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Prevalence of HBeAg Positive Cases among Hepatitis B Virus Infected Patients

Submitted to

Ministry of Health

Ramshah Path, Kathmandu, Nepal

2002

Submitted by

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ABSTRACT

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INTRODUCTION:

Hepatitis B is an infection due to Hepatitis B virus. It causes both acute and chronic diseases of liver. Nepal is a country with mixed prevalence of hepatitis B virus infection.

OBJECTIVES:

The study was carried out to detect the presence of HBeAg positivity among all the HBV infected patients.

METHOD:

A cross sectional prospective study was carried out in 100 consecutive HBV positive patients at liver unit of Bir hospital. In then HBeAg was tested by ELISA.

RESULTS:

Among 97 patients, 19 patients were found to be positive for HbeAg, indicating that the percentage of positivity is 19.6 %. The HBsAg and HBeAg were both found to be most prevalent in the age group of 20-29. The most productive age.

ABBREVIATIONS

1. HBV Hepatitis B Virus
2. DNA Deoxyribonuleic Acid
3. HBsAg Hepatitis B Surface Antigen
4. WHO World Health Organization
5. HBeAg Hepatitis B e Antigen
6. HBcAg Hepatitis B c Antigen
7. AST Aspartate Aminotransferase
8. ALT Alanine Aminotransferase
9. OPD Out Patient Department
10. ELISA Enzyme Linked Immunoabsorbant Assay

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1. INTRODUCTION

1.1 Introduction

Hepatitis B virus (HBV) is an important course of acute and chronic diseases of liver. HBV is a DNA virus belonging to Hepadnaviridae family. Though both acute and chronic infection may generally be without any symptoms, it may lead to serious illness in human beings from acute liver failure to hepatocellular carcinoma. Presence of HBsAg in blood indicates on going hepatitis B infections.

1.2 Statement of the Problem

Hepatitis B is one of the most common viral infections affecting mankind. It is a major public health problem occurring endemically in all parts of the world. It is hyper-endemic in many countries of Asia and Africa with the prevalence of current and past infections ranging from 30 to 100 %. Worldwide there are over 350 million courses of surface antigen of Hepatitis B virus (HBsAg)[1,2]. More than 10 % of the population in some areas may suffer from chronic liver disease due to Hepatitis B. In 1996, the WHO estimated that about 2,000 million people had serological markers of HBV infection. Without immunization, it is anticipated that this figure will increase to 4,000 million in the near future. It is estimated that about 65 million from the group of chronic carries will die due to liver diseases.

Nepal is a country with mixed prevalence of Hepatitis B virus infection. Prevalence of Hepatitis B in general population is low (HBsAg 1 %, anti HBsAg 8 %)[2]. But moderate to high incidence of infection are observed in certain ethnic groups e.g. Tibetans (HBsAg 16 %, anti HBsAg 95 %) Manangis (HBsAg 7.3 %, anti HBsAg 5 %), Sherpas (HBsAg 3.8 %) and in some areas e.g. Surkhet (HBsAg 6.6 %, anti HBsAg 30 %).

1.3 Rationale of the Study

The acute Hepatitis B infection causes a variety of manifestations ranging from sub-clinical infection to fulminant hepatitis and death.

The sequelae of acqute infection could be chronic carrier state, chronic hepatitis and carcinoma of liver. The vigor of the immune system determines the severity of acute HBV hepatitis and the probability of the infection entering a chronic phase. An exuberant response can produce fulminant hepatic failure, whereas a lesser response many fail to clear the virus.

After exposure to HBV, there is an incubation period of several weeks to 6 months before the onset of the systems. HBsAg appears in the serum, followed shuttly by HBeAg late in incubation period.

HBeAg positivity shows active replication of virus, which helps to ascertain the infectivity & communicability of the case.

HBeAg positive status of HBV infected cases helps to decide the need for anti viral treatment. HBeAg positive pregnant patients are more prolonged source of perinatal transmission of HBV, which helps to decide about vaccination of neonate at birth and also the need of HBIg prophylaxis.

Presence of HBeAg for more than 3 months may help to decide the chronicity of the disease. Disappearance of HBeAg later on during follow up and appearance of anti HBeAg will help to decide the status of seroconversion and cessation of replication.

