

RESEARCH ARTICLE

CLINICOHEMATOLOGICAL PROFILES OF HEPATITIS B VIRUS (HBV): OBSERVATIONS FROM A TERTIARY CARE CENTRE

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ABSTRACT: Aim: In humans, Hepatitis B virus (HBV) is arguably the most common organ specific virus affecting the liver. The pathological sequelae and stages especially in the liver are well studied. However, reports on the effect of HBV on the extrahepatic organs are lacking. The present study was carried out to ascertain clinical presentations and the alterations on the hematological and hepatic parameters. **Material and Methods:** This was a retrospective study and was conducted in a tertiary care hospital in India. Data was collected and analyzed in people who were confirmed to be affected only by HBV by the standard diagnostic method using the HB surface Antigen (HBsAg) for the period January 2016 to December 2016. **Results:** The results indicated that during the study period, a total of 233 people were included in the study and compared with healthy individuals who were coming for regular health check up and were tested negative for any infectious and chronic diseases. Of these 46 were symptomatic, while 187 were asymptomatic and were diagnosed incidentally during routine/mandatory investigation before surgery. In the 46 symptomatic patient's fever (73.91%), jaundice (63.04%), loss of appetite (39.12%), nausea & vomiting (52.17%), fatigue (28.26%), abdominal pain (17.39%) and Ascites (8.69%) were seen. There was a significant difference in the various hematological, hepatic and electrolyte endpoints ($p < 0.05$ to 0.0001). **Conclusion:** The study indicates that acute infection with HBV causes changes in the alterations in hematological, hepatic and electrolytes in the serum.

KEY WORDS: Hepatitis B Virus (HBV); clinical, hematological, electrolytes.

INTRODUCTION:

Hepatitis B virus (HBV) is a DNA virus belonging to the family Hepadnaviridae, is the most prevalent infectious cause for acute and chronic liver disease, worldwide¹. It is an important proven factor in the development of hepatocellular carcinoma (HCC)². Worldwide, 500 million people

are estimated to be chronically infected with HBV and accounts for 500,000-1,000,000 deaths, annually. It has emerged as an important indication of liver transplantation in the modern world, which varies from 5% in western countries to up to 90% in China³. Highest prevalence is seen

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in South East Asia, China and Africa⁴. In the developing world, perinatal and early life exposures continue to be major sources of infection due to lack of policy of universal vaccination for newborns. Sexual contact and injection drug use account for most new cases of HBV in adults in low prevalence areas⁵. Maintenance hemodialysis is a high-risk environment for transmission of HBV and other blood-borne viruses⁶.

It has a circular closed and partially double stranded DNA with unique life cycle, due to its transcription into pregenomic RNA and then back to DNA- resulting in drug resistant mutations^{7,8}. The immune response to HBV involves both innate and adaptive immunity. The 4 viral genes components include the core, surface, X, and polymerase genes which encodes for core nucleocapsid protein, surface proteins, X protein and DNA polymerase respectively. The X protein may have an important role in hepatic carcinogenesis due to its transactivating properties⁵. Based on genomes it is subdivided into 10 subtypes from A to J⁹ and genotype C is associated with increased risk of HCC¹⁰.

The immunologic phases are dynamic and the 4 phases are immune tolerance, immune clearance, the inactive carrier state, and reactivation. The immune tolerant phase is prolonged in patents who acquire infection early in life⁵. The spectrum of clinical manifestations of hepatitis B infection varies in both acute and chronic disease. During the acute phase, manifestations range from subclinical or anicteric hepatitis to icteric hepatitis and, in some cases, fulminant hepatitis; during the chronic phase, manifestations range from an asymptomatic carrier state to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. Extrahepatic manifestations can also occur with both phases. Approximately, 70% of patients with acute HBV infection, have subclinical or anicteric hepatitis¹¹. Around 95% of population who were exposed perinatally will convert into chronic HBV carrier state due to immunologic tolerance to the virus. In contrast, children exposed during the first

5 years of Life and adulthood has 30% and 2-5% chance, respectively. Many of these are unaware that they carry the infection, and only a small percentage receives routine follow-up to monitor disease status. Chronic infection will have a dynamic course with phases of active inflammation and inactive state. Disease progression is influenced by various factors, including viral genotype and specific mutations, demographic features and social and environmental factors¹². The reactivation of hepatitis B is more being noted in patients of inflammatory Bowel Disease who are on Immunosuppressive therapy¹³.

