

# FREQUENCY OF HBeAg POSITIVITY IN CHRONIC HEPATITIS B INFECTED PATIENTS

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## ABSTRACT

**Objective:** To determine the frequency of HBeAg positivity in chronic hepatitis B infected patients.

**Methodology:** This descriptive cross-sectional study was carried out for one year between June 01, 2014 till May 30, 2015 in a private consulting clinic at Ibrahimi Hospital, Dabgari Gardens, Peshawar - Pakistan. A total of 149 patients were included in the study. All patients of either gender between 15 to 70 years of age, newly diagnosed with HBV infection in the form of positive HBsAg on third generation ELISA were included in the study. In all the patients, HBeAg was checked. Data were analyzed using SPSS version 20.0.

**Results:** Out of the total 149 patients between 20 to 60 years (mean 41 ±8.7) included in the study, the males 112 (75.2%) outnumbered the females 37 (24.8%). The prevalence of HbeAg in chronic HBV was 28.2 % (males 16.10 %, females 12.08%) with more patients (22.14%) between 21 and 40 years of age.

**Conclusion:** The frequency of HbeAg was found in a significant number of chronic HBV patients. Its frequency was more in males and in the age group of 21 to 40 years.

**Key Words:** Chronic hepatitis B, HBeAg, Seroprevalance

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## INTRODUCTION

Any acute or chronic inflammation of the liver is defined as hepatitis. Hepatitis due to hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most important causes. Worldwide, HBV infection is the most common cause of hepatitis. It is estimated that 2 billion of the total population is suffering from HBV infection and 350 million alarmingly are the chronic carriers while 180 million of the world population have HCV infection, which is more alarming knowing the fact that 3-4 million are added as new cases every year<sup>1</sup>.

Cirrhosis of liver and hepatocellular carcinoma (HCC) are the potential end points of silent chronic HBV infection. The Asia-Pacific is the worst endemically infected region<sup>2</sup>. Magnius and Espmark in 1972 discovered the HbeAg and over years the exact functions still have to be completely understood<sup>3</sup>. It is an established fact the seroconversion from HBeAg to Anti HBeAb is associated with slowing of HBV replication and in most cases improvement in the liver histology<sup>4</sup>. Nevertheless there is a significant population of patients where such like HBeAg negative results do not show any decrease in the viremia and slowing the progression of liver disease<sup>5,6</sup>.

More recently the quantitative titers of the HBsAg and HBeAg have been used to measure the viral loads and predicting the response to antiviral therapy<sup>4</sup>.

It has been observed that the pattern of decline in the HBeAg titers during antiviral therapy has profound effects on the clinical outcome and chances of viral breakthrough<sup>7</sup>. In non-immunized pregnant mothers with HBeAg positive chronic HBV infection, the chances of spread to the fetus remains 70-90%<sup>8</sup> while the risk drops to 40% in HBeAg negative mothers<sup>9</sup>. The chances of such transmission further declines to 5-10 % with appropriate immunoprophylaxis. The review of the evidence highlights the fact that in spite of immunoprophylaxis, 8-32% of the children born to mothers with high HBV titers end up with perinatal infection<sup>10-12</sup>. In a population study conducted in Islamabad including women and children with chronic HBV infection, 10.3% mothers and 25% of children with chronic HBV infection were positive for HBeAg<sup>13</sup>. In another Turkish study, 25.4% of patients were positive for HBeAg<sup>14</sup>.

It is clearly evident that HBeAg is a good predictor in chronic HBV infected patients with regard to the treatment outcome and risk of progression to grave com-

plications. A thorough review of the available literature suggested that no local study in North of Pakistan has been carried out to find the frequency of HBeAg among patients who are suffering from chronic HBV infection. This study is first of its kind in our local population and the results of this study are to be a beginning of a long strategic framework towards fight against rising HBV infection locally and also formulating the local treatment recommendations.

## METHODOLOGY

This descriptive cross-sectional study was carried out for one year between June 01, 2014 till May 30, 2015 in a private consulting clinic at Ibrahim Hospital, Dabgari Gardens, Peshawar, Pakistan. A total of 149 patients were included in the study following non-probability consecutive sampling technique.

All patients of either gender between 15 to 70 years of age, newly diagnosed with HBV infection in the form of positive HBsAg on third generation ELISA with or without high ALT levels were included in the study. Patients who were previously diagnosed as chronic HBV, who had received any type of treatment in the past or those with acute HBV infection were excluded from the study. The purpose and benefits of the study were explained to all the included patients and a written informed consent was obtained. From all the patients, 5ml blood was obtained in a disposable sterile syringe under strict aseptic techniques and was sent immediately to the hospital laboratory for the detection of HBeAg.

Data were analyzed using SPSS version 20.0. For quantitative variables like age, mean and standard deviation were calculated and for qualitative variables like gender and HBeAg, frequencies and percentages were calculated. All results were presented in the form of tables.

## RESULTS

Out of the total 149 patients included in the study, the males 112 (75.2%) outnumbered the females 37 (24.8%). The included patients were between 20 to 60 years of age with a mean age of  $41 \pm 8.7$  years.

The distribution of the sample with respect to age is shown in table 1. The distribution of HBeAg positivity in chronic HBV infected patients is shown in table 2. The gender wise stratification is shown in table 3 while the age wise stratification is shown in table 4.

