Preventing vertical transmission of HCV in Canada

Chelsea Elwood MD, Laura J. Sauve MD, Neora Pick MD

Cite as: *CMAJ* 2019 June 17;191:E650-1. doi: 10.1503/cmaj.181662

In Canada, the seroprevalence rate of hepatitis C virus (HCV) in pregnancy is thought to be about 1%, which translates to about 3500 pregnant women who have HCV infection during pregnancy each year.[1] Vertical transmission rates range from 5% to 6% among HCV-monoinfected women to 10% among those with HIV co-infection.[2] Almost half of women who are infected with HCV may be unaware of their infection and, therefore, will not go on to be treated in a timely fashion. We argue that the elimination of vertical transmission of HCV would be achievable in Canada with universal screening of women who are pregnant and engagement in a plan for treatment either postpartum or preconception. Similar to HIV and hepatitis B virus (HBV), eliminating perinatal transmission is achievable, and our goal for rates of perinatal transmission should be the same as that for HIV (i.e., 0%), particularly since HCV infection is now curable. However, current Canadian guidance recommends universal screening for HBV and HIV in pregnancy, but not for HCV in pregnancy.[3]

More years of life are lost because of HCV than any other infectious disease in Canada.[4] Hepatitis C virus infection does not appear to worsen maternal health; however, rates of preterm birth, low birth weight, obstetrical cholestasis and adverse neonatal outcomes, such as admission to a neonatal intensive care unit, are increased for pregnancies complicated by HCV infection.[5,6]

Perinatal transmission is one of the ways of acquiring HCV. The timing of vertical transmission, either antepartum or intrapartum, has not been fully clarified, although risk factors for vertical transmission include prolonged rupture of membranes and high viral load during pregnancy.[2,7] Cesarean delivery does not prevent vertical transmission.[8] Breastfeeding does not appear to be a risk for transmission.[7] Clearly, however, a woman who is cured before pregnancy cannot transmit HCV to her infant.

The treatment of HCV has been transformed with the introduction of direct-acting antiviral regimens. Previous treatment regimens for HCV were limited by their low success rates and substantial adverse effects of interferon-based therapies. Furthermore, ribavirin-based regimens were contraindicated in pregnancy because of their known teratogenic effects, which meant HCV infection was usually not treated in pregnancy. There are scarce data available to suggest that treatment with direct-acting antivirals in pregnancy or during breastfeeding is safe.[9] However, the perinatal period is an excellent opportunity for screening, to diagnose women who are infected and engage them in care to cure the HCV infection. When planning pregnancy or during pregnancy, women are often motivated to make modifications to lifestyle risk factors such as intravenous drug use and to consider curative treatment for HCV infection when information about HCV treatment and access to it is offered.[10] This approach has the potential for improving a woman's own health trajectory, allowing for risk mitigation during the current pregnancy (avoiding prolonged rupture of membranes, internal fetal monitoring), and preventing vertical transmission in a subsequent pregnancy.

KEY POINTS

- The rate of vertical transmission by women who are monoinfected with hepatitis C virus (HCV) is 5%–6%.
- Only half of women who are infected with HCV are identified by screening based on risk factors.
- Canadian guidelines should recommend universal screening for HCV in pregnancy as they do for hepatitis B virus and HIV.
- Treatment of women who are HCV positive and of reproductive age could eliminate the risk of vertical transmission.

Universal HCV screening is currently recommended in the United States (https://hcvguidelines.org/unique-populations/pregnancy), but it is not routine in Canada. Universal HCV screening in pregnancy was recently shown to be cost effective in France and the US when treatment is started regardless of the stage of liver fibrosis.[11,12] Guidance from Canada and the US suggests screening based on the presence of risk factors, yet it is increasingly clear that this approach identifies only about half of women who are infected with HCV.[1,3,13]

For infants, a diagnosis of HCV acquired perinatally involves either testing with HCV RNA polymerase chain reaction on 2 occasions between 2 and 6 months of age or at 18 months using serology; the National Institutes of Health have suggested earlier polymerase chain reaction–based testing to avoid loss to follow-up.[14] Yet, a 2018 study found that only 31% of infants born to mothers with HCV were tested for perinatally acquired HCV.[2] Mothers may not be aware of

their HCV status, the risk of transmission of HCV or of testing recommendations for their children.[2]

With care gaps in both maternal screening in pregnancy and postnatal infant screening, Canada likely has a large cohort of infants, children and young adults with progressive liver disease who could have been cured of the HCV infection if it had been identified early or, quite simply, would not have been infected at all.

