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Original Article

Seroprevalence and predictors of hepatitis E infection in Nigerian children

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Abstract

Introduction: Hepatitis E is a hepatotropic virus transmitted through the fecal-oral route and is prevalent in developing countries where sanitation is still a public health issue. There is no epidemiological data about this virus in Nigerian children. All the existing studies are hospital based, with obvious limitations. This study was conducted to establish the seroprevalence and predictors of viral hepatitis E antibody in children in Akpabuyo Local Government Area of Cross River State, Nigeria.

Methodology: This was a community-based, cross-sectional study. A multi-staged sampling technique was used to select ten communities from which 406 children were recruited. The study period was April to June 2012. A structured interviewer-administered questionnaire was used for data collection. Blood samples were screened for anti-HEV IgG antibody using the enzyme-linked immunoassay technique. Multivariate logistic regression was used to identify factors that independently predicted the occurrence of the anti-HEV IgG antibody. A p value of < 0.05 was considered significant.

Results: The seroprevalence rate of anti-HEV IgG antibody was 7.7% (95% CI = 5.1–10.3). The study population mainly (94.1%) comprised the lower social class. Levels of social amenities in these communities were generally poor, with virtually no piped water and modern sewage disposal systems. After multivariate analysis, the predictor of infection was the duration of residence in the study communities.

Conclusions: HEV infection was prevalent in the study population. Educational campaigns and provision of good sewage disposal and piped water are of high necessity.

Key words: hepatitis E virus; seroprevalence; predictors; anti-HEV IgG antibody; children; Nigeria.

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Introduction

Hepatitis E virus (HEV) is a non-enveloped RNA virus that is transmitted through the fecal-oral route [1,2]. HEV is noted to be responsible for epidemic and sporadic cases of enterically transmitted non-A, non-B viral hepatitis in many developing countries [3-6]. Areas with endemic infection and high incidence are found in Asia, Africa, Central America, and the Middle East [7], where the virus has been known to produce self-limiting acute viral hepatitis with mortality rates of 1%–3% [8].

The largest documented outbreak of HEV infection was in China between 1986 and 1988, involving over 100,000 individuals [9]. In industrialized countries, the disease occurs sporadically, and most infections occur in individuals who travel to countries where HEV is endemic [7]. Hepatitis E is endemic in the West African sub-region. Outbreaks of hepatitis E have been described in Chad and Cote d'Ivoire, and the virus was responsible for 66% of sporadic hepatitis cases in Chad, at least 22% in Cote d'Ivoire, and 44% of cases of acute hepatitis in Senegal [10]. The reported seroprevalence rates of anti-HEV antibodies in the West African region varies from 4.4% in Ghana [11] (increasing from 1% in school-age children to 8.1% in older adolescents) to 8% in Sierra Leone [12]. The case fatality rate in a reported outbreak in Ghana was 3.2% [10]. The 2010 World Health Organization (WHO)'s systematic review on the global prevalence of HEV infection did not report any prevalence or case fatality study in Nigeria. Furthermore, no outbreaks were recorded [10]. However, Adesina *et al*. [13], in a hospital-based study in Ekiti State, southwest Nigeria, reported a prevalence of 13.4% in individuals between 3 and 72 years of age. No community-based study has been done, to our knowledge, of HEV in Nigeria.

This study was therefore designed to provide the first community-based data on hepatitis E seroprevalence in Nigerian children.

Methodology

Setting

The study was a community-based, cross-sectional, analytical study in Akpabuyo Local Government Area (LGA) of Cross River State, south-south geopolitical zone, Nigeria. Akpabuyo LGA is a suburb of LGA, bounded by Akamkpa LGA in the north, Calabar Municipality in the west, Bakassi LGA in the east, and the Cross River in the south. It comprises 10 electoral wards with a total population of 313,097. The occupations of the residents include farming, trading, civil service, and fishing. The aim of the study was to determine the seroprevalence and predictors of viral hepatitis E in children.

Study period

The study was carried out between April and June 2012.

