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# Seroprevalence of Hepatitis A and Hepatitis E Viruses among Pregnant Women in Haiti

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*Abstract.* Hepatitis E virus (HEV) infection is associated with a high fatality rate among pregnant women, and gestational complications have been reported among pregnant women infected with hepatitis A virus (HAV). The aim of this study was to determine the seroprevalence of HAV and HEV infections among pregnant women in Haiti. We stratified the population ($n$ = 1,307) between West and non-West regions. Specimens were tested for total HAV antibody (anti-HAV), and IgM and IgG HEV antibody (anti-HEV). Overall, 96.8% pregnant women were positive for total anti-HAV, 10.3% for IgG anti-HEV, and 0.3% for IgM anti-HEV. The prevalence of IgG anti-HEV in the non-West region (12.3%) was significantly greater than that in the West region (5.3%) ($P < 0.0001$). Most pregnant women in Haiti had evidence of past exposure and immunity to HAV. The non-West region had a higher prevalence of HEV. Improvement in water and sanitation will help in the prevention and control of these infections in Haiti.

Globally, there are approximately 20 million new hepatitis E virus (HEV) infections every year. More than three million acute cases of hepatitis E and 44,000 hepatitis E–related deaths were reported in 2015. Four of the seven HEV genotypes affect humans.[1–4] However, there was a single human case of genotype 7, which is found in camels. Genotypes 1 and 2 are a major cause of large outbreaks and epidemics and are commonly seen in developing countries that lack access to safe water, sanitation, and hygiene services, and where contaminated water is the main source of infection. Hepatitis E virus infection is often a self-limiting disease. Hepatitis E virus genotype 1 is associated with a high case fatality rate among pregnant women, particularly during the third trimester.[1] The infection may cause maternal death (15–25%), intrauterine fetal deaths, and postpartum hemorrhage.[3] Hepatitis E virus genotypes 1 and 3 have been reported in the Caribbean; however, no data on HEV prevalence are available from Haiti.[1,4]

Hepatitis A virus (HAV) has similar transmission routes to HEV. It causes infection in an estimated 1.4 million people worldwide each year, with 11–22% requiring hospitalization.[5] There have been reports of associations between preterm delivery and neonatal cholestasis of mothers infected with HAV during the second and third trimesters, with gestational complications developing in 69% of pregnant women infected with HAV.[6,7] There are strategies to prevent HAV and HEV infections through improvements in food and water safety, such as implementation of the Water, Sanitation, and Hygiene (WASH) program.[8] The aim of this study was to determine the seroprevalence of HAV and HEV infections among pregnant women in Haiti.

In this study, we selected a total of 1,307 specimens from 6,241 residual serum specimens collected during the 2012 Biannual Sentinel Serosurvey for HIV among Pregnant Women, which included 18 geographically representative antenatal care sites. Further details on the sampling can be found elsewhere.[9] The protocol was approved by the Haiti National Bioethics Committee and deemed nonhuman subjects research for the CDC's role of analyzing de-identified specimens.

All 1,307 specimens were first tested for total HAV antibody (anti-HAV) immunoglobulins (anti-HAV IgM/IgG) with an automated platform using a chemiluminescent immunoassay (Vitros Eci; Ortho Clinical Diagnostics, Rochester, NY). Samples with ≥ 1 signal-to-cutoff ratio were considered positive. Only 1,279 (97.8%) specimens had sufficient volume for HEV antibody (anti-HEV) IgM and anti-HEV IgG testing. Detection of anti-HEV antibodies was performed using commercially available enzyme immunoassays (Wantai Biopharmaceutical, Inc., Beijing, China). Those that tested positive for anti-HEV IgM were tested for HEV RNA as described previously.[10]

Demographic and socioeconomic characteristics (age, education level, and marital status) were available for each selected specimen. Age was categorized into five age groups (15–19 years, 20–24 years, 25–29 years, 30–34 years, and ≥ 35 years). Education level was categorized as no education, primary (1–8 years of school), secondary (9–12 years of school), and postsecondary (any additional years after secondary school). We adjusted for weights considering the selection probability in each region. We evaluated the association between HAV and HEV seroprevalence by geographic region and demographic and socioeconomic characteristics using $\chi^2$ tests for independence. The analysis was conducted in SAS v. 9.4 (The SAS Institute, Cary, NC). $P$-values ≤ 0.05 were considered statistically significant.

