SEROLOGICAL PROFILES OF HEPATITIS B CARRIER PATIENTS IN SINGAPORE WITH SPECIAL REFERENCE TO THE FREQUENCY AND SIGNIFICANCE OF CONCURRENT PRESENCE OF HBsAg AND ANTI-HBs

Y M Wang, W C Ng, J Y Kang, I Yap, B L Seet, J Teo, R Smith, R Guan

ABSTRACT

Hepatitis B serological markers were investigated in 1,132 consecutive Singaporean HBV carriers. Hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (anti-HBs) were found concurrently in 234 carriers (234/1132 or 21%). Serum anti-HBs levels were more than 10 mIU/mL in 80 of these carriers (80/234 or 34%). There were no difference in HBeAg positive status, as well as HBV-DNA positive status in concurrent HBsAg/anti-HBs carriers compared to carriers without anti-HBs. Our results suggested that concurrent HBsAg and anti-HBs is a common serologic pattern in Singaporean HBV carriers.

Keywords: HBV carriers, HBsAg, anti-HBs, HBeAg, HBV-DNA

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INTRODUCTION

The concurrent presence of hepatitis B surface antigen and antibody has been noticed in both acute and chronic hepatitis B infection[1,2]. In patients with chronic hepatitis B, the presence of anti-HBs is not associated with the disappearance of the virus[3]. The immune response in these patients resulting in anti-HBs production may have resulted from infection with a different subtype of HBV virus or the infecting virus developing point mutations, deletions and genetic recombination in the surface genes, thereby causing amino acid changes in the virus antigenic sites[4,5].

We studied the serological profiles of hepatitis B carrier patients attending the Gastroenterology Clinic at the National University Hospital and determined the frequency and significance of concurrent HBsAg and anti-HBs in Singaporean HBV chronic carriers. The possible mechanisms of such serologic patterns are discussed.

Hepatology Laboratory
Department of Medicine
National University of Singapore
5 Lower Kent Ridge Road
Singapore 119074

Y M Wang, MD
Research Scholar

W C Ng, PhD
Research Scientist

J Y Kang, MD, FRCP, FRACP
Associate Professor

I Yap, MBBS, M Med (Int Med)
Associate Professor

B L Seet
Senior Technician

J Teo, BSc (Hons)
Research Assistant

R Smith, SRN
Research Nurse

R Guan, FAMS, MBBS, FRCP
Associate Professor

Correspondence to: A/Prof R Guan
3 Mt Elizabeth #17-02
Mt Elizabeth Medical Centre
Singapore 228510

MATERIALS AND METHODS

Materials

Consecutive sera from 1,132 consecutive hepatitis B carriers seen at National University Hospital Singapore between 1986-1994 were studied. There were 1,073 (94.8%) Chinese, 35 (3.1%) Malays and 12 (1.1%) Indians.

Laboratory Tests

Serum samples were tested for HBsAg, HBeAg, anti-HBe and anti-HBc by commercially available enzyme linked immunoassay kit (Auszyme II for HBsAg, EIA for HBeAg/anti-HBe, Abbott Laboratories, North Chicago Ill). Serum HBV deoxyribonucleic acid (HBV-DNA) were measured by dot blot hybridization[6,7]. Anti-HBs levels were tested using the IMx AUSAB assay, which is a Microparticle Enzyme Immunoassay (MEIA) for the qualitative and quantitative determination of anti-HBs. Specimen with an absorbance greater than or equal to the cut-off value were considered positive for the presence of anti-HBs

Statistical Analysis

The statistical significance of the data were evaluated with chi-squared analysis test for comparing dichotomous variables.

RESULTS

Sera from 742 (65.5%) men and 390 (34.4%) women were evaluated. Their ages ranged from less than 11 to 79 years. The age distribution of the HBsAg positive carrier population is shown in Fig 1. The relative frequencies of HBeAg and HBV-DNA status in HBsAg carriers with respect to age are shown in Fig 2 and Fig 3. Fig 4 shows the frequency of occurrence of anti-HBs in the different age groups in hepatitis B carriers.

Two hundred and thirty-four HBV carriers (20.6% or 234/1132) had both HBsAg and anti-HBs in their sera. Serum anti-HBs levels were more than 10 mIU/mL in 80 of them (80/1132 or 7.0%). The HBeAg and HBV-DNA positivity rates in the two groups (HBsAg/anti-HBs positive and HBsAg only) were similar (Table I).

DISCUSSION

There was a progressive decrease in the frequency of HBeAg and HBV-DNA positivity rate with age showing a reduction in

