

Hepatitis C Virus (HCV) Screening and Treatment for Pediatrics and Pregnancy

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Hepatitis C in Pregnancy

Prevalence of Hepatitis C in pregnant women has increased significantly over the past decade



AASLD, ACOG, CDC, & USPSTF now recommend universal screening for HCV in all pregnant women

Maternal Risks in HCV+ Pregnancy

Increased rates of:

- Preterm delivery
- Cesarean delivery
- Intrahepatic cholestasis of pregnancy



Risks increase further with active HCV viremia during pregnancy

Infant Risks in HCV+ Pregnancy

Increased rates of:

- Maternal to child transmission (MTCT)
- Low birthweight



Treatment Considerations:

- Initial studies are showing safety and efficacy of direct acting antivirals (DAA) for treatment of HCV during pregnancy
- Use of DAA during pregnancy and/or breastfeeding should be individually discussed between patients and their healthcare providers (not FDA approved)
- Infants should be tested for HCV at 18 months. DAA treatment should be initiated in infected children starting at age 3
- Efforts should be made to link infected mothers and infants to specialized care post-partum

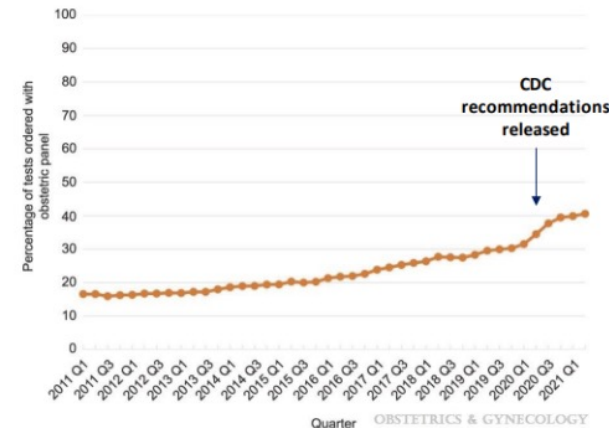
Lange, et al. *Clinical Liver Disease*.

CLD CLINICAL LIVER DISEASE
A MULTIMEDIA REVIEW JOURNAL

HCV in Pregnancy

- ▶ Since 2010 rates of acute HCV infection have more than tripled among reproductive-aged persons
- ▶ Overall rates of HCV infection during pregnancy increased 10-fold from 2000 to 2019 and by 20% between 2016 and 2020 alone

HCV testing among pregnant persons before and after 2020 CDC universal screening recommendations



