Low Prevalence Of Hepatitis B 'E' Antigen In Asymptomatic Adult Subjects With Hepatitis B Virus Infection In Enugu, South East Nigeria

U Ijoma, S Nwokediuko, B Onyenekwe, C Ijoma

Citation

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Abstract

Background: Hepatitis B Virus (HBV) infection is a worldwide problem and reaches endemic proportion in developing countries including Nigeria, where an estimated 18 million people are infected. The sequelae of HBV infection are serious and account for about 25% to 40% of the mortality from chronic HBV infection. There is a direct relationship between HBeAg and progression of disease and eventual sequelae of chronic liver disease. The fraction of the individuals with HBV infection who are HBeAg positive in Nigeria is not known.Aim: To determine the hepatitis B 'e' antigen status of asymptomatic subjects with hepatitis B virus infection in Enugu, Nigeria.Design: Prospective cross sectional studySubjects and method: Consecutive adult subjects with HBsAg in serum who met the study criteria were recruited from the Gastroenterology clinic of the University of Nigeria Teaching Hospital, Enugu, Nigeria from May 2004 to August 2005. Subjects were clinically evaluated and serological markers of HBV were assayed by immunochromographic method.Results: Thirteen (8.6%) of the study population were HBeAg positive while 114 (75.5%) were positive for antiHBe antibody. Ninety seven percent were positive for anti HBc IgG antibody. None of the subjects was positive for anti HBc IgM antibody indicating that none of the subjects had acute infection.Conclusion: This study has demonstrated that less than 9% of asymptomatic adult subjects with hepatitis B Virus (HBV) infection in Enugu, Nigeria, have e antigen.

INTRODUCTION

Hepatitis B virus infection is a world wide problem and reaches endemic proportions in South East Asia, sub-Saharan Africa and other parts of the developing world [1]. The disease burden is large and of public health concern. The morbidity and mortality associated with the Hepatitis B virus (HBV) infection is considerable with serious complications including acute viral hepatitis, chronic viral hepatitis, liver cirrhosis and primary liver cell carcinoma. It is estimated that about 2 billion people have been previously infected and there are about 350 million sufferers worldwide [2]. Approximately 18 million Nigerians are chronically infected with HBV and about 4 – 7 million (25 – 40%) of these die from long term complications of cirrhosis and liver cancer [3].

Up to 10% of those infected with HBV may not clear the virus after six months and may go on to develop a chronic carrier state. The progression to chronicity and complication is directly related to high viral replication demonstrable serologically by the presence of markers of pathogenicity and infectivity [4]. These serological markers include Hepatitis B surface antigen (HBsAg), IgG anti core antibody (anti HBc IgG), Hepatitis e antigen (HBeAg), anti hepatitis e antibody (anti HBeAb), and HBV DNA [5]. HBe antigen reflects high viral replication and infectivity [6], and thus, its measurement in serum.

AIM OF THE STUDY

The aim of the study was to determine the HBeAg/anti HBe status in asymptomatic adult subjects with chronic HBV infection in Enugu, Nigeria.

MATERIALS AND METHODS

Consecutive adult subjects who fulfilled the study criteria were recruited from May 2004 to August 2005 from the Gastroenterology outpatient clinic of University of Nigeria Teaching Hospital, Enugu, Nigeria. Individuals 18 year and above of both sexes found to be HBsAg positive were included in the study. Subjects were excluded if they had

significant history of alcohol consumption more than 60 gram for males and 30 grams for females daily, evidence of acute or chronic liver disease from history, physical examination and relevant laboratory investigations, or use of antituberculous or antihypertensive drugs in the past 6 months. Ethical clearance was obtained from the hospital Ethics committee. Written informed consent was obtained from all subjects. A detailed history and physical examination was done for all subjects. Four millilitres of venous blood was drawn from each subject and spun at 4000 rpm for 5 minutes. Serum was separated and tested for serological markers: HBsAg, HBeAg, anti HBe, anti HBc IgG and HBc IgM using immunochromatographic method, (Linear Chemicals SL, Montgat, Barcelona, Spain). Test strips were pre-coated with synthetic and recombinant antigen or antibody. During testing, the serum specimen migrates chromatographically by capillary action and reacts with the antigen or antibody to produce a colour change. The presence of a coloured line in the test region indicates a positive result.

