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Medicine

SPECTRUM OF HEPATITIS B INFECTION IN A TERTIARY CARE CENTRE OF EASTERN INDIA

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ABSTRACT

BACKGROUND AND AIM: Hepatitis B virus (HBV) infection is a global health problem. HBV- related liver disease is not uncommon in India. There are very few report on spectrum of hepatitis B infection from eastern India. In this study we shall try to elaborate the spectrum of hepatitis B infection of those patients among patients attending the Virology OPD in a tertiary referral center.

MATERIALS AND METHODS: Hepatitis B surface antigen (HBsAg) positive patients registered in the Tropical Medicine Virology OPD or who were admitted under Tropical Medicine department between July 2017 and December 2018 were included in the study. All patients had baseline liver function tests, serological markers for HBV infection (hepatitis B e antigen [HBeAg], anti-HBe, anti-HBc IgM and total, and HBV DNA quantification), and ultrasound. Serum alpha-fetoprotein was done only in elderly (>50 years) patients. Based on the viral profile and transaminase levels and ultrasound findings, patients were categorized as HBeAg pos chr infection or immune tolerant, HBeAg pos chr hepatitis or immune reactive, HBeAg neg chr infection or inactive carrier, HBeAg neg chr hepatitis and chronic liver disease with compensated cirrhosis or Decompensated cirrhosis.

RESULTS: Majority of patients were asymptomatic and incidentally detected to be positive during any health checkup, pre-anesthetic checkup, pregnancy or blood donation camps. Among the study population 29% of patients were in immune inactive carrier phase and 49% had features of chronic hepatitis without features of cirrhosis. Alanine aminotransferase (ALT) levels were similar in both HBeAg-positive and negative patients. HBV DNA quantity was significantly high in patients who were HBeAg positive.

CONCLUSION: A significant proportion of HBsAg-positive patients is in HBeAg negative chronic infection or inactive carrier phase and do not require treatment. Patients with elevated ALT and HBV DNA levels need further evaluation to categorize them into immune clearance or immune reactive phase.

KEYWORDS : Chronic hepatitis B, spectrum of the disease, need of treatment.

INTRODUCTION

Hepatitis B is a global health problem that affects over four hundred million people worldwide and causes over a million deaths every year. Following an acute HBV infection, the rate of progression from acute to chronic hepatitis B is approximately 90% for a perinatally acquired infection, 20–50% for infections acquired between the age of 1 and 5 years, and <5% for an adult-acquired infection [1]. The prevalence is decreasing in several highly endemic countries due to improvements in the socioeconomic status, universal vaccination programs and perhaps effective antiviral treatments [2]. Still this infection remains a serious threat to public health in India [3]. The natural history of chronic HBV infection has been schematically divided into five phases, taking into account the presence of HBeAg, HBV DNA levels, alanine aminotransferase (ALT) values and eventually the presence or absence of liver inflammation [4]. Chronic HBV infection is a dynamic process reflecting the interaction between HBV replication and the host immune response and not all patients with chronic HBV infection have chronic hepatitis (CHB). Other factors that may play a role in the progression of HBV-related liver disease include gender, alcohol consumption, and concomitant infection with other hepatitis virus (es). The phases of chronic HBV infection are not necessarily sequential [4].

Phase 1: HBeAg-positive chronic HBV infection, previously termed "immune tolerant" phase; characterised by the presence of serum HBeAg, very high levels of HBV DNA and ALT persistently within the normal range according to traditional cut-off values [upper limit of normal (ULN) approximately 40 IU/L]. In the liver, there is minimal or no liver necroinflammation or fibrosis but a high level of HBV DNA integration and clonal hepatocyte expansion suggesting that hepatocarcinogenesis could be already underway in this early phase of the infection. This phase is more frequent and prolonged in subjects infected perinatally. The rate of spontaneous HBeAg loss is very low in this phase. These patients are highly contagious due to the high levels of HBV DNA.

Phase 2: HBeAg-positive chronic hepatitis B is characterised by the presence of serum HBeAg, high levels of HBV DNA and elevated ALT. In the liver, there is moderate or severe liver necroinflammation and accelerated progression of fibrosis1. Most patients can achieve HBeAg seroconversion and HBV DNA suppression and enter the HBeAg-negative infection phase. Other patients may fail to control HBV and progress to the HBeAg-negative CHB phase for many years.