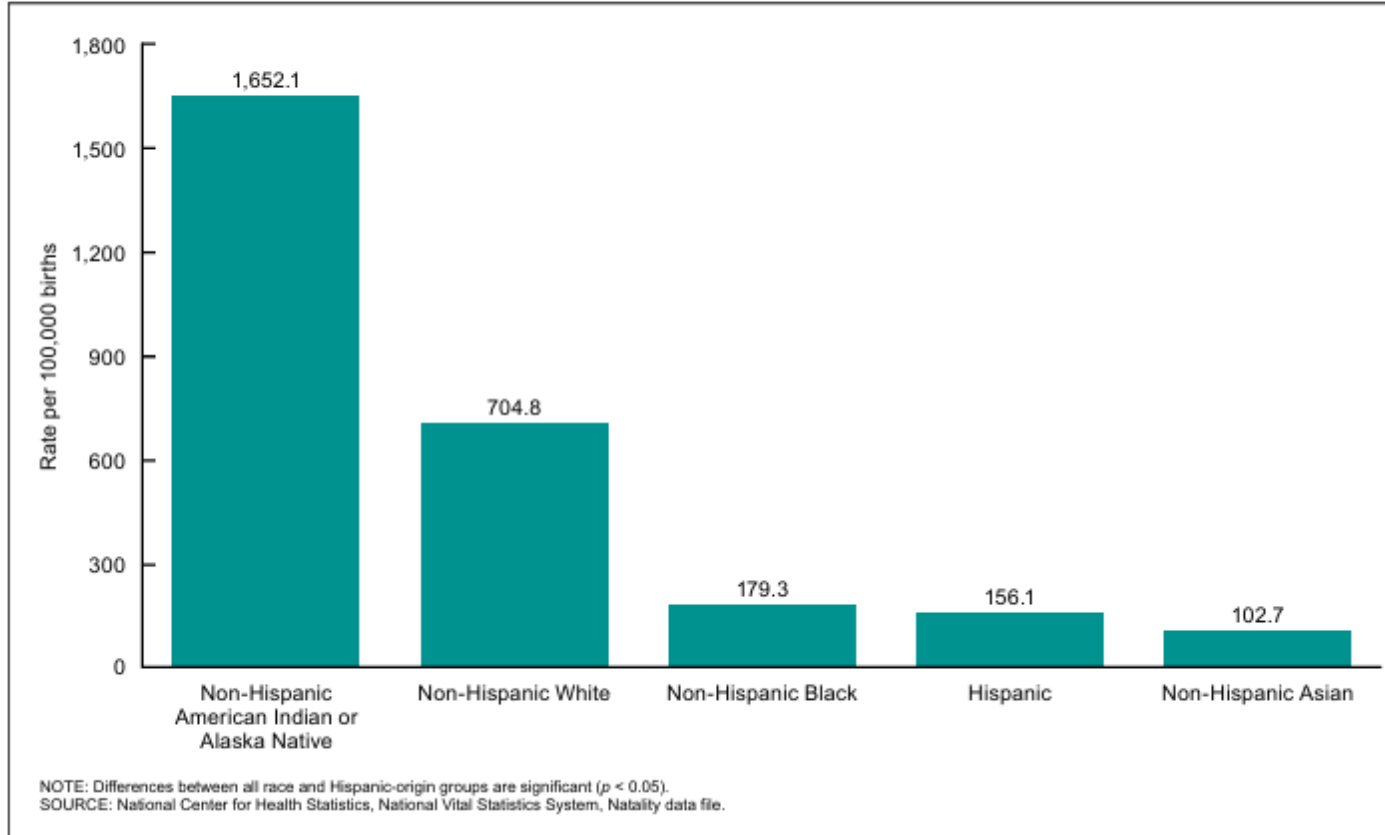
- Hepatitis C antibody testing among pregnant persons increased from 16.6% in 2011 to 40.6% in 2021

Kaufman, Harvey W.; Osinubi, Ademola; Meyer, William A. III; Khan, Mohammed; Huang, Xiaohua; Panagiotakopoulos, Lakshmi; Thompson, William W.; Nelson, Noele; Wester, Carolyn. Obstetrics & Gynecology 140(1):99-101, July 2022.

HCV in Pregnancy

4 National Vital Statistics Reports, Vol. 72, No. 3, April 11, 2023

Figure 3. Rate of maternal hepatitis C virus infection, by race and Hispanic origin of mother: United States, 2021



HCV Adverse Effects in Pregnancy

▶ Increases the risk for mother of:

- ▶ Cholestasis of pregnancy
- ▶ Gestational hypertension
- ▶ Need for cesarean section
- ▶ Need for intensive care unit admission

▶ Increases the risk for the neonate of:

- ▶ Preterm birth
- ▶ Low birthweight
- ▶ Fetal growth restriction
- ▶ Admission to the neonatal intensive care unit
- ▶ Congenital anomalies

Source: Trends and Characteristics in Maternal Hepatitis C Virus Infection Rates During Pregnancy: United States, 2016–2021 by Danielle M. Ely, Ph.D., and Elizabeth C.W. Gregory, M.P.H.

Perinatal Transmission of HCV

- ▶ Mothers infected with HCV have been shown to have about a 7.2% risk of perinatal transmission (increases to 12.1% in HIV co-infection)
- ▶ It has been suggested that HCV transmission occurs as early as the second trimester through delivery

PERINATAL HEPATITIS C

SCREEN patients for hepatitis C during each pregnancy.

TEST all perinatally exposed infants for hepatitis C infection at age 2 – 6 months.

MANAGE infants with an HCV RNA+ test alongside a provider with pediatric hepatitis C expertise.



Perinatal Transmission of HCV

- ▶ Risk factors associated with increased risk of perinatal transmission include HCV RNA greater than 10^6 IU/ml and antepartum hemorrhage
- ▶ Breastfeeding and mode of delivery have not been associated with an increased risk of transmission

4 Can I breastfeed with hepatitis C?

Yes, you cannot pass hepatitis C through breast milk.

