

Full Length Research Paper

Anti-hepatitis E virus antibodies in sick and healthy Individuals in Ekiti State, Nigeria

O. A Adesina^{1,2*}, M. O Japhet^{1,2}, E. Donbraye^{1,3}, T. E. Kumapayi² and A. Kudoro²

¹Department of Virology, University College Hospital, Ibadan, Nigeria. ²Department of Microbiology, Obafemi Awolowo University, Ile-Ife, Osun, State, Nigeria. ³Department of Medical Microbiology and Parasitology, College of Health Sciences, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria.

Accepted 19 July, 2020

A cross-sectional serosurvey of 186 healthy and sick individuals between ages 3 and 72 years in Ekiti State, Nigeria was conducted for the presence of antibodies to hepatitis E virus (HEV) using a commercial enzyme immunoassay kit. Antibody to HEV was detected in 25(13.4%) of the samples analyzed. The prevalence of antibodies was greater among males (20%) than among females (11.3%) and increased with age for both sexes from 7.8% among subjects 11-20 years to 20% among subjects 61-70 years old. Five pregnant women (8.3%) and 4 (22.22%) children also had detectable anti HEV antibodies in them. Five (8.3%) healthy and 20(15.9%) sick individuals had detectable anti – HEV antibodies in them. There is a dearth of information about HEV infection in Ekiti State and in Nigeria as a whole thus making it difficult to compare with other states. HEV is likely to be endemic in the study areas as there are no portable water and good toilet facilities in most of the places. The pregnant women and the healthy but anti – HEV antibodies positive individuals suggest that HEV had been in the study area before the study was conducted.

Key words: Hepatitis E Virus (HEV), seroprevalence, antibodies, endemic, immunoassay.

INTRODUCTION

Hepatitis E virus (HEV) is an enterically transmitted virus implicated in the cause of viral hepatitis alongside hepatitis A Virus (HAV) and other percutaneously transmitted viruses like hepatitis B, C, D and G. HEV is the only member of the genus Hepesvirus of the family Hepeviridae. It is a non-enveloped, single stranded, positive sense RNA virus (Purcell and Emerson, 2001). HEV infections have been known to produce self-limiting acute hepatitis with mortality as low as 1-3%. Case fatality rate in pregnant women is as high as 20% (Emerson and Purcell, 2004) while Yuel and Kaut (2006) placed it at 20-30% especially those in the third trimester and it can cause premature birth (Vasickova et al., 2007).

Hepatitis E is the only hepatitis virus that apparently

has this virulent impact on pregnant women. Based on its mode of transmission, HEV infections have been found to mostly affect young adults.

Poor hygienic conditions as a result of poor environmental sanitation facilities have been implicated in the wide distribution of HEV infections in Africa and Asia. This condition has made some developing countries of Asia and Africa and Mexico endemic for the virus and its infections (Smith, 2001). The spread of HEV to the Industrialized countries had been made possible via travelers to and from endemic regions (Piper- Jenks et al., 2000; Dawson et al., 1992). Sporadic cases of acute hepatitis E without an implicated travel history have also been reported in Europe and the United States (Dawson et al., 1992; Heath et al., 1995).

The sequence analyses of HEV isolates obtained from sporadic cases in the US, Europe, Taiwan and Japan in people who had not traveled to countries where HEV is endemic revealed genetically divergent isolates

*Corresponding author. E-mail: Adesinafat@yahoo.co.uk. Tel: +234 803 413 5898.

(Garkavenko et al., 2001; Schlauder et al., 1999, Schlauder et al., 1998, Worm et al., 2000; Pei and Yoo, 2002). The human and swine HEV isolates from Industrialized countries are genetically clustered together in the same genotype (either genotype 3 or 4) raising concerns of hepatitis E as a zoonotic disease (Meng et al., 1997, Nishizawa et al., 2003; Banks et al., 2004).

Although transmission of HEV is generally via the faecal-oral route, person-to-person transmission and transmission via the parenteral route or blood transfusion have been suggested. The possibility of hepatitis E being a zoonotic disease is also being researched into. Meng et al., (2002) demonstrated the ability of swine HEV to infect across species thus supporting the zoonotic nature of the virus. Also, HEV transmission after the consumption of wild boar meat and uncooked deer meat has been reported (Li et al, 2005).

