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Vertical Transmission of Hepatitis E Virus Infection Among Antenatal Attendees in Ekiti, Nigeria: A Longitudinal Cohort Study

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Abstract

Hepatitis E virus (HEV) infection in pregnancy is a serious health issue associated with spontaneous miscarriage, preterm labour and also accounts for 30% maternal mortality in the third trimester. This study was carried out to determine the anti-HEV prevalence, HEV vertical transmission and possible pregnancy complications among the antenatal attendees attending the two tertiary facilities in Ekiti State. This longitudinal cohort study involved 300 antenatal attendees recruited over a period of 15 months. Plasma samples were initially screened for anti-HEV antibodies using rapid enzyme immunoassay followed by ELISA assay as the gold standard. Seropositive mothers were followed up till delivery. Pregnancy complications and vertical transmission were reported. Descriptive statistics was used to obtain frequency, percentages, mean and standard deviation using SPSS software version 21 software for data analyses. Correlation between viral prevalence age was also tested and a p-value of < 0.05 was considered statistically significant. Performance characteristics of the rapid immunochromatographic technique was evaluated. The HEV seroprevalence of 2.0% was recorded among the antenatal attendees with vertical transmission rate of 16.7%. The sensitivity and

negative predictive values of rapid kit for both HEV-IgM and HEV-IgG antibodies were 100%, the specificity was 90% for HEV-IgG and 99.7% for HEV-IgM. Study also showed that 25.67%, 14% and 6.0% of the participants respectively had abortion, preterm deliveries and postpartum complications. HEV infection still remains a significant public health burden in view of its contribution to maternal and neonatal morbidity and mortality especially in the third trimester. Vertical transmission of HEV is still a challenge and inculcation of routine screening for HEV antibodies into antenatal care protocol will help to identify at risk mothers and reduce pregnancy complications.

Keywords: HEV, Infection, vertical transmission, Antenatal attendees, Ekiti, Nigeria

Introduction

Hepatitis E virus causes mild and self-limiting viral hepatitis in general population, chronic hepatitis in immuno-compromised individuals (Nimigaonkar *et al.*, 2018). It is a more severe infection in pregnant women with attendant preterm labour and account for about 30% maternal mortality in the second and third trimesters (Nimigaonkar *et al.*, 2018). Hepatitis E virus also results in extra-hepatic conditions such as

pancreatitis, neurological disorders, haematological disorders, glomerulonephritis and cryoglobulinemia (Bazerbachi *et al.*, 2016; Nimgaonkar *et al.*, 2018). The global burden of these viral infections approximates 20 million, out of which about 3.3million are symptomatic with acute HEV infection, with 60,000 deaths annually (Nimgaonkar *et al.*, 2018; WHO, 2019). In developing countries HEV infection has manifested as large outbreaks of increasing frequency and the majority of these outbreaks occur in Asia (59%) and Africa (39%) while Latin America accounts for the remaining 2% (Adjei *et al.*, 2009; Carratala *et al.*, 2019; Fierro *et al.*, 2016). Although, the prevalent rates of between 2.6% and 33% have been recorded among the general population (Adjei *et al.*, 2009; Goumba *et al.*, 2010; Huang *et al.*, 2013; Ahumibe *et al.*, 2014; Cong *et al.*, 2015), the average prevalent rate among the pregnant women in Africa including Nigeria, has been reported as 26% with a wide range between 0.4% and 84% (Lindemann *et al.*, 2010; Gu *et al.*, 2015; Zaki *et al.*, 2015; Abebe *et al.*, 2017; Ifeora *et al.*, 2017; Nimgaonkar *et al.*, 2018). The wide variation in the prevalence rate is adduced mainly to geographical differences. The vertical transmission of HEV has been reported to vary between 33% to 100% (Abebe *et al.*, 2017). Those mothers who are HEV-RNA positive are more likely to have higher vertical transmission than those who are only anti-HEV positive (Zaki *et al.*, 2015). Pregnancy in mothers with active HEV infection usually results in preterm birth or infants with icterus at birth with associated perinatal morbidity and mortality. HEV in neonates usually runs a self-limiting course except in few cases that present with fulminant hepatic failure. However, HEV infection hardly runs a chronic course in pregnancy and in neonates (Carratala *et al.*, 2019). It is obvious that HEV infection runs a more fatal course in pregnancy and in neonates than the known self-constraining course seen in other populations. Therefore, pregnant women should be screened for this HEV infection and the rate of vertical transmission in the newborns should be determined.

