time.

What is the ideal screening test for HCV?

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.[48] HCV viremia or the presence of HCV RNA indicates active infection and can first be detected 1 to 3 weeks after exposure.[49]

The standard screening test for HCV is an anti-HCV antibody test. A positive test result indicates one of the following: the patient has active HCV infection (acute or chronic), the patient has had a past infection that has resolved, or the result is a false positive.[9] Thus, a positive

antibody test result can indicate the patient is currently positive, was positive, or is negative. Therefore, a positive anti-HCV antibody result should be followed by a quantitative nucleic acid test for HCV RNA. The recombinant immunoblot assay is no longer available or recommended (Figure 2). If a patient who tested negative for HCV RNA within the past 6 months is newly found to be viremic, acute HCV infection is confirmed. If a patient with no previous testing for hepatitis C tests positive for both anti-HCV antibodies and HCV RNA, it is not possible based on the test results alone to distinguish acute from chronic HCV infection. If the anti-HCV antibody test result is positive and the HCV RNA test result is negative, distinguishing a false-positive antibody test from a prior infection requires testing for anti-HCV antibodies with a different antibody assay platform (such as polymerase chain reaction or immunoblot) (Figure 2).[50] If the anti-HCV antibody test result on the different platform is negative, the initial test result should be considered a false positive.[51] If the anti-HCV antibody test result on the different platform is positive, then the infection can be considered cleared (20% of all infections clear).[51]

Treatment and outcomes

Once hepatitis C is diagnosed, what additional evaluation should be performed?

Because there are no formalized pregnancy-specific guidelines for laboratory testing in HCV infection, SMFM has adapted guidelines from the American Association for the study of Liver Disease (AASLD) and the Infectious Disease Society of America (IDSA) for pregnancy.[9] For pregnant patients with confirmed active HCV infection, a quantitative HCV RNA test should be performed to determine the baseline viral load. Basic laboratory testing to evaluate the extent of liver disease should include the following laboratory tests: bilirubin, ALT, aspartate

aminotransferase (AST), albumin, platelet count, and prothrombin time. Testing for HCV genotype should also be performed if not done previously to help plan future treatment (Box 1).

In light of 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).** The CDC, IDSA, and AASLD recommend screening for HIV and HBV specifically in this scenario.[8,9] HBV has overlapping risk factors for HCV and can lead to accelerated liver damage and adverse effects during pregnancy. Hepatitis A virus (HAV) infection can also worsen hepatic damage if present with HCV infection. Pregnant patients with HCV should be screened for immunity to HAV. The Advisory Committee on Immunization Practices recommends that patients with HCV infection who are found to be nonimmune to HBV or HAV be vaccinated against both of these infections,[52] which is safe to do during pregnancy. **We recommend vaccination against HAV and HBV (if not immune) for patients with HCV (GRADE 1B).**

What are the principles of medical management of HCV?

Any woman who receives a diagnosis of HCV infection during pregnancy should ideally be referred to a specialist experienced in the management of hepatitis to establish long-term care.

HCV is a genetically diverse RNA virus; it has six different genotypes that affect the choice and efficacy of treatment regimens. The goal of treatment is to achieve sustained virologic response (SVR), defined as undetectable HCV RNA 12 to 24 weeks after completing treatment. Since 99% of patients who achieve SVR remain HCV RNA-negative during long-term follow-up, treatment that achieves SVR is considered curative. In patients who do not have cirrhosis, SVR is associated with resolution of liver disease. In patients with cirrhosis, regression of

hepatic fibrosis may be seen, and the risk of complications, such as hepatic failure, hepatocellular carcinoma (HCC), and portal hypertension, while still possible, is lower than in untreated individuals.[53]

