OCCULT HEPATITIS B IN PATIENTS WITH DECOMPENSATED CHRONIC LIVER DISEASE: A CROSS-SECTIONAL STUDY AT TERTIARY CARE HOSPITAL, PESHAWAR

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ABSTRACT

OBJECTIVES

The objective of this study was to find the frequency of occult hepatitis B in patients presenting with Decompensated chronic liver disease.

METHODOLOGY

This descriptive, cross-sectional study was conducted at a tertiary care hospital at Peshawar-KP from 31st December 2021 to 31st May 2022.143 patients were enrolled. Informed consent was taken from all patients who were enrolled in this study. We included patients aged 18-60 years of either gender. All patients admitted to medical units or visiting Medical OPDs having decompensated Chronic liver disease were enrolled. A consecutive sampling technique was used to enroll patients for our study. Baseline characteristics, demographics and laboratory data were collected on predesigned proforma. All patients were screened for Hepatitis B infection by performing HBsAg with ELISA, and patients with negative surface antigens were eligible for the study.

RESULTS

Our study population age range was from 18 to 60 years, with a mean age of 43.30±8.00 years. There were 100 male (69.9%) patients and 43 female (30.1%) patients. Occult Hepatitis B was observed in 40(28%) patients with decompensated chronic liver disease. Among these patients, 26 were male, and 14 were female. Stratification for Occult Hepatitis B was done concerning age & gender to see any significant difference in distribution. There was no significant difference in the distribution of Occult Hepatitis B among different age groups and gender.

CONCLUSION

This study has shown that a significant proportion of decompensated chronic liver disease patients had evidence of occult hepatitis B infection.

KEYWORDS: *Cirrhosis, Decompensated Chronic Liver Disease, Occult Hepatitis B Infection*

INTRODUCTION

Occult Hepatitis B infection (OBI) is when a patient infected with the Hepatitis B virus has negative viral surface antigen (HBsAg). However, HBV DNA is detected in the liver parenchyma and possibly in the serum sample of patient.[1] Other investigations and markers of HBV infection, like antibodies to the core (anti-HBc) or surface antigen (anti-HBs), are often detected. Seronegative OBI can also occur in which HBV DNA is the only positive marker of Hepatitis B virus infection with all negative serological tests.[2] The clinical manifestations of OBI include decompensating cirrhosis, the persistent risk of reactivation if there is any immunosuppression and the risk of transmission to other people as they are labelled as Hepatitis B negative with routine Hepatitis B surface antigen testing being negative.[3] OBI is more prevalent in populations at higher risk of infection (People living with HIV infection, IV drug users, patients on hemodialysis and in endemic regions of the world.[3,4] Hepatitis B virus infection is prevalent at intermediate endemicity (2-7%) in areas like South Asia and Sub-Saharan Africa, and a substantial number of patients might have Occult Hepatitis B infection.[5] OBI can be further classified as true or false according to HBV DNA levels. True OBI occurs due to suppressed replication activity of the virus and genome expression of covalently closed circular DNA (cccDNA) in the hepatocytes, which leads to very low HBV DNA levels in the blood (<200 IU/mL). False OBI, in contrast, occurs due to S-gene escape mutants, which cause alteration in the surface antigen that cannot be detected with routine HBsAg testing, with higher HBV DNA levels that occur in chronic active Hepatitis B patients.[6] Hepatitis B is a common cause of cirrhosis that can lead to liver decompensation, liver cancer and ultimately, death of the patient. Patients with chronic liver disease can be

asymptomatic or symptomatic, depending on whether their liver functions are clinically compensated or decompensated. Occult hepatitis B is associated with liver decompensation, and the oncogenic potential of the Hepatitis B virus can lead to Hepatocellular carcinoma.[7,8] Available literature shows a very high prevalence of Occult hepatitis B in patients with cirrhosis. For instance, a study by Chemin I et al. has shown that frequency of occult hepatitis B was 61% in patients with cirrhosis.[9] HBV and HCV infections related to chronic liver diseases are common in Pakistan.[10] It will be important to determine the burden of Occult hepatitis in patients with negative screening with Hepatitis B surface antigen in patients with chronic liver disease. Therefore, this study was planned to determine the frequency of occult HBV infection in patients with decompensated chronic liver disease. This study will help estimate the burden of OBI and pave the way to study the possible influence of occult HBV infection on the clinical outcomes of patients with decompensated chronic Liver Disease. Moreover, it would have implications for routine screening of blood products for OBI and investigating all patients with cryptogenic decompensated chronic liver disease for evidence of occult hepatitis B. The rationale of this study was to find the frequency of occult hepatitis B in patients with decompensated chronic liver disease at the Peshawar Institute of Medical Sciences, Peshawar.