Selection of subjects

The study population comprised children 1 to 18 years of age. A multi-stage sampling technique was used in this study and involved three stages. The first stage was a simple random sampling technique used to select four out of ten wards by balloting. In the second stage, a proportionate sampling method was used to select ten villages from the four selected wards. In the third stage, 40 children from alternate households in the selected villages were chosen from those eligible after a screening form was administered. Children who had resided in Akpabuyo for less than one year were excluded from the study. An interviewer administered a structured questionnaire to the heads of the households.

Ethical approval

The study was approved by the ethical review committee of University of Calabar Teaching Hospital and the Cross River State Health research ethics committee. Informed consent was obtained from each parent or legal guardian of the eligible participants prior to enrolment.

Data collection

The following data were collected using a structured, interviewer-administered questionnaire:

1) General characteristics (age, sex);
2) Family socioeconomic characteristics and sanitation : parent's/guardian's occupation and education, total number of persons in the household, toilet types, method of disposal of domestic household waste, source of drinking water. The social class of parents/guardians was determined using the social classification proposed by Olusanya *et al*. [14] considering the parents/guardian's occupation and educational qualifications; and
3) Clinical history to determine eligibility for the study.

Laboratory investigations

Two milliliters of venous blood was collected from each participant into a clean, plain bottle, properly labeled. The sera were tested for anti-HEV IgG antibody by a competitive enzyme immunoassay (EIA) test with test kits from DRG International (Springfield Township, USA). The anti-HEV IgG antibody tested for IgG antibody for HEV. Test results were interpreted as a ratio of the absorbance of the sample (A_s) and the cut-off absorbance (A_c). A level of < 0.9 mIU/mL was considered negative; 0.9 to 1.1 mIU/mL equivocal; and > 1.1 mIU/mL positive. A negative result indicated that the subject was not infected with HEV. In subjects with equivocal results, a second sample taken two weeks later was retested. A positive result was indicative of previous HEV infection. The sensitivity and specificity of the test kits were over 98%.

Statistical analysis and presentation

The data obtained were analyzed using the Statistical Package for Social Sciences (SPSS) version 17.0. Quantitative variables were summarized as median (interquartile range [IQR]), and categorical data were summarized as frequency (percentage). Chi square was used to test for association between categorical variables. Likelihood ratio Chi square and Fisher's exact test were applied where required. Multivariate logistic regression analysis was used to control for anticipated confounders. A p value of < 0.05 was considered statistically significant. Results are presented in Tables 1–4.

Results

General characteristics of the children

A total of 406 children between 1 and 18 years of age participated in this study. The 1–4 year age group was the most represented, with a total number of 150 (37.0%). The 15–18 year age group was least represented, with a total of 51 (12.6%). The median age was 6 years, and the interquartile range was 3–12 years. A total of 207 (51.0%) of the children were females and 199 (49.0%) were males, for a female-to-male ratio of 1:1.

Table 1. Age and sex distribution of the study population

Age group (years)	Female n (%)	Male n (%)
1–4	62 (30.0)	88 (44.2)
5–9	58 (28.0)	51 (25.6)
10–14	57 (27.5)	39 (19.6)
15–18	30 (14.5)	21 (10.6)
Total	207 (100)	199 (100)

The 1–4 year age group was the highest represented with a total number of 150 (37.0%). The 15–18 year group was least represented, with a total of 51 (12.6%). The median age was 6 years, and the interquartile range was 3–12 years. Two hundred and seven (51.0%) were females and 199 (49.0%) were males, for a female-to-male ratio of 1:1.

Table 2. Prevalence of HEV antibody in relation to the age of subjects

Age group (years)	Anti-HEV IgG antibody	
	Positive n (%)	Negative n (%)
1–4	5 (16.1)	143 (38.5)
5–9	7 (22.6)	100 (26.9)
10–14	9 (29.0)	87 (23.5)
15–19	10 (32.3)	41 (11.1)
Total	**31 (100)**	**371 (100)**

Age was significantly associated with anti-HEV IgG antibody positivity (p = 0.039)

Table 3. Prevalence of anti- HEV IgG antibody positivity with sex

Sex	Anti-HEV IgG antibody	
	Positive n (%)	Negative n (%)
Female	17 (54.8)	188 (50.7)
Male	14 (45.2)	183 (49.3)
Total	**31 (100)**	**371 (100)**

There was no significant association with sex (p = 0.66).