Phase 3: HBeAg-negative chronic HBV infection, previously termed 'inactive carrier' phase, is characterised by the presence of serum antibodies to HBeAg (anti-HBe), undetectable or low (\2,000 IU/ml) HBV DNA levels and normal ALT according to traditional cut-off values (ULN _40 IU/L). These patients have low risk of progression to cirrhosis or HCC if they remain in this phase, but progression to CHB, usually in HBeAg-negative patients, may occur.

Phase 4: HBeAg-negative chronic hepatitis B is characterised by the lack of serum HBeAg usually with detectable anti-HBe, and persistent or fluctuating moderate to high levels of serum HBV DNA (often lower than in HBeAg-positive patients), as well as fluctuating or persistently elevated ALT values. The liver histology shows necroinflammation and fibrosis. This phase is associated with low rates of spontaneous disease remission.

Phase 5: HBsAg-negative phase is characterised by serum negative HBsAg and positive antibodies to HBcAg (anti-HBc), with or without detectable antibodies to HBsAg (anti-HBs). This phase is also known as "occult HBV infection".

Liver biopsy has long been the gold standard to stage fibrosis in the liver and it is crucial to identify patients who need antiviral treatment . In particular, liver biopsy has been used to evaluate patients with viral hepatitis (particularly those with hepatitis B virus [HBV] or hepatitis C virus [HCV] infection), to stage disease, and to determine whether treatment should be pursued. Fibroscan (transient elastography-TE) is noninvasive test, and it offers several advantages compared to liver biopsy [5] . TE is of great value in the detection of patients with CHB-related cirrhosis. The optimal cut-off values of TE were 7.25 kPa for diagnosing significant fibrosis and 12.4 kPa for diagnosing cirrhosis, respectively [6] . The current evidence suggests that FibroScan is of good accuracy in the diagnosis of early hepatic fibrosis [7]. Apart from TE, another alternative to percutaneous liver biopsy (PLB), Aminotransferase Platelet Ratio index (APRI) score was recently validated by the WHO [8].

The 5-year cumulative incidence of cirrhosis ranges from 8% to 20% in untreated CHB patients and, among those with cirrhosis, the 5-year cumulative risk of hepatic decompensation is 20% [9]. The annual risk of HCC in patients with cirrhosis has been reported to be 2–5% [10].

MATERIALS AND METHODS

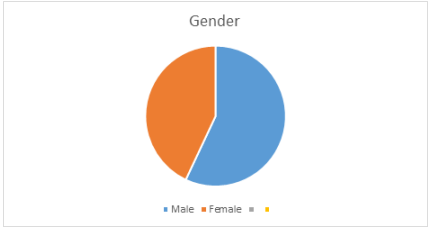
It was a single centre, retrospective study. In the School of Tropical Medicine, Kolkata, we have virology OPD, for which we get referrals from other centers for the management of liver disease due to hepatitis B. As pregnant women are routinely screened for HBsAg, many pregnant patient were also referred. The study was done for one and half year period and we collected data of 100 patients from previous record from July 2017 to December 2018.

Further evaluation for those found to be HBsAg positive included baseline liver function tests, hepatitis B e antigen (HBeAg), anti-HBe, anti-Hbc (total and anti-HBc IgG), and HBV DNA quantification and ultrasound examination. Serum alpha-fetoprotein was done only in elderly (>50 years) patients. Liver biopsy was not considered mandatory for analysis, but we did fibroscan of liver for the analysis of fibrosis. Individuals who were positive for HBsAg for at least 6 months or who were negative for anti-HBc IgM were included in the study.

Based on the clinical presentation, viral profile and transaminase levels and ultrasound findings the sequel of chronic HBV infection was categorized as HBeAg pos chr infection or immune tolerant, HBeAg pos chr hepatitis or immune reactive, HBeAg neg chr infection or inactive carrier, HBeAg neg chr hepatitis and chronic liver disease with compensated cirrhosis or Decompensated cirrhosis. Patient information included age, gender, date of detection and duration of HBsAg positivity, family history of liver disease including HCC, past history of tattoo, blood transfusion, jaundice, and surgery. A pre-designed proforma was used to collect information from the hospital records. By using the proforma data were collected from hospital records of total of 100 patients with chronic HBV infection. Standard statistical methods was used for data analysis.

