

## Original article

# Seroprevalence and associated risk factors of hepatitis E virus infection among pregnant women attending Maiduguri Teaching Hospital, Nigeria

*Babajide Bamidele Ajayi*<sup>1</sup>, *Imaan Igwegbe*<sup>2</sup>, *Semsari Latbone*<sup>2</sup>, *Ibrahim Musa Kida*<sup>3</sup>, *Bamidele Soji Oderinde*<sup>2</sup>, *Samuel Oyeboode Oyinloye*<sup>4</sup>, *Kayode Adelowo*<sup>5</sup>, *Ballah Akawu Denu*<sup>3</sup>, *Calvin Chama*<sup>6</sup>, *Idris Nasir Abdullahi*<sup>7</sup>

1- Department of Microbiology, School of Sciences, Federal University of Technology Akure, Nigeria.

2- Department of Medical Laboratory Science, College of Medical Sciences, University of Maiduguri.

3- Department of Medicine, University of Maiduguri Teaching Hospital, Maiduguri Nigeria.

4- Department of Microbiology, Faculty of Science, University of Maiduguri, Borno State, Nigeria.

5- Department of Immunology, University of Maiduguri Teaching Hospital, Maiduguri Nigeria.

6- Department of Obstetrics and Gynaecology, University of Maiduguri Teaching Hospital, Maiduguri Nigeria.

7- Department of Medical Laboratory Science, College of Medical Sciences, Ahmadu Bello University, Zaria, Nigeria.

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## ABSTRACT

**Background:** Hepatitis E virus (HEV) is a major public health problem in developing countries and often fatal among pregnant women in the third trimester. **Objective:** The study investigated the sero-prevalence and risk factors of HEV infection among pregnant women attendee of University of Maiduguri Teaching Hospital, Maiduguri, Nigeria. **Method:** The cross-sectional study was carried out between 4<sup>th</sup> January 2016 to 30<sup>th</sup> May, 2016. One hundred and eighty blood samples from pregnant women who consented and enrolled for the study were analyzed for anti-HEV IgM using a quality assured commercial enzyme linked immunosorbent assay (ELISA) kit. Structured questionnaires were used to collate the sociodemographic characteristics and risk factor of study subjects. **Results:** Out of the 180 pregnant women sampled, the anti-HEV IgM seroprevalence of 13.3% was recorded. The seroprevalence was significantly higher in the age range of 31 – 35 years (26.5%) and least in age range  $\leq 20$  years (4.9%) ( $p=0.009$ ). The highest seroprevalence was recorded in the third trimester 14.1% followed by second ( $p>0.05$ ). After logistic regression, nature of toilet system, and source of water consumption were significant risk factors for active HEV infection ( $p<0.05$ ). **Conclusion:** Based on the 10.8% pooled national prevalence of HEV infection in Nigeria, this study recorded a significantly high level of anti-HEV IgM seropositivity, an indication of recent and active HEV infection among pregnant women at the study area. Also, these infections are most among the pregnant women in their third trimester. Hepatitis E virus infection was related to personal, water and environmental hygiene.

## Introduction

Hepatitis E virus (HEV) is a single stranded positive sense RNA virus, member of the *Orthohepevirus* genus, that belongs to the family

*Hepeviridae* [1,2]. The virus has 4 distinct genotypes (genotype 1–4) and only 1 serotype. Genotype 1 and 2 are isolated solely from humans while 3 and 4 have

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\* Corresponding author: Idris Nasir Abdullahi

E-mail address: cedris888@yahoo.com

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been isolated from swine and other animals [3,4]. Hepatitis E virus, the causative agent of hepatitis E represents considerable public health concern in many developing countries of Asia, Africa and Central America where infections are contracted via faecal-oral route due to consumption of contaminated food and water (poor food hygiene and sanitation) [5,6].

Water contaminated by HEV has been reported more than food in Africa and Asia where it has caused an epidemic hepatitis E [7,8]. The World Health Organization (WHO) reported that approximately 2 billion persons live in areas that are endemic for HEV and estimated that more than 20 million infections occur annually, leading to about 44,000 deaths worldwide [9].

Hepatitis E virus infection due to genotypes 1 and 2 occasionally has severe maternal complications such as acute liver failure (ALF), hemorrhage, eclampsia and high case-mortality rate of 20-30% among infected pregnant women, particularly those in their third trimester., however, it does not cause chronic disease in the general population [10].