Use of even modest amounts of alcohol has been associated with progression of liver disease in patients with HCV. Thus, patients with HCV, including pregnant patients, should refrain from using alcohol.[54] For patients with advanced liver disease, dosage adjustments may be required for some medications. For patients with HCV who have normal hepatic function, dosage adjustments in most prescription and over-the-counter medications are not required. Patients do not need to avoid acetaminophen, although it is advisable to set a lower maximum daily dosage of 2 g rather than 4 g in patients with cirrhosis related to HCV.[55] Patients with HCV should receive counseling about transmission prevention, such as avoidance of sharing personal hygiene articles (eg, razors, nail clippers, scissors, toothbrushes) with close contacts and avoidance of needle-sharing in the setting of intravenous drug use.[51]

Serial laboratory surveillance of liver function or serial viral load assessment during pregnancy in HCV-positive patients is generally not recommended. As discussed previously, serum levels of ALT tend to decrease during the second and third trimesters of pregnancy.[20-23]

Should HCV be treated during pregnancy?

Currently, none of the antiviral therapies recommended for HCV infection are approved for use during pregnancy. Among nonpregnant women, according to guidelines released in 2016 by AASLD/ISDA, direct-acting antiviral (DAA) regimens are first-line treatments as they typically achieve SVR rates of >90%, are tolerated better than interferon-based regimens, and require a shorter duration of treatment.[9] Specific treatment regimens are beyond the scope of this

document but are based on genotype, presence of cirrhosis, and prior treatments. Treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be extended by treatment.[9]

Studies are limited on the effects of second-generation DAA therapy in pregnancy. There are no adequate human data regarding any of these antiviral medications, and safety data come entirely from animal reproduction studies. Due to the lack of human studies, no DAA therapy has yet been approved to treat HCV infection in pregnancy.[1] Given the availability of ribavirin-free DAA regimens that demonstrated high efficacy in nonpregnant adults and no adverse fetal effects in animal studies, the assessment of these regimens for use in pregnancy should be actively investigated. A phase 1 trial assessing ledipasvir plus sofosbuvir for the treatment of chronic HCV infection during pregnancy showed 100% cure rates, large declines in viral loads within 10 to 21 days of starting treatment, and no clinically significant adverse effects on the maternal/infant dyad.[56] In the meantime, 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.[1] 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 people 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 as it can help to expedite therapy following pregnancy.

Methods to reduce vertical transmission

Is prenatal diagnostic testing safe in patients with HCV?

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.[57] No association between amniocentesis and vertical transmission was found in a case-control study of 51 HCV-infected children that evaluated risk factors for vertical transmission or in a case series of 22 HCV-positive women who underwent amniocentesis.[57] 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 are counseled 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.

Does mode of delivery affect the risk of vertical transmission?

Vaginal delivery has not been shown to be a risk factor for vertical transmission of HCV. Cottrell et al published a systematic review in 2013 that included 14 observational studies evaluating the association between mode of delivery and vertical transmission of HCV.[58] Eleven studies compared the risk of transmission between vaginal and cesarean delivery without differentiating between elective and emergent cesarean deliveries; of these, 10 found no association between mode of delivery and transmission rate. Two studies specifically compared cesarean delivery before the onset of labor with vaginal or emergent (after onset of labor) cesarean delivery. There was no difference in the risk of vertical transmission according to mode of delivery in either of these two studies.[40,41] Moreover, a 2011 meta-analysis of studies on HCV

vertical transmission by mode of delivery found no significant difference. This meta-analysis did not distinguish between elective and emergent cesarean deliveries and included 8 studies, all of which were observational rather than prospective.[59] 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.[60] **We recommend against cesarean delivery solely for the indication of HCV (GRADE 1B).**

Does labor management affect the risk of vertical transmission?

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. One study reported that membrane rupture for greater than 6 hours was associated with an increased risk of vertical transmission.[41] Another study found that the median duration of membrane rupture was significantly longer among women who transmitted HCV to their infants than among those who did not (28 vs 16 hours).[61] Regarding invasive fetal monitoring, a retrospective study including 710 HCV-infected women and a prospective study including 242 HCV-infected women both reported that internal fetal monitoring was associated with increased risk of transmission compared with no internal monitoring.[41,62] In contrast, a retrospective study with 724 women found no such association.[63] One of these studies also found that episiotomy was significantly associated with an increased risk of vertical transmission.[62] Based on the available evidence, **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). Based on these data, another potential benefit of screening all pregnant patients for HCV is the potential impact of an HCV diagnosis on intrapartum and neonatal management.

