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Retrospective analysis of Hepatitis B serology profiles of a cohort of Hepatitis B Surface antigen positive patients, Sri Lanka

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Abstract

Introduction: Currently more than 350 million people are estimated to be chronically infected with Hepatitis B (HBV). The prevalence of HBV in Sri Lanka is estimated to vary between 0.1-2.5 percent. A detailed descriptive statistical analysis has not yet been performed on the available HBV serology profiles in Sri Lanka.

Objective: To describe the serology profiles of Hepatitis B surface antigen positive (HBsAg+) patients tested at the Medical Research Institute of Sri Lanka during 2007-2017

Methods: A sample of 517 test reports of patients with positive HBsAg was extracted during the period from 2007 to2017 for analysis. The serology profiling had been done using ELISA technique available at the time of testing. The data collected for each patient consisted of available data on the MRI request form which included age and gender.

Results: The mean age of the sample was 36 years (Mdn=36, 95% CI=36-38 years) and 5% of them were <12 years of age. Male to female ratio was 2:1. Out of 517 profiles, 23% (118) had serologically acute hepatitis, 12% (63) chronic hepatitis, 12% (63) early acute hepatitis, 3%(17) acute resolving hepatitis, 2% (10)immune tolerant or immune active chronic hepatitis, 11%(55) chronic HBeAg negative, and 3%(18) chronic inactive carrier stage. Out of the total, 22.4%(116)were positive for HBeAg with high infectivity. HBeAg positivity among the age groups of <10 years, 11-19 years, > 20 years was 72%, 22% and 20% respectively. There was a significant difference in infectivity ($p<0.05$) among the three age groups.

Conclusions: More than1/5 of HBV infected is of high infectivity. HBeAg positivity appears to be higher in the age group <10 years.

Key words: Hepatitis B serology profiles, Hepatitis B surface antigen positive.

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Full article

Introduction

Currently more than 350 million people are estimated to be chronically infected with Hepatitis B (HBV).(1) Annual deaths due to HBV are around 780,000. (2) Exact prevalence of HBV infection in SL is unknown.It is estimated to vary between 0.1-2.5 percent. (3)

HBV infection results in a spectrum of liver diseases ranging from acute hepatitis to chronic liver diseases.(3) With increasing age, the risk of chronicity decreases. The one to five age group has a 30% - 50% risk whilst the adult group has a 6%-10% risk. There for prevention of infections in younger age groups is important.(4)

Staging, assessing severity and infectious status based on HBV profile can significantly improve disease prognosis. HBV profile inferred natural history and infectivity patterns among different age groups will help health care prevention measures against HBV. HBV markers helps in decision on management of HBV infection. Hepatitis B e Antigen (HBeAg) testing is a qualitative marker of HBV replication, showing high infectivity and identifies individuals with a high risk of developing liver cancer.(5) Hepatitis B core Antibody (HB IgM and HB IgG) testing enables categorization into recent or chronic infection.

A detailed descriptive statistical analysis has not yet been performed on the available HBV serology profiles in Sri Lanka.

Method

Retrospective descriptive analysis of 517 test reports of patients with positive HBsAg was extracted from Medical Research Institute (MRI), during the period from 2007 to 2017. MRI is the reference laboratory for HBV testing in Sri Lanka. The data collected for each patient consisted of available data on the MRI request form which included age and gender. Data collection was done using a data extraction sheet. HBV profiles of same patient and incomplete HBV serology profiles were excluded.

The serology profiling was done using ELISA technique which was available at the time of testing. HBsAg positive samples were re-tested for hepatitis B serology profile with ELISA. Serology profile contained; Hepatitis B core total (HBc IgM and HBc IgG), Hepatitis B core IgM (HBc IgM), Hepatitis B e Antigen (HBeAg), Hepatitis B e Antibody (HBeAb).

Data analysis was done using SPSS Statistics 17 and Microsoft Excel. Interpretation of hepatitis B serological markers was done using the United Kingdom National Guideline on the Management of the viral hepatitis A, B and C 2015.

Results

Out of the 517 HBsAg positives, 293 (56%) were males, 148 (29%) were females and 76 (15%) gender was not indicated.

The mean age of the sample was 36 years (Mdn=36, 95% CI=36-38 years) and 5% of them were <12 years of age.

Table 1: Distribution by age

Mean	36 years (95% CI=36-38 yrs.)
Median	36 years
Patients <12 years	5%

Out of 517 profiles, 23% (118) had serologically acute hepatitis, 12% (63) chronic hepatitis, 12% (63) early acute hepatitis, 3% (17) acute resolving hepatitis, 2% (10) immune tolerant or immune active chronic hepatitis, 11% (55) chronic HBeAg negative, and 3% (18) chronic inactive carrier stage.