Fig 1 – Age frequency of HBsAg-positive carriers

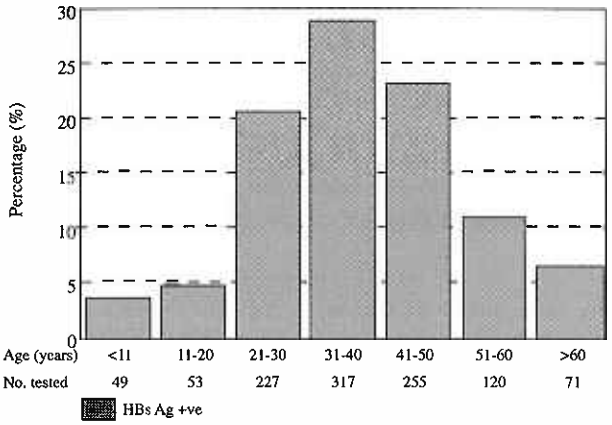


Fig 2 – Frequency of HBeAg positive and negative status according to age groups

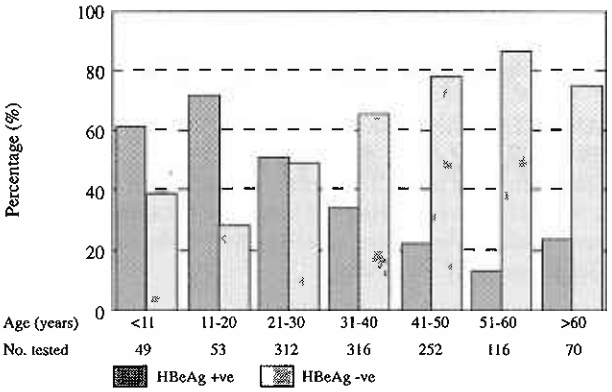
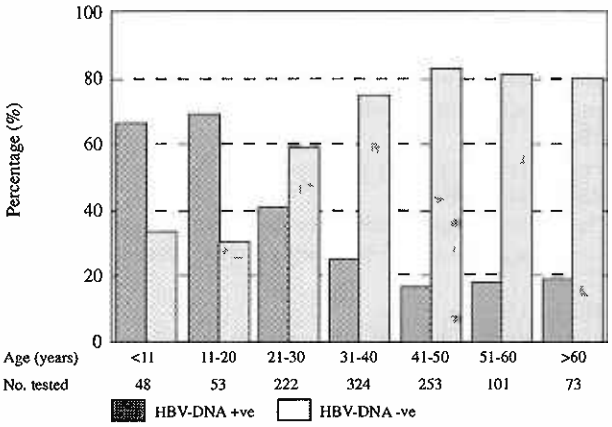


Fig 3 – Frequency of HBV-DNA positive and negative status according to age groups



virus replication with time. These results are in accordance with other reports[8].

Twenty-one percent of HBV carriers have concurrent presence of HBsAg and anti-HBs. Thirty-four percent of these patients have anti-HBs levels more than 10 mIU/mL. Snields and his colleagues reported 32% (73/228) of patients with acute and chronic hepatitis B harboured HBsAg and anti-HBs[1].

Serum HBeAg and HBV-DNA are markers of HBV replication and infectivity. Both the HBsAg and HBsAg/anti-HBs groups of HBsAg carriers had similar HBeAg positive HBV-DNA positive rates (Table I). These results are in accordance

Fig 4 – Frequency of occurrence of anti-HBs in HBV carriers in the different age groups

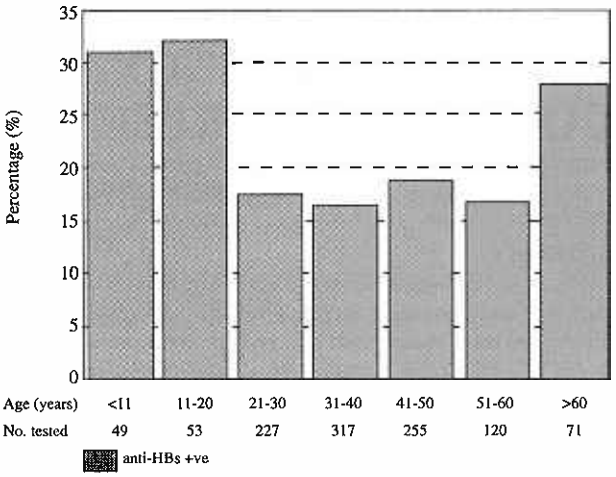


Table I – HBeAg and HBV-DNA status in HBV carrier patients with or without anti-HBs

	HBeAg		HBV-DNA	
	+ve	-ve	+ve	-ve
anti-HBs +ve(%)	79 (34)	155 (66)	71 (30)	163 (70)
anti-HBs -ve(%)	290 (32)	608 (68)	263 (29)	635 (71)

with that in the literature[9-11] and suggested that simultaneous HBsAg/anti-HBs positivity does not appear to reflect a distinct clinical entity. Wang and his colleagues[12] reported a case of acute hepatitis B viral infection in a patient with anti-HBs level of less than 100 mIU/mL prior to his acute illness. This antibody level is supposed to be above the protective level and the infection, in spite of protection, was thought to be due to the fact that the patient's antibody was to a different subtype of the HBV.

Our study showed that these HBV carriers with concurrent anti-HBs still have active virus replication indicating that the anti-HBs offered no protection against the hepatitis B virus. HBV carrier patients having concomitant hepatitis B surface antigen and antibody appear to behave like patients without anti-HBs.

One possible explanation for this serological pattern is that some of the infecting virus are surface antigen mutants which can influence and alter the immune response and clinical course of their hosts. The other possible mechanism is that the antibody developed against only a subdeterminant of HBsAg, as the HBV genomes are comprised of subtypes adw, adr, ayr and ayw. Variants of the virus are conveniently identified by distinct antigenic determinants carried on their surface antigen. A recent report[13] has described another pair of allelic determinants: i/t, besides d/y and w/r. It was thought that each of d/y, w/r and i/t conversion is induced by changing the second letter of the codon. Since antigenic determinant of HBsAg, coded by the pre-s and s gene, have not been fully characterised, other allelic determinants regulated by single amino acid substitutions induced by point mutations may occur. Trepo[14] proposed that another mechanism is strong antibody response to continued viral replication. This is possible although DNA levels were not measured in his patients.

Further studies to delineate the cause of concurrent HBsAg and anti-HBs in HBV carriers are being carried out in our

laboratory.

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