2. AIMS & OBJECTIVE

2.1 Primary Aim

The purpose of the research is to detect the prevalence of HBeAg positive cases among HBV infected patients thereby detecting the infectivity and communicability of the cases.

2.2 Secondary Aim

- To decide about the need for the anti-viral treatment in HBeAg positive chronic cases.

- To have an ideas about mass vaccination if there's a higher prevalence of HBeAg in the general population.

3. REVIEW OF LITERATURE

The existence of hepatitis is not new to mankind. It has been documented through descriptions of jaundice dating to several centuries B.C. [3].

The contagious nature of this disease was first recognized in the 8th century A.D. by Pope Zacharias. However it is likely that most of the reports of large population epidemics over the last centuries were due to internal transmission of what is now known as hepatitis A.

A serological marker for hepatitis B was first identified by Blumberg in 1965[4], although its association with parentally transmitted entity known as serum hepatitis, was not recognized until two years later.

Hepatitis B remains a major health problem worldwide. There are over 30 millions carriers of surface antigens of Hepatitis B virus (HBsAg) worldwide.

The prevalence of Hepatitis B is clarified in the basis of carrier rate of surface antigen of hepatitis B (HBsAg) in the population. Countries with the carrier rate between 0.2 % and 2 % are classified as low prevalence countries while these with carrier rate between 2 % and 7 % are designated as countries with intermediate prevalence rate. High prevalence rate countries are those that have a carrier rate frequency in excess of 7 %.

Nepal belongs to the group of countries with low prevalence rates. The average prevalence of hepatitis B in the general population is low (HBsAg 1 % and anti HBsAg 8 %). But moderate to high increase of infection are observed in certain ethnic groups e.g. Tibetans (HBsAg 16 %, anti HBsAg 45 %), Manangis (HBsAg 7.3 %, anti HBsAg 35 %), Sherpas (HBsAg 3.8 %) and in some areas e.g. Surkhet (HBsAg 6.6%, anti HBsAg 30 %).

The Hepatitis B Virus:

Hepatitis B virus (HBv) is a member of the family Hepadnaviridae. HBV is an enveloped spherical DNA virus. The complete virion has an outer envelop of protein, lipid and carbohydrate enclosing a nucleocapsid core. The genome of the HBV is a

partially double stranded circular DNA molecule. The organization of the HBv genome is unique in that all regions of the viral genome encoded protein sequences including the nucleocapsis (Hepatitis B core Antigen (HBcAg), the envelop glycoprotein (Hepatitis B surface antigen (HBsAg), DNA polymerase (a product of the P gene), and a protein from the X gene, which may play a role in replication. HBeAg is a polypeptide virtually identified to HBcAg, which contains a slightly longer pre core region that directs the polypeptide towards secreting into the blood.

Modes Transmission[5]

HBV is highly infectious virus and can be transmitted through extremely minute amount of body fluid. Even as low as 0.00004 ml of blood can transmit the infection (compare this with HIV where the infectivity rise is 0.1 ml).

HBV is present in blood serum, vaginal secretion, saliva, breast milk, bile and amniotic and ascitic fluid. These are several modes of transmission:

1) Parenteral or percutaneous:

Blood plasma, factor VIII and IX transfusion, fibrinogen injection with contaminated needles, dental procedures, operations, tattooing, acupuncture needles,

ear perching, improperly sterilized needles and syringes, sharing needles and syringes, razors, nail clippers, toothbrush etc.

2) Veneral or Premucosal:

Contact of mucosa with body fluids like saliva, semen e.g. during sexual contact.

3) Vertical or Perinatal Transmission:

Transmission from mother to infant can occur either from chronic carrier or when the mother suffers from acute viral hepatitis during the last trimester of pregnancy. The infection occurs during birth or due to close contact in perinatal period. It is known to occur via breast feeding and handling by mother in the postnatal period.

The overall efficacy of vertical transmission is 30-40 % . This increases to 70-90 % if mother is also HBeAg positive, but drops to less than 30 % of she has anti HBe Antibodies.