Objectives of the Study:

The study was designed to:

1. Determine the anti-HEV prevalence among the antenatal attendees at two Tertiary Hospitals in Ekiti State, Southwestern, Nigeria
2. Determine the vertical transmission rate among the HEV positive mothers

3. Examine the pregnancy and the neonatal outcomes of HEV infection
4. Evaluate Biopanda Immunochromatographic rapid test device's performance for HEV antibodies based on this independent research.

Materials and Methods

Study Design

This is a longitudinal cohort study among pregnant women accessing antenatal care at the study centers. All pregnant women who fulfilled the study criteria and consented to participate were screened for HEV using ELISA and those who were positive were followed up to delivery. The infants of the positive mothers were then screened for HEV infection.

Data Collection and Analysis

A structured questionnaires were administered to consenting pregnant women to obtain their socio-demographic characteristics and risk factors associated with HEV infection. All data were analyzed with the identity of the participants concealed.

Sample Collection

Five milliliters of whole blood samples were collected by venipuncture from 300 antenatal subjects and dispensed into EDTA blood collection tubes after obtaining informed consent and ethical approval. Plasma was separated by centrifugation at 2500 rpm for 5 minutes for HEV IgM and HEV IgG antibodies analyses by both rapid and ELISA assays.

HEV Antibodies Testing

The initial screening of antenatal patients for HEV antibodies was based on an immunochromatographic assay for HEV IgM/IgG by rapid technique (Biopanda Diagnostic Limited, UK). Seropositivity of any or both of HEV IgM and HEV IgG antibodies advanced screening for the HEV antibodies by ELISA technique (Melsin Medical Co. Limited, China). The ELISA technique served dual purposes. The first is that of serving as gold standard against which the rapid technique's statistical indices were compared while the other role is its elimination of cross-reactivities with markers of other disorders such as systemic lupus erythematosus and Rheumatoid arthritis with

proper preanalytical and analytical quality control measures in place. The analyses were carried out according to the manufacturers' instructions.

Statistical Analysis

The descriptive statistics of the Statistical Package for Social Sciences version 21 was used to analyze data and results were presented in tables. The sensitivity, specificity, positive predictive value and negative predictive value of the Biopanda immunochromatographic HEV antibody test device were derived using the ELISA assay as the gold standard and minimum diagnostic device approved for use.

Results

Age, Gravidity and Educational Status of Antenatal Patients Screened for Hepatitis E Virus
 The total number of pregnant women recruited into the study was 300. Table 1 shows the age, gravidity and educational status of the participants. While the mean age was 31.2 ± 0.3 years, the modal age group was 30-34 years with 115 subjects (38%). The extreme age groups of 15-19 years and 45 years were less represented with 2 women (0.7%) in each age group. There were more multigravidae, 255 (85%) than primigravidae, 45 (15%). The majority of the participants had tertiary education, 277 (92.3%).

Table 1: Age, Gravidity and Educational Status of Antenatal Patients Screened for Hepatitis E Virus

Demographic Variable	Mean Age /Absolute Numbers	Percentage (%)
Number of Enrollees	300	100
Number of Enrollees/Study Site		
EKSUTH	140	46.7
FETHI	160	53.3
Age Group of Enrollees		
15 – 19	19.0 ±0.0	2 (0.7)
20 – 24	22.4 ± 0.3	20 (6.7)
25 – 29	27.6 ± 0.1	94 (31.3)
30 – 34	31.9 ± 0.1	115 (38.3)
35 – 39	36.7 ± 0.2	54 (18.0)
40 – 44	41.0 ± 0.5	13 (4.3)
45 – 49	46.0 ± 1.0	2 (0.7)
Multigravida Status		
2	101	33.7
3	71	23.7
4	35	11.7
5	23	7.5
6	14	4.7
7	9	3.0
9	2	0.7
Educational Status		
No Formal Education	3	1.0
Primary	8	2.7
Secondary	12	4.0
Tertiary	277	92.3

Key: EKSUTH = Ekiti State University Teaching Hospital; FETHI = Federal Teaching Hospital, Ido Ekiti; SD = Standard deviation; % = Percentage

Table 2: Marital, Tribal and Occupational Status of Antenatal Enrollees Screened for Hepatitis E Virus
 Significant number of the participants was married (77.4%) and understandably, majority were of Yoruba ethnicity (90.7%). There were more self-employed participants (60.3%) than government workers (31.7%) in the study and unexpectedly students represented a small proportion (8%) of the participants.

