

Coexistence of HBsAg/Anti-HBs and HBeAg/Anti-HBe in Sudanese Patients with Chronic Hepatitis B Virus Infection: A Cross-Sectional Study

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Abstract

Background: Seroconversion of hepatitis B surface antigen (HBsAg) to hepatitis B surface antibody (anti-HBs) is a recognized goal of HBV therapy. This dynamic transition responsible for the coexistence of HBsAg and anti-HBs is rarely detected in clinical cases. However, with vaccination and the use of various antiviral drugs, as well as the development of new medical technologies, recognizing the coexistence of HBsAg and anti-HBs has become more common. In addition, mutations in viral genomes, immune status, and human genetic factors may also contribute to such coexistence. The current study was designed to determine the prevalence of the coexistence of HBsAg and anti-HBs and HBeAg and anti-HBe in CHB patients in Sudan.

Methods and Results: This was a descriptive cross-sectional study conducted in Khartoum state from November 2018 to January 2019. The study included 70 HBV-infected patients who were positive for HBsAg for more than six months. Blood samples were tested for HBsAg/Anti-HBs and HBeAg/Anti-HBe using Commercial ELISA Kits (Foresight, United Kingdom) and (PRECHEK, USA). Demographic data were collected using a structured questionnaire, and any antiviral agent and laboratory results were also recorded for each participant. The current study showed that one case (1.4%) was reactive for the coexistence of HBsAg/HBsAb and two cases (2.8%) for the coexistence of HBeAg/HBeAb. There was no statistical difference between the coexistence of HBsAg/HBsAb and HBeAg/HBeAb with age, gender, residence, and treatment status.

Conclusion: Our study indicates that the frequencies of the coexistence of HBsAg/HBsAb and HBeAg/HBeAb among Sudanese patients with chronic HBV infection were low compared to previous studies in a different population. (**International Journal of Biomedicine. 2023;13(4):281-285.**)

Keywords: hepatitis B virus • HBsAg • HBeAg • anti-HBs • anti-HBe

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Abbreviations

anti-HBs, hepatitis B surface antibody; **anti-HBe**, HBe antibody; **anti-HBc**, total antibody to hepatitis B core antigen; **CHB**, chronic hepatitis B; **HBsAg**, hepatitis B surface antigen; **HBV**, hepatitis B virus; **HBeAg**, hepatitis B e antigen.

Introduction

Hepatitis B virus (HBV) infection is a universal public health problem and a common cause of liver cirrhosis and hepatocellular carcinoma. Globally, a probable 257 million people are living with chronic HBV, which affects primarily many African countries and the western Pacific region, according to the WHO.⁽¹⁾

HBV clearance is classically characterized by the occurrence of hepatitis B surface antibody (anti-HBs) homologous to hepatitis B surface antigen (HBsAg), which contains several important antigenic epitopes, in particular a determinant that spans amino acids 124-147 within its major hydrophilic region (MHR).⁽²⁻⁴⁾ Thus, anti-HBs and HBsAg are characteristically not recognized in sera of people with present HBV infection in routine clinical practice.⁽⁵⁾

However, several studies have depicted the manifestation of HBsAg linked with anti-HBs in CHB patients.⁽⁶⁻¹⁰⁾ With variable rates of coexisting anti-HBs and HBsAg in chronic patients, the HBsAg carriers were projected to be 2.43%-8.9%.^(5,11-14) Further, the mechanism underlying the advent of anti-HBs in patients with chronic hepatitis B drugs is indistinct. Still, numerous studies have disclosed that HBV mutations could be attributed to the selection of immune escape mutations.^(10,12,14-17)

The key methods widely used for testing hepatitis B serology are the tests for detecting HBsAg and HBeAg and their matching with antibodies anti-HBe, anti-HBc IgM, anti-HBs, and anti-HBc (total). A previous study showed that succeeding infection with HBV naturally, HBsAg can be noticeable in serum during the cultivation period of 3-5 weeks before the presence of clinical symptoms and continues for 2-4 weeks after the augmentation of transaminase level; it is not detected in 2-6 months as the patient recovers and after a window period, protective anti-HBs antibody appears. The perseverance of HBsAg beyond six months after acute infection is putative evidence of chronic infection. Occasionally, the seroconversion of HBeAg to anti-HBe consensuses with the reduction or normalization of serum ALT concentration and a very low level of HBV duplication. However, recent studies have established that the serum HBV DNA concentration is not associated with the presence or absence of HBeAg.⁽¹⁸⁾

