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A STUDY OF THE EPIDEMIOLOGY OF HEPATITIS B VIRUS INFECTIONS IN PATIENTS OF CHRONIC LIVER DISEASE IN A TERTIARY CARE HOSPITAL: AN OBSERVATIONAL STUDY

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ABSTRACT **Background:** Hepatitis B virus is an enveloped, partially double-stranded DNA virus belonging to family Hepadnaviridae, genus Orthohepadnavirus. Chronic infection results in slowly progressive liver disease that can lead to cirrhosis, chronic liver failure, and hepatocellular carcinoma (HCC). Chronic Hepatitis B infection is defined by the continued presence of HBsAg in the blood for longer than six months. Chronic liver disease (CLD) is a progressive deterioration of liver functions, leading to fibrosis and cirrhosis, over more than six months. **Aims:** To assess the prevalence and incidence, mortality, complications of Hepatitis B infection in Chronic Liver Disease. **Materials And Methods:** This is a prospective observational study of 535 patients of clinically suspected Chronic liver Disease conducted from January 2021 to June 2022. Patient's detailed case history was taken, and blood or serum samples were tested for HBsAg by ELISAN using Merilisa HBsAg kits. **Results:** Of 535 samples 79.4% were Male while the 20.6 % female. Maximum number of patients were in the age group 41 to 60. Increased alcohol consumption was the most common risk factor. 25.04% tested reactive to HBsAg where 86.56% were male and 13.43% female. 29.85% cases progressed to Cirrhosis while 0.75% had Hepatocellular Carcinoma. The in-hospital mortality was 9.52 %. The mortality rate among HBsAg seropositive cases was 30.59%. The incidence and prevalence of HBsAg reactivity among the patients of Chronic Liver Disease seen in the patients of this study in the study duration was 21.12 % and 25.46% respectively.

KEYWORDS : Hepatitis B, Chronic Liver Disease, ELISA, Incidence, Prevalence, Mortality

INTRODUCTION

Hepatitis B virus is an enveloped, partially double-stranded DNA virus belonging to family Hepadnaviridae, genus Orthohepadnavirus. The complete virus particle called the Dane particle, is spherical, 42nm in size, consists of an outer envelope containing Hepatitis B surface antigen (HBsAg) in a lipid membrane surrounding an inner core consisting of pre-core antigen (HBeAg) and core antigen (HBcAg) and partially double stranded DNA. Viral genome consists of four overlapping genes; S which encodes for HBsAg, Core or C gene which codes for hepatitis B e antigen (HBeAg) and hepatitis B core antigen HBcAg , X gene coding for HBxAg and the P gene coding for polymerase (P) protein. Australia antigen or HBsAg was first discovered by Blumberg in 1963. [1,2,3,4,5,6,7]

Hepatitis B virus infection is a major public health problem worldwide, with serologic evidence of current or past infection present in approximately 30% of the world's population. WHO estimates that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections per year. Hepatitis B is most commonly transmitted by parenteral route (blood and blood products and needle prick injuries) where even 0.00001ml of blood can be infectious. Also transmitted by sexual and parenteral routes. Alcoholics, drug addicts, sex workers and healthcare workers are the high-risk groups. Phases of Chronic Hepatitis B Infection include Immune tolerant phase, HBeAg positive immune active phase, Inactive phase, HBeAg negative immune reactivation phase. Hepatitis B virus has a long incubation period (45 to 120 days). Chronic infection results in slowly progressive liver disease that can lead to cirrhosis, chronic liver failure, and hepatocellular carcinoma (HCC). Chronic viral hepatitis ranks as the fifth leading cause of death globally. [8,6,9,10,11]
Hepatitis B Virus Serological and Virological Markers include: HBsAg, HBeAg , Anti-HBc (IgM) , Anti-HBc (IgG) , Anti-HBs , Anti-HBe, Anti-HBc (IgG) and anti-HBs , Anti-HBc (IgG) and HBsAg, Anti-HBc (IgG) and/or anti-HBs and HBV DNA (PCR)[12]