Table 2: Marital, Tribal and Occupational Status of Antenatal Enrollees Screened for Hepatitis E Virus Demographic Variable

Demographic Variables		
Marital Status		
Variable	Frequency	Percentage (%)
Single	66	22.0
Married	232	77.4
Divorced/Separated	1	0.3
Widow	1	0.3
Tribe		
Yoruba	272	90.7
Igbo	18	3.0
Hausa	1	0.3
Ebira	3	1.0
Others	6	6.0
Occupational Status		
Civil Servants	95	31.7
Self-employed	181	60.3
Poultry	0	0
Livestock Farming	0	0
Students	24	8.0

Key: % = Percentage

Seroprevalence of Hepatitis E Virus Antibodies by Biopanda HEV Rapid Antibody Technique According to Antenatal Attendees' Age Group

Table 3 shows the sero-prevalence of Hepatitis E antibodies among the different age groups participants. The HEV antibodies (HEV IgM, HEV IgG and combination of HEV IgM and HEV IgG) were detected in 6 out of the 300 participants using the rapid technique, giving a prevalence rate of 2%. HEV IgG was detected in three (1.0%) participants while HEV IgM was found in one (0.3%) woman and both antibodies were present in two (0.7%) participants. Although, the distribution of the HEV antibodies appears to be more among the older age groups, there was no statistically significant age difference in anti-HEV prevalence reported in this study ($p > 0.05$).

Table 3: Seroprevalence of Hepatitis E Virus Antibodies by Biopanda HEV Rapid Antibody Technique According to Antenatal Attendees Age Group.

Age Group	Frequency (%)	Hepatitis E Virus Antibody Seropositive Cases					
		HEV IgM	P- value	HEV IgG	P-value	HEV IgM & IgG	P-value
15 -19	2 (0.7)	-	0.09	-	0.44	-	0.09
20 - 24	20 (6.7)	-		-		-	
25 - 29	94 (31.3)			-			
30 - 34	115 (38.3)	1 (0.3)		1 (0.3)		2 (0.7)	
35 - 39	54 (18.0)	-		1 (0.3)		-	
40 - 44	13 (4.3)	-		1 (0.3)		-	
45 - 49	2 (0.7)	-		-		-	
Total:	300 (100.0)	1 (0.3)		3 (1.0)		2 (0.7)	

Key: p 0.05 is statistically significant.

Biopanda Rapid Immunochromatographic & ELISA Assay Results of HEV Testing and Vertical Transmission of HEV by Seropositive Mothers

Table 4 shows the performances of Biopanda rapid immunochromatographic technique and ELISA technique in detecting the presence of the various HEV antibodies among the participants. While the yield by the rapid technique was 2 % (6/300), the yield by the ELISA technique was 1% (3/300). That gave a false positive rate of 50% using the rapid kit. The false positivity is more with the HEV IgG antibodies where 1 out of the 3 detected by rapid technique was confirmed by ELISA technique. The HEV antibody (IgG) was detected in one infant, delivered to one of the mothers with combined HEV IgM and IgG antibodies (HEV antibody total), giving a mother-to- child transmission rate of 16.7% with the ELISA technique.