Expectant management of ruptured membranes should be avoided at term. There are inadequate data regarding the risk of perinatal HCV transmission with expectant management in the setting of prolonged preterm premature rupture of membranes (PPROM). Therefore, usual obstetric management for PPROM 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 was 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, 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

Is breastfeeding safe in HCV-positive mothers?

Breastfeeding does not appear to affect the risk of vertical transmission of HCV. A systematic review including 14 cohort studies examined breastfeeding and HCV transmission, and none found a significant association.[58] Therefore, the American College of Obstetricians and Gynecologists and the CDC state that breastfeeding is safe in those with HCV infection;[11,49] however, the CDC recommends abstaining from breastfeeding if the nipples are bleeding or cracked.[49] **We recommend that HCV status not alter standard breastfeeding counseling and**

recommendations unless nipples are cracked or bleeding (GRADE 1A). In those with cracked or bleeding nipples, breast milk should be expressed and discarded.

How should infants born to HCV-positive patients be screened for HCV infection?

Because anti-HCV antibodies can be transmitted across the placenta to the fetus, the presence of anti-HCV antibodies in a neonate's serum soon after delivery is not diagnostic of neonatal infection. In a prospective study of vertical transmission of HCV that included 235 uninfected infants, anti-HCV antibodies were found in 96.8% of infants at birth, 15.3% at age 12 months, 1.6% at age 18 months, and 1.0% at age 24 months.[41] This study defined infants as HCV infected if they were positive for HCV RNA on at least 2 occasions at age ≥1 month or older or if they were anti-HCV positive at 24 months of age.[41] The American Academy of Pediatrics and CDC recommend screening of infants born to HCV-positive women for anti-HCV antibodies >18 months of age or for HCV RNA on 2 occasions in infants >1 month of age.[64]

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**	2C

	with a diagnosis of ICP at an early gestational age or with significant elevation of bile acids.	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 pregnancyand that people who become pregnant while taking a DAA should 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

406 Abbreviations: DAA: direct-acting antiviral; HBV, hepatitis B virus; HCV, hepatitis C virus;

407 HIV, human immunodeficiency virus; ICP, intrahepatic cholestasis of pregnancy.

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409 **Society for Maternal-Fetal Medicine Grading System: Grading of Recommendations**

410 **Assessment, Development, and Evaluation (GRADE) Recommendations** [65,a]

411

Grade of Recommendation	Clarity of Risk and Benefit	Quality of Supporting Evidence	Implications
1A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa.	Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	Strong recommendation that can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risks and burdens, or vice versa.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation that applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present.
1C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risks and burdens, or vice versa.	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.	Strong recommendation that applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality.
2A. Weak	Benefits closely	Consistent evidence from	Weak

recommendation, high-quality evidence	balanced with risks and burdens.	well-performed randomized controlled trials or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.	recommendation; best action may differ depending on circumstances or patients or societal values.
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens.	Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens.	Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation, other alternatives may be equally reasonable.
Best practice	Recommendation in which either (i) there is an enormous amount of indirect evidence that clearly justifies strong recommendation (direct evidence would be challenging, and inefficient use of time and resources, to bring together		

	and carefully summarize), or (ii) recommendation to the contrary would be unethical.		

[a]Adapted from Guyatt GH, et al.[66], 2008

Guidelines

The content of this document reflects the national and international guidelines related to the management of hepatitis C virus infection in pregnancy.