Table 4. Logistic regression of anti-HEV IgG antibody

Variables	Univariate		Multivariate	
	Odds ratio (95% CI)	P value	Odds ratio (95% CI)	P value
Age (years)	1.08 (1.01–1.16)	0.02	1.07 (0.95–1.20)	0.25
Gender	0.85 (0.41–1.77)	0.66	0.89 (0.41–1.93)	0.76
Source of water				
Pipe water		1		1
Others	0.72 (0.34–1.52)	0.39	0.78 (0.36–1.72)	0.54
Duration of residence (years)				
1–5		1		1
6–10	4.32 (1.72–10.82)	0.004	3.2 (1.22–8.39)	0.02
> 10	3.6 (1.29–10.1)	0.02	1.9 (0.46–7.80)	0.37
Number of persons in household	0.91 (0.80–1.04)	0.19	0.90 (0.79–1.03)	0.13
Fecal disposal method				
Water cistern		1		1
Others	0.75 (0.25–2.23)	0.76	0.61 (0.19–1.98)	0.41

At the univariate level, age and duration of residence were significant predictors of HEV; for every one year increase in age, there was 8% increase risk of having anti-HEV IgG antibody (95% CI = 1.01–1.16, p = 0.02). Number of persons in the household was not statistically significant (95% CI = 0.80–1.04, p = 0.19) with positivity to anti-HEV IgG antibody at the univariate level; After multivariate analysis, duration of residence in the community predicted infection with HEV after adjusting for the effect of all the other factors in the model. Individuals who had spent 6–10 years (compared to those who spent 1–5 years) had a 3.6 times increased risk of having HEV infection after adjusting for other variables.

Table 1 shows the age and sex distribution of the study population. Twenty-four (5.9%) of the subjects belonged to the middle class, and 382 (94.1%) were of the lower social class; no subjects were in the higher social class.

Results for HEV

Four hundred and six subjects were tested for the anti-HEV IgG antibody. Twenty-eight subjects were initially positive for HEV. Seven subjects had equivocal results, and a second test done two weeks later showed three positive results in two females and one male, while four subjects remained equivocal (two males and two females). These were excluded from further analysis. The total number of subjects positive was thus 31 out of 402, giving a seroprevalence rate of 7.7% (95% CI = 5.1–10.3). The median age of those positive was 9 years, with an interquartile range of 6–14 years, while the median age of those negative was 6 years, with an interquartile range of 3–12 years. Table 2 shows the prevalence of HEV antibody in relation to the age of the subjects. Age was significantly associated with anti-HEV IgG antibody positivity ($p = 0.039$). Table 3 shows the distribution of anti-HEV IgG antibody positivity with gender. There was no significant association with sex ($p = 0.66$). Table 4 shows the logistic regression of variables to anti-HEV IgG antibody positivity. At the univariate level, age and duration of residence were significant predictors of HEV; for every one-year increase in age, there was an 8% increased risk of having the anti-HEV IgG antibody (95% CI = 1.01–1.16, $p = 0.02$). Number of persons in the household was not statistically significant (95% CI = 0.80–1.04, $p = 0.19$) with positivity to anti-HEV IgG antibody at the univariate level. After multivariate analysis, duration of residence in the community predicted infection with HEV after adjusting for the effect of all the other factors in the model. Individuals who had lived for 6–10 years (compared to those who had lived 1–5 years) in the community had a 3.6 times increased risk of having HEV infection after adjusting for other variables.