Anti-HBs appears late, some 3 months after the onset, and then persists. Anti-HBs levels are rarely high and 10-15 % of patients with acute type B hepatitis never develop the antibody. Anti-HBs accounts for recovery and immunity. In the past,

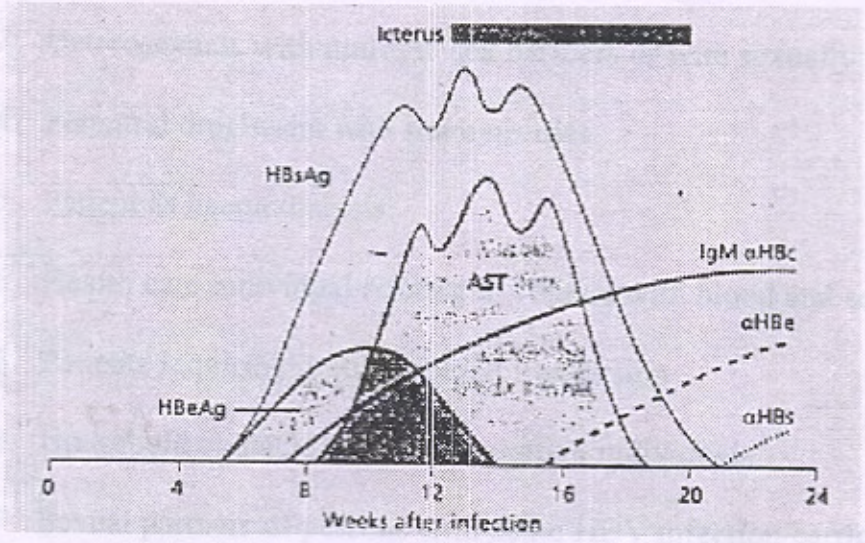
HBsAg and HBsAb were believed to be mutually exclusive. However, as many as one-third of carriers of HBsAg also have HBsAb. The mechanism is uncertain, but it has been attributed to simultaneous infection with different sub-types.

HBeAg correlates with ongoing viral synthesis and with infectivity. It is transiently present during the acute attack. It is present for a shorter time than HBsAg. Persistence for more than 10 weeks strongly suggest the development of chronicity.

Anit-HBc is a marker of relatively low infectivity. The appearance of anti-HBe is strong evidence that the patient will recover completely.

HBcAg cannot be detected in circulating blood, but its antibody (anti-HBc) can. High titres of IgM anti-HBc mark present acute virus hepatitis. This antibody is detected after HBsAg has been cleared from the serum. This is true of 5-6% of cases with acute hepatitis B and is encountered particularly in fulminant hepatitis. It is also useful in determining whether an acute attack of hepatitis is due to virus B or to superinfection with another virus. Persistence of IgM anti-HBc implies ongoing virus B-related chronic disease, usually chronic active hepatitis. Lower titres of IgG anti-HBc with antiHBs mark hepatitis B infection in the remote past. Higher titres of IgG anti-HBc without anti-HBs indicate persistence of viral infection. The significance of high titres of IgG anti-HBc without anti-HBs is uncertatin. It may

indicate the late phase of an acute attack. It may be sue to inability to produce HBsAb. Some have immune complex-associated HBsAg and HBV DNA may be positive. Some still have ongoing HBV infection.



The course of acute type hepatitis. HBsAg = Hepatitis B surface antigen; HBeAg = Hepatitis B e antigen; AST = Aspartate Transminase; IgMα = IgM antibody against hepatitis B core antigen; αHBe = antibody against hepatitis e antigen; αHBs = antibody against hepatitis B surface antigen.

The course of acute type hepatitis: HBsAg = Hepatitis B surface antigen; HBeAg

HBV DNA is the most sensitive index of viral replication.

It is detected by polymerase chain reaction. Using PCR, HBV DNA can be found in serum and liver after the loss of HBsAg, particularly in those receiving antiviral treatment. HBV DNA in serum detected by PCR is a good marker of the liver viraemia, can be correlated with serum transaminase levels and parallels the presence of HBsAg in serum. Patients with an HBV precore mutant are HBeAg negative and HBV DNA positive.