Organization	**Title**	**Year of Publication**
American Association for the Study of Liver Diseases and the Infectious Diseases Society of America [9]	Recommendations for testing, managing, and treating hepatitis C	2020
American Academy of Pediatrics[64]	Hepatitis C	2018
European Association for the Study of the Liver[53]	EASL recommendations on treatment of hepatitis C	2020
Centers for Disease Control and Prevention[8]	CDC recommendations for hepatitis C screening among adults—United States,	2020

	2020	
American College of Obstetricians and Gynecologists[11]	Viral hepatitis in pregnancy. Practice Bulletin No. 86	2007

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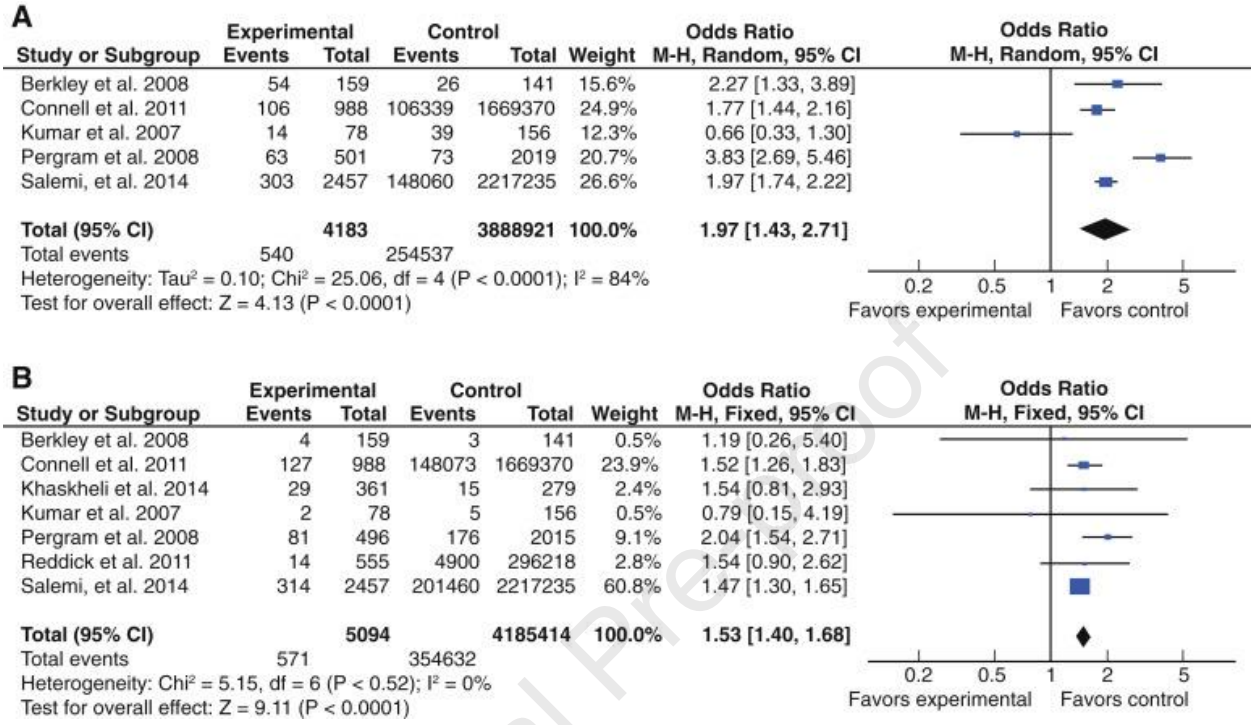

423

424 **Figure 1. Meta-analysis of infants of hepatitis C virus-positive women.** Odds of A, low birth

425 weight and B, fetal growth restriction in infants of hepatitis C virus-positive women: results of

426 meta-analysis. CI, confidence interval; df, degrees of freedom; M-H, Mantel-Haenszel.

427 (Huang Q, Hang L, Zhong M, Gao Y, Luo M, Yu Y. Maternal HCV infection is associated with

428 intrauterine fetal growth disturbance. Medicine (Baltimore) 2016;95:1-7.)