The age of pregnant women included in this study ranged from 15 to 46 years. Of the 1,307 specimens tested for HAV, 96.8% (95% CI: 95.7–97.9) were positive for total anti-HAV. Of the 1,279 specimens tested for HEV, 10.3% (95% CI: 8.4–12.3) were positive for anti-HEV IgG (Table 1) and 0.3% (95% CI: 0.2–0.3) tested positive for anti-HEV IgM. Only one sample was positive for both anti-HEV IgM and IgG. Hepatitis E virus RNA was not detectable in any of the samples.

Total anti-HAV prevalence was similar in West and non-West regions (Table 1). The prevalence of anti-HEV IgG in the non-West region (12.3%) was greater than that in the West region (5.3%) ($P < 0.0001$), but there was no significant difference between anti-HEV IgM positivity in the West and non-West regions (0.2% in West versus 0.3% in non-West, $P = 0.6$). Prevalence of total anti-HAV and anti-HEV IgG increased with

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TABLE 1

Hepatitis A and hepatitis E seroprevalence by demographic and socioeconomic characteristics among pregnant women attending antenatal care clinics—Haiti, 2012

| | | Total anti-HAV positive | | | | Anti-HEV IgG positive | | |
|---|---|---|---|---|---|---|---|---|
| | *N* | *n* | % (95% CI) | *P*-value | *N* | *n* | % (95% CI) | *P*-value |
| Total | 1,307 | 1,265 | 96.8 (95.7–97.9) | – | 1,279 | 123 | 10.3 (8.4–12.3) | – |
| Department | | | | | | | | |
| West | 634 | 613 | 96.8 | 1.000 | 622 | 34 | 5.3 | < 0.001 |
| Non-West | 673 | 652 | 96.8 | | 657 | 89 | 12.3 | |
| Age (years) | | | | | | | | |
| 15–19 | 183 | 169 | 92.1 | 0.008 | 178 | 8 | 6.0 | 0.050 |
| 20–24 | 352 | 340 | 96.4 | | 348 | 27 | 8.7 | |
| 25–29 | 356 | 347 | 98.1 | | 350 | 33 | 9.5 | |
| 30–34 | 241 | 238 | 98.6 | | 234 | 29 | 13.2 | |
| ≥ 35 | 173 | 169 | 97.5 | | 167 | 26 | 16.1 | |
| Education level | | | | | | | | |
| None | 124 | 122 | 98.6 | 0.300 | 121 | 11 | 8.2 | 0.200 |
| Primary | 463 | 450 | 97.5 | | 449 | 58 | 13.1 | |
| Secondary | 659 | 636 | 96.1 | | 649 | 49 | 9.0 | |
| Postsecondary | 61 | 57 | 94.5 | | 60 | 5 | 8.3 | |
| Marital status | | | | | | | | |
| Married | 312 | 299 | 96.3 | 0.600 | 305 | 22 | 8.2 | 0.200 |
| Other | 995 | 966 | 97.0 | | 974 | 101 | 11.0 | |

Anti-HAV = hepatitis A virus antibody; anti-HEV IgG = hepatitis E virus IgG antibody. Percentages were weighted to account for the study design.

age (Table 1). Both HAV and HEV infection prevalence increased with increasing age. Compared with pregnant women aged 15–19 years, women aged ≥ 35 years had a higher prevalence of both anti-HAV (98% versus 92%) and anti-HEV IgG (16% versus 6%).

We evaluated the seroprevalence of HAV and HEV infections among pregnant women in Haiti because the morbidity and mortality associated with HAV and HEV infections increase significantly during pregnancy.[1,7] Our findings demonstrate that Haiti is highly endemic for HAV infections and endemic for HEV infections.[11,12] The 10-year cholera elimination plan launched in February 2013 by Haiti's Ministry of Public Health and Population and the National Directorate for Potable Water and Sanitation aims to implement strategies to improve WASH. According to the 2017 update and Sustainable Development Goals baselines on the progress on drinking water, sanitation, and hygiene, Haiti had limited or no progress in those areas.[13] Hopefully, with WASH implementation, the rates of HAV and HEV infections will decrease.