Presently, the definite mechanism for the unreasonably high mortality among pregnant women has not been fully elucidated [11]. However, in developed countries, HEV infection due to genotypes 3 and 4 in pregnancy has a milder course with low risk of complications [11]. Hepatitis E virus infection generally remains asymptomatic or presents as mild and self-limiting disease. The humoral immune response begins with the rise of anti-HEV IgM antibodies straggled by the development of a robust anti-HEV IgG response [12].

In Nigeria, a recent meta-analysis and systematic review reported a pooled HEV prevalence of 10.8% and 65.7% in humans and animals, respectively [13]. The disease in pregnant women, however, has been associated with a substantially increased risk of childbearing conditions such as abortion, stillbirth, low birth weight and preterm labour [13–17]. Thus, the current study sought to determine the sero-prevalence of anti-HEV IgM antibodies and associated risk factors among pregnant women attending the University of Maiduguri Teaching hospital, Maiduguri, Nigeria.

## Materials and Methods

### Study area

The cross-sectional study was carried out between 4<sup>th</sup> January 2016 to 30<sup>th</sup> May 2016 at the University of Maiduguri Teaching Hospital (UMTH), Maiduguri, Borno State, Nigeria. The UMTH is a tertiary health

facility designated center of excellence in immunology and infectious diseases situated in Maiduguri. The hospital has a bed capacity of 530 and provides health services to the States in the northeast geopolitical zone of Nigeria and neighboring Niger, Chad and Cameroon.

### Ethical consideration

Ethical approval for the study was obtained from the ethical research committee of the University of Maiduguri Teaching Hospital. All subjects gave written or verbal (and accent) informed consent before enrolled into the study. This study was conducted in accordance with the declaration of Helsinki of human Experimentation (as revised in 2003). All data were analyzed anonymously, and women were treated with respect and care.

### Study population

A total of 180 pregnant women attending the antenatal clinic who consented to participate in the study were enrolled. Their age ranged from 15 – 40 years with mean of  $26.8 \pm 6.4$  SD. Structured questionnaires were used to collect data on the demographics and risk factors associated with HEV infection. Subjects included were apparently healthy pregnant women  $\geq 18$  years.

### Sample size

Being a cross-sectional study, the minimum sample size was determined the expression:

$$n = \frac{Z^2 Pq}{d^2}$$

$d^2$

$p$  = prevalence rate from a previous study at  $Z = 3.94$  and standard error of 0.05. Using the prevalence of 0.92% of HEV infection among pregnant women in Northcentral Nigeria [17], a minimum sample size of 15 was calculated. However, 180 pregnant women who voluntarily consented for participation were enrolled.

### Sample collection, processing and laboratory analysis

Five milliliters of venous blood samples were collected from the subjects into a plain vacutainer container which was allowed to clot. The samples were spun at 10000g for 15 minutes and serum was harvested into 2 ml cryovials bottles. The serum samples were stored at  $-20^\circ\text{C}$  and thawed once at room temperature and were screened for the presence of HEV IgM antibodies by commercially available ELISA kits (Diagnostic Automation/ Cortez Diagnostics Inc. Calabasas, USA). The tests were conducted, and results interpreted according to kits manufacturer's instruction. Analysis were done on samples collected every 48 hours interval.

### Statistical analysis

Statistical Package for Social Sciences Version 20.0 (IBM, California, USA) was used for all analysis. Univariate logistic regression was done to determine significant association between seroprevalence of anti-HEV IgM and risk factors of infection. *P values* <0.05 at 95% confidence interval were considered statistically significant.

### Results

Out of the total 180 pregnant women tested 13.3% were positive for HEV IgM antibodies (**Figure 1**). The seroprevalence of anti-HEV IgM was highest among women between 31 – 35 years, 26.5%, this was followed by ages > 36 years, 22% and least among those between 21 – 25 years, 4.4%. There was a significant association between the age of pregnant women and seroprevalence of anti-HEV IgM ( $p=0.009$ ) (**Table 1**).