429

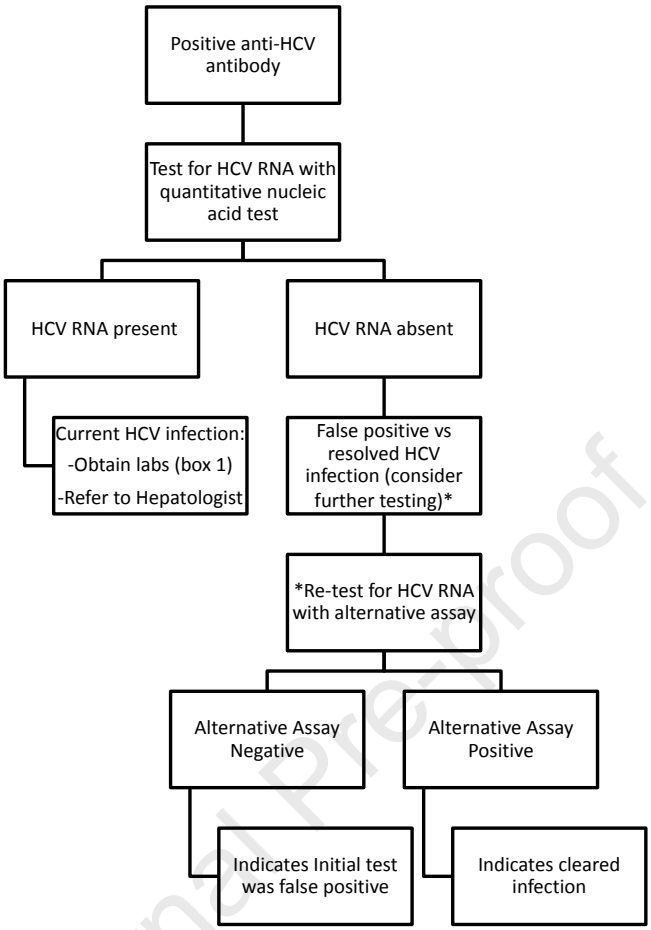

Figure 2. Recommended testing sequence for identifying current hepatitis C virus infection.

*HCV antibody assays vary according to their antigens, test platforms, and performance characteristics, so biologic false positivity is unlikely to be exhibited by more than one test when multiple tests are used on a single specimen

Note: Repeat HCV RNA testing if the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Modified from Centers for Disease Control and Prevention. Available at https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a5.htm?s_cid=mm6218a5_w#fig

Box 1. 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)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; RNA, ribonucleic acid; STI, sexually transmitted infection.

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SMFM Consult #56: Hepatitis C in Pregnancy: Updated Guidelines – Summary of Evidence Table

<table>
<tr><td colspan="3">Clinical question</td></tr>
<tr><td colspan="3">What is the impact of HCV on obstetric and neonatal outcomes?</td></tr>
<tr><td colspan="3">Recommendation statement</td></tr>
<tr><td colspan="3">Antenatal testing is not indicated in the setting of HCV diagnosis alone.</td></tr>
<tr><td colspan="3">GRADE</td></tr>
<tr><td colspan="3">2C- Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens. Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.</td></tr>
<tr><td colspan="3">Other organization recommendations</td></tr>
<tr><td colspan="3">n/a</td></tr>
<tr><td>Category A Evidence:</td><td>Category B Evidence:</td><td>Category C Evidence:</td></tr>
<tr><td>n/a</td><td>Huang 2016- Meta-analysis of observational studies; 7 studies of 4,185,414 participants and 5094 HCV infection cases. HCV+ status associated with growth restriction (OR=1.53, 95% CI: 1.40–1.68, fixed effect model) and low birth weight (OR=1.97, 95% CI: 1.43–2.71, random effect model).</td><td>Pergram 2008- Retrospective cohort; 506 HCV+ pregnant women vs 2022 HCV- mothers vs 1439 drug-using HCV- mothers. Infants of HCV+ mothers were more likely to be low birth weight (OR, 2.17; 95% CI, 1.24, 3.80) and small for gestational age (OR, 1.46; 95% CI, 1.00, 2.13).