Frequency of developing hepatic decompensation in HBV-associated cirrhosis is 5% to 8%, and HCC is 2% to 4% per year¹⁴. The disease may have more severe, protracted and complicated course when coinfecting with other hepatitis virus or with pre-existing liver disease¹¹. Chronicity will push them to lifelong risk of developing cirrhosis or hepatocellular carcinoma (HCC) or both¹². The antigen-antibodies which help in detection, progression and assessment of infectivity are HBsAg, HBeAg, Anti-HBsAg, Anti- HBeIgM, Anti- HBeIgG and Anti-HBeAg. Clinically the HBsAg (Australian antigen), the hallmark antigen is usually detectable between 1-10 weeks after exposure and its persistence beyond 6 months signifies chronicity, which occurs in approximately 1% of exposed population¹⁵. Quantification of HBV DNA by PCR helps in deciding the candidates for Treatment¹⁶. The present study was undertaken to analyze the clinical, hematological, biochemical parameters in patients diagnosed with HBV in a tertiary care center at Mangalore, Karnataka, India

MATERIALS AND METHODS:

This was a retrospective study and was conducted by Department of Microbiology of the tertiary care center for three months during January 2016 to December 2016. The study was

undertaken after approval by the Institutional Ethics Committee. All patients who were admitted and diagnosed as HBV infection by chemiluminescent immunoassay vitro ECI - HBs Ag assay (Ortho Clinical Diagnostics), in one year i.e. January to December 2016, were included in the study. All the clinical manifestations, haematological, biochemical parameters were considered were noted in detail for the study. For HBV negative data used as concomitant controls, people who had come for general health checkups were considered. The data from individual patients were noted and entered in to the Microsoft excel. All the data was recorded as mean $\pm$ standard deviation (SD) and are represented in each of the tables. The demographic and other details were categorized in to frequency. To assess the HBV-induced changes all the lab parameters were compared with HBV negative subjects using the students "t" test. A p value of 0.05 was considered significant.

RESULTS:

Table 1. Symptoms in the HBV infected people with symptomatic (46) features.

Symptoms	Frequency (N=46)	Percent age
Jaundice	29	63.04
Loss of appetite	18	39.13
Nausea and vomiting	24	52.17
Fever	34	73.91
Fatigue	13	28.26
Abdominal pain	8	17.39
Ascites	4	8.69

Table 2: Comparison of hematological and biochemical parameters in HBV infected and healthy individuals.

Haematological Parameters	Control	HEPATITIS B	p Value
Hb	12.49 $\pm$ 1.05	12.71 $\pm$ 2.49	0.227
TC	8201.61 $\pm$ 1729.13	9273.68 $\pm$ 3831.82	0.0002
N	58.31 $\pm$ 8.29	65.09 $\pm$ 14.25	<0.0001
L	35.89 $\pm$ 9.15	23.25 $\pm$ 11.07	<0.0001
E	3.66 $\pm$ 2.14	3.67 $\pm$ 3.84	0.813
M	2.53 $\pm$ 1.73	7.67 $\pm$ 2.82	<0.0001
ESR	5.38 $\pm$ 1.88	22.81 $\pm$ 25.18	<0.0001
PCV	39.63 $\pm$ 4.09	37.78 $\pm$ 6.82	0.007
Liver function test	Control	Hepatitis B	p Value
AST	23.18 $\pm$ 8.48	115.03 $\pm$ 282.81	<0.0001
ALT	21.58 $\pm$ 12.39	170.00 $\pm$ 532.69	0.0002
ALP	73.09 $\pm$ 19.02	108.23 $\pm$ 66.67	<0.0001
T. Bil	0.63 $\pm$ 0.407	1.76 $\pm$ 3.42	<0.0001
T. Protein	7.30 $\pm$ 0.41	6.99 $\pm$ 0.84	<0.0001
Albumin	4.29 $\pm$ 0.42	3.76 $\pm$ 0.77	<0.0001
Globulin	2.98 $\pm$ 0.33	3.23 $\pm$ 0.77	0.0001
A/G Ratio	1.46 $\pm$ 0.25	1.24 $\pm$ 0.41	<0.0001
Electrolytes	Control	Hepatitis B	p Value
Na	136.81 $\pm$ 17.51	135.14 $\pm$ 8.87	<0.0001
K	4.28 $\pm$ 0.38	4.13 $\pm$ 0.73	0.014
Cl	99.93 $\pm$ 12.74	96.41 $\pm$ 6.22	<0.0001
Renal function test	Control	Hepatitis B	p Value
Urea	20.96 $\pm$ 8.03	30.09 $\pm$ 32.65	0.0001
Creatinine	0.24 $\pm$ 0.19	1.18 $\pm$ 1.36	<0.0001

