

Status of Hepatitis Be Antigen in Chronic Hepatitis B Patients from Various Regions of Pakistan

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Abstract

Background: To determine the distribution of HBeAg in chronic hepatitis B patients from different regions of Pakistan.

Methods: In this study a total of 677 individuals infected with hepatitis B for a minimum period of 6 months, were included in the study. The information like age, gender along with area of residence, were recorded in a proforma filled for each study subject. A 3 ml blood sample was taken from each person. HBsAg, HBeAg and Anti HBe testing was carried out by ELISA.

Results: Out of 677 study subjects, 517 (76.4%) were males and 160 (23.6%) females with an overall mean age of 35.42 ±12.4 years. HBeAg was positive in 66 (9.7%) . All HBeAg positive cases were negative for Anti HBe. HBeAg positivity was 9.4% in Punjab, 14.8% in KPK, 4.89 % in Sindh, 8.3% in AJ & K and 13.3% in Gilgit Baltistan.

Conclusion: There was a male predominance among Hepatitis B virus infected patients .Maximum cases were between 20 to 50 years of age. HBeAg positive cases were significantly less as compared to HBeAg negative cases.

Key Words: HBsAg, HBeAg, Anti HBe,

Introduction

Hepatitis B virus infection is one of the major health problems in Pakistan. Lot of advances have been seen in the recent past regarding management of this infection. Hepatitis B e Antigen (HBeAg) status of hepatitis B infected person has a great role in management of hepatitis B, in the light of guidelines by American Association for Study of Liver Diseases (AASLD). Study of HBeAg status in a population can give us an idea about magnitude of the aggressive disease in that particular area, which would be beneficial for all concerned and decision makers for

allocation of resources for the management of the patients, as well as for implementing the control/preventive measures. It is a global health problem and an estimated 257 million people are living with HBV infection (defined as hepatitis B surface antigen positive) worldwide.¹ HBV is found in almost every region of the globe and is highly endemic in Asia, sub-Saharan Africa, South America and the Middle East.² World Health Organization (WHO) has divided the world into areas of high (more than 8%), high intermediate (5-7%), low intermediate (2-4%) and low (less than 2%) endemic areas for HBV, based on Hepatitis B surface Antigen (HBsAg) prevalence rates.³ Being a chronic disease the risk of developing cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC) is increased in carriers of HBV as compared to general public because 15% to 40% of HBV infected may develop serious sequelae during their lifetime.⁴ Life-long surveillance of HBV infected individuals is therefore, required through testing them repeatedly for HBV DNA and parameters like Hepatitis Be Antigen (HBeAg), antibodies to Hepatitis Be antigen (Anti HBe) and alanine aminotransferase (ALT). HBV infected persons are divided into various categories like active carriers, inactive carriers, and resolved HBV infection, based upon their HBeAg, Anti HBe serostatus, HBV DNA load and ALT levels.⁵ Presence of HBeAg in chronic HBV infection is generally associated with active viral replication and infectivity, whereas Anti HBe shows loss of infectivity and viral replication. Few exceptions are those patients with core/ pre-core mutations, where there is viral activity in the absence of detectable HBeAg.⁶ HBeAg is a surrogate marker for HBV and is used as an alternate to HBV DNA in decision making for treatment, in patients with HBeAg positive serostatus along with ALT level more than twice of the upper limit of the normal.⁷ In majority of cases the loss of HBeAg is associated with a decrease in levels of HBV DNA,

normalization of ALT and significant clinical improvement despite the presence of HbsAg.⁸

The prevalence as well as severity of the disease is not uniform in all segments of society because of certain high risk groups, high prevalence of HDV co-infection in certain areas as well as difference of HBV genotypes.⁹ According to a nationwide survey compiled by Pakistan Medical Research Council, the prevalence of HBsAg is 2.5% in Pakistan. Therefore, in a country of 180 million people, there are approximately 4.25 million hepatitis B carriers.¹⁰ As HBeAg positivity indicates active disease, generally requiring treatment, testing for HBeAg in different areas can give us an idea about severity of the disease in that population. This information can help us in allocation of resources for prevention/ control measures.

Patients and Methods

Ethical approval of research ethics committee of Armed Forces Institute of Pathology (AFIP) Rawalpindi was obtained. Total 677 hepatitis B carriers (HBsAg positive for a minimum period of 6 months), were included. Those, with HCV or HIV co-infection, on immunosuppressive drugs, patients on antiviral therapy for HBV and those not willing for participation in study, were excluded. HbsAg, HBeAg and Anti HBe testing was carried out with enzyme linked immunosorbent assay (ELISA). Patients' serum was incubated with horseradish peroxidase linked antibody for formation of antigen antibody complexes, the presence of which is detected by adding a substrate. The resulting change in colour was read calorimetrically with help of an ELISA micro plate reader. Positive and negative controls were run in each batch.

Results

HBsAg tested positive in all 677 cases. Majority (76.4%) were males. Mean age of the patients was 35.42±12.4 years. HBeAg was positive in 66 (9.7%) out of 677 tested (Table 1). The maximum study subjects 446 (65.9%) were from Punjab (Table 2). All HBeAg positive cases were negative for Anti HBe.