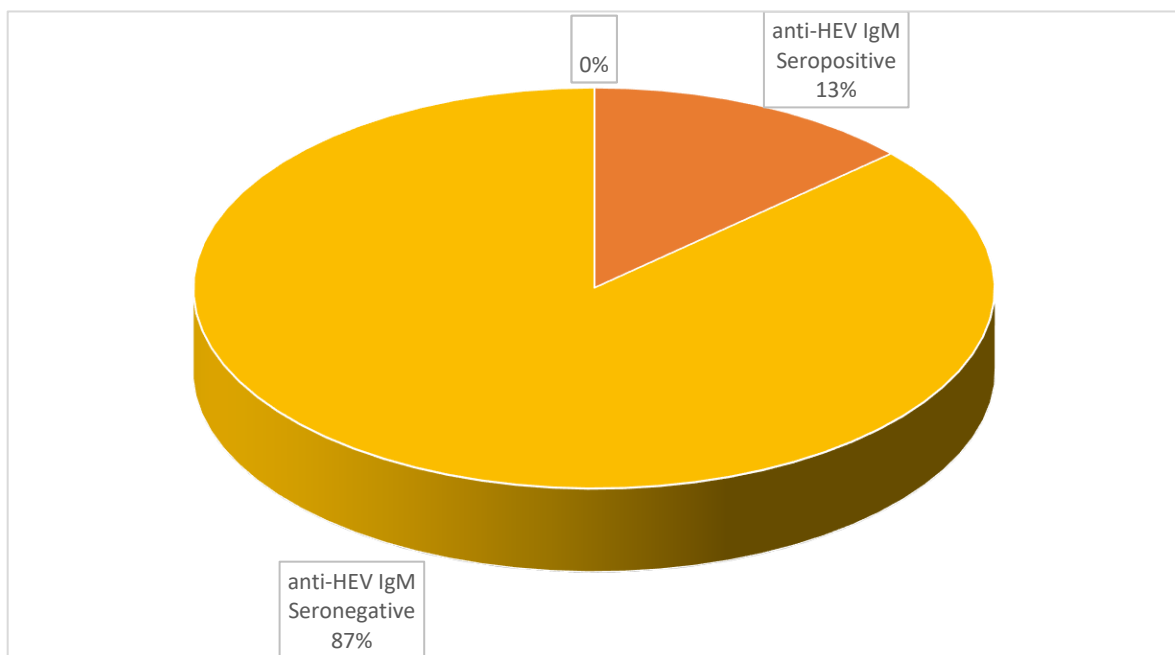
From this study, the highest seroprevalence of anti-HEV IgM of 33.3% was recorded among pregnant women who used stream as source of water, followed by well water, 20.0% and lowest in women who used bore holes, 8.4% (**Table 1**). There was a statistically significant association between anti-HEV IgM seroprevalence and source of water used by pregnant women ( $p=0.005$ ). Anti-HEV IgM seroprevalence was highest in pregnant women that used pit latrine 16.7% followed by those that practice open defecation, 10.0%

and least in those that used water closet system with 8.1%. There was a significant association between seroprevalence of anti-HEV IgM and the type of toilet system used by the pregnant women ( $p<0.0001$ ).

Women in their third trimester of pregnancy had the highest seroprevalence of anti-HEV IgM, 14.1%. This was followed by those in their second trimester, 12.8% and least in those at their first trimester, 10.0%. There was no statistically significant association between seroprevalence of anti-HEV IgM and gestation period of the pregnant women ( $p>0.05$ ).

Pregnant women with the presence of tattoo and or scarification had a relatively higher seroprevalence of anti-HEV IgM (20.0%) than those who do not (13.2%). The prevalence of anti-HEV IgM was highest among subjects who had primary education (17.1%), and least in those with tertiary education (6.7%). Pregnant women with >3 parity had relatively higher seroprevalence of anti-HEV IgM, 30.2% than those with <3 parity, 6.3%. There was significant association between the seroprevalence of anti-HEV IgM with the presence of tattoo and scarification ( $p=0.032$ ). However, no significant association between seroprevalence of anti-HEV IgM and education level and parity of pregnant women ( $p>0.05$ ).

**Figure 1.** Seroprevalence of hepatitis E virus IgM antibodies among pregnant women.



**Table 1.** Risk factors associated with serological evidence of recent hepatitis E virus infection.

Variables	No. of subject tested	No. seropositive (%)	OR	95% (CI)	p-value
<b>Age (years)</b>					
≤ 20	41	2 (4.9)	0.174	0.040 – 0.751	0.009*
21-25	45	2(4.4)	0.140	0.320 - 0.599	
26-30	42	7(16.6)	0.657	0.272 – 1. 587	
31-35	34	9(26.5)	1.546	0.662 – 3.611	
≥ 36	18	4(22.2)	1		
<b>Gestation</b>					
First Trimester	10	1(10.0)	4.250	0.796-22.704	0.068
Second Trimester	78	10(12.8)	0.192	0.093-0.398	
Third Trimester	92	13(14.1)	1		
<b>Source of water</b>					
Well	70	14(20.0)	2.545	1.318-4.914	0.005*
Stream	3	1(33.3)	0.032	0.002-0.458	
Bore Holes	107	9(8.4)	1		
<b>Parity</b>					
> 3	53	16(30.2)	1.036	0.531 – 2.022	0.917
< 3	127	8 (6.3)	1		
<b>Educational status</b>					
Primary	35	6(17.1)	1.167	0.450 – 3.027	0.751
Secondary	40	10(25.0)	0.857	0.386 – 1. 902	
Tertiary	30	2(6.7)	2.800	0.633 – 12.388	
None	75	6(8.0)	1		
<b>Presence of tattoo and body scarifications</b>					
Yes	5	1(20.0)	0.114	0.011-1.216	0.032*
No	175	23(13.1)	1		
<b>Toilet system</b>					
Pit latrine	108	18(16.7)	7.500	4.168 – 13.495	<0.0001*
Water cistern	62	5(8.1)	5.990	2.283 – 15.714	
None	10	1(10.0)	1		