We could not determine the HEV genotype/s circulating in Haiti as none of the samples tested positive for HEV RNA. However, it is possible that HEV genotypes prevalent in Haiti are closer to those found in West Africa, such as genotypes 1 and 2, which pose increased mortality among pregnant women.[12,14]

The anti-HEV IgG prevalence was lowest among the 15- to 19-year age group (6%), although prevalence steadily increased with age. In a study conducted among pregnant women in Durango, Mexico, the prevalence for anti-HEV IgG also increased with age.[15] In Burkina Faso, HEV seroprevalence in pregnant women was reported at 11.6%, and in Gabon, it was reported at 14.1%, which are similar to the seroprevalence rate we found in Haiti.[16,17] The higher prevalence of HEV in the non-West region than the West department needs to be further investigated.

In conclusion, HAV is highly prevalent in Haiti. Given the very high immunity against HAV, vaccination is not currently recommended in Haiti.[11] Hepatitis E virus prevalence is intermediate with variability between regions. Improvement in WASH will help in the prevention and control of HAV and HEV infections in Haiti.

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## REFERENCES

1. Rein DB, Stevens GA, Theaker J, Wittenborn JS, Wiersma ST, 2012. The global burden of hepatitis E virus genotypes 1 and 2 in 2005. *Hepatology 55:* 988–997.
2. Andonov A, Robbins M, Borlang J, Cao J, Hatchette T, Stueck A, Deschambault Y, Murnaghan K, Varga J, Johnston L, 2019. Rat hepatitis E virus linked to severe acute hepatitis in an immunocompetent patient. *J Infect Dis* jiz025, https://doi.org/10.1093/infdis/jiz025.
3. Patra S, Kumar A, Trivedi SS, Puri M, Sarin SK, 2007. Maternal and fetal outcomes in pregnant women with acute hepatitis E virus infection. *Ann Intern Med 147:* 28–33.
4. Villalba ML, Lay LL, Chandra V, Corredor MB, Frometa SS, Moreno AG, Jameel S, 2008. Hepatitis E virus genotype 1, Cuba. *Emerg Infect Dis 14:* 1320–1322.
5. Matheny SC, Kingery JE, 2012. Hepatitis A. *Am Fam Physician 86:* 1027–1034.

6. Elinav E, Ben-Dov IZ, Shapira Y, Daudi N, Adler R, Shouval D, Ackerman Z, 2006. Acute hepatitis A infection in pregnancy is associated with high rates of gestational complications and preterm labor. *Gastroenterology 130:* 1129–1134.
7. Urganci N, Arapoglu M, Akyildiz B, Nuhoglu A, 2003. Neonatal cholestasis resulting from vertical transmission of hepatitis A infection. *Pediatr Infect Dis J 22:* 381–382.
8. WHO, 2017. *Global Hepatitis Report 2017*. Available at: https://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/. Accessed January 8, 2019.
9. Tohme RA et al., 2016. Hepatitis B virus infection among pregnant women in Haiti: a cross-sectional serosurvey. *J Clin Virol 76:* 66–71.
10. Jothikumar N, Cromeans TL, Robertson BH, Meng XJ, Hill VR, 2006. A broadly reactive one-step real-time RT-PCR assay for rapid and sensitive detection of hepatitis E virus. *J Virol Methods 131:* 65–71.
11. WHO, 2012. WHO position paper on hepatitis A vaccines – June 2012. *Wkly Epidemiol Rec 87:* 261–276.
12. WHO, 2015. Hepatitis E vaccine: WHO position paper, May 2015. *Wkly Epidemiol Rec 90:* 185–200.
13. WHO, 2017. *Progress on Drinking Water, Sanitation and Hygiene: 2017 Update and SDG Baselines*. Available at: https://www.who.int/mediacentre/news/releases/2017/launch-version-report-jmp-water-sanitation-hygiene.pdf. Accessed January 8, 2019.
14. Andernach IE, Nolte C, Pape JW, Muller CP, 2009. Slave trade and hepatitis B virus genotypes and subgenotypes in Haiti and Africa. *Emerg Infect Dis 15:* 1222–1228.
15. Alvarado-Esquivel C, Sanchez-Anguiano LF, Hernandez-Tinoco J, 2014. Hepatitis E virus exposure in pregnant women in rural Durango, Mexico. *Ann Hepatol 13:* 510–517.
16. Caron M, Kazanji M, 2008. Hepatitis E virus is highly prevalent among pregnant women in Gabon, central Africa, with different patterns between rural and urban areas. *Virol J 5:* 158.
17. Traore KA, Rouamba H, Nebie Y, Sanou M, Traore AS, Barro N, Roques P, 2012. Seroprevalence of fecal-oral transmitted hepatitis A and E virus antibodies in Burkina Faso. *PLoS One 7:* e48125.