Hepatitis A infection during pregnancy

Shahnaz A. Chaudhry MD MRCOG **Gideon Koren** MD FRCPC FACMT

Abstract

Question Many of my patients are from Southeast Asia, where hepatitis A virus (HAV) infection is quite common. What precautions can I suggest my pregnant patients take before traveling to these areas and what is the risk of contracting HAV during pregnancy?

Answer Hepatitis A virus is a water-borne pathogen transmitted by the fecal-oral route. To reduce the risk of contracting HAV while traveling to endemic areas, it is important to maintain hygienic practices such as hand washing with safe water, particularly before handling food, avoiding drinking water or using ice cubes of unknown purity, and avoiding eating unpeeled fruits and vegetables. An HAV vaccine is available and can be administered before traveling to endemic countries. Hepatitis A virus infection has a largely favourable expected outcome even during pregnancy. Infection occurring in the second or third trimester has been reported to be associated with preterm labour.

Infection par l'hépatite A durant la grossesse

Résumé

Question Bon nombre de mes patientes sont originaires de l'Asie du Sud-Est, où l'infection par le virus de l'hépatite A (VHA) est assez courante. Que dois-je suggérer à mes patientes enceintes comme précautions à prendre avant de se rendre dans ces régions et quel est leur risque d'être infectées par le VHA durant la grossesse?

Réponse Le virus de l'hépatite A est un pathogène hydrique transmis par la voie fécale-orale. Pour réduire le risque de contracter le VHA durant un voyage dans les régions où il est endémique, il est important de maintenir de bonnes pratiques d'hygiène, comme se laver les mains avec de l'eau salubre, surtout avant de manipuler de la nourriture, éviter de boire de l'eau ou d'utiliser des glaçons dont la pureté est inconnue et éviter de consommer des fruits et des légumes non pelés. Il existe un vaccin contre le VHA qu'on peut administrer avant un voyage vers des pays endémiques. Le pronostic d'une infection par le virus de l'hépatite A est largement favorable, même durant la grossesse. On a associé une infection se produisant au deuxième ou troisième trimestre avec un travail prématuré.

Hepatitis A virus (HAV) is a common cause of acute viral hepatitis across the globe and is preventable by a safe and effective vaccine. Hepatitis A virus is a single-stranded RNA virus that belongs to the Picornaviridae family.[1] Hepatitis A virus infection is typically self-limited and rarely life-threatening, with an estimated mortality rate of 0.3% to 0.6%. The mortality rate increases to 1.8% in adults older than 50 years.[2,3] It is highly endemic in South and Central Asia, sub-Saharan Africa, Latin America, North Africa, the Middle East, and Oceania.[4] Approximately 1.5 million new cases are reported annually, although the true incidence is likely much higher, as milder cases are under-reported.[5]

Mode of transmission

Hepatitis A virus is transmitted via the fecal-oral route either by direct contact with an infected person or indirectly by ingestion of fecally contaminated food, especially raw and undercooked shellfish.[6,7] The incubation period for HAV is 15 to 50 days, with a mean of 28 days.[8] In a dried state, the virus can survive for at least 1 week in ambient conditions, and it can survive in fresh or salty water for up to 12 months.[9,10] Hepatitis A virus infection is common in developing countries owing to poor hygiene and sanitation systems, resulting in contaminated food and water supplies, which typically leads to infection in early childhood and a mild form of the disease.[11] Transmission of HAV from the mother to the fetus is uncommon, although there are numerous case reports of vertical transmission, with 2 cases associated with meconium peritonitis and perforation of the distal ileum requiring surgery.[11-13] Nosocomial spread is also possible from pregnant women and neonates to other infants, adults, or health care workers.

Effects of hepatitis on pregnancy

Hepatitis A infection is the most common cause of acute viral hepatitis in the general population but it is

infrequently reported among pregnant women. Hence, data on the incidence and outcome of HAV infection during pregnancy are scarce.[14-16] Overall, HAV infection during pregnancy is not associated with serious outcomes.[17] However, the available data show a causal relationship between HAV infection and preterm labour, especially if infection occurs in the second or third trimester.[11] Hepatitis A virus infection has also been reported to be associated with other gestational complications such as increased premature uterine contractions, placental abruption, and premature rupture of membranes.[11] The markers for a more aggressive course of the disease are fever and hypoalbuminemia. Overall, no mortality was reported among mothers and infants exposed to HAV infection, with full resolution of the infection.[18] Most infants born to mothers with HAV infection were not affected and had normal antibody and transaminase levels. However, in the rare cases in which mother-to-child HAV infection occurs, it can be associated with fetal ascites, meconium peritonitis, neonatal icteric HAV infection, and distal ileum perforation.[19]

Breastfeeding

Although mothers infected with HAV have anti-HAV antibodies and HAV RNA in their breast milk, there is no evidence that breastfeeding transmits HAV to suckling infants. Therefore, breastfeeding should not be discouraged; the child should be protected through administration of immunoglobulin or the inactivated vaccine.[20]

Prevention

To reduce the risk of contracting HAV while traveling to endemic areas, it is important to maintain hygienic practices such as hand washing with safe water, particularly before handling food, avoiding drinking water or using ice cubes of unknown purity, and avoiding eating unpeeled fruits and vegetables. Before visiting HAV-endemic countries or underdeveloped countries with poor sanitation and hygienic standards, pregnant women and women of reproductive age need protection against HAV.[4] The HAV vaccine is available both in a monovalent form and in combination with hepatitis B virus. Hepatitis A virus vaccine is prepared from the inactivated virus and is considered safe during pregnancy, but there should be a clear indication for administering the vaccine during pregnancy.[21] About 70% of individuals develop protective levels of antibodies 2 weeks after the first dose of the vaccine.[22] Hence, if the vaccine is administered immediately before travel, it can ensure adequate protection, as the incubation period for HAV is 15 to 50 days. Adequate levels of antibodies will likely persist for at least 10 to 29 years, if not for life, after receiving the second dose.[23]

Conclusion

Overall, infection with HAV is a result of poor hygiene and can be prevented through appropriate food handling and water sanitation. Hepatitis A virus infection is preventable with a vaccine and has a largely favourable expected outcome with regard to the mother and the fetus. However, infection in the second and third trimesters has been associated with preterm labour and other complications. Breastfeeding should not be discouraged in mothers with HAV infection. Infants should be protected by administration of either immunoglobulin or the inactivated HAV vaccine.