Table 4: Table Showing Rapid & ELISA Assay Results of HEV Testing & Vertical Transmission of HEV by Seropositive Mothers

HEV Viral Marker	N (Percent) Positive by Rapid Technique	Outcome of HEV Assay By ELISA Technique		HEV Vertical Transmission
		IgM-Positive N (%)	IgG-Positive (%)	
HEV IgM	01 (0.3)	01(0.3)	-	HEV IgM = 0 (0%)
HEV IgG	03 (1.0)	-	01(0.3)	HEV IgG = 0 (0%)
HEV IgM & IgG	02 (0.7)	01(0.3)	01(0.3)	HEV IgG= 01 *(0.3%)
TOTAL	06 (2.0)	02 (0.7)	02 (0.7)	HEV IgG= 01 (0.3%)

Key: = Approximated prevalence by ELISA technique; N= Absolute number; HEV Vertical transmission: mother-to-child transmission of hepatitis E virus; *0.3% was an approximate value; The actual HEV IgG detected among the infants was 0.33% which represented vertical transmission rate of 16.7%.

Pregnancy and Neonatal Outcomes of HEV Infection among Antenatal

This study also revealed that 25.67% of the participants had abortion, 14.0% had postpartum complications, 6.0% had preterm deliveries and the rest (54.33%) had no pregnancy-related complications.