Statistical analysis was done with statistical package for social sciences (SPSS) version 13.5. Normally distributed variables were expressed as mean ± SD. Pearson chi square was used to determine association between gender and HBeAg. P values < 0.05 were accepted as significant. The student t-test and chi square respectively were used to compare the means of parametric and non parametric variables.

RESULTS

One hundred and fifty one subjects comprising 103 (68.2%) males and 48 (31.8%) females fulfilled the study criteria and completed the study. Table 1 shows the demographic data of the study population. The age of the study population ranged from 18 to 73 years with a mean of 33.66 ±12.43. The mean age of the males was 35.82±14.0 while that of the females was 29.04±5.99, p = 0.002. The age distribution of the study population by gender is shown in figure 1.

Table 2 shows the pattern of serological markers of hepatitis B virus infection in the study population. Thirteen (8.6%) of the subjects were positive for HBeAg while 138 (91.4%) were negative for HBeAg. Out of the 13 HBeAg positive subjects, 9 were males and 4 were females. There was no statistical difference in the prevalence of HBeAg in the male (8.7%), and the females (8.3%) subjects, p = 0.938. (Table 3) One hundred and forty one (75.5%) of the group studied were positive for HBeAb while 37 (24.5%) were negative for HBeAb. The distribution of the other serological markers is as shown in table 2. The pattern and combination of serological markers in the study is shown in table 4. One hundred and fourteen subjects had HBsAg, anti HBc IgG, and anti HBe without HBeAg. Twenty one subjects had HBsAg and anti HBc IgG as the only positive markers. Three subjects, though positive for HBsAg were negative for all other markers of HBV infection. HBeAg and anti HBe were not found together in any of the subjects. None of the subjects had a combination of HBsAg and anti HBeAb as serological markers. Thirteen subjects were positive for HBsAg, anti HBc IgG and HBeAg only.

Figure 1

Table 1: Demographic data of the study population.

	SUBJECTS			
	ALL	MALE	FEMALE	p-VALUE
	N=151	N=103	N=48	
Age (years)±SD	33.66±12.43	35.82±14.00	29.04±5.99	0.002
Range	18-73	18-73	18-40	
Gender (%)		103 (68.2%)	48 (31.8%)	<0.001

Figure 2

Table 2: Serological markers of hepatitis B virus infection in the study population

SEROLOGICAL MARKER	NUMBER POSITIVE (%)	NUMBER NEGATIVE (%)
HBsAg	151 (100)	0 (0)
Anti HBc IgM	0 (0)	151 (100)
Anti HBc IgG	147 (97.4)	4 (2.6)
HBeAg	13 (8.6)	138 (91.4)
HBeAb	114 (75.5)	37 (24.5)

HBsAg; hepatitis B surface antigen, Anti HBc IgM; IgM antibody to hepatitis B core antigen, Anti HBc IgG; IgG antibody to hepatitis B core antigen, HBeAg; hepatitis B é'antigen, HBeAb; hepatitis B é'antibody

Figure 3

Table 3: Association between gender and HBeAg positivity

	SEX		
	MALE (%)	FEMALE (%)	TOTAL (%)
HBeAg positive	9 (8.7)	4 (8.3)	13 (8.6)
Negative	94 (91.3)	44 (91.7)	138 (91.4)
Total	103 (100)	48 (100)	151 (100)

Pearson chi square .007, df 1, p = 0.938

Figure 4

Table 4: Pattern of serological markers in the study group

HBV MARKER					
HBsAg	AntiHBc IgM	AntiHBc IgG	HBeAg	HBeAb	NUMBER
+	–	+	+	–	13
+	–	+	–	+	114
+	–	+	–	–	21
+	–	–	–	–	3

HBsAg; hepatitis B surface antigen, Anti HBc IgM; IgM antibody to hepatitis B core antigen, Anti HBc IgG; IgG antibody to hepatitis B core antigen, HBeAg; hepatitis B é'antigen, HBeAb; hepatitis B é'antibody

DISCUSSION

This study has demonstrated a low prevalence (8.6%) of HBeAg in the study population indicating a low level of infectivity and viral replication in asymptomatic individuals infected with Hepatitis B virus in Enugu, South East Nigeria.

