Hepatitis E Virus Infection among Asymptomatic Pregnant Women at the University College Hospital, Ibadan

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Abstract

Introduction: The high mortality associated with fulminant Hepatitis E infection in pregnancy justifies the need to assess the epidemiologic proportion of this underestimated virus. **Objectives:** This study aimed to determine the burden of HEV infection among pregnant women attending antenatal Clinic in Ibadan. **Methodology:** HEV IgG and IgM serological surveys were carried out among 230 pregnant women attending antenatal clinic in Ibadan, Nigeria. Serum and stool samples from HEV IgM positive women were further analysed using two independent reverse transcriptase polymerase chain reactions (RT-PCR) assays, targeting ORF1 region of HEV genome. Socio-demographic variables associated with HEV in these women, were analyzed to estimate statistical significance ($p < 0.05$). **Results:** Eleven (4.8%) women had HEV IgM, while 39 (17.0%) women had HEV IgG. Three (27.3%) of the 11 anti-HEV IgM positive samples were positive for HEV RNA while all stool samples tested negative for HEV RNA. HEV infection among pregnant women was statistically associated with age ($p = 0.044$), and educational status ($p = 0.005$). **Conclusion:** Recent HEV infection among this pregnant population is on the lower part of the scale, compared with other Sub-Saharan African countries. However, the HEV IgG seroprevalence rate suggests indirect evidence of past contact with HEV.

Keywords: Hepatitis E, Ibadan, pregnant women

Introduction

Infection with hepatitis E virus (HEV) is particularly fatal for pregnant women with fulminant hepatitis, for whom the mortality rate can be as high as 10%–20%.[1] Pregnancy appears to be a potential risk factor for viral replication and leads to extremely low immune status among African, Indian, and Asian pregnant women.[2] The current study therefore aimed to determine the burden of HEV infection among pregnant women in our environment.

Methods

This prospective study was carried out at the University College Hospital, Ibadan, Southwestern Nigeria. Sera were tested for antibodies by ELISA (HEV IgG and IgM, DiaPro, Milan, Italy) kits. HEV IgM seroreactive samples were confirmed by two independent polymerase chain reaction (PCR) assays, targeting ORF1 of the HEV genome. PCR amplification was carried out using the primers selected from the nonstructural ORF1 region. The primers used were – external sense: 5′-CCG GAT CCA CAC ACA TCT GAG CTA CAT TCG TGA GCT-3′, external anti-sense: 5′-CCG AAT TCA AAG GCA TCC ATG GTG TTT GAG AAT GAC-3′, internal sense: 5′-GGA ATT CGA CTC CAC CCA GAA TTA CTT-3′, and internal anti-sense 5′-GGA ATT CAC AGC CGG CGA TCA GGA CAG-3′. These two sets of primers were designed to amplify 343 bp segment of the ORF1 region.

Results

The mean age of the 230 participants was 32.1 ± 4.8 years, with more than half (55.6%) aged between 29 and 35 years. Other sociodemographic characteristics are summarized in Table 1.

HEV IgM antibodies were detected in 11 (4.8%) of the participants while HEV IgG antibodies were detected in 39 (17.0%). None of the HEV IgM-positive participants was positive for HEV IgG antibodies. Of the 11 HEV IgM-seropositive women, three (27.3%) were confirmed positive for HEV RNA by PCR. All the 11 stool samples were negative for HEV RNA.

There was a significant association between the age of respondents and their HEV RNA status ($\chi^2 = 5.18$, $P = 0.044$) and between educational

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Table 1: Association between sociodemographic characteristics and hepatitis E virus RNA status

Variable	HEV RNA		Total (%)	χ^2	*P*
	Yes (%)	No (%)			
Age (years)					
<20	0	15 (6.6)	15 (6.5)	5.18	0.044
20-29	1 (0.6)	87 (38.3)	88 (38.3)		
30-39	2 (0.7)	125 (55.1)	127 (55.2)		
40-49	0	0	0		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Residential area					
Within Ibadan	2 (0.9)	222 (96.5)	224 (97.4)	11.29	0.08*
Outside Ibadan	1 (0.4)	5 (2.2)	6 (2.6)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Level of education					
Primary uncompleted	0	2 (0.9)	2 (0.9)	10.73	0.005
Primary completed	3 (1.3)	4 (1.7)	7 (3)		
Secondary uncompleted	0	9 (3.9)	9 (3.9)		
Secondary completed	0	35 (15.2)	35 (15.2)		
Post-secondary	0	12 (5.2)	12 (5.2)		
University graduate	0	144 (62.6)	144 (62.6)		
Others (specify)	0	21 (9.1)	21 (9.1)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Employment status					
Employed government/private	2 (0.9)	90 (39.1)	92 (40.0)	1.17	0.95
Unemployed	0	19 (8.3)	19 (8.3)		
Self-employed	1 (0.4)	92 (40.0)	93 (40.4)		
Homemaker	0	11 (4.8)	11 (4.8)		
Student	0	6 (2.6)	6 (2.6)		
Others (specify)	0	9 (3.9)	9 (3.9)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Type of housing					
Personal house	0	37 (16.1)	37 (16.1)	1.56	0.67
Rented flat	3 (1.3)	149 (64.8)	152 (66.1)		
Self-contain	0	30 (13.0)	30 (13.0)		
Single rooms	0	11 (4.8)	11 (4.8)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Source of drinking water					
Surface stream	0	129 (56.1)	129 (56.1)	1.36	0.72
Underground water	2 (0.9)	42 (18.2)	44 (19.1)		
Bore-hole	1 (0.4)	38 (16.5)	39 (17.0)		
Pipe-borne	0	18 (7.8)	18 (7.8)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Total monthly income of both partners					
<50,000	0	20 (8.7)	20 (8.7)	4.64	0.46
50,000-100,000	0	57 (24.8)	57 (24.8)		
100,000-150,000	1 (0.4)	72 (31.3)	73 (31.7)		
150,000-200,000	2 (0.9)	45 (19.6)	47 (20.4)		
200,000-250,000	0	23 (10.0)	23 (10.0)		
Above 250,000	0	10 (4.3)	10 (4.3)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		