However, if you have a cracked or bleeding nipple, stop breastfeeding on that side and talk to a midwife for advice.

hepatitis
australia



Outcomes in Vertically Transmitted HCV

- ▶ In a large scale study, an estimated 65% of confirmed infections cleared by 5 years, at a median of 12.4 months.
- ▶ In 7 (6.6%) confirmed infections, RNA was not detectable until after 6 weeks and not until after 6 months in 2 (1.9%). However, all such cases subsequently cleared.

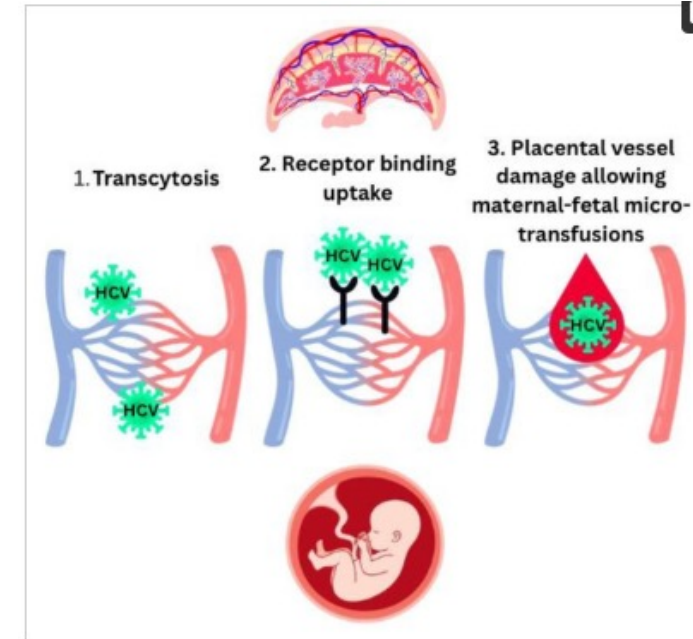


Figure 5. Pathways of HCV IUT transmission [27,32,60].

Testing for Perinately Acquired HCV

- ▶ Until 2023 professional societies recommended HCV antibody testing at 18 months (to avoid persistence of maternal antibody).
- ▶ However, 70% of children exposed perinately were not being tested due to being lost to follow-up by 18 months.



Recommendations for Counseling Parents Regarding Transmission and Prevention in Children with HCV Infection

RECOMMENDED	RATING ⓘ
Parents should be informed that hepatitis C is not transmitted by casual contact and, as such, children with HCV infection do not pose a risk to other children and can participate in school, sports, and athletic activities, and engage in all other regular childhood activities without restrictions.	I, B
Parents should be informed that universal precautions should be followed at school and in the home of children with HCV infection. Educate families and children about the risk and routes of HCV transmission, and the techniques for avoiding blood exposure, such as avoiding the sharing of toothbrushes, razors, and nail clippers, and the use of gloves and dilute bleach to clean up blood.	I, B

Source: HCV in Children – HCV Guidance

Treatment-Naive or Interferon-Experienced Children and Adolescents Without Cirrhosis or With Compensated Cirrhosis^a

RECOMMENDED	DURATION	RATING ⓘ
Combination of glecaprevir/pibrentasvir (weight-based dosing; see Table 1) for children aged ≥ 3 years with any genotype ^b	8 weeks	I, B
Combination of sofosbuvir/velpatasvir (weight-based dosing; see Table 2) for children aged ≥ 3 years with any genotype	12 weeks	I, B
Combination of ledipasvir/sofosbuvir (weight-based dosing; see Table 3) for children aged ≥ 3 years with genotype 1, 4, 5, or 6	12 weeks	I, B

^a Child-Pugh A

^b A longer duration of therapy (ie, 16 weeks) may be needed for children or adolescents with genotype 3 infection and interferon-experience.