Competing interests
None declared

References

1. Koff RS. Hepatitis A. *Lancet* 1998;351(9116):1643-9.
2. Wheeler C, Vogt TM, Armstrong GL, Vaughan G, Weltman A, Nainan OV, et al. An outbreak of hepatitis A associated with green onions. *N Engl J Med* 2005;353(9):890-7.
3. Advisory Committee on Immunization Practices; Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2006;55(RR-7):1-23.
4. Public Health Agency of Canada [website]. *Canadian immunization guide. Part 4. Active vaccines. Hepatitis A vaccine.* Ottawa, ON: Public Health Agency of Canada; 2007. Available from: **www.phac-aspc.gc.ca/publicat/cig-gci/p04-hepa-eng.php**. Accessed 2015 Sep 24.
5. World Health Organization. Hepatitis A vaccines. *Wkly Epidemiol Rec* 2000;75(5):38-44.
6. Ornoy A, Tenenbaum A. Pregnancy outcome following infections by coxsackie, echo, measles, mumps, hepatitis, polio and encephalitis viruses. *Reprod Toxicol* 2006;21(4):446-57. Epub 2006 Feb 9.
7. Lemon SM, Thomas DL. Vaccines to prevent viral hepatitis. *N Engl J Med* 1997;336(3):196-204.
8. Spira AM. A review of combined hepatitis A and hepatitis B vaccination for travelers. *Clin Ther* 2003;25(9):2337-51.
9. McCaustland KA, Bond WW, Bradley DW, Ebert JW, Maynard JE. Survival of hepatitis A virus in feces after drying and storage for 1 month. *J Clin Microbiol* 1982;16(5):957-8.
10. Tallon LA, Love DC, Moore ZS, Sobsey MD. Recovery and sequence analysis of hepatitis A virus from springwater implicated in an outbreak of acute viral hepatitis. *Appl Environ Microbiol* 2008;74(19):6158-60. Epub 2008 Aug 15.
11. Elinav E, Ben-Dov IZ, Shapira Y, Daudi N, Adler R, Shouval D, et al. Acute hepatitis A infection in pregnancy is associated with high rates of gestational complications and preterm labor. *Gastroenterology* 2006;130(4):1129-34.
12. McDuffie RS Jr, Bader T. Fetal meconium peritonitis after maternal hepatitis A. *Am J Obstet Gynecol* 1999;180(4):1031-2.
13. Leikin E, Lysikiewicz A, Garry D, Tejani N. Intrauterine transmission of hepatitis A virus. *Obstet Gynecol* 1996;88(4 Pt 2):690-1.
14. Khuroo MS, Kamili S. Aetiology, clinical course and outcome of sporadic acute viral hepatitis in pregnancy. *J Viral Hepat* 2003;10(1):61-9.
15. Acharya SK, Dasarathy S, Kumer TL, Sushma S, Prasanna KS, Tandon A, et al. Fulminant hepatitis in a tropical population: clinical course, cause, and early predictors of outcome. *Hepatology* 1996;23(6):1448-55.
16. Dahiya M, Kumar A, Kar P, Gupta RK, Kumar A. Acute viral hepatitis in third trimester of pregnancy. *Indian J Gastroenterol* 2005;24(3):128-9.
17. Cuthbert JA. Hepatitis A: old and new. *Clin Microbiol Rev* 2001;14(1):38-58. Erratum in: *Clin Microbiol Rev* 2001;14(3):642.
18. Fiore S, Savasi V. Treatment of viral hepatitis in pregnancy. *Expert Opin Pharmacother* 2009;10(17):2801-9.
19. Motte A, Blanc J, Minodier P, Colson P. Acute hepatitis A in a pregnant woman at delivery. *Int J Infect Dis* 2009;13(2):e49-51. Epub 2008 Sep 6.
20. Daudi N, Shouval D, Stein-Zamir C, Ackerman Z. Breastmilk hepatitis A virus RNA in nursing mothers with acute hepatitis A virus infection. *Breastfeed Med* 2012;7:313-5. Epub 2012 Apr 26.
21. Duff B, Duff P. Hepatitis A vaccine: ready for prime time. *Obstet Gynecol* 1998;91(3):468-71.
22. Werzberger A, Mensch B, Kuter B, Brown L, Lewis J, Sitrin R, et al. A controlled trial of a formalin-inactivated hepatitis A vaccine in healthy children. *N Engl J Med* 1992;327(7):453-7.
23. Wiedermann G, Kundi M, Ambrosch F, Safary A, D'Hondt E, Delem A. Inactivated hepatitis A vaccine: long-term antibody persistence. *Vaccine* 1997;15(6-7):612-5.

MOTHERISK Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Dr Chaudhry** is a clinical pharmacology and toxicology fellow in the Motherisk Program. **Dr Koren** is the founder of the Motherisk Program.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future **Motherisk Updates**. Published **Motherisk Updates** are available on the *Canadian Family Physician* website (**www.cfp.ca**) and also on the Motherisk website (**www.motherisk.org**).