Meanwhile, the marker for the resolution of acute infection can be identified by the appearance of the antibodies to HBeAg, which is used to monitor treatment, and the appearance of anti-HBe differentiates between the two stages. A negative result of the HBeAg may designate an early severe infection before the peak of viral duplication or early recovery when HBeAg has dropped below detectable levels. It is important to state a subset of CHB patients is not obvious HBeAg in serum but is positive for anti-HBe; these

types of patients may also be positive for serum hepatitis B virus DNA.

Additionally, when treating CHB patients, the antigen/antibody seroconversion can be used as a marker of virological response.⁽¹⁹⁾ The coexistence of HBsAg and anti-HBs contains an atypical serological profile in patients with HBV infection. Hence, in the presence of a circulating immune complex with optimal proportion and new subtype infection, the coexistence of anti-HBs and HBsAg might reveal the strictness of liver disease and the active replication or reactivation of the virus.⁽²⁰⁾ It is unusual for patients with prolonged HBV to relate to more advanced liver diseases.⁽¹²⁾

According to many publications, Sudan is classified among the countries with high HBV seroprevalence endemicity, with infection rates ranging from 6.8% in central to 26% in southern Sudan, and this infection is common among patients hospitalized with hepatocellular carcinoma. Also, there are many challenges facing healthcare workers in the country in combating severe health problems like hepatitis infection, cancer, HIV, and Dengue virus.⁽²¹⁻²⁵⁾

The current study was designed to determine the prevalence of the coexistence of HBsAg and anti-HBs and HBeAg and anti-HBe in CHB patients in Sudan.

Materials and Methods

This was a descriptive cross-sectional study conducted in Khartoum state from November 2018 to January 2019. The study included 70 HBV-infected patients (54[77.1%] male and 16[22.9%] female; age range from 19 to 65 years with mean age of 34.35 years) who were positive for HBsAg for more than six months, attending Saba Medical Complex, Ibrahim Malik Teaching Hospital, and The Hospital of ibn Sina in Khartoum. The blood samples (2.5 ml in a plain container) were collected, let to clot, and then separated to obtain serum. All samples were tested for HBsAg/Anti-HBs and HBeAg/Anti-HBe using Commercial ELISA Kits (Foresight, United Kingdom) and (PRECHEK, USA). Demographic data were collected using a structured questionnaire, and any antiviral agent and laboratory results were also recorded for each participant.

Statistical analysis was performed using the statistical software package SPSS version 20.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages. Group comparisons were performed using chi-square test or, alternatively, Fisher's exact test when expected cell counts were less than 5. A probability value of $P < 0.05$ was considered statistically significant.

The study was approved by the Ethics Committee at the Al Neelain University.

Results

Of 70 patients with chronic HBV infection, there were 37(52.8%) under specific HBV treatment, while 33(47.1%) were treated naïvely. The participants were classified into two groups, from 19 to 40 years and from 41 to 65 years, which were distributed as 58/70(82.9%) and 12/70(17.1%),

respectively. Out of the 70 participants, 61(87.1%) resided in Khartoum, 2(2.8%) in Omdurman, and 7(10%) in North Khartoum (Bahri).

The current study showed that one case (1.4%) was reactive for the coexistence of HBsAg/HBsAb and two cases (2.8%) for the coexistence of HBeAg/HBeAb. Among 70 patients, 6(8.6%) carried HBeAg and 58(82.9%) carried HBeAb. There was no statistical difference between the coexistence of HBsAg/HBsAb and HBeAg/HBeAb with age, gender, residence, and treatment status (Tables 1 and 2).

Table 1.

Coexistence of HBsAg/HBsAb regarding age, gender, residence, and treatment status.

Variable		HBsAg/HBsAb		P-value
		Reactive n (%)	Non-reactive n (%)	
Age	19—40	0 (0)	58 (82.9)	0.171
	41—65	1 (1.4)	11 (15.7)	
Gender	Male	1 (1.4)	53 (75.7)	1.0
	Female	0 (0)	16 (22.8)	
Treatment	Specific HBV treatment	0 (0)	37 (52.8)	0.471
	Treatment-naïve	1 (1.4)	32 (45.7)	
Residence	Khartoum	1 (1.4)	60 (85.7)	0.928
	Bahri	0 (0)	7 (10.0)	
	Omdurman	0 (0)	2 (2.8)	

Table 2.