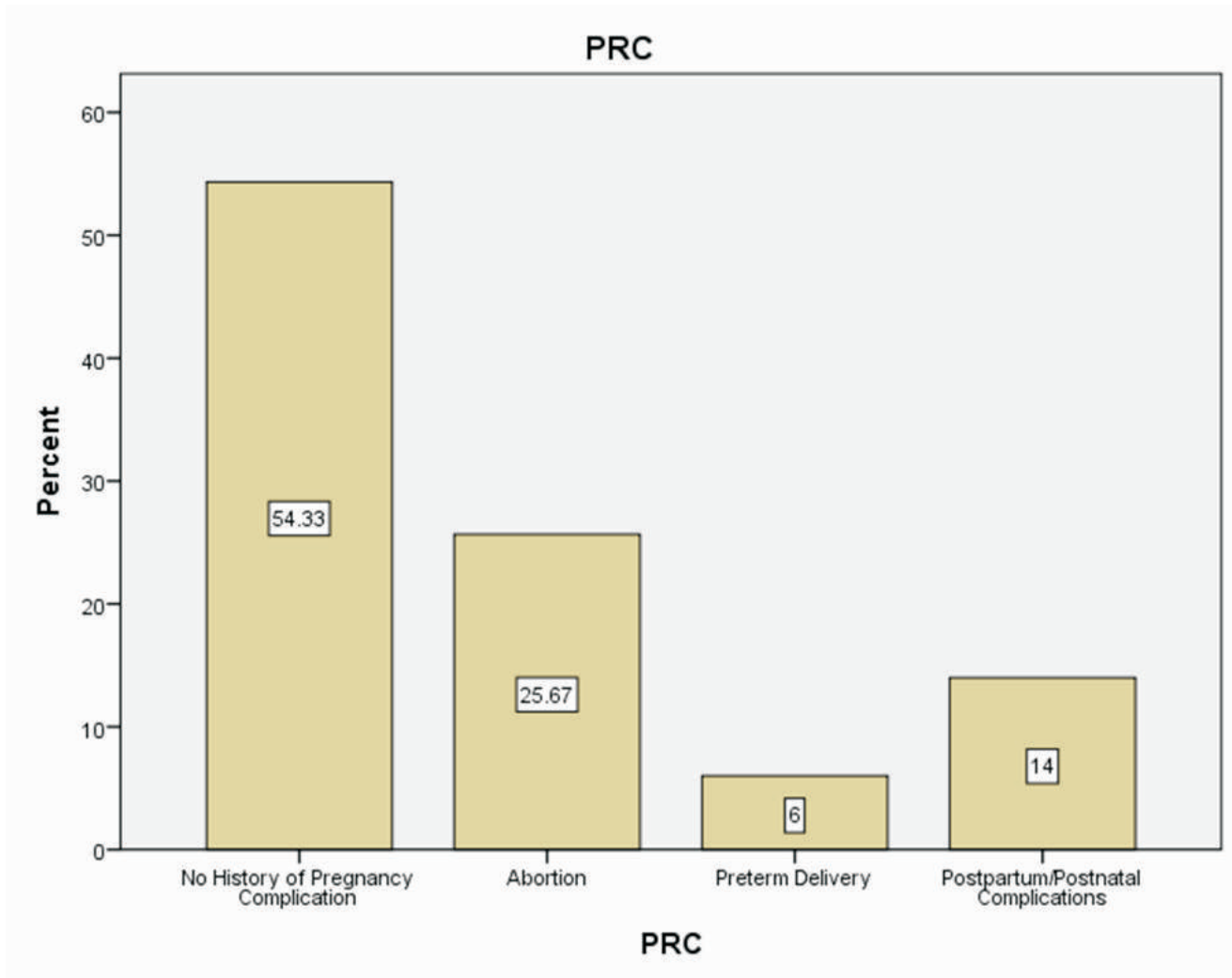


Figure 1: Pregnancy and the Neonatal Outcomes of HEV Infection among the Antenatal Attendees

Legend: PRC: Pregnancy complications

Evaluation of Biopanda Rapid Screening Test Performance Based on HEV Antibodies Confirmation with ELISA Technique (Gold Standard)

Table 5 shows the performance of the Biopanda immunochromatographic rapid test kit for detection of HEV antibodies using the ELISA assay as the gold standard. While the sensitivity and negative predictive values (NPV) for both IgM and IgG were 100%, the specificity was 90% for IgG and 99.7% for IgM. The Positive predictive values (PPV) were 66.7% and 40% for IgM and IgG respectively.

Table 5: Biopanda Immunochromatographic Rapid Screening Test Performance Characteristics Using the ELISA Technique as the Gold Standard

HEV Antibody Markers	Number Screened by ELISA Technique (Gold Standard)			Number Screened with Biopanda Rapid HEV Antibody Technique (Investigated Method)			Assessment Biopanda HEV Rapid Test Kit Performance Using ELISA Technique as the Gold Standard			
	Pos.	Neg.	Total	*Pos.	Neg.	Total	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
HEV IgM	2	298	300	3	297	300	100.0	99.7	66.7	100.0
HEV IgG	2	298	300	5	295	300	100.0	90.0	40.0	100.0

Key: HEV = Hepatitis E Virus; ELISA = Enzyme-linked immunosorbent assay; HEV IgM = Hepatitis E Virus immunoglobulin M; HEV IgG = Hepatitis E Virus immunoglobulin G; *Pos. = The number of HEV IgM and HEV IgG seropositivity obtained by Biopanda Rapid immunochromatographic kit both singly and in combination as HEV antibody total; Neg. = Negative

Discussion

The mean age of the participants in this study was 31.2 ±0.3 years, and the modal age group was 30-34, with 115 women (38%). This mean age is higher than 26.4years (±6.23 years) reported by Ehi Airiohuodion *et al.* (2022) in the Northern Nigeria. The majority of the participants were multiparae (277 or 85%), compared to primiparae (23 or 15%) which might result from cumulative HEV infection over the distant past and risk associated with each pregnancy. Also, majority has tertiary education (277 or 92.3%) which is far higher than the reported 57% in a similar study (Okwara *et al.*, 2021) in Nigeria. This may be attributable to regional variation in educational status. There were more self-employed participants (60.3%) than government workers (31.7%) in this study similar to findings by Ehi-Airiohuodion *et al.* (2022) that reported 25% for civil servants in their study. Our study, however, unexpectedly reported the proportion of the students to be 8% compared to 30% reported by Ehi Airiohuodion *et al.* (2022).

Hepatitis E virus is an old and underestimated infection due to inappropriate diagnosis and lack of awareness among physicians in both developed and developing countries of the world

(Mansu *et al.*, 2004; La Fauci *et al.*, 2017). In recent years, both in developing and developed countries, surveillance and seroprevalence-based research has gained more attention. However, there are significant gaps in the published literature. Therefore, this study aimed to estimate the burden and pooled prevalence of HEV antibodies in pregnant women in Ekiti State, Nigeria and by extension add to the awareness of HEV infection the world over.