We encourage all care providers to consider the reproductive implications of HCV, to consider HCV screening in pregnancy and referral for treatment of HCV. The time has come to move toward universal HCV screening in women who are pregnant, with initial prenatal investigations that are then repeated based on risk factors in the third trimester. All providers of prenatal care should consider HCV screening, diagnosis and referral to HCV treatment for women with HCV infection who are considering pregnancy. They should also counsel women who are pregnant about the potential for cure with new treatment and encourage them to seek treatment postpartum to prevent vertical transmission in future pregnancies. Achieving a 0% vertical transmission rate for HCV in Canada is possible, but it requires buy-in and action from a broad spectrum of health care providers and public health officials.

References

1. Blasig A, Wagner EC, Pi D, et al. Hepatitis C infection among pregnant women in British Columbia: reported prevalence and critical appraisal of current prenatal screening methods. *Can J Public Health* 2011;102:98-102.
2. Chappell CA, Hillier SL, Crowe D, et al. Virus screening among children exposed during pregnancy. *Pediatrics* 2018;141. pii: e20173273. doi: 10.1542/peds.2017-3273 [Epub 2018 May 2].
3. Boucher M, Gruslin A, Jones G, et al. The reproductive care of women living with hepatitis C infection. *J Soc Obstet Gynaecol Can* 2000;22:820-44.
4. Shah H, Bilodeau M, Burak KW, et al. The management of chronic hepatitis C: 2018 guideline update from the Canadian Association for the Study of the Liver. *CMAJ* 2018;190:E677-87.
5. Huang QT, Huang Q, Zhong M, et al. Chronic hepatitis C virus infection is associated with increased risk of preterm birth: a meta-analysis of observational studies. *J Viral Hepat* 2015;22:1033-42.
6. Money D, Boucoiran I, Wagner E, et al. Obstetrical and neonatal outcomes among women infected with hepatitis C and their infants. *J Obstet Gynaecol Can* 2014;36:785-94.
7. Cottrell EB, Chou R, Wasson N, et al. Reducing risk for mother-to-infant transmission of hepatitis C virus: a systematic review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2013;158:109-13.
8. Ghamar Chehreh ME, Tabatabaei SV, Khazanehdari S, et al. Effect of cesarean section on the risk of perinatal transmission of hepatitis C virus from HCV-RNA+/HIV– mothers: a meta-analysis. *Arch Gynecol Obstet* 2011;283:255-60.
9. Chappell CA, Krans EE, Bunge K, et al. Abstract 87: a phase 1 study of ledipasvir/sofosbuvir in pregnant women with hepatitis c virus. In: *Proceedings of the Conference on Retroviruses and Opportunistic Infections* 2019 Mar. 4–7; Seattle (WA). San Francisco (CA): CROI Foundation/IAS–USA; 2019:36.
10. Ordean A, Kahan M, Graves L, et al. Integrated care for pregnant women on methadone maintenance treatment: Canadian primary care cohort study. *Can Fam Physician* 2013;59:e462-9.
11. Deuffic-Burban S, Huneau A, Verleene A, et al. Assessing the cost-effectiveness of hepatitis C screening strategies in France. *J Hepatol* 2018;69:785-92.
12. Chaillon A, Rand EB, Reau N, et al. Cost-effectiveness of universal hepatitis C virus screening of pregnant women in the United States. *Clin Infect Dis* 2019 Jan. 28. [Epub ahead of print]. doi: 10.1093/cid/ciz063.
13. Waruingi W, Mhanna MJ, Kumar D, et al. Virus universal screening versus risk based selective screening during pregnancy. *J Neonatal Perinatal Med* 2015;8:371-8.
14. NIH consensus statement on management of hepatitis C: 2002. *NIH Consens State Sci Statements* 2002;19:1-46.

Competing interests: Neora Pick is a member of the advisory boards for Merck, VIIV and Gilead, as an expert in women's reproductive health and infectious diseases. No other competing interests were declared.

This article has been peer reviewed.

Affiliations: On behalf of the Society of Obstetricians and Gynaecologists of Canada Infectious Diseases Committee (Elwood); Department of Obstetrics and Gynaecology (Elwood), University of British Columbia; Oak Tree Clinic, BC Women's Hospital (Elwood, Sauve, Pick); Department of Pediatrics, BC Children's Hospital (Sauve), University of British Columbia, Vancouver, BC

Contributors: Chelsea Elwood contributed substantially to the concept and writing of the commentary. Laura Sauve and Neora Pick contributed substantially to the writing of the manuscript. All of the authors contributed substantially to the editing of the work, revised the manuscript critically for important intellectual content, gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Correspondence to: Chelsea Elwood, Chelsea.elwood@cw.bc.ca