Individuals at high rate Hepatitis B Infection

1. Infants born to HBsAg positive mothers.
2. Homosexuals
3. Heterosexuals with multiple sex partners or with sexually transmitted diseases.
4. Perentral drug users who share needles.
5. Patient as haemodialysis.
6. Health care individual coming in contact with blood and secretions.
7. Patients requiring multiple blood transfusion.
8. Household contacts of HBsAg positive individuals.
9. Sexual partners of persons with acute HBV infection/carriers.
10. In Nepal, certain ethnic groups. (HBsAg 3.8 to 16 %)

Natural Course of Hepatitis B Infection in Children & Adults

Natural infection with hepatitis B virus has different course in children as compare to adults. Earlier the age at which it occurs, milder is the clinical course. One higher is the chance of becoming a chronic carrier.

Newborns infected perinatally rarely develop clinical disease but their chances of bearing carrier are as high as 90 % if mother is HBeAg positive and 22-30 % if she is HBeAg negative.

Adults infected with HBV suffer from acute hepatitis and 10 % of them become chronic carrier. Of the carrier some would develop chronic liver diseases are liver cancer after a decade or two.

If the adults with acute HBV hepatitis has marginally raised liver enzymes then chances of becoming chronic carrier are high as compared to the ones with markedly raises enzymes.

Fulfillment hepatitis with HBV occurs in 1-2 % of cases.

Chronic Features:

The acute Hepatitis B infection causes a variety of manifestations ranging from sub-clinical infection to fulminant hepatitis and death.

Acute Hepatitis has a long incubation period (6 weeks to 6 months). It occurs sporadically and has a gradual or abrupt onset. Symptoms include marked anorexia, vomiting and fever for a few days. HBV infection cannot be differentiated from that due to other virus clinically. Signs of hepatic dysfunction, principally jaundice and hepatomegaly may be seen. Very rarely, the hepatitis is fulminant, with acute liver failure leading to hepatic encephalopathy, hepatorenal syndrome and coagulopathy. Extrahepatic manifestations of acute infections are mainly the result of antigen antibody complex formation and can be seen in 20 % of individuals. The main disorders include

or serum sickness like syndrome Polyarthritis nodosum and popular acrodermatitis of childhood.

Serological Diagnosis[6,7,8]

HBsAg appears in the blood about 6 weeks after infection and has disappeared by 3 months. Persistence for more than 6 months implies a carrier state.

Viral hepatitis B: Significance of serological markers

HBsAg	-	Acute or Chronic hepatitis B carrier.
Anti HBcIgM	-	Acute hepatitis B (High titre).
Anti HBcIgG	-	Chronic hepatitis B (Low titre).
	-	Past exposure to hepatitis B (with negative HBsAg).
	-	Chronic hepatitis B (with positive HBsAg).
Anti-HBs	-	Immune to hepatitis B.
HBeAg	-	Acute hepatitis B. Persistence means continual infection state.
Anti-HBe	-	Convalescent or continual infection state.
HBV-DNA	-	Continual infection state.

Anti-HBs appears late, some 3 months after the onset, and persists. Anti HBs levels are rarely high and 10-15 % of patients.

4. RESEARCH METHODOLOGY

4.1 Research Design: This is a cross sectional prospective study of 100 consecutive patients.

4.2 Research Study: The study was carried out in the Liver unit at Bir Hospital, which is a tertiary hospital of the country.

4.3 **Research Population:** 100 consecutive patients of varying ages and different sexes who had attended the Bir Hospital for OPD, or who were admitted in the ward were enrolled for the study, during the period extending form 1st Baishakh 2059 to 31st Jestha 2059.

4.4 **Research Method:** All the patients whose blood were positive for the HBsAg, and who attended the Bir Hospital, either in the liver OPD or in the ward, were taken as the study population.

The blood was taken out in each of those patients under strict aseptic precaution and HBsAg was reconfirmed by the confirmatory method. Those whose blood was positive for the HBsAg by the confirmatory method, HBeAg was tested. The presence of HBeAg was done by ELISA method at Bir Hospital. All the patients were informed of the research and they were allowed to fill the subject's consent form.