Treatment of HEV is basically symptomatic through bed rest and fluid replacement. Prevention is by improving sanitation. A recombinant hepatitis E vaccine is currently being studied for its effectiveness and safety.

Hepatitis E has been found to be endemic in sub-Saharan African countries yet there is a dearth of information about its incidence and prevalence in Nigeria compared to what obtains in Asian countries. This prompted this study especially in the part of Nigeria associated with heavy rains. The objective of this study is to determine the prevalence of antibodies to HEV in healthy and sick individuals and pregnant women.

MATERIALS AND METHODS

Study population

Three hundred and sixty serum samples were collected from both sick and healthy individuals from a Federal Medical Centre (FMC) and a University Teaching Hospital (UTH) both in Ekiti State, Nigeria. The mean age of sample collected from FMC was 28.71 years while that of UTH was 30.9 years. The samples included those from healthy pregnant women on routine check up and those on booking as well as sick and healthy individuals on routine check up too. The samples were collected from April 2007 to December 2007 from people of ages between 3 and 72 years old and a mean of 29.82 years after ethical approval had been obtained. One hundred and eighty six (186) samples were randomly selected for anti-HEV antibodies screening.

Serological test

The samples were tested for antibodies to HEV using a commercial enzyme immunoassay (EIA) kit (HEV Ab EIA Dia Pro, Italy) according to the manufacturer's instructions. The kit is for the determination of antibodies to HEV in human serum and plasma. The cut off was defined with positive and negative control sera that were included in each assay according to the manufacturer's instruction.

RESULTS

Anti -Hepatitis E virus antibodies were detected in 25 (13.4%) of the 186 serum samples analyzed. Out of the

Table 1. Age distribution of Anti-HEV antibody prevalence in Ekiti State.

Age range	Total No	Number Positive	% Positive
1-10	18	4	22.2
11-20	10	2	20.0
21-30	64	5	7.8
31-40	64	8	12.5
41-51	17	3	17.6
51-60	7	2	28.6
61-70	5	1	20.0
>70	1	0	0

Table 2. Subjects variables associated with the prevalence of antibodies to the HEV in Ekiti Sate.

Variables	No. +ve (Prevalence %) (95% CI)	No Screened
Sex		
Male	9 (20.00)	45
Female	16(11.3)	141
Study Location		
FMC	20(15.9)	126
UTH	5(8.3)	60
Gravidity		
Pregnant	5(8.3)	60
Non-Preg. Female	11(13.6)	81
Health Status		
Healthy	5(8.3)	60
Sick	20(15.9)	126

twenty five that had detectable HEV antibodies in them, 20 (15.9%) were sick showing symptoms like fever, body/joint pains, gastroenteritis and jaw swelling. The remaining five showed no symptoms. Twenty (16%) of the samples collected from the Federal Medical Centre (FMC) had detectable anti - HEV antibodies while 5 (8.3%) out of 60 samples obtained from the University Teaching Hospital (UTH) had the antibodies in them. Out of 18 children aged between 2-10 years screened, 4 (22.22%) had detectable anti-HEV antibodies. Two of them were females while the other two were males.

With respect to age distribution, positivities to anti -HEV antibodies are as shown in Table 1.

Nine (20.00%) out of 45 males and 16 (11.3%) out of 141 females tested positive for the HEV antibodies. Worthy of note and further study were the 5(8.33%) out of 60 pregnant women and 4 (22.22%) out of 18 children aged between 3 and 10 years who demonstrated antibodies to HEV in their sera. Table 2 gives the summary of the results. The most common symptoms among the sick individuals were fever and jaw swelling.

DISCUSSION

In Africa, some Central Asian republics and some parts of the Middle East, Hepatitis E is a significant public health concern. It is both endemic and epidemic, with human outbreaks generally associated with faecal contamination of drinking water. Hepatitis E generally results in asymptomatic or mild illness similar to Hepatitis A, except in pregnant women who experience up to 20% mortality (Chin, 2000).