Similar studies by Otegbayo et al [7], in Ibadan and Abiodun et al [8], in Benin City documented prevalence rates of HBeAg in HBsAg positive subjects of 10.8% and 8.8% respectively. These rates are similar to that (8.6%) in this study. Ibadan, Benin City and Enugu are in the same geographical rain forest region and it will appear that the prevalence rate of HBeAg in the Nigerian rain forest region is low. In contrast, a similar study by Mbaawuaga et al [9], in Makurdi in the Savannah middle belt in pregnant women documented a higher prevalence of HBeAg of 30.3%. The reason for this geographical difference is not clear. Ojo et al [10], recorded a much higher prevalence rate of 48% in Ile-Ife, Nigeria in the same geographical location as Ibadan, but these patients had established chronic liver disease (CLD).

The presence of HBeAg is a marker of infectivity and continuing viral replication in blood and portends a less favorable prognosis. It is thought that 80% to 95% of HBeAg positive individuals maintain high viral replication and severe necroinflammation with high levels of alanine transaminase (ALT) in serum. The elevated levels of aminotransferases correlate highly with on-going chronic hepatitis which begins the sequalea of complications. A large prospective study of Taiwanese men [11], showed that men who were positive for both HBsAg and HBeAg had a much higher cumulative incidence of PLCC than those who were positive for only HBsAg and an even higher incidence than those who were negative for both. The relative risk for PLCC among men who were positive for HBsAg alone was 9.6 and 60.2 among those who were positive for both. In sub-Saharan Africa, various workers, [10, 12, 13], have highlighted the fact that HBV is probably the most important aetiological factor associated with chronic liver disease (CLD) in this environment.

Chronic HBV infection can be subdivided into two based on the presence or absence of HBeAg. The HBeAg negative variant has been found to be more prevalent in Asia and Far East [14, 15]. Such persons have HBV organisms that are unable to produce HBeAg due to a mutation either at the pre core or basic core promoter region of the viral genome. Sequence analysis have revealed a point mutation, guanine to adenine (G to A) at nucleoside position 1896 that results in the production of a translational stop codon predicted to stop the translation of HBeAg [16]. An increased level of HBeAg in regions of high endemicity maintains a reservoir for chronic HBV infection. Further studies to define pre-core and core promoter variants in HBeAg negative subjects in Nigeria is warranted. This may probably explain the difference in the prevalence of HBeAg between the rain forest and Savannah regions of Nigeria.

Anti HBe antibody was documented in 75.5% of this study population. Other studies done within Africa have also shown lower values for anti HBe antibody ranging from 25% to 59.5%. [17, 18]. It is accepted that in sub Saharan Africa, most HBV infections are acquired horizontally in childhood and the level of HBsAg is expected to be high [8, 19, 20] With advancing age, spontaneous seroconversion takes place leading to a reduction in the frequency of HBeAg and an increase in anti HBe antibody.

In this study, we observed a male to female ratio of HBsAg of 2.1:1 in keeping with the preponderance of HBV infection globally. Various studies locally and internationally have recorded a male preponderance in individuals infected with hepatitis B virus [7, 8, 17, 18, 21]. The age group 15-29 years and 30-44 years accounted for 81.4% of the study population and this follows the normal pyramidal structure of the population. Older individuals may have manifested with complications of HBV infection and would have been excluded from the study. The study population also had a bias for younger persons as these are more likely to be potential blood donors or need medical certification for employment or school admission. This is comparable to an Indian study with 43% of the study group in the age range 30 – 39 years [22].

CONCLUSION

This study has shown a low prevalence of HB e antigen and high prevalence of HBe antibody in asymptomatic chronic hepatitis B virus infected subjects. These findings may indicate a low level of active disease in the region.

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Author Information

Uchenna N Ijoma
Department of Medicine, University of Nigeria Teaching Hospital

Sylvester C Nwokediuko
Department of Medicine, University of Nigeria Teaching Hospital

Belonwu Onyenekwe
Department of Medicine, University of Nigeria Teaching Hospital

Chinwuba K Ijoma
Department of Medicine, University of Nigeria Teaching Hospital