Discussion

In this study, the prevalence of hepatitis E was 7.7%. This was similar to a prevalence of 8% reported by Hodges *et al*. [12] in Sierra Leone. Adesina *et al*. [13], working in Ekiti State in southwest Nigeria, found a prevalence rate of 22.2% in sick and healthy children. He studied only 20 children between the ages of 3 and 10 years, and these included sick children. Martinson *et al*. [11], working in Ghana, found a prevalence rate of 4.4% in children 6–18 years of age in a rural community. This rather lower value in rural Ghana may be due to variation in the sensitivity of the immunoassay kits in different laboratories. Colak *et al*. [15] found a prevalence rate of 0.9% in children in Turkey. Turkey is a country in the European Union, and socioeconomic conditions there are better than those in the community where this study was done. Goumba *et al*. [16] found a prevalence rate of 78% during an epidemic of HEV infection in Bangui, Central African Republic. The prevalence of hepatitis E in an epidemic period would obviously be higher than in a non-epidemic period. Age was significantly associated with the prevalence of the anti-HEV antibody in this study. The prevalence increased from 16.1% in the 1–4 year age group to 38.7% in the 15–18 year group. Martinson *et al*. [11] also showed increasing seroprevalence, from 1% in children between 6 and 7 years of age to 8.1% in adolescents 16 to 18 years of age. This age-specific antibody profile was also reported by Fix *et al*. [17], working in two rural Egyptian communities. Arrankalle [18] speculated that this age-specific antibody profile might be due to the increased exposure to HEV in young adults through exposure to high-risk environments through work and consumption of high volumes of contaminated food and water. In the present study, there was no significant association of sex with positivity to anti-HEV antibody. Females, however, had a prevalence rate of 54.8%, and the males had a rate of 45.2%. Adesina *et al*. [13] showed no significant difference in both sexes. This could be due to the fact that both sexes live in the same endemic environment and are exposed to the same predictors of the infection.

Source of drinking water, method of human waste disposal, and method of domestic waste disposal were not significantly associated with seropositivity to anti-HEV antibody in this study. It is important to note that in this study, 18 (58.1%) of the 31 subjects positive for anti-HEV antibody used a borehole as a source of drinking water and 12 (38.7%) got their drinking water from a stream. Twenty-six (83.9%) of the subjects positive for HEV used a pit latrine, and four (12.9%) used a water closet. Though these differences were not statistically significant, it is important to note that social amenities were generally poor, and it will be important for the community to be educated about how HEV infection is spread, about the need for improved personal hygiene, and also about boiling drinking water.

Social class was not significantly associated with positivity to anti-HEV antibody. However, In Spain, Buti *et al*. [19] showed a significant association of social class with positivity to anti-HEV antibody, using parents' professions and the English classification of social classes. HEV is endemic in areas with poor hygiene and among those of lower socioeconomic background who are not fully aware of the mode of transmission of the disease and the importance of improving personal hygiene [10]. In this study, 30 (96.8%) of the 31 subjects with positive anti-HEV antibody belonged to the lower social class, while one (3.2%) belonged to the middle class. None were of the upper social class. It would be therefore difficult to demonstrate statistically the effect of social class.

The number of persons in the household was not significantly associated with positivity to anti-HEV antibody. This is in keeping with the findings of Colak *et al*. [15] and Aggarwal *et al*. [20], who showed that intrafamilial transmission of HEV was rare. This could be due to the fact that there is a low level of fecal secretion of HEV [20], and so intrafamilial or person-to-person transmission is low.

At the multivariate level, duration of residence was significantly associated with anti-HEV antibody in the community. Longer duration of residence increases the subjects' risk of re-exposure to risk factors, and the probability of infection increases.

A limitation of this study was that the kit used tested for the anti-IgG antibody and therefore made it impossible to test for new infections in the study populations.

Conclusions

An educational campaign about the mode of transmission of this virus and prevention of the infection is recommended. Though the effects of waste disposal systems and water sources were not demonstrated, probably because they were almost universally poor, provision of pipe-borne water and modern sewage disposal systems could help to curb the prevalence of this infection and prevent an epidemic.

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Authors' contributions

EE conceptualized the study and had a final overview of the manuscript. JI collected the data and wrote up the manuscript. HO carried out the laboratory analysis. JU had an overview of the manuscript. All authors reviewed and approved the final manuscript.

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