Connell 2011- Retrospective cohort; 988 HCV+ pregnant women vs 1,669,370 HCV- pregnant women. Infants of HCV+ mothers were more likely to be low birth weight (10.7% vs 6.37%, p<0.0001) and preterm birth <37 weeks (13.1% vs 8.84%, p<0.0001).</td></tr>
<tr><td colspan="3">Recommendation statement</td></tr>
<tr><td colspan="3">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.</td></tr>
<tr><td colspan="3">GRADE</td></tr>
<tr><td colspan="3">2C- Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens. Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.</td></tr>
<tr><td colspan="3">Other organization recommendations</td></tr>
<tr><td colspan="3">n/a</td></tr>
</table>

Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	**Wijarnpreecha 2016**- Two meta-analyses of observational studies. 3 studies (n= 95,429); HCV+ pregnant women compared to HCV- pregnant women, pooled OR of ICP was 20.40 (95% CI, 9.39—44.33, I2 = 55%). 2 studies (n=94,326); ICP patients compared to non-ICP patients, pooled OR of later HCV infection was 4.08 (95% CI, 3.13—5.31, I2 = 0%).	**Smith 2020**- Editorial. Reports population-based studies have linked several chronic liver diseases to the development of intrahepatic cholestasis, namely hepatitis C infection. **Williamson 2014**- Editorial. Lists viral hepatitis as a differential diagnosis of intrahepatic cholestasis of pregnancy.

Clinical question		
Who should be screened for HCV during pregnancy?		
Recommendation statement		
We recommend that obstetric care providers screen all pregnant patients for HCV by testing for anti-HCV antibodies in every pregnancy.		
GRADE		
1B- Benefits clearly outweigh risks and burdens or vice versa. Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.		
Other organization recommendations		
CDC- CDC is augmenting previous guidance with two new recommendations: 1) hepatitis C screening at least once in a lifetime for all adults aged ≥18 years, except in settings where the prevalence of HCV infection is <0.1% and 2) hepatitis C screening for all pregnant women during each pregnancy, except in settings where the prevalence of HCV infection is <0.1%. **USPSTF**- The USPSTF recommends to screen all asymptomatic adults (including pregnant persons) aged 18 to 79 years without known liver disease for hepatitis C virus (HCV) infection (Grade B). There is limited information about the specific screening interval that should occur in persons who continue to be at risk for new HCV infection or how pregnancy changes the need for additional screening.		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	**Rossi 2020**- Population-based retrospective cohort study evaluating change in rates of HCV infection in pregnancies in the US. Between 2009-2017, there were 94,824	**Sheffield 2020**- Editorial. Reports support for one-time screening during the index pregnancy, with repeat screening during subsequent pregnancies if new risk factors

	reported cases of maternal HCV infection among the 31,207,898 live births in the US. The rate of maternal HCV infection increased from 1.8 cases per 1,000 live births in 2009 to 4.7 cases per 1,000 live births in 2017 (relative risk [RR] 2.7, 95% CI 2.6–2.8).	are identified. **Delgado-Borrego 2012-** Population-based retrospective cohort study evaluating expected and actual ascertainment of childhood HCV infection cases. Between 2000-2007, 12% of the number of children expected to have positive HCV antibody tests were identified in Florida; 4.9% of expected cases were identified nationally. **Tasillo 2019**- Cost-effectiveness study of universal prenatal HCV screening compared with current practice. Using a stochastic individual-level microsimulation model, with universal screening: HCV+ pregnant women lived 1.21 years longer and had 16% lower HCV-attributable mortality, which had an ICER of $41,000 per QALY gained compared to current practice. In this model, universal screening compared with current practice increased identification of infants exposed to HCV at birth from 44% to 92%.