*Tested by Fisher's exact test. HEV: Hepatitis E virus

status and the participants' HEV infection status ($\chi^2 = 10.73$, $P = 0.005$). Of the eight respondents with a history of jaundice, anti-HEV IgM antibody was present in three (37.5%) and all three were positive for HEV RNA, suggesting a positive association between history of jaundice and HEV RNA status ($\chi^2 = 0.12$, $P = 0.00$) [Table 2].

Discussion

The HEV seroprevalence rates in some endemic areas are often in excess of the population burden of hepatitis E-associated symptomatic illnesses. The current study revealed a HEV IgM seroprevalence of 4.8% and a higher HEV IgG seroprevalence

Table 2: Association between clinical characteristics and hepatitis E virus RNA status

Variable	HEV RNA		Total (%)	χ^2	*P*
	Yes (%)	No (%)			
History of jaundice in previous or present pregnancy					
Positive	3 (1.3)	5 (2.2)	8 (3.5)	0.12	0.00*
Negative	0	222 (96.5)	222 (96.5)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
History of premature delivery of newborn in previous pregnancies					
Yes	1 (0.4)	10 (4.4)	11 (4.8)	5.41	0.14*
No	2 (0.9)	216 (94.3)	218 (95.2)		
Total	3 (1.3)	226 (98.7)	229 (100.0)		
History of abortion					
Yes	0	57 (24.8)	57 (24.8)	1.00	0.42*
No	3 (1.3)	170 (73.9)	173 (75.2)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
Gestational age					
1st trimester	0	42 (18.3)	42 (18.3)	1.95	0.38
2nd trimester	3 (1.3)	137 (59.6)	140 (60.9)		
3rd trimester	0	48 (20.9)	48 (20.9)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
HIV status					
Positive	0	16 (6.9)	16 (6.9)	4.34	0.11
Negative	2 (0.9)	198 (86.1)	200 (87.0)		
Unknown	1 (0.4)	13 (5.7)	14 (6.1)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		
History of threatened abortion					
Yes	1 (0.4)	60 (26.1)	61 (26.5)	0.07	0.61*
No	2 (0.9)	167 (72.6)	169 (73.5)		
Total	3 (1.3)	227 (98.7)	230 (100.0)		

*Tested by Fisher's exact test. HEV: Hepatitis E virus

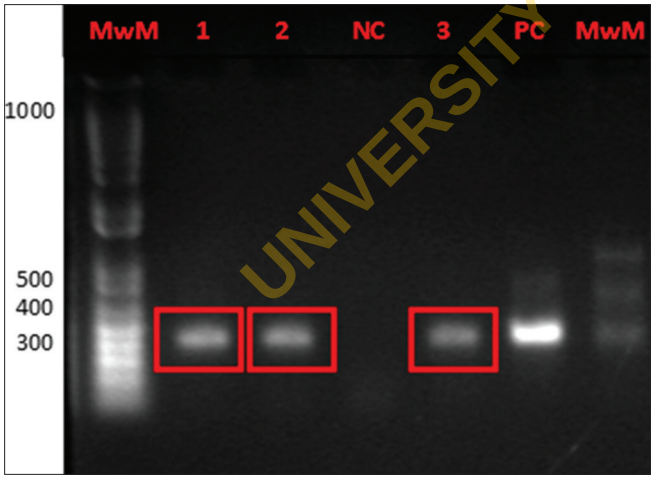

Figure 1: Agarose gel electrophoregram showing PCR results of the three HEV positive samples runs separately, with positive control (PC) and Negative Control (NC; water in lieu of template DNA) and a 100Kb Molecular Weight Marker (MwM). Samples S1, S2 and S3 were positive with PCR product size corresponding to the band with molecular weight 343bp. NC= Negative control, PC = Positive contro,l S1-S3 = Positive samples

of 17.0%, thus suggesting the possibility of previous exposure and self-limiting infection among this cohort. HEV RNA was detected in only 3 (1.3%) of the pregnant women. Acute viral hepatitis E is evidenced by HEV IgM seropositivity and presence of HEV RNA. Only three out of the 11 HEV IgM (27.3%) seropositive were HEV RNA positive [Figure 1]. This might be attributed to the nonoptimal performance of serological tests compared with genomic tests.

The results of this study bring to light the burden of hepatitis E in Ibadan and the risk factors among pregnant women attending the antenatal clinic. It also highlights the independent risk factors for HEV infection in the study which were age of the participants and educational status. There is need for multicenter large-scale study on hepatitis E infection in pregnancy, to accurately determine the burden of hepatitis E in Nigeria, and also to define the impact of pregnancy on the immunological dynamics of HEV infection.

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Conflicts of interest

There are no conflicts of interest.

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