RESULTS

In the present study age of the patient range from 6- 75 years with mean 37.89. Most of the patients were in 3 and 4 decade of life. Out of 100 patients, 57% were males and 43% were females with male: female (1.32:1).



Majority of patients were asymptomatic and incidentally detected to be positive during any health checkup, pre-anesthetic checkup, pregnancy or blood donation camps. Table 1 shows the risk factors for HBV transmission and spectrum of chronic liver disease amongst the different category of study subjects.

Table 1: Risk factors for HBV transmission and spectrum of chronic liver disease among the study subjects

Risk factors	HBeAg neg chr infection-inactive carrier	HBeAg pos chr infection-immune tolerant	High ALT high DNA(HBeAg neg+ pos)
Incidental	17	0	49
Family history (? vertical)	4	3	14
Pregnancy	3	0	5
Past blood transfusion	1	0	1
Sexual	0	0	3

Among the study population 29% of patients were in immune inactive carrier phase and 49% had features of chronic hepatitis without features of cirrhosis. 8 patient was detected during pregnancy, among them 4 had high ALT and DNA and one had cirrhosis and remaining 3 patient were in inactive carrier state. We got cirrhosis in 19 patients, among them 13 were HBeAg nonreactive and 7 were HBeAg reactive. Among them 9 patient had esophageal varix and 8 patient had decompensated cirrhosis and was admitted in our hospital. Varix was not found in noncirrhotic patient.

Table 2: Spectrum of Hepatitis B Infection

Spectrum of Hepatitis B Infection	Percentage
HBeAg neg chr infection-inactive carrier	29%
HBeAg neg chr hepatitis	40%
HBeAg pos chr infection- immune tolerant	3%
HBeAg pos chr hepatitis- immune reactive	9%
Cirrhosis (HBeAg neg+ pos)	19 (13+6)%

Alanine aminotransferase (ALT) levels were similar in both HBeAg-positive and negative patients. The mean ALT levels were higher in HBeAg-negative patients. HBV DNA quantity was significantly high in men and women who were HBeAg positive indicating higher infectivity and transmissibility rates. There was no correlation between HBsAg and HBV DNA quantity with HBeAg positivity.

One patient in the entire series was positive for both HBV and retrovirus, and one was positive for HBV, HCV and retrovirus. One patient was on chemotherapeutic drugs and required prophylactic antivirals. There was no patients who had HBV-related HCC during the study period though three patient showed high AFP.

DISCUSSION

The goals of hepatitis B therapy are to prevent disease progression and improve patient survival and quality of life. Treatment protocol for an individual depends on the phase of HBV infection.

Currently, treatment is recommended for according to EASL clinical practice guidelines 2017- All patients with HBeAg-positive or -negative chronic hepatitis B, defined by HBV DNA >2,000 IU/ml, ALT >ULN and/or at least moderate liver necroinflammation or fibrosis, cirrhosis with any detectable HBV DNA level regardless of ALT levels, patients with HBV DNA>20,000 IU/ml and ALT>2xULN regardless of the degree of fibrosis, patients with HBeAg-positive chronic HBV infection (persistently normal ALT and high HBV DNA) with age> 30 years, patients with HBeAg-positive or HBeAg-negative chronic HBV infection and family history of HCC or cirrhosis and extrahepatic manifestations.

In the present study, a significant number of patients were in the inactive phase not requiring treatment which is similar to Balasubramanian S et al [1] study. Age and duration of illness possibly predict severity of liver injury in the presence of high HBV DNA levels [11, 12]. We got only three patient in immune tolerant phase which quite low from Balasubramanian S et al [1] study. A significant proportion of our patients despite being asymptomatic had high ALT and HBV DNA levels. The study, however, could not differentiate the immune clearance from the reactive group of patients as the study was a retrospective study.

CONCLUSION

A significant number of HBsAg-positive patients belong to immune inactive (chronic carrier) phase not requiring treatment. Patients with elevated ALT and HBV DNA levels need an in-depth evaluation to

categorize these patients into immune clearance and immune reactive phase, which was not possible in the present study, as the study was a retrospective study.

Conflicts of interest

There are no conflicts of interest.

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