

Research article

PREVALENCE OF HBeAg AMONG HEPATITIS B SEROPOSITIVE INDIVIDUALS IN MAKURDI, NIGERIA

Odimayo Michael Simidele¹; Nwadioha Samuel Ihinacho, Nwokedi Emmanuel Prince

Department of Medical Microbiology and Infectious Diseases,
College of Health Sciences,
Benue State University/Benue State University Teaching Hospital,
Makurdi, Benue State, Nigeria

E-mail: simideledimayo@yahoo.com

¹ Corresponding Author

Abstract

This retrospective study aimed at determining the prevalence of Hepatitis B 'e' Antigen (HBeAg) among hepatitis B surface antigen positive patients in Makurdi, Nigeria. We review of HBeAg among Hepatitis B surface antigen (HBsAg) sero-positive patients aged 0-65 years from July 2009 to February 2012 in Delight Specialist Clinic and Maternity, Makurdi. In a total of 467 patients recruited in the study, 20.6% (n=96/467) was HBsAg sero positive. Among the HBsAg sero positive patients, only 3.1% (n=3/96) was HBeAg sero positive. Sixty-seven per cent of HBeAg detection in was females while 33% was males. A total 100% number of Hepatitis B 'e' Antigen sero-positive patients were under age of 22 years. The study showed a low sero-prevalence of HBeAg in a high hepatitis B sero-positive endemic population with adolescent age posing a higher risk for HBeAg. **Copyright © AJBCPS, all rights reserved.**

Key words: Hepatitis B virus, Hepatitis B 'e' antigen, prevalence

INTRODUCTION

The problem of hepatitis B virus (HBV) associated morbidity and mortality is still a concern [1-3]. The silent nature of the disease coupled with the significant untimely death calls for early, reliable and affordable method of diagnosis [3].

The current Laboratory diagnosis of HBV includes detection of Hepatitis B surface antigen, Hepatitis B e Antigen, Hepatitis B surface antibody, Hepatitis B e antibody and Hepatitis B core antibodies in the serum [4]. Several techniques have been used in the time past, but enzyme linked immunoabsorbent assay (ELISA) and recombinant immunoblot assay (RIBA) are still currently relevant [5]. Polymerase chain reaction (PCR) is useful for amplifying and quantifying serum DNA [5]. Liver biopsy permits tissue diagnosis of hepatitis. Enzyme tests for abnormal liver functions can supplement clinical, pathologic and epidemiologic findings. While Viral Cultures in various primate cell lines are slow in growth and repeated blind passages are required [6].

The complete infectious Hepatitis B virion (Dane particle) is a 42nm spherical particle consisting of hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), hepatitis B e antigen (HBeAg), DNA and DNA polymerase [7]. HBsAg is an outer lipoprotein surface envelope that mediates the attachment of HBV to hepatocytes. It is the first viral marker to appear following infection with the virus. The detection of HBsAg in the blood indicates either an inactive HBV carrier state or acute or chronic infection with Hepatitis B Virus. HBsAg positivity also means potential infectivity. HBeAg is a marker of viral replication. When viral replication slows, HBeAg disappears and anti-HBe is detected. Anti-HBe may persist for years. Other important markers include HBcAg and its antibodies; DNA and DNA polymerase [8].

The present study examines the prevalence of Hepatitis B e antigen among hepatitis B surface antigen positive patients in Makurdi, Nigeria.

MATERIALS & METHODS

This is a retrospective study conducted in Delight Specialist Clinic and Maternity, Makurdi in which randomly selected patients who were screened for hepatitis B virus sero positivity using HBsAg and HBeAg as markers between July 2009 and February 2012 were reviewed. Patients found to be positive for HBsAg after repeated screening were usually further tested for the presence of hepatitis B e antigen (HBeAg) seropositivity. HBsAg screening of patients was done by aseptically collecting 2mls of blood from the antecubital vein, using HBsAg rapid test kits manufactured by Clinotech Diagnostics Incorporated, (Lot SAG90808; expiry date 03/2013). Manufacturer's instructions were strictly followed. Patients found to be sero positive were confirmed by rescreening with a second rapid test kits manufactured by Exact diagnostics and then interpreted. Samples positive after repeated testing were documented as positive. Patients diagnosed hepatitis B positive were then tested for Hepatitis B e antigen (HBeAg) using HBeAg rapid test kits. Manufacturer's instructions were strictly followed. Additional investigations did include liver function test and urinary bilirubin. Facility for molecular detection of hepatitis B viral genome in patients' sample was not available for definitive diagnosis of hepatitis B viral infection. Patients diagnosed chronic hepatitis were placed on ternofovir-emcitrabin combination or

lamivudine. Every patient was on monthly follow up clinical assessment and 3 to 6 monthly liver function tests, HBsAg and HBeAg check. Additional data extracted include age and sex. Any patient with previous hepatitis B vaccination was excluded from the study. Patients negative for HBsAg were given 3 doses of hepatitis B virus vaccine.

The results were analyzed using SPSS 11.0 statistical software; chi-square(X^2) was used to compare association between proportions and P-values <0.05 was considered significant at 95.0% confidence level.