The prevalence of anti-HEV (HEV-IgG and HEV-IgM and combination of both) in this study was 2.0% (6/300). According to our searches from the literature, the prevalence of HEV IgG range from 3.4% (La Fauci *et al.*, 2017) in Italy to 61.2% (Musa *et al.*, 2016) in Sudan. The seroprevalence from this study is lower than pooled prevalence of 42.6% (La Fauci *et al.*, 2017), 6.3% (Musa *et al.*, 2016), and 13.3% (Junaid *et al.*, 2014) obtained from similar studies conducted in Nigeria and 7.8% reported from Senegal (Diouara *et al.*, 2021), but higher than 0.4% reported by Ifeorah *et al.* (2017) in pregnant women in their study and 0.8% by Sadeghi *et al.*, (2021). The individual HEV antibodies of participants showed that out of the 6 seropositive mothers, HEV IgG was detected in

3 (1.0%) participants while HEV IgM was found in 1 (0.3%) woman and both antibodies were present in 2 (0.7%) participants as compared to 0.4% and 7.4% for HEV-IgM and HEV-IgG respectively observed in a previous report (Diouara *et al.*, 2022) from Senegal. The differences in the reported prevalence might be due to differences in the sample size, host risk factors, HEV antibodies assay characteristics, and the study environment. Anti-HEV (IgM) is evidence of acute infection while the anti-HEV (IgG) is evidence of past or ongoing infection (Aslan *et al.*, 2020).

Based on the overall assessment of the six seropositive mothers, a vertical transmission rate of 16.7% was obtained in this study. There was a past or ongoing HEV infection in the neonate evidenced by the detectable anti-HEV antibody. None of the infants of HEV seropositive mothers had detectable vertical transmission at birth. Our observed prevalence of vertical transmission of HEV is lower than a 78.9% prevalence observed in a study in India by Khuroo *et al.* (2016).

Most of the participants had no complication during pregnancy (54.33%) while 25.67% had second trimester miscarriages and 6% had preterm deliveries. HEV infection is known to be associated with spontaneous abortions and pre-term births. The low anti-HEV seroprevalence reported in this study might explain why few complications in the participants were observed when compared with 11% (7/63) intrauterine foetal death and 8% (5/63) neonatal death among HEV positive mothers (63/200) reported in Northern Nigeria (Ehi-Airiohuodion *et al.*, 2022). No maternal death among the HEV seropositive mothers during the study as compared to 0.5% (1/56) maternal death recorded by Okwara *et al.* (2021).

Furthermore, study showed the high sensitivity (the ability of the test device to correctly identify HEV infection in a known seropositive subject) and negative predictive value (the likelihood that a negative antenatal enrollee with a negative test result did not have HEV infection). The Biopanda immunochromatographic rapid kit's specificity (that is, the ability of the kit to test an antenatal subject negative who did not have HEV infection)

was also high for anti-HEV IgM (99.67%) but lower for anti-HEV IgG antibody (90.0), the reason for more false positives anti-HEV IgG cases. However, the positive predictive values (the likelihood that an antenatal subject with positive test results do have HEV infection) of the kit are very low for both anti-HEV IgM (60.0%) and anti-HEV IgG (40.0%). For any diagnostic test device to be validated for use in any laboratory, such kit must have high assay performance characteristics (Bohm *et al.*, 2017). The World Health Organization recommended screening for hepatitis E infection particularly among at risk populations such as pregnant women, individuals living in camps for displaced persons, and in outbreak situations (WHO, 2015). However, these outcomes might not actually be kit-based but might be connected with the low seroprevalence of HEV antibodies among the studied population (Bohm *et al.*, 2017).

Limitation

Larger population of antenatal enrollees could not be screened due to travel restrictions at the geographic location of study, and we could not determine the HEV genotype of infected mothers due to limited funds. Further studies involving large population of pregnant women with anti-HEV IgM and anti-HEV IgG antibodies should be carried out to correctly evaluate the positive predictive value of the study rapid kit.

Conclusion: HEV infection still remains a significant public health burden in view of its contribution to maternal and neonatal morbidity and mortality especially in the third trimester. Vertical transmission of HEV is still a challenge and the inclusion of routine screening for HEV antibodies into antenatal care protocol will help to identify at risk mothers, promote optimal care and reduce pregnancy complications. Infants of HEV positive mothers should be followed up immediately after delivery to identify vertically acquired HEV infection and institute appropriate surveillance as life progresses.