Source: HCV in Children – HCV Guidance

Table 1: Weight-Based Dosing of Glecaprevir/Pibrentasvir for Children Aged ≥3 Years

Body Weight	Once Daily Dose of Glecaprevir/Pibrentasvir
<20 kg	150 mg/60 mg
≥20 kg to <30 kg	200 mg/80 mg
≥30 kg to <45 kg	250 mg/100 mg
45 kg and greater or 12 years of age and older	300 mg / 120 mg / day

Source: HCV in Children – HCV Guidance

Management of Pediatric HCV

- ▶ Routine liver biochemistries at initial diagnosis and at least annually thereafter are recommended to assess for disease progression.
- ▶ Although uncommon, cirrhosis occurs occasionally in children and adolescents (aged <18 years) with HCV infection.
- ▶ The presence of extrahepatic manifestations—such as cryoglobulinemia, rashes, and glomerulonephritis—as well as advanced fibrosis should lead to early antiviral therapy to minimize future morbidity and mortality.

AASLD/IDSA Guidelines on DAA treatment during Pregnancy

- ▶ “DAA treatment can be considered during pregnancy on an individual basis after a discussion between the pregnant person and their physician about the potential risks and benefits. ”

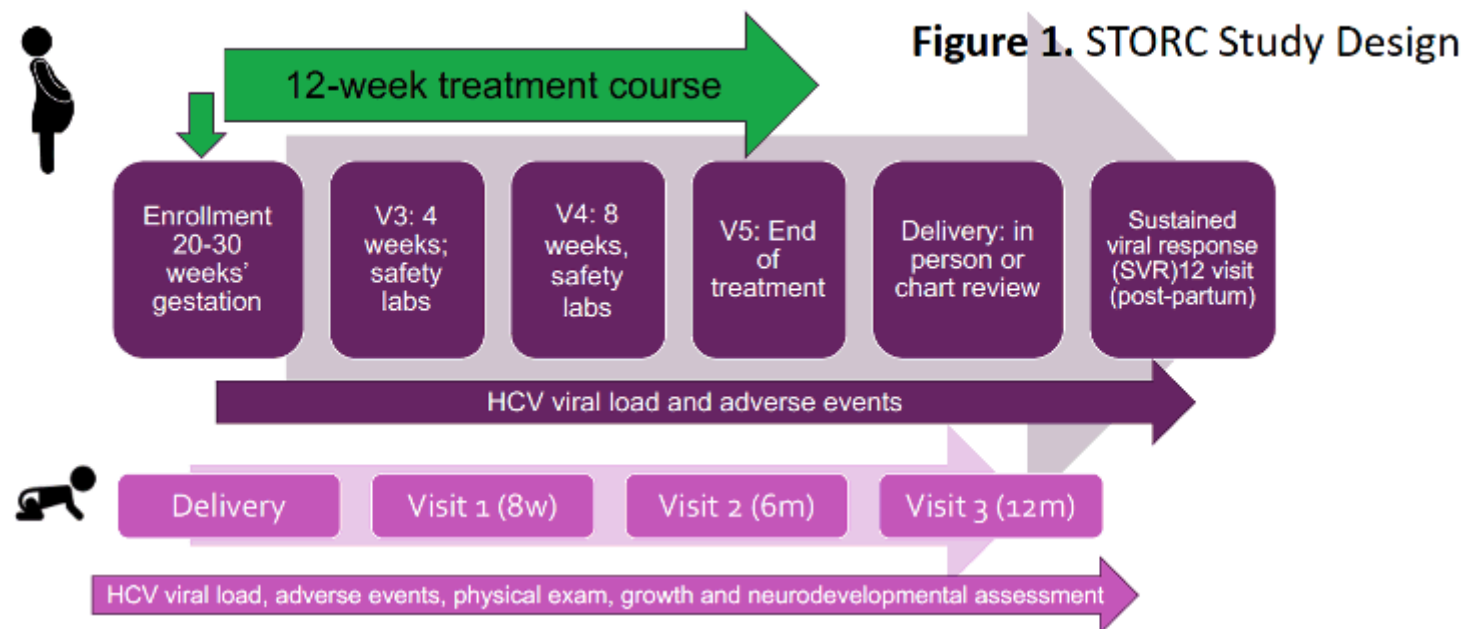


STORC TRIAL FOR HCV IN PREGNANCY

The **STORC trial** (NCT05140941) is a **phase 4, multicenter, single-arm study** evaluating the safety and efficacy of **sofosbuvir/velpatasvir (SOF/VEL)** for treating **chronic hepatitis C virus (HCV) infection during pregnancy**