During the study period, a total of 233 people were diagnosed with positive for HBsAg. Among them, 161 (69.09%) were males and 72 (30.91%) were females. The afflicted people belonged to the age group of 18 to 72 years. Among these 46 people were symptomatic. Other 187 patients were asymptomatic and were incidentally diagnosed when they were routinely investigated for HBsAg. Among these patients, majority of the symptoms of fever (73.91%), jaundice (63.04%), loss of appetite (39.12%), nausea & vomiting (52.17%), fatigue (28.26%), abdominal pain (17.39%) and Ascites (8.69%) were seen (Table 1).

The mean hematological parameters in the HBV patients were deranged with respect to Total Leukocyte count, differential counts (Neutrophils, Lymphocyte, Monocyte) and Erythrocyte Sedimentation Rate (ESR). The statistical analysis showed significant difference among these parameters when compared to healthy individuals (Table 2). The mean serum total bilirubin level is elevated and Serum Albumin is reduced. The liver enzymes, Aspartate amino-transferase (AST) and Alkaline phosphatase (ALP) were elevated (Table 2). The liver biochemical parameters like Total Bilirubin, Total protein, S.albumin, S Globulin and A/G ratio had increased. The serum of Sodium and Chloride were reduced significantly compared to healthy individuals (Table 2)

DISCUSSION:

With the high prevalence of HBV infection in South Asian countries and high chronic carriers in India¹⁷, it is important to study the epidemiology of HBV in our local population. The present study demonstrates the incidence of HBV infection among the patients admitted at a tertiary care centre in South India. A total of 260 patients with HBsAg were diagnosed in our hospital during the study period. Incidence of HBV varies from 16-43% in acute viral hepatitis patients in Indian population^{18,19}.

In our study population, HBV infection was presented mainly with fever (73.91%), in contrast to fever with right hypochondriac region pain and Anorexia with Vomiting was the commonest symptoms in patients with HBV in North Indian¹⁹ and Western Indian patients¹⁸, respectively. In western Indian population, HBV infected patients have not shown any derangement of the hematological parameters like haemoglobin and total leukocyte count¹⁸, whereas we have seen statistically significant change in TLC (Table 2)

The liver parenchymal cells are the primary target for HBV there is very high derangement in the liver function tests i.e., decrease in serum albumin, total protein, and increase in total bilirubin and hepatic enzymes²⁰. The liver enzymes like ALT, AST, ALP were raised in more than 70% of the HBV patients and increased in total bilirubin in 80% of the case has been reported in Indian population¹⁸ as we have observed in our cohort of study population.

CONCLUSION:

HBV targets the hepatic parenchyma and leads to all the signs and symptoms of hepatic dysfunction. The hematological and biochemical parameters in our patients are deranged as given in literature. Even though, the four phases of the HBV infection is known; many of the infected individuals will have minor symptoms or are asymptomatic. So it is very important to diagnose the seropositive HBV infected cases, so as to prevent transmission from these individuals. Future studies are also planned at to observe the clinic hematological profiles of cancer patients with HBV positive results and as to how they would respond to the proposed chemo and radiotherapy. The efforts are underway in this direction.

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