METHODOLOGY

This descriptive Cross-sectional Study has conducted at the Peshawar Institute of Medical Sciences Hospital, Peshawar, after taking institutional ethical approval from IRB. The study was conducted from 31st December 2021 to 31st May 2022. Informed consent was taken from all patients who were approached in this study. We included patients aged 18-60 years of either gender. All patients admitted to medical units or visiting Medical OPDs having decompensated Chronic liver disease were enrolled. A consecutive sampling technique was used to enroll patients for our study. Baseline characteristics, demographics and laboratory data were collected on predesigned proforma. All patients were screened for Hepatitis B infection by performing HBsAg with ELISA, and patients with negative surface antigens were included in the study. We excluded patients who have Hepatitis C virus infection, are on hemodialysis, have a History of IV drug abuse and ones with HIV infection (patients are usually using tenofovir). We also excluded patients with a History of Hepatitis B treatment in the past. Decompensated chronic liver disease was defined as patients with chronic liver disease with episodes of hepatic encephalopathy/variceal bleeding or having Splenomegaly/ascites on Ultrasound imaging or Albumin less than 3.5 g/l with prothrombin time greater than 3 seconds from control. Occult hepatitis B was defined as the patient having negative hepatitis B virus (HBV) surface antigen (HBsAg) with detectable HBV DNA in the serum by Real-Time PCR (persistence of HBV RNA level >50 IU/ml). A total of 143 patients were recruited for this study. The sample size was calculated with WHO sample size software, using a 95% confidence interval and 8% margin of error and expected frequency of occult hepatitis B by 55.9 % in patients with cirrhosis.[11] With aseptic measures, 5 ml of blood sample was taken with a disposable syringe. The blood samples of patients fulfilling the criteria for decompensated chronic liver diseases were sent for analyzing HBsAg by ELISA and Antibodies to Hepatitis C virus (Anti HCV). Patients with negative Hepatitis B surface antigen tests and negative Anti-HCV were further tested for HBV DNA by performing qualitative PCR. Patients were labelled as having Occult Hepatitis B when their Hepatitis B surface antigen was negative, and PCR detected the HBV DNA virus. These patients were referred to a hepatologist to consider antiviral therapy. Data were entered and analyzed with a statistical analysis program (IBM-SPSS V-23). Frequencies and percentages were computed for categorical variables like gender and occult hepatitis B. Mean ±SD was determined for variables like age. Occult hepatitis B was stratified by age and gender. The post-stratification chi-square test was applied, and the P value of ≤0.05 was considered statistically significant.

RESULTS

Our study population age range was from 18 to 60 years, with a mean age of 43.30±8.00 years. There were 100 male (69.9%) patients and 43 female (30.1%) patients. Occult Hepatitis B was observed in 40(28%) patients with decompensated chronic liver disease. Stratification for Occult Hepatitis B was done concerning age & gender to see any significant difference in distribution. There was no significant difference in the distribution of Occult Hepatitis B among different age groups and gender.

Table 1: Frequency and %age of Patients According to Gender n=143

Gender	F	%age
Male	100	69.9%
Female	43	30.1%

Table 2: Frequency and %age of Patients with OHB n=143

Occult Hepatitis B	F	%age
Yes	40	28%
No	103	72%

Table 3: Stratification of Occult Hepatitis B Concerning Age

Age(Years)	Occult Hepatitis B		P-Value
	Yes	No	
18-40	14(29.2%	34(70.8%)	0.821
41-60	26(27.4%)	69(72.6%)	

Table 4: Stratification of Occult Hepatitis B for Gender

Gender	Occult Hepatitis B		P-Value
	Yes	No	
Male	26(26%)	74(74%)	0.423
Female	14(32.6%)	29(67.4%)	