## DISCUSSION

Chronic HBV infection continues to remain a major part of the world health problems with long-term complications especially in the less developed countries like Pakistan with scarce health care resources. Even the introduction of HBV vaccine has not reduced the occur-

rences of new cases. Pakistan has been placed under the endemic zones by WHO, with 3 % of population suffering from chronic HBV infection<sup>14</sup>.

Chronic HBV infection has been observed across the globe including countries of the Middle East and Asia including Japan<sup>15,16</sup> & Hong Kong<sup>17</sup>. Chronic HBV infection is rarely reported in United States<sup>18,19</sup>. Various studies across Pakistan have not found clearly the exact exposure rate of HBV but limited data predicts 35-38% prevalence<sup>20</sup>. Most acute infections with HBV are self-limiting secondary to spontaneous clearance of virus and resultant immunity. Nevertheless, both the adults (5% to 10%) and the children (85-95%) end up in having chronic HBV infection<sup>14,20</sup>.

Milich et al<sup>21</sup> have reported the down regulation of the host Th2- like immune response in individuals with chronic HBV infection with HbeAg positivity. Vertical transmission reduces from 70-90% (HbeAg reactive chronic HBV) to 40 % in HbeAg negative mothers<sup>8</sup>. HbeAg is known to cross the placenta inducing immune tolerance in fetus with resultant chronic HBV infection<sup>22</sup>. Alarmingly infants born to mothers with high HBV-DNA levels during pregnancy, despite immunoprophylaxis, 8-32% of infants are destined to develop perinatal chronic HBV infection<sup>23-25</sup>.

In our study 75.8% of the patients were between 31 and 50 years of age. The overall prevalence of HbeAg was 28.2% in our study population with 16% males having HbeAg as compared to 12% in females. Multiple community-based studies recruiting patients of different age groups, from different parts of the world, have found HbeAg negativity in 70-90%<sup>26-29</sup>. A survey of 10 years between 1975 to 1985 across Italy found 41 % of patients with negative HbeAg but the proportion increased to 90 % in the following decade<sup>30,31</sup>. A cross sectional study involving a total of 350 Chinese patients (230 men and 120 women) with chronic HBV infection found 69% (243) patients with negative HbeAg, of whom 15% had clinical cirrhosis<sup>32</sup>.

Despite careful attempts to choose a representative population sample, there were more males (75.2%) than females (24.8%) surveyed, due to the predominance of males among the adults tested. This difference is probably due to the fact that males in our society have more approach to health care facilities and better treatments. Although this gender inequity is unfortunate, the literature does consistently suggest a gender difference in the prevalence of HBsAg among adults of this age. Various other epidemiological studies have documented the similar male predominance<sup>33,34</sup>.

In patients with negative HBeAg, the age ranges of studied populations in most studies have varied between 40 and 55 years which have also been observed in our study population with 88.6% (132) of the patients

**Table 1: Age-wise distribution of sample (n=149)**

Age ranges [in years]	No. of Patients	Percentage
20-30	17	11.4%
31-40	51	34.2%
41-50	62	41.6%
51-60	19	12.8 %
Total	149	100%

**Table 2: Distribution of HBeAg among HBsAg positive patients (n=149)**

HBeAg	No. of Patients	Percentage
Yes	42	28.2%
No	107	71.8%
Total	149	100%

**Table 3: Gender-wise stratification with HBeAg among HBsAg patients (n=149)**

HBeAg	Male	Female	Total	P Value
Yes	24 (16.10%)	18(12.08%)	42(28.18%)	0.04
No	88 (59.06%)	19(12.75%)	107(71.81%)	
Total	112(75.16%)	37(24.83%)	149(100%)	

**Table 4: Age wise stratification with HbeAg among chronic HBV positive patients (n=149)**

HbeAg	20-30	31-40	41-50	51-60	Total	P Value
Yes	3 (2.01%)	11(7.38%)	22(14.76%)	6(4.02%)	42(28.18%)	0.217
No	14(9.39%)	40(26.84%)	40(26.84%)	13(8.72%)	107(71.81%)	
Total	17(11.40%)	51(34.22%)	62(41.61%)	19(12.75%)	149(100%)	

between 30 and 59 years of age.

Hadziyannis<sup>30</sup>, Rizzetto<sup>35</sup> and Hamasaki<sup>36</sup> have observed that the younger population with Chronic HBV infection has increased proportion of positive HBeAg as compared to the older individuals. These observations are in contrast to our results with only 2% of the individuals between 20 to 30 years of age having a positive HBeAg.

Another interesting fact is the rarity of finding HBeAg in individuals who have multiple sexual partners, who are homosexuals or having problems of drug addiction<sup>37</sup>. The significance of this observation is not known and beyond the scope of this study project.

### LIMITATIONS

Our study has lacked in the sample size mainly because of absence of any funding. There remains a need

to conduct wider population based studies with recruitment from across the province to know the true prevalence of HBeAg in our population with chronic HBV infection. The findings are expected to help in formulating cost effective local guidelines and treatment protocols.

### CONCLUSION

The frequency of HbeAg was found in a significant number of chronic HBV patients. Its frequency was more in males and in age group of 21 to 40 years.

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### CONTRIBUTORS

MTM conceived the idea, planned the study, and drafted the manuscript. HK helped acquisition of data and did statistical analysis. NUI supervised the study and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.