The enzyme-linked immunosorbent assay (ELISA) is the most commonly used serological method for the detection of Hepatits B antigens and antibodies. Chronic Hepatitis B infection is defined by the continued presence of HBsAg in the blood for longer than six months. HBsAg can be detected by rapid diagnostic tests or by laboratory-based immunoassays. [13,14,15]

HBV DNA testing is used for the assessment of level of viral replication. HBV DNA can be detected in the blood in more than 90% of infected hosts who are positive for hepatitis B surface antigen (HBsAg) and hepatitis B e antigen (HBeAg). The use of detection and quantification of HBV DNA has become the preferred method for measuring the quantity of infectious particles and provides important diagnostic and prognostic information, mainly as a marker of virus replication. [12,16]

Chronic liver disease (CLD) is a progressive deterioration of liver functions, due to a continuous process of inflammation, destruction, and regeneration of the liver parenchyma, leading to fibrosis and cirrhosis, over more than six months, including synthesis of clotting factors and other proteins, detoxification of harmful products of metabolism, and excretion of bile. The most common aetiologies are: Alcoholic liver disease, Non-alcoholic Fatty Liver Disease, Chronic Viral Hepatitis most commonly caused by Hepatitis B, C, and D viruses, Autoimmune Causes. [17]

AIMS & OBJECTIVES

To assess the prevalence and incidence, mortality, complications of Hepatitis B infection in Chronic Liver Disease.

MATERIALS AND METHODS

This is a prospective observational study of 535 patients of clinically suspected Chronic liver Disease above 18 years of age in a Tertiary Care Centre, Mumbai conducted from January 2021 to June 2022.

METHODOLOGY

After taking informed consent, patient's detailed case history was taken according to a questionnaire. Blood or serum samples were tested for presence of Hepatitis B surface antigen using Merilisa HBsAg kits by Meril Diagnostics which is a direct sandwich solid-phase enzyme linked immunoassay. Samples and controls were added to the microwells coated with monoclonal anti-HBsAg antibodies followed by the addition of the enzyme conjugate (polyclonal anti-HBsAg antibodies labelled with Horseradish peroxide). After incubation and washing, an antibody– antigen sandwich complex is formed in the well wherein HBsAg is "trapped" or "sandwiched". The bound enzyme is developed by the addition of substrate containing 5, 5'-Tetramethylbenzidine and hydrogen peroxide developing a blue colour develops in the wells with bound conjugate. Reaction is stopped using sulfuric acid stop solution to develop a yellow colour which is finally read at 450nm spectrophotometrically. The intensity of the colour produced in the wells is directly proportional to the concentration of HBsAg in sample. Wells containing negative sample remain colourless.

OBSERVATIONS AND RESULTS

A total of 535 cases of Chronic Liver disease was considered for this study and were tested for positivity to HBsAg surface antigen using ELISA. 425 (79.4%) were Male while the 110 (20.6 %) were females. The male to female ratio was 3.86: 1. Maximum number of patients were in the age group 41 to 60 [280 (52.34%)], followed 61-80 years [162(30.28 %)], 21-40 years [93 (17.38 %)]. The mean age of the total study population was 53.25 years with standard deviation of 12.66, that of males was 52.53 with a standard deviation of 12.34 and of females was 56.03 with a standard deviation of 13.53. 396 gave a history of risk factors where increased alcohol consumption was the most common risk factor [186 (34.76%)], followed by a history of blood transfusion (79,14.77%), history of injectable drug use (63), history of having a tattoo inscribed (20, 3.73%), history of having multiple sexual partners (16, 2.99%.)134 (25.04%) tested reactive to HBsAg where 116 (86.56%) were male and 18 (13.43%) were female. Male to female ratio was 6.4:1. 40 cases had progressed to Cirrhosis that is 29.85% while 1 (0.75%) had Hepatocellular Carcinoma.