The overall prevalence of anti HEV antibodies among the 186 screened individuals in this study was 13.44% while it was 22.22% among children aged 3 – 10 years. This result is quite challenging and calls for urgent attention as it suggests that the children could have been exposed to the virus at a much younger age. Maria et al., (2008) reported a prevalence of anti-hepatitis E virus IgG in 4.6% (n = 1,249) of children in the Northeast of Spain, which is much smaller than that obtained from this study. This study did not follow up the sick individuals involved in this research but worthy of note are two children who had detectable HEV antibodies in them with one presenting with fever and the other jaw swelling. It is therefore becoming important to consider other types of hepatitis viruses apart from Hepatitis B and C as potential aetiological agents of various forms of infections. The connection between jaw swelling and HEV infection was not studied but it could be an area to look into by clinicians. Fever, jaw swelling and gastroenteritis were the common symptoms observed in the individuals that had the anti HEV antibodies in them. Hepatitis had been implicated in fever/pyrexia of unknown origin (PUO) with no particular emphasis on hepatitis E. It is suggested, therefore that a closer look at the role of HEV in PUO be considered. Also it is important to further study the pathogenesis of HEV to ascertain its role in jaw swelling.

It has been previously observed that the prevalence of anti – HEV antibodies is always higher in people aged between 20 and 40 years. HEV had been implicated to have a peak clinical attack rate in young adults, high rate of fulminant disease in pregnancy and produce epidemics of waterborne disease. This study is in support of this as 5 (7.8%) of people aged between 21 – 30 years and 8 (12.5%) from ages 31 – 40 years had detectable anti- HEV antibodies in them. A decreasing number of positive individuals from ages 31-70 years was observed. This study suggests that many people in the study area of Ekiti State had been exposed to the Hepatitis E virus. This may be attributed to the tropical nature of the region and possibly poor hygienic conditions of the people and proximity to likely domesticated and wild animals that can transmit the virus. It could be said therefore that HEV is endemic in Ekiti State.

Hepatitis E has been described as life threatening for pregnant women. Being the only hepatitis that apparently has this virulent impact on pregnant women, it has been implicated to cause death rate ranging between 15-25% among pregnant women. It is also able to cause miscar-

riages. A much lower prevalence, 8.3% (n = 60), of HEV antibodies was observed in pregnant women in this study compared to 84.3% (n = 2,428) that Sonia et al., (2006) observed in Egyptian pregnant women with most of the infected women having no history of liver disease. The source of HEV infection in this area could not be ascertained but it may be due to zoonotic transmission since antibodies to HEV have been detected in many animals in areas where HEV is endemic and in domestic swine and rats in the United States (Junkun et al., 2002). However, it was observed that most of the neighbouring towns where people came from to use the health services were rural areas with no potable water supply and proper toilet facilities.

Although, there is a dearth of information about HEV infection in Ekiti State and in Nigeria as a whole thus making it difficult to compare with other states yet it is worthy of note that the region with the highest prevalence had that is required for the transmission of the virus like poor hygiene, proximity to domesticated animals and a larger population of young adults. Prompt actions are recommended to improve the standard of living in the area so as to prevent further spread of the virus and hence its complications.

ACKNOWLEDGEMENTS

The authors wish to thank Dr. K. Oyebode and Mrs. Philip who assisted in sample collection and Mrs. O.T. Awotipe for her assistance in the laboratory.

REFERENCES

- Banks M, Heath GS, Grierson SS, King DP, Gresham A, Girones R, Widen F, Harrison TJ (2004). Evidence for the presence of hepatitis E virus in pigs in the United Kingdom. *Vet. Rec.* 154: 223-227.
- Chin J (2000). ed. *Viral hepatitis E*. In: *Control of Communicable Diseases Manual*. Washington, DC: APHA pp. 255-257.
- Dawson GJ, Mushahwar IK, Chau KH, Gitnick GL (1992). Detection of long-lasting antibody to hepatitis E virus in a US traveler to Pakistan. *Lancet.* 340: 426-427.
- Emerson S, Purcell R (2004). Running like water – the omnipresence of hepatitis E. *N. Engl. J. Med.* 351: 2367-2368.
- Garkavenko O, Obriadina, A, Meng J, Anderson DA, Benard HJ, Schroeder BA, Khudyakov YE, Fields HA, MC Croxson (2001). Detection and characterization of swine hepatitis E virus in New Zealand. *J. Med. Virol.* 65: 525-529.
- Heath TC Burrow JN, Currie BJ, Bowden FJ, Fisher DA, Demediuk BH (1995). Locally acquired hepatitis E in the Northern Territory of Australia. *Med. J. Aust.* 162: 18-19.
- Junkun HE, Innis BL, Shrestha M, Clayton ET, Scott RM, Linthicum KJ, Musser GG, Gigliotti SC, Binn LN, Kuschner RA, Vaughn DW (2002). Evidence that rodents are a reservoir of hepatitis E virus for humans in Nepal. *J. Clin. Microbiol.* 40(12): 4493-4498.
- Krawczynski K, McCaustland K, Must E, Yarbough PO, Purdy M, Favorov MO, Spellbring J (1996). Elements of Pathogenesis of HEV infection in man and experimentally infected primates, pp. 317-328.
- Li TC, Chijiwa K, Sera N (2005). Hepatitis E virus transmission from wild boar meat. *Emerging Infect. Dis.* PMID 16485490. 11(12): 1958-1960.
- Maria Buti, Plans P, Dominguez A, Jordi R, Frias FR, Estaban R, Salleras L, Plasencia A (2008). Prevalence of Hepatitis E Virus Infection in Children in the Northeast of Spain. *Clin. Vaccine Immunol.*