Coexistence of HBeAg/HBeAb regarding age, gender, residence, and treatment status.

Variable		HBeAg/HBeAb		P-value
		Reactive n (%)	Non-reactive n (%)	
Age	19—40	2 (2.8)	56 (80.0)	1.0
	41—65	0 (0)	12 (17.1)	
Gender	Male	2 (2.8)	52 (74.3)	1.0
	Female	0 (0)	16 (22.8)	
Treatment	Specific HBV treatment	1 (1.4)	36 (51.4)	1.0
	Treatment-naïve	1 (1.4)	32 (45.7)	
Residence	Khartoum	2 (2.8)	59 (84.3)	0.859
	Bahri	0 (0)	7 (10.0)	
	Omdurman	0 (0)	2 (2.8)	

Discussion

The coexistence of anti-HBs and HBsAg in patients with HBV infection is uncommon⁽²⁰⁾ but may be associated with more progressive liver diseases.⁽¹²⁾ The HBeAg is a significant marker of viral replication in chronic infection, infectivity, and constant liver injury.

The antibody to HBeAg is noticeable as HBeAg vanishes from the serum, and the existence of anti-HBe is linked with the probability of impulsive resolution of severe infection.

In patients enduring HBV infection, the downfall of HBeAg and the gaining anti-HBe tend to be allied with biochemical and histological upgrading.⁽²⁷⁾ Previous studies have shown the prevalence of coexistence of anti-HBs with HBsAg and anti-HBe with HBeAg in patients with chronic hepatitis B infection, with significant variation in many different countries. Our study found that the frequency of the coexistence of HBsAg and HBsAb was 1.4%, which is comparable to a previous study on patients with chronic HBV infection by Wang et al.,⁽²⁸⁾ who found that the dominance of atypical serological pattern was 2.93% (122/4169). The prevalence progressively increased with age from 40 to 70 years old. In addition, the rate of HBeAg positive and detectable HBV DNA were both significantly higher in carriers with this pattern than in carriers who were HBsAg positive but anti-HBs negative ($P=0.046$ and $P<0.001$, respectively).

Our findings were similar to a study by Liu et al.,⁽¹⁵⁾ which showed a 2.9% prevalence of the coexistence of HBsAg and anti-HBs in Chinese CHB patients. There was no significant difference between patients with and without anti-HBs regarding age, gender, alanine aminotransferase level, and the proportion positive for HBeAg and HBeAb.

The present findings found that 2.8% (2/70) of patients were positive for the coexistence of HBeAg and HBeAb, which was closely similar to the study by Rabbie et al. in Dhaka,⁽²⁷⁾ in which out of 72 chronic HBsAg positive carriers, 28(38.9%) patients were HBeAg positive and anti-HBe negative, 38(52.8%) patients were HBeAg negative and anti-HBe positive, only 3(4.2%) patients were positive for both HBeAg and anti-HBe and the rest 3(4.2%) patients were negative for both markers.

In a study by Xiang et al.,⁽²⁹⁾ among 124,865 patients with CHB infection, 324(0.3%) were concurrently positive for HBsAg and anti-HBs, and 206(0.2%) were concurrently positive for HBeAg and anti-HBe. The HBeAg+/anti-HBe+ group was composed of younger patients ($P<0.05$). There were no significant difference in the sex, ALT, AST, and HBV DNA level between the HBsAg+/anti-HBs+ and the HBeAg+/anti-HBe+ groups. In our study, the percentage of positive results for the HBeAg/HBeAb coexistence was higher among the patients between 19-40 years than among the older group, but with an insignificant difference. This result contrasts with a study by Xiang et al.⁽²⁹⁾ This current study revealed no substantial relationship between the coexistence of HBsAg/HBsAb and HBeAg/HBeAb with gender, age and treatment, residence, and the incidence of anti-HBe.

Conclusion

The frequencies of the coexistence of HBsAg/HBsAb and HBeAg/HBeAb among Sudanese patients with chronic HBV infection are low compared to previous studies in a different population.

Competing Interests

The authors declare that they have no competing interests.

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