Table 2: Distribution by disease state

Disease State	No	%
Early acute hepatitis	63	12%
Acute resolving hepatitis	17	3%
Immune tolerant or immune Active chronic hepatitis	10	2%
Chronic HBeAg negative	55	11%
Chronic inactive carrier stage	18	3%

Out of the total, 22.4% (n=116) were positive for HBeAg+ with high infectivity. Majority 78% (n=116) were negative for HBeAg.

There was a significant difference in HBeAg positivity (p=0.000196) between <10 year age group and 11-19 year age group. There was a significant difference in HBeAg positivity (p=0.00001) between <10 year age group and 11-19 year age group.

The prevalence of HBe Ag positivity was similar for the two sexes (p=0.466)

Table 3: HBeAg positivity distribution by age category

Age Category	HBeAg Negative	HBeAg positive	Total
<10 years	28%	72%	4%
11-19 years	78%	22%	10%
>20 years	80%	20%	86%
Total	78%	22%	100%

Table 4: HBeAg positivity distribution by gender

	HBeAg positive	HBeAg negative	Total
Females	25%	75%	26%
Males	24%	76%	74%
Total	22%	78%	100%

Twenty four were HBc total negative, HBc IgM positive, HBeAg negative and HBeAb positive. Therefore 19.8% of acute hepatitis patients had developed antibodies, thus has become less infective.

Discussion

Male:Female ratio was 2:1 and mean age of the sample was 36 years. The age distribution and Male:Female ratio of the sample was comparable to data from the epidemiology unit, SL.(2) Somewhat similar trends were reported in a study done in Gujarat, India.(6) However since this study was a lab record based one, it could not comment on Sri Lankan population level data.

In areas where the disease is rare, HBV transmission is found to be most frequent through intravenous drug use and sexual transmission.(3) The age, gender and mean age(36 yrs, 95% CI=36-38 yrs) of HBsAg positive individuals correlates with such methods of transmission. But proper clinical studies are needed to prove this.

Following HBV infection, development of hepatitis B core IgM antibodies are followed by development of HBc IgG antibodies. Categorization in to acute and chronic infection is possible with the presence of HBc IgM class antibodies, which persists only during the first 6 months of infection.(5) In this study, out of 517 profiles, 23% (n=118) had serologically acute hepatitis (IgM positives) and 12% (n=63) chronic hepatitis (IgM negative but IgG positive). HBsAg positive patients were not followed up for 6 months to categorize to chronic hepatitis B stage, which was a study limitation. Liver enzymes and HBV DNA viral load was not available to differentiate Chronic immune tolerant HBV infection from Immune active chronic hepatitis.

HBeAg positivity was 22%, this highly infectious fraction contributes to maintain the viral transmission. It predicts the future burden of liver cancer.(5) Similar trends have been observed in a study done in Taiwan.(7)

A proportion of HBV infected persons are HBeAg-negative due to mutations in the precore or core promoter regions of the HBV genome which prevents HBeAg formation.(8) Detection of these mutations was not done in this study. Therefore, the actual HBeAg positive proportion could be higher.

HBeAg positivity among <10 year age group was 72%. Significant difference in infectivity ($p<0.05$) was observed compared to other three age groups. Higher HBeAg positivity among younger ages have been observed in studies done in Taiwan and Nigeria.(7,9) HBeAg seroconversion has been shown to be infrequent amongst children. (8) HBeAg seroconversion tends to occur in the second decade of life in 70% to 80% of childhood acquired infections. Also it had been shown that HBeAg negative infection(pre core mutant) occurs infrequently in children.(8) High HBeAg positivity rates amongst less than 10 year age group could be explained by these facts. But future clinical studies are needed to prove such findings.

It was not known whether less than 10 year group category had acquired the HBV infection perinataly since in-depth analysis of this age group was not done.

Infant HBV vaccination was introduced to the EPI in Sri Lanka in 2003.(3) A study in 2014, in Kaluthara district showed 76% protective levels of HBsAb status amongst children (1-5 years), despite 100% HBV vaccination status.(2)

Infectivity patterns also need to be monitored through HBeAg testing. During childhood, horizontal transmission through infected saliva and blood is the most common method of transmission. (3) Therefore, strengthening the vaccination and infection control measures for all contacts of hepatitis B infected children needs to be considered.

Conclusions

This study shows the importance of strengthening the hepatitis B surveillance, vaccination and infection control measures for all contacts of hepatitis B infected.

More than 1/5 of HBV infected is of high infectivity. HBeAg positivity appears to be higher in the age group <10 years.

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