Clinical question
Once hepatitis C is diagnosed, what additional evaluation should occur?
Recommendation statement
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- Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens. Evidence from

observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.		
Other organization recommendations		
CDC 2020- Management of persons with HCV infection includes HIV risk assessment and testing. **AASLD/IDSA 2021**- Evaluation for other conditions that may accelerate liver fibrosis, including hepatitis B and HIV infections, is recommended for all persons with active HCV infection.		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	n/a	n/a
Recommendation statement		
We recommend vaccination against Hepatitis A virus and Hepatitis B virus (if not immune) for patients with HCV.		
GRADE		
1B- Benefits clearly outweigh risks and burdens or vice versa. Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate. [Recommendation unchanged from Consult 43]		
Other organization recommendations		
CDC ACIP 2021- HAV and HBV vaccination recommended for adults with the additional risk factor of Chronic liver disease (e.g., persons with hepatitis B, hepatitis C, cirrhosis, fatty liver disease, alcoholic liver disease, autoimmune hepatitis, alanine aminotransferase [ALT] or aspartate aminotransferase [AST] level greater than twice the upper limit of normal).		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	n/a	n/a

Clinical question
Should HCV be treated during pregnancy?
Recommendation statement
We recommend that direct-acting antiviral regimens should be initiated only in the setting of a clinical trial during pregnancy and that people 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 - Benefits appear to outweigh risks and burdens or vice versa. Evidence from observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.

Other organization recommendations		
AASLD/IDSA- Women 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. There are no large-scale clinical trials evaluating the safety of direct-acting antivirals (DAAs) in pregnancy. A small study evaluating the pharmacokinetics of sofosbuvir in pregnancy demonstrated 100% SVR12 and no safety concerns (Chappell, 2019). Similarly, an international case series of 15 pregnant women treated with ledipasvir/sofosbuvir reported 100% SVR12 and no early safety concerns in the women or their infants (Yattoo, 2018). 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.		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	**Chappell 2020**- Open-label, phase 1 pharmacokinetic evaluation of ledipasvir–sofosbuvir administration; 8 HCV+ pregnant women. All participants had an undetectable viral load by the third pharmacokinetic visit between 33 and 35 weeks of gestation and 12 weeks after completion of treatment. Five participants had an adverse event related to ledipasvir–sofosbuvir. 1 infant delivered <37 weeks, 0 infants were LBW, had detectable HCV RNA by cord blood sampling at birth or at 12-month follow up, or had congenital abnormalities at birth.	**Spera 2016**- Editorial. Concludes that given the lack of human studies, no DAA has yet been approved for use in pregnancy or during breast feeding.

Clinical question
Is invasive prenatal diagnostic testing safe in women with HCV?
Recommendation statement
We suggest that if prenatal diagnostic testing is requested, patients be counseled that data on the risk of vertical transmission are reassuring but limited.
GRADE
2C- Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens. Evidence from

<table>
<tr><td colspan="3">observational studies, unsystematic clinical experience, or randomized controlled trials with serious flaws. Any estimate of effect is uncertain.</td></tr>
<tr><td colspan="3">Other organization recommendations</td></tr>
<tr><td colspan="3">SOGC- Amniocentesis in women infected with hepatitis C does not appear to significantly increase the risk of vertical transmission, but women should be counselled that very few studies have properly addressed this possibility (II-2C). More research on this topic is recommended. (III-L)</td></tr>
<tr><td>Category A Evidence:</td><td>Category B Evidence:</td><td>Category C Evidence:</td></tr>
<tr><td>n/a</td><td>n/a</td><td>n/a</td></tr>
<tr><td colspan="3">Recommendation statement</td></tr>
<tr><td colspan="3">We recommend against cesarean delivery solely for the indication of HCV.</td></tr>
<tr><td colspan="3">GRADE</td></tr>
<tr><td colspan="3">1B- Benefits clearly outweigh risks and burdens or vice versa. Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate. [Recommendation unchanged from Consult 43]</td></tr>
<tr><td colspan="3">Other organization recommendations</td></tr>
<tr><td colspan="3">n/a</td></tr>
<tr><td>Category A Evidence:</td><td>Category B Evidence:</td><td>Category C Evidence:</td></tr>
<tr><td>McIntyre 2006- Cochrane systematic review. Currently, there is no evidence from RCTs regarding planned caesarean section versus vaginal delivery for preventing mother to infant hepatitis C virus transmission.</td><td>Cottrell 2013- Systematic review; 4 low-quality cohort studies (n=2080) found no significant association between elective cesarean versus vaginal delivery and risk for transmission of HCV; 11 moderate-quality cohort studies (n=2308) found no significant association between any cesarean versus vaginal delivery and risk for transmission of HCV.