- 15(4): 732-734.
- Meng XJ, Purcell RH, Halbur PG, Lehman JR, Webb DM, Tsareva TS, Haynes JS, Thacker BJ, Emerson SU (1997). A novel virus in swine is closely related to the human hepatitis E virus. *Proc Natl. Acad. Sci. U. S. A.* 94: 9860-9865.
- Meng XJ, Wiseman B, Elvinger F, Guenette DK, Toth TE, Engle RE, Emerson SU, Purcell RH (2002). Prevalence of antibodies to hepatitis E virus in veterinarians working with swine and in normal blood donors in the United States and other countries. *J. Clin. Microbiol.* 40(1): 117-122
- Nishizawa T, Takahashi M, Mizuo H, Miyajima H, Gotanda Y, Okamoto H (2003). Characterization of Japanese swine and human hepatitis E virus isolates of genotype iv with 99% identity over the entire genome. *J. Gen. Virol.* 84: 1245-1251.
- Pei Y, Yoo D (2002). Genetic characterization and sequence heterogeneity of a Canadian isolate of swine hepatitis E virus. *J. Clin. Microbiol.* 40: 4201-4029.
- Piper-Jenks N, Horowitz HW, Schwartz E (2000). Risk of hepatitis E infection to travelers. *J. Travel Med.* 7: 194-199.
- Purcell RH, Emerson SU (2001). Hepatitis E virus, In D.M. Knipe, PM Howley (ed.), *Fields Virology*, 4th ed., Lippincott Williams and Wilkins, Philadelphia, Pa. 2: 3051-3061.
- Schlauder GG, Dawson GJ, Erker JC, Kwo PY, Knigge MF, Smalley DL, Rosenblatt JE, Desai SM, Mushahwar IK (1998). The sequence and Phylogenetic analysis of a novel hepatitis E virus isolated from a patient with acute hepatitis reported in the United States *J. Gen. Virol.* 79: 447-456.
- Schlauder GG, Desai SM, Zanetti AR, Tassopoulos NC, Mushahwar IK (1999). Novel hepatitis E. virus (HEV) isolates from Europe: Evidence for additional genotypes of HEV. *J. Med. Virol.* 57: 251.
- Smith JL (2001). A review of hepatitis E virus. *J. Food Prot.* 64: 572-86.
- Sonia KS, Mohamed A, Doa'a AS, Sherif E, Shaker N, Yousry H, Fatma MS, Mai E, Ahmed S, Enas K, Nabel M, Ronald EE, Mohamed S, Soraya S, Alan DF, Suzanne UE, Robert HPG, Thomas S (2006). High prevalence of hepatitis E anti-bodies in pregnant Egyptian women. *Trans. R. Soc. Trop. Med. Hyg.* 100: 95-101.
- Vasickova P, Psikal I, Kralik P, Widen F, Hubalek Z, Pavlik I (2007). Hepatitis E virus: *Rev Vet. Med.* pp.365-377.
- Worm HC, Schlauder GG, Wurzer H, Mushahwar IK (2000). Identification of a novel variant of hepatitis E virus in Austria: Sequence phylogenetic and Serological analysis. *J. Gen. Virol.* 81: 2885-2890
- Yuel VI, Kaur V (2006). HEV infection in pregnancy. *Obstet. Gynecol. India* 56(2): 146-148.