Hepatitis E infection during pregnancy

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Abstract

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

Answer Hepatitis E is a water-borne pathogen transmitted by the fecal-oral route. To reduce the risk of contracting HEV 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. Currently there is no vaccine available in Canada for HEV. Hepatitis E infection during pregnancy, especially in the third trimester, is characterized by a more severe infection that sometimes results in fulminant hepatitis, increasing maternal and fetal mortality and morbidity.

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Hepatitis E virus (HEV) is an emerging infectious agent causing acute viral hepatitis worldwide.[1] Each year more than 20 million estimated cases of HEV infection occur globally, resulting into 70 000 deaths.[1] Hepatitis E virus was first recognized in 1978 during an epidemic in Kashmir Valley in northern India, with 52 000 cases of hepatitis resulting in 17 000 deaths.[2]

Hepatitis E is a single-stranded RNA virus with 4 genotypes, of which genotypes 1 and 2 exclusively infect humans and can lead to endemic HEV or outbreaks in countries with poor sanitation systems. Genotypes 3 and 4 can infect humans, pigs, and other animals, and can result in sporadic infection in both developed and developing countries.[3] Distribution of HEV varies across the globe, with genotype 1 being more common in Asia, Africa, and Latin America, while genotype 2 is more common in sub-Saharan Africa and Mexico. Genotypes 3 and 4 can infect both medically vulnerable and healthy populations, and are mostly detected in sporadic cases in developed countries.[4,5]

There is increasing evidence that HEV is an important contributor to maternal morbidity and mortality in South Asia, especially if infection occurs in the third trimester with genotype 1.[6,7]

Hepatitis E virus is a water-borne pathogen that has fecal-oral transmission, mostly due to ingestion of fecally contaminated water. Direct person-to-person transmission is uncommon.[8] The incubation period ranges from 15 to 64 days with a mean of 6 weeks.[9] The virus has a 50% rate of vertical transmission.[7,10]

During pregnancy

Hepatitis E infection during pregnancy and in the third trimester, especially with genotype 1, is associated with more severe infection and might lead to fulminant hepatic failure and maternal death.[11-13] Although the mechanism of liver injury is not yet clear, it is possible that interplay of hormonal and immunologic changes during pregnancy, along with a high viral load of HEV, renders the woman more vulnerable.[14] Immunologic changes during pregnancy promote the maintenance of the fetus in the maternal environment by suppression of T cell–mediated immunity, rendering pregnant women more susceptible to viral infections like HEV infection. During pregnancy, levels of progesterone, estrogen, and human chorionic gonadotropin increase as pregnancy advances. These hormones play a considerable role in altering immune regulation and increasing viral replications.[15]

Hepatitis E infection with genotype 1 during the third trimester can lead to maternal mortality in up to 15% to 25% of cases.[16] Most of the studies showing high maternal mortality are from India, where infection occurs in epidemics. There is a very high risk of vertical transmission of HEV from the mother to the fetus. During a Delhi epidemic, a hospital-based study revealed that HEV infection during pregnancy was associated with miscarriage, stillbirth, or neonatal death in 56% of infants.[6] One recent study[1] highlights that HEV infection might be responsible for 2400 to 3000 stillbirths each year in developing countries, with many additional fetal deaths linked to antenatal maternal deaths.[11] There is a very

high risk of preterm delivery in pregnant women with HEV infection, with poor neonatal survival rates.[11,17] In 2 separate studies from India, 15% to 50% of live-born infants of mothers with HEV infection died within 1 week of birth.[11,18] During an outbreak in Sudan in 2010 to 2011, among 39 pregnant women with HEV infection there were 14 intrauterine deaths and 9 premature deliveries.[19]

Breastfeeding

Breastfeeding is considered safe in asymptomatic women infected with HEV despite the presence of anti-HEV antibodies and HEV RNA in the colostrum. However, it is considered unsafe if the mother has acute hepatic disease or an increased viral load. In these cases, feeding formula is advised, as there is a possibility of transmission from infected breast milk or lesions on the nipple through suckling.[20,21]

Prevention

Currently there is no commercially available HEV vaccine in North America. Hepatitis E vaccine using recombinant capsid protein has been shown in phase 2 and 3 clinical trials to be safe and effective in the general adult population.[22,23] The recombinant hepatitis E vaccine, the first prophylactic vaccine against HEV infection, was approved in China in December 2011.[24] Women traveling to HEV-endemic countries should strictly follow food and water precautions, such as drinking only bottled water, not adding ice cubes to beverages, avoiding unpeeled fruits and vegetables, and washing hands, fruits, and vegetables thoroughly with safe water before eating.[25]

Conclusion

Hepatitis E infection is a result of poor hygiene and can be prevented by practising good hygiene, handling food appropriately, and drinking safe water. Hepatitis E infection during pregnancy, especially in the third trimester with genotype 1, has a more severe outcome that might lead to fulminant hepatitis, increasing maternal and fetal mortality. It is relatively safe for women with hepatitis E infection to breastfeed, except for those with symptomatic HEV infection, for whom breastfeeding is not advisable.

Competing interests
None declared

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MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont.

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