Ghamar Chehreh 2011- Meta-analysis; 8 studies of 641 HCV+/HIV- mother-infant pairs. HCV transmission rate did not vary significantly by among study mothers who underwent cesarean versus control mothers who gave birth vaginally [pooled odds ratio,</td><td>European Pediatric HCV Network 2005- European multicenter prospective observational study; 1787 HCV+ mother-child pairs. HCV transmission rate did not vary significantly by mode of delivery (elective CS, 7.3% [35/480]; vaginal delivery or emergency CS, 5.4% [50/924]; unadjusted OR, 1.37 [95% CI, 0.88–2.15]; P=0.16).

Mast 2005- Prospective cohort study; 181 infants born to HCV+ mothers. HCV transmission rate did not vary significantly by mode of delivery (vaginal: 4%, 6/151; elective cesarean: 0%, 0/12; emergency cesarean: 1/18, 5.5%).</td></tr>
</table>

	1.1 (95% CI 0.45–2.67)].	

Clinical question		
Does labor management affect the risk of vertical transmission?		
Recommendation statement		
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- Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, and burdens. Evidence from randomized controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an effect on confidence in the estimate of benefit and risk and may change the estimate.		
Other organization recommendations		
n/a		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	n/a	**Mast 2005**- Prospective cohort study of 181 HCV infants born to HCV+ mothers. HCV transmission rate varied according to duration of membrane rupture (less than 1hr, 0%; 1-5hr, 1.7%; 6-12hr, 10%; greater than 13 hr, 6.7%; p=0.02). HCV transmission rate also varied for internal (18.8%; 3/16 infants) vs external (2.4%; 4/165 infants) fetal monitoring (p=0.02). **Spencer 1997**- Prospective cohort study of 89 HCV+ pregnant women. HCV transmission rate was higher among women with longer duration of membrane rupture (p=0.03). **Garcia-Tejedor 2015**- Retrospective cohort

		study of 711 infants born to 710 HCV+ mothers. HCV transmission rate did not vary according to duration of membrane rupture (p=0.44). HCV transmission rate was higher among women who had an episiotomy than those who did not (p=0.085) and among women who had fetal scalp blood sampling and/or internal electrode compared to those who did not (p=0.016). **European Pediatric HCV Network 2001-** Pooled retrospective analysis of prospective cohort data; 1655 HCV+ mother-child pairs. HCV transmission rate did not vary among those in which a fetal scalp monitor was used during delivery (11.8%, 11/93) and those in which monitoring was not used (9.2%, 58/631) (OR=1.33, 95%CI 0.63-1.13).

Clinical question
Is breastfeeding safe in HCV-positive mothers?
Recommendation statement
We recommend that HCV status not alter standard breastfeeding counseling and recommendations, unless nipples are cracked or bleeding.
GRADE
1A - Benefits clearly outweigh risks and burdens or vice versa. Consistent evidence from well-performed, randomized controlled trials, or overwhelming evidence of some other form. Further research is unlikely to change confidence in the estimate of benefit and risk.
Other organization recommendations
ACOG- Breastfeeding has not been associated with an increased risk of neonatal HCV infection and, therefore, is not contraindicated in HCV-infected mothers.

CDC- Women with HCV infection do not need to avoid pregnancy or breastfeeding. HCV has not been shown to be transmitted through breast milk, although mothers with HCV infection should consider abstaining from breastfeeding if their nipples are cracked or bleeding.		
Category A Evidence:	Category B Evidence:	Category C Evidence:
n/a	**Cottrell 2013**- Systematic review; 14 cohort studies (n=2971) found no significant association between breastfeeding and risk for transmission of HCV.	n/a