RESULTS

A total of 467 individuals were tested during the study period consisting of 247 males and 220 females among them 96 (20.6%) were positive for HBsAg (Table 1). Among the 96 HBsAg seropositive patients, 3 (3.1%) were HBeAg sero positive while the remaining 93 (96.9%) were sero negative showing that only about 3% of HBsAg positive patients were elaborating the 'e' antigen or actively replicating the virus. Among the individuals with active 'e' antigen elaboration, 2 (67%) of them were females while 1 (33%) was a male. Among these 3 patients, 2 of them were below 15 years while 1 was 22 years. However, among our study population, two of the HBsAg seropositive patients aged above 35 years were diagnosed of hepatocellular carcinoma.

DISCUSSION

The study recorded 3.1% (3/96) of hepatitis B 'e' antigen (HBeAg) in a total 21% (96/467) hepatitis B seropositive individuals. A similar work carried out at the blood donor clinics across two teaching hospitals in Lagos, S.W. Nigeria showed a higher sero-prevalence rate of 8.2% of HBeAg positivity in chronic hepatitis [9]. Lesi and co-workers in Nigeria recorded HBeAg positivity in 25% of the subjects with HBV /HIV co-infections [10]. A growing evidence from Congo and Zambia are in support of the findings of high prevalence of HBeAg, and suggests that higher prevalence of HBeAg may be due to reactivation of hepatitis B virus (HBV) infection in previously immune subjects or chronic carriers[11,12].

Among the 3.1% HBeAg sero-positive patients in the study, all were 22years and below of age. An earlier study done on changes in HBeAg status with age in HBV chronic carriers in Gambia [13], recorded that HBeAg was lost at a much faster rate than HBsAg. Eighty-six percent of the carriers who were recruited at the age of 1-4 years lost HBeAg by the age of 19 years compared to 30% who lost HBsAg. However, small proportion (10-20%) retained HBeAg and continued to have high levels of viral replications [13]. Other studies have shown that early in the carrier state, HBV infected individuals test positive for HBsAg and HBeAg in the serum, however, the serum of older carriers shows clearance of HBeAg with detectable antibody to hepatitis B 'e' antigen (anti-HBe)[13,14]. Important occurring changes that have impacted on the natural history of HBeAg include the development of mutant forms of the virus mainly pre-core (pre-C) and basal core promoter (BCP) mutants. Pre-core mutants are unable to express HBeAg due to the presence of a stop codon within the pre-core region. Such mutants retain the ability to replicate and express HBcAg [15]. The fact that HBeAg tend to wane with increasing age and majority of adults carriers have maintained inactive status plus the possibility of mutant

forms of the virus not to express HBeAg could explain the low level of sero-prevalence of HBeAg vis-avis HBsAg recorded in the present study.

Hepatitis B 'e' antigen has been considered a biomarker of active viral proliferation in hepatocytes and infectivity and is associated with risk of hepatocellular carcinoma (HCC) [16]. A study showed an 87% cumulative hepatocellular risk from age 30 to 70 years for those who were persistently sero-positive for HBsAg and HBeAg and 12% for those with seropositivity for HBsAg only [16]. In some further studies, the viral mutant forms (basal core promoter mutant forms) were implicated in the development of advanced liver diseases in the Gambia [17]. Although several selected commercial laboratories now offer the assays that identify the precore and core promoter mutations, in clinical practice, the diagnosis of HBeAg-negative chronic hepatitis B is generally made by identifying a high HBV DNA load in an HBeAg-negative patient.

The treatment of HBeAg-negative chronic hepatitis B has several features that differ from treatment of HBeAg positive chronic hepatitis B, including lower response rates, longer duration of therapy, greater use of interferon, and higher relapse rates. Thus, the treatment endpoint in patients with HBeAg-negative chronic hepatitis B is based on suppression of HBV DNA and normalization of alanine transaminase enzymes (ALT).

The degree of severity/infectivity of chronic hepatitis B virus therefore is best ascertained by study of HBV DNA in order to rule out viral core promoter mutant forms of chronic HBeAg negative viral hepatitis.

The present work is limited by small sample size, further studies including multicentre studies are recommended since only a handful of HBeAg studies has been done in our locality. Serologic testing is the primary way to identify persons with chronic hepatitis B virus infection. This testing is recommended for infants born to HBsAg positive mothers, household contacts and sex partners of HBV infected persons, persons born in countries with HBsAg prevalence of $\geq 8\%$, blood donors or individual with exposures to body fluid that may warrant postexposure prophylaxis (e.g., needlestick injury to a health-care worker or sexual assault), and persons infected with human immunodeficiency virus [19]. Sero negative individuals who fall into this category should be promptly immunized.

In conclusion, this study showed a low sero-prevalence of HBeAg in a high hepatitis B sero-positive endemic population with adolescent age posing a higher risk for HBeAg.

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Tables

Table 1: Sex distribution of positive and negative subjects

Sex	No. Positive	No. Negative	Total
Male	57	190	247
Female	39	181	220
Total	96	371	467

Table 2: Sex distribution of HBeAg positive and negative subjects

Sex	No. Positive	No. Negative	Total
Male	1	56	57
Female	2	37	39
Total	3	93	96