Table 2: Distribution of study population

Area	No(%)
Punjab	446(65.9)
Khyber Pakhtunkhwa	108(16)
Sindh	62 (9.2)
Azad Jammu & Kashmir	36(5.3)
Baluchistan	10(1.5)
Gilgit Baltistan	15(2.2)

Table 1: HBeAg percentage positivity in different regions of Pakistan

	Patients' number	HBeAg Postive	Percentage positivity
Punjab	446	42	9.4%
Khyber Pakhtoonkhwa	108	16	14.8%
Sindh	62	3	4.89%
Azad Jammu and Kashmir	36	1	3.8%
Balochistan	15	2	13.3%
Gilgit Baltistan	10	2	20%
Total	667	66	9.89%

Discussion

Pakistan generally is a male dominated society where men have a central role in the families, being mostly responsible for earning bread and butter for their home-mates. In this study, there was a male preponderance which might be due to the better access and opportunities for males to the testing and treatment facilities for HBV infected cases. This male predominance was also observed in different studies carried out by Ghani et al, Khokhar et al and Khan et al.¹¹⁻¹³ The age of HBV infected persons in this study ranged between 1 to 80 years, with a mean of 35.42 years (SD±12.3). This was similar to a study conducted in Hong Kong by Yuen et al, in which the mean age of presentation was 38 years with an age range of 1 to 85 years.¹⁴ In both genders, the maximum cases were between 21 and 50 years. Similar result were seen in studies conducted by Khan et al and Castolo et al.^{13,15} This age distribution indicates ongoing acquisition of HBV peri-natally and during childhood and highlights the importance of complete and comprehensive childhood immunization coverage against HBV infection. The overall result indicates that maximum number of patients have this problem during the prime of their lives when they are supposed to be the most useful members of their families as well as the society.

The maximum study subjects (446) were from province of Punjab followed by 108 from KPK 62 from Sindh, 36 from AJK, 15 from GB and 10 from Baluchistan. This region wise distribution of the cases in our study was logical keeping in view geography of the country, the population density in various regions and location of the testing laboratory. This study was carried out in northern Punjab, so the maximum cases were from this province. The next highest number was from the province of KPK, the boundaries of which are

common with the northern Punjab. The Sindh province is situated in the southern part of the country and it was difficult for the study subjects to report due to the distances involved, as was the case in Balochistan, AJK and GB.

A male preponderance was seen in all our regions under study including Punjab, Sindh, KPK, Baluchistan, AJK and GB., A similar male predominance was observed in various studies conducted in different areas of Punjab including Manzoor et al in 1997, Alam et al in 2007, Moosa et al in 2009 and Khan et al in 2011, in which males were more as compared to females.¹⁶⁻¹⁸ This was also observed in patients from KPK as well and mentioned in a study conducted by Farooqi et al in Peshawar in 2007. Out of 62 persons from Sindh, 57 (91.9%) were males and 5 (8.1%) were females.¹⁹ This trend was also noticed in a study conducted by Aziz et al in Sindh in 2010²⁰. The total number of cases from AJK was 36, out of which 26 (72.2%) were males and 10 (27.8%) females. A similar male to female ratio was also seen in a study conducted by Naz et al in Muzaffarabad in 2002.²¹

The mean age of patients from Punjab was 35.46±12.9 years,, 33.06±14.2 years for patients from KPK, 40 + 9.5 years for AJK patients and 31±6.2 years for patients from Sindh, The lowest mean age for Sindhi patients can be understood due to the fact that the disease generally reported from Sind areas is relatively aggressive. The higher mean age of the patient from AJK needs to be further explored because of the limited number of patients from AJK in this study.

The overall HBeAg positivity in our study was 9.7 % which is higher than 7.5% reported in neighboring India, and less than a study conducted in Southern China, where the HBeAg positivity was 18.5%.^{22,23} This difference was probably due to higher prevalence of HBV in Southern China. In another study conducted in Italy, an overall HBeAg positivity of 11% was noted which was close to our percentage.²⁴ In this Italian study the immigrant group had a much higher HBeAg positivity of 18 % as majority of them were from developing countries. In Bangladesh, the prevalence of HBeAg was found to be 19.2% which was higher as compared to our study.²⁵ Moreover, in this study it was established that the HBeAg positivity decreased with increasing age showing that sero-conversion occurs with advancing age.

The percentage of positivity for HBeAg in Punjab (9.4%) was almost same as reported for all cases (n=677). It was however, higher (14.9%) in cases from KPK. The less positivity of HBeAg in Sindh (4.89%)

might be incidental as the number of patients was low, otherwise areas of Sindh and adjoining Southern Punjab are well known for the aggressive nature of the disease. There was a lower percentage (3.8%) in cases from AJK but the total number of the patients was only 26 which is too low a number to give any statistically significant results. The number of patients was also less in Baluchistan as well as for the patients from GB. These studies show that HBeAg positivity is different in different geographical areas. There was no previous study showing HBeAg distribution in different areas of Pakistan. This study can serve as base-line for future studies of the problem from different angles.

Conclusion

1. A male predominance was noted in this study. The maximum numbers of chronic hepatitis B carriers were found between 20 to 50 years.
2. HBeAg positive cases were less as compared to what has been reported earlier.

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