Study Design & Population:

- **Participants:** ~100 pregnant people with chronic HCV, screened between 12+0 and 29+6 weeks gestation, enrolled between 20+0 and 30+0 weeks
- **Treatment:** Fixed-dose SOF/VEL (400 mg/100 mg tablet) taken **once daily for 12 weeks** (84 days)
- **Follow-up:** Maternal follow-up until 12 weeks postpartum; infants followed from birth to 1 year



STORC Key Findings (Interim Analysis)

- ▶ **SVR12 rate:** 96.9% of participants (63/65) with an SVR assessment achieved SVR12. Two treatment failures were reported: 1 participant missed 20 doses and was re-exposed to HCV via sex, and 1 participant missed 28 doses and was re-exposed to HCV via injection drug use.
- ▶ No perinatal transmission occurred in the 61 infants with available data.
- ▶ Most common maternal adverse events were nausea/vomiting and GERD (3 participants stopped treatment due to GI side effects)
- ▶ No infant adverse effects deemed related to SOF/VEL

IMPAACT 2041 – Phase I/II Study of Glecaprevir/Pibrentasvir in Pregnancy

- ▶ **IMPAACT 2041** is a **Phase I/II, multi-site, open-label, single-arm study** evaluating the **pharmacokinetics (PK) and safety** of **glecaprevir/pibrentasvir (GLE/PIB)** in pregnant women with hepatitis C virus (HCV) infection, with or without HIV, and assessing infant safety through 10 weeks postpartum



Treatment of HCV during Pregnancy

Submit Cases to the TiP-HepC Registry

Submit Cases to the TiP-HepC Registry

Contribute existing data on outcomes of mothers and infants exposed to DAA medications in pregnancy by submitting to the Treatment in Pregnancy for Hepatitis C (TiP-HepC) Clinical Case Registry [by clicking here](#).

Explore the TiP-Hep C Evidence Base

Evidence briefs

Community of Practice

HCV and Breastfeeding

Recommendations Regarding Breastfeeding and Postpartum Care for Persons With HCV Infection

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

- ▶ **Glecaprevir/pibrentasvir (GLE/PIB)** is 97-99% bound to maternal plasma proteins, so amounts in breastmilk are likely to be very low.
- ▶ Limited information indicates that typical doses of sofosbuvir produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months.

Source: NIH LactMED

Spontaneous Clearing in the Postpartum Period

- ▶ Spontaneous clearance of HCV can occur in the postpartum period.
- ▶ Previous studies with small numbers of participants demonstrated that up to 10% of postpartum persons became HCV RNA undetectable.
- ▶ A study from Egypt demonstrated a 25% rate of spontaneous resolution that was strongly associated with the favorable IL28B allele.
- ▶ The possibility of spontaneous viral clearance should be considered for any person who is being assessed for DAA treatment in the postpartum period.

Sources

- ▶ Chen, Po-Hung, et al. "Trends in the prevalence of hepatitis C infection during pregnancy and maternal-infant outcomes in the US, 1998 to 2018." *JAMA Network Open* 6.7 (2023): e2324770.
- ▶ Benova, Lenka, et al. "Vertical transmission of hepatitis C virus: systematic review and meta-analysis." *Clinical infectious diseases* 59.6 (2014): 765-773.
- ▶ Wasuwanich, Paul, et al. "A composite score for predicting vertical transmission of hepatitis C: a multicenter study." *Pathogens* 13.1 (2024): 45.
- ▶ A E Ades, Fabiana Gordon, Karen Scott, Intira Jeannie Collins, Claire Thorne, Lucy Pembrey, Elizabeth Chappell, Eugènia Mariné-Barjoan, Karina Butler, Giuseppe Indolfi, Diana M Gibb, Ali Judd, Spontaneous Clearance of Vertically Acquired Hepatitis C Infection: Implications for Testing and Treatment, *Clinical Infectious Diseases*, Volume 76, Issue 5, 1 March 2023, Pages 913–991,