Author Contributions

Conceptualization (KAF, AAA and AWA); Methodology (KAF, AAA, AOA); Software (KAF, AAA and AWA); Validation (OBB, OMA and MY); Formal Analysis (OAA, AIO, OEA);

Investigation (KAF, AAA, MOA); Resources (AAA and KAF, AB); Data Curation (AAA); Writing (OMA, AAA, KAF); Writing Review & Editing (AA, MIA, YDO, OTA, AOB); Visualization (BAO, EOO, POA); Supervision (ASA, MAM, AAI); Project Administration (AAA, ZAJ, KAF) and Funding Acquisition (All Authors contributed).

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Institutional Review and Board Statement

Ethical approval was obtained from the ethical review committees of both Federal Teaching Hospital (ERC/2020/06/378A) and Ekiti State University Teaching Hospital (EKSUTH/A67/2020/06/006).

Informed Consent Statement

Patient's oral and written informed consent was obtained for voluntary participation and prior sample collection for this study.

Data Availability Statement

For reasons of confidentiality and data security, data were not made public, but data will be made available upon request to interested researchers.

Acknowledgment

None.

Conflict of Interest

Authors declare that there is no conflict of interest regarding this study.

References

- Abebe, M., Ali, I., Ayele S. *et al.* (2017). □ Seroprevalence and risk factors of Hepatitis E Virus infection among pregnant women in Addis Ababa, Ethiopia, □ *PLoS ONE*; **12(6)**: e0180078.
- Adjei, A.A., Tettey, Y., Aviyase, J.T. *et al.* (2009). Hepatitis E virus infection is highly prevalent among pregnant women in Accra, Ghana, *Virology Journal*; **6**: 108.
- Ahumibe, A.A., Okonkwo, G., Shehu, S.M., Waziri, E.N., Nguku, P. (2014). Prevalence of hepatitis E markers in primary health care antenatal attendees in Abuja, Nigeria, *International Journal of Infectious Diseases*; **21(S1)**: 397.
- Aslan, A.T., Balaban, H.Y. (2020). Hepatitis E virus: Epidemiology, diagnosis, clinical manifestations, and treatment. *World Journal of Gastroenterology*; **26(37)**: 5543-5560.
- Bazerbachi, F., Haffar, S., Garg, S.K., Lake, J.R. (2016). Extra-hepatic manifestations associated with hepatitis E virus infection: a comprehensive review of the literature. *Gastroenterology Reports*; **4**: 1 □ 15.
- Bohm, K., Strompl, J., Krumbholz, A, Zell, R., Krause, G., Sievers, C. (2020). Establishment of a highly sensitive assay for detection of hepatitis E virus-specific immunoglobulin. *Journal of Clinical Microbiology*; **58**: e01029-19.
- Carratala, A., Joost, S. (2019). Population density and water balance influence the global occurrence of hepatitis E epidemics. *Science Report*; **9 (1)**: 10042. 10.1038/s41598-019-46475-3.
- Cong, W., Sui, J.C., Zhang, X.Y., Qian, A.D., Chen, J., Zhu, X.Q. (2015). □ Seroprevalence of hepatitis E virus among pregnant women and control subjects in China, □ *Journal of Medical Virology*; **87(3)**: 446 □ 450.
- Diouara, A.A.M., Nguer, L.S., Senghor C.M., Di A., Ndiaye, H., Manga N.M. *et al.* (2022). Hepatitis E virus Seroprevalence and associated Risk Factors in Pregnant Women Attending Antenatal Consultations in Senegal. *Viruses*; **9**; **14(8)**: 17- 42.
- Ehi-Airiohuodion, P., Wartel A., Yako, A.B., Mac, A.P. (2022). Seroprevalence and burden of hepatitis E viral infection among pregnant women in central Nigeria attending antenatal clinic at a Federal Medical Centre in Central Nigeria. *Frontiers Medicine*; **9**: 888218.
- Fierro, N.A., Realpe, M., Meraz-Medina T., Roman S., Panduro A. (2016). Hepatitis E virus: an ancient hidden enemy in Latin America. *World Journal of Gastroenterology*; **2(7)**: 2271-2283.
- Goumba, C.M., Yandoko-Nakoune E.R., Komas N.P. (2010). A fatal case of acute hepatitis e among pregnant women, Central African Republic. *BMC Research Notes*; **3**: 103.
- Gu, G., Huang, H., Zhang, L., Bi, Y., Hu Y., Zhou, Y.-H. (2015). Hepatitis E virus seroprevalence in pregnant women in Jiangsu, China, and postpartum evolution during six years, *BMC Infectious*