Distribution of HBsAg Reactivity Based On Risk Factors

HBsAg Reactive Risk factors	TOTAL	MALE	FEMALE	MALE TO FEMALE RATIO
ALCOHOL	53	43	10	4.3:1
BLOOD TRANSFUSION	7	6	1	6:1
TATTOOS	4	4	0	All male
MULTIPLE SEXUAL PARTNERS	8	8	0	All male
INJECTABLE DRUG USE	16	16	0	All male

Distribution of HBsAg Reactivity Based On SGOT Levels

SGOT LEVELS	HBsAg Reactive
25-250	4
251-500	23
501-750	60
751-1000	35
>1000	1

The in-hospital mortality in this study was 51(9.52 %) where 36 (70.58%) were male and 15 (29.41%) were female. The mortality rate among HBsAg seropositive cases was 30.59%. 18 (14.6%) had been known positives from before this study was conducted while 105 (85.4%) were newly diagnosed cases. The incidence and prevalence of HBsAg reactivity among the patients of Chronic Liver Disease seen in the patients of this study in the study duration was 21.12 % and 25.46% respectively.

DISCUSSION

In this study, 425 (79.4%) were Male while 110 (20.6 %) were female and the male to female ratio was 3.86: 1. Grewal et al [18] reported 80% male and 20% female with a male to female ratio of 4:1 while Singh et al [19] and Xess et al [20] reported a Male to female ratio of 2.3:1 and 3.7:1 respectively. Bukhtiari et al. reported 46.4% females and 53.6% males.[8] A maximum number of patients were in the age group of 41- 60 years [280 (52.34%)] with a mean age of 53.25 years with a standard deviation of 12.66. The mean age among males and females were 52.53 with a standard deviation of 12.34 ± 0.59 and 56.03 with a standard deviation of 13.53 ± 1.29 respectively. The average age of the patients in studies by Grewal et al, Singh et al, and Bukhtiari et al was 47.44 ± 14.56 years , 46.5 years and 51.6 years respectively. In our study, 396 had history risk factors where majority of the patients had a history of alcohol addiction (186 - 34.76%) followed by history of blood transfusion (79 - 14.77%). Grewal et al reported that a majority of the patients either had a history of alcohol/drug addiction (42.2%) or blood transfusion (35.2%) and 15.5% of patients exclusively had a history of injecting drug use (IDU). The major risk factors reported by Devi et al [21] was blood transfusion (35.3%), history of multiple sexual contacts (29.4%) and Injectable drug use (14.7%), by Singh et al. wasblood transfusion (30%) and alcohol addiction (15%) as the major risk factors.In this study, 134 (25.04%) tested reactive to HBsAg where 86.56% were male and 13.43% were female with a Male to female ratio of 6.4:1. HBsAg reactivity reported by Grewal et al., Devi et al., Mathur et al. [22], Kumar et al. [23]. Singh et al, Bukhtiari et al. and Sagnelli et al.[24] was 26%, 17.3%, 5.89%, 17.34%, 4%, 24.7% and 13.4% respectively. Grewal et al. and Kumar et al. showed a higher prevalence of HBsAg in males than females with male: female ratio being 7.6:1 and 2.5:1 respectively. In our study, men with history of multiple sexual partners had the highest rate of HBsAg reactivity (31.25%) followed increased alcohol consumption [53 (28.49%)]. Grewal et al reported the major risk factor to be alcohol (26.9%) followed by unsafe blood transfusion (15.4%). Tiwari et al. and Curciarello et al. [25] reported prevalence of HBsAg seropositivity in alcohol addicts to be 23.6% and 13.9% respectively. Grewal et al, Nandi et al. [26] and Curciarello et al. reported 16%, 10.58% and 3.75% prevalence of HBsAg positivity in patients with blood transfusion.Among those that were reactive to HBsAg, SGOT levels are most commonly in the range of 501 to 750IU/L (48.8%). 18 had been known positives while 105 were newly diagnosed cases. The incidence was 21.12 % while the prevalence was 25.46%. 40 cases had progressed to Cirrhosis while 1 developed Hepatocellular Carcinoma.

SUMMARY AND CONCLUSION

To assess the prevalence and incidence, mortality, complications of Hepatitis B infection in Chronic Liver Disease. 535 cases of chronic liver disease were studied and tested using ELISA and analysed. 134 (25.04%) tested reactive to HBsAg. Male to female ratio was 6.4:1. 40 cases had progressed to Cirrhosis that is 29.85% while 1 (0.75%) had Hepatocellular Carcinoma. The incidence of Hepatitis B virus infection was 21.12 % while the prevalence of Hepatitis B in the study population in the study period was 25.46%.

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