5. RESULTS

Between 1st Baishakh to 31st of Jetha 2059, a total of 100 consecutive patients who were positive for HBsAg, attending the liver unit of Bir Hospital were enrolled in the study. When they were subjected to the confirmatory test only 97 patients were found to be suffering from HBsAg positive. The results of this study is as follows:

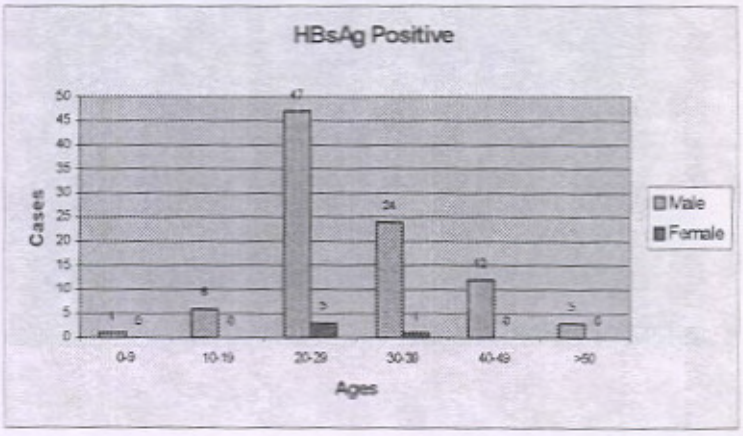
HBsAg by positive cases by confirmation Method:

1. **Age:** The age of the patient in whom the HBsAg was positive by confirmation test varies from 5 to 60 years.
2. **Sex:** These 93 % males and 4 % female with male preponderance over female in the ratio of 23:1.

The age & sex distributions of the patients are shown in bar diagram no. A & B.

(A) HBsAg by Confirmatory Text

Ages	Male	Female
0 - 9	1	-
10 -19	6	-
20 - 29	47	3
30 - 39	24	1
40 - 49	12	-
>50 Yrs	3	-
	93	4 = 97



The maximum numbers of patients belong to age group 20-29 accounting for 52 % of cases.

Result of HBeAg in HBsAg positive Case:

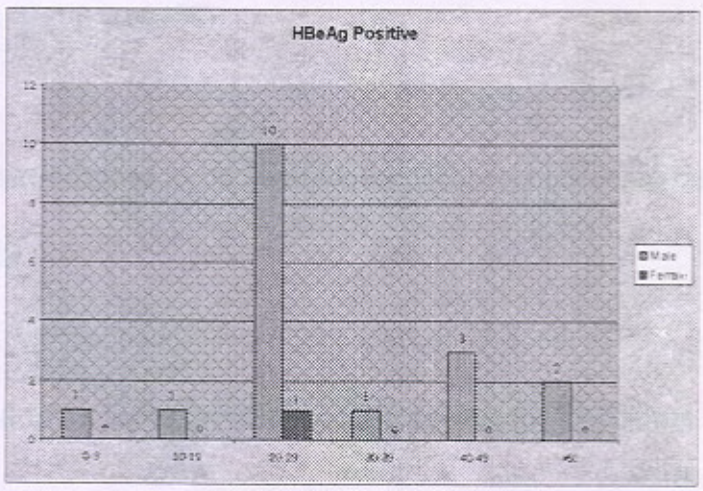
Among 97 patients, HBeAg was found in 19 patients, which accounts for 19.6 %.

3. **Age:** The youngest patient in whom HBeAg was positive was 50 years and oldest one was 60 years.

4. **Sex:** Among 19 positive patients 18 were males and 1 was female.

(B) **HBeAg Positive**

Ages	Male	Female
0 - 9	1	-
10 -19	1	-
20 - 29	10	1
30 - 39	1	-
40 - 49	3	-
>50 Yrs.	2	-
	18	1 = 19



Age group 20-29 holds the maximum number of HBeAg positive code, which accounts for 58 % of total cases.

- Conclude as result
- Should compare with other research
- And add some reasons

6. DISCUSSION

This prospective study was conducted at liver unit, Bir Hospital between 1st of Baishakh to 31st of Jestha 2059.

A total of 100 patients whose sera was positive for HBsAg was taken as the study population, which was reconfirmed by the confirmation test. It was seen that 97 out of 100 patients were positive for HBsAg by the confirmatory method indicating the false positive results of other method was 3/100 (0.03%).

Among the 97 patients, 19 patients were found to be positive for HBeAg indicating that higher rate of infectivity is seen in 19.6 %.

HBsAg and HBeAg were both found to be most prevalent in the age group 20-29, the most productive age group.

So, if they become carries, then there is higher chances that they would transmit the disease to their respective wives and hence to the new born babies.

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