\* Significant association determined by Univariate Logistic regression. OR = Odd Ratio, CI = Confidence Interval

## Discussion

Hepatitis E Virus is a major public health problem in low and middle - income countries and more frequently fatal in the third trimester period of

pregnant women [13-17]. The study revealed a prevalence rate of 13.3% of HEV IgM antibody among pregnant women in the study area suggesting the appreciable presence of HEV in the study area. Anti –

HEV IgM antibody observed in this study also indicates some recent and active infection. This is however, the first study on HEV carried out on pregnant women in the study area. The 13.3 % prevalence rate reported in this study is higher to the findings by **Bello et al.** [18] who reported the prevalence of 9.9% anti – HEV IgG in Sokoto, North Western Nigeria and much lower than the report of **Surajudeen et al.** [19] who observed the prevalence of 42.6% among pregnant women in Jos North Central, Nigeria. However, the results from this study is comparable to a study carried out in Gabon with prevalence rate of 14.1% of HEV infection [20]. A study carried out in Ghana found a high prevalence rate of 28.66% of HEV antibody among pregnant women [21]. Also, **Musa et al.** [22] reported a higher prevalence rate of 61.2% among pregnant women in Khartoum Sudan. The high rate in Sudan and Ghana suggest that they are endemic areas for HEV infection which may be attributed to the poor sanitation and contamination of water supply by fecal materials. The prevalence is also lower than that of who reported 47.4%, 45% and 37% respectively in India [23–26]. These variations could be due to degree of endemicity of HEV and socioeconomical statuses in these locations.

This study showed that pregnant women who had primary educational status had the highest seroprevalence of HEV IgM seroprevalence. This is in agreement with most studies where women with tertiary educational status have the lowest seropositivity [27– 29]. This may be connected with the literacy level and its influence on the practice and adherence to personal, food and environmental hygiene.

The finding from this study revealed the highest prevalence rate of HEV IgM was found in pregnant women in their third trimester. Our findings corroborated with the study of **Kumar et al.** [6] who reported that the majority of pregnant women infected with HEV were in their third trimester. A study indicated that HEV infection during pregnancy especially in second and third trimester may lead to hepatic failure with increased risk of mortality [19]. Reported data from HEV studies have shown that chronic infections elevate viral load, prolonged viremia has been documented during pregnancy [30–32]. These contribute to severe liver injury or liver failure in the mother and vertical transmission from mothers to fetus [33]. There are reports that mother to child transmission of HEV infection has been documented with the rate of transmission, which

ranged from 30 to 100% [33]. Our cross-sectional study, however, did not account for these clinical features.

From this study, pregnant women that used stream as source of water supply had the highest seroprevalence of HEV IgM. This finding corroborates with the findings of **Bello et al.** [18] who reported a prevalence of 37.5% and 5.4% among pregnant women who used river and borehole as source of water respectively. The high prevalence among those that used stream as source of water may be attributed to the contamination of the stream with human faeces. This is in agreement with reports from other studies in the USA, France, Spain and Turkey [31– 34].

Findings from this study revealed significant association between seroprevalence of HEV IgM and tattoo and scarification. Although, tattooing and scarification were not associated with HEV seropositivity from the report of **Vilibic-Cavlek et al.** [35], this reflect the possibility of HEV contamination of equipment used for these practices.

#### **Conclusion**

Based on the 10.8% pooled national prevalence of HEV infection in Nigeria, this study recorded a significantly high level of anti–HEV IgM seropositivity, an indication of recent and active HEV infection among pregnant women at the study area. Also, this infection is most among the pregnant women in their third trimester. Hepatitis E virus infection was related to personal, water and environmental hygiene.

There is the need for further studies to assess the implication of HEV infection over the maternal and fetal outcome in pregnant women and to determine the genotypes predominant the study location.

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