- Diseases*; **15(1)**: 560.
- Huang, F., Ma, T., Li, L., Zeng, W., and Jing, S. (2013). □ Low seroprevalence of hepatitis E virus infection in pregnant women in Yunnan, China, □ *The Brazilian Journal of Infectious Diseases*; **17(6)**: 716-717.
- Ifeorah, I.M., Faleye, T.O.C., Bakarey, A.S., Adewumi, M.O., Akere, A., Omoruyi E.C., et al. (2017). □ Acute Hepatitis E Virus Infection in Two Geopolitical Regions of Nigeria □, *Journal of Pathogens*: <https://doi.org/10.1155/2017/4067108>.
- Junaid, A.S.E., Abubakar, K.A. (2014). Epidemiology and associated risk factors of hepatitis e virus infection in Plateau state, Nigeria. *Virology Research and Treatment*; **5**:15-26.
- Khuroo M.S., Khuroo M.S., Khuroo N.S. (2016). Transmission of Hepatitis E Virus in Developing Countries. *Viruses*; **8(9)**: 253.
- Kmush, B.I., Labrique, A.B., Dalton, H.R. et al. (2015). Two generations of □ gold standards □: the impact of a decade in hepatitis E virus testing innovation on population seroprevalence. *American Journal of Tropical Medicine and Hygiene*; **93**:714-717.
- La Fauci, V., Facciola, A., Riso, R., Calimeri, S., Giudice, D.L., Squeri, R. (2017). Seroprevalence of HEV antibodies in a sample of pregnant women in the city of Messina. *Annals of Immunoglobulins*; **29**: 232-238.
- Lindemann M.L.M., Gabilondo, G., Romero, B., De La Maza, O.M.S., Pérez-Gracia, M.T. (2010) Low prevalence of hepatitis E infection among pregnant women in Madrid, Spain, *Journal of Medical Virology*; **82(10)**:1666-1668.
- Mansu, J.M., Peron, J.M., Abravanel, F., et al. (2004). Hepatitis E in the Southwest of France in individuals who have never visited an endemic area. *Journal of Medical Virology*; **74**: 419-424.
- Musa, A.O., Osman, O.H., Jaffer, A., Ali, A.A., Ibrahim, M.E.A., Abuzeid N. (2016). Seroprevalence of HEV infection and risk factors among Sudanese pregnant women in Khartoum state. *Mediterranean Journal of Bioscience*; **1**:83-91.
- Nimgaonkar, I., Ding Q., Schwartz, R.E., Ploss A. (2018). Hepatitis E virus: advances and challenges. *Nature Review in Gastroenterology and Hepatology*; **15**:96 □ 110.
- Okwara, V.C., Mbachu, I.I., Ndububa, I.V., Okpara, H.C., Mbachu, C.P. (2021). Seroprevalence, associated factors and foeto-maternal outcome in pregnant women that tested positive to hepatitis e antibodies in Nigeria. *Obstetrics and Gynecology International*: 9341974.
- Sadeghi, F., Zahra, G., Javadian, Maryam, J., Baray, M., Parisa, S., Socheil, E. et al. (2021) Seroprevalence of Hepatitis A and E viruses among pregnant women in Northern Iran. *Infectious Diseases in Obstetrics and Gynecology*: 5130586.
- World Health Organization (2024). Hepatitis E. <https://www.who.int/en/news-room/factsheets/detail/hepatitis-e.RRRRRYTTV467U> (Accessed 8 July 2024).
- World Health Organization. Hepatitis E Vaccine: WHO position paper; 2015. <https://www.who.int/wer/2015/wer9018>. (Accessed 7 March 2025).
- Zaki, ME., El Razek, M.M.A., El Razek, H.M.A. (2014). Maternal-Fetal Hepatitis E Transmission: Is It Underestimated □ *Journal of Clinical and Translational Hepatology*; **2**:117-123.

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