DISCUSSION

Hepatitis B virus infection-induced cirrhosis is among developing countries most common causes of liver cirrhosis.[4,12] We screened all HBsAg-negative patients with decompensated chronic liver disease for occult hepatitis B. In our study, 28% of patients with Decompensated chronic liver disease had Occult hepatitis B, which is significantly high. Occult hepatitis B infection has been proposed as a possible cause of Cirrhosis in HBV-endemic regions.[13] This study describes for the first time the prevalence and characteristics of OBI among patients having decompensated chronic liver disease. In our study, almost one-third of decompensated cirrhotic patients with no evidence of Hepatitis B infection with HBsAg screening test had detectable HBV DNA by PCR. Occult hepatitis B is due to mutations in regulatory regions of the HBV virus genome where the HBV virus remains in liver tissue and blood in low levels and can promote liver inflammation and, ultimately, decompensation and hepatocellular carcinoma.[14] A study conducted in Ethiopia showed a higher prevalence, with 44.4% of patients having OHB in patients labelled as cryptogenic Cirrhosis.[15] Another study done in India showed the prevalence of 14.6% of Occult hepatitis B based on testing with Hepatitis B core antibodies. Their results were different compared to our studies due to different diagnostic methods used.[16] Similarly, another study done in Eastern India showed a prevalence of 17.8 per cent, which is lower than our results.[17] Their study population was HIV-infected patients, and using tenofovir as ARV therapy could be the reason for the lower prevalence. In a study conducted in Yemen, the frequency of OHB in patients with CLD was 4.3%, which was quite lower compared to our results.[18] There is wide variation in the prevalence of Occult hepatitis B in different populations, and it depends on diagnostic tests and the overall prevalence and endemicity of Chronic Hepatitis B infection. Different studies from Iran have also found a higher prevalence of OBI in patients with cryptogenic cirrhosis and reported 2%, 14% and 22%.[13] Another study from China showed a 28.3% prevalence of OBI among patients with cryptogenic CLD.[4] A study from Egypt showed the prevalence of OBI as 22.5% when HBC DNA PCR was done from a blood sample and 62.5% when HBV DNA PCR was performed on liver tissue.[19,20] Another study done in Israel showed that 30 per cent of patients with negative Hepatitis B surface antigen had detectable HBV DNA by PCR.[21] A study conducted in Pakistan in patients having HCV infection showed an Occult hepatitis B prevalence of 30 %, which is almost similar to our results, where the prevalence was 28%, but the study population was different.[22] The literature shows significant variation in the prevalence of OBI among cirrhotic patients. The frequency of Occult hepatitis B infection among patients varies and depends on whether HBV DNA by PCR was performed on serum or liver biopsy specimens. Other factors that can explain wide variability include the detection limit of the PCR method, fluctuation of HBV DNA levels and spontaneous mutation in the Hepatitis B virus genome.[23,24] Superimposed HCV or HDV infection can decrease HBsAg titer to undetectable levels, contributing to variation in the prevalence of Occult hepatitis B infection.[25] Our study population was HCV-negative, but due to financial limitations, we could not check our patients for Hepatitis D virus coinfection. Occult Hepatitis B is strongly associated with HCC, and its oncogenic potential is well-established. Several studies have shown that Occult Hepatitis B can lead to the early development of HCC, and patients with evidence of OHB have a greater chance of developing Liver malignancy than patients with no evidence of current or previous hepatitis B infection.[8,26] Therefore, clinicians should always consider a full panel of investigation for Hepatitis B in patients with CLD, especially in HBV-endemic regions like Pakistan and should keep a low threshold to screen for the development of Hepatocellular carcinoma. It is the first study in our regional setting to check for OBI among decompensated cirrhotic patients with a negative screening test for hepatitis B surface antigen. In Hepatitis B endemic regions like our country, this study shows that all patients diagnosed with Chronic liver disease should be considered for a full Hepatitis B-related panel, including PCR testing if risk factors are present. There were a few limitations in the study. Firstly, we couldn't do HBV DNA PCR testing on liver tissue as it could underestimate the true prevalence of Occult Hepatitis B infection in our study population. Secondly, our sample size was small. Thirdly, financial implications meant we couldn't do HBeAg and HBeAg-related antibodies. Lastly, Hepatitis D virus infection can affect hepatitis B virus surface antigen detection, which was again not checked in our population due to financial constraints. Occult hepatitis B can contribute

to the development of cirrhosis and liver cancer and implementation of national vaccination program and community awareness is the only way to prevent occult hepatitis B. Complete eradication from the liver genome and recovery from Hepatitis B infection based on serological recovery should not be declared. All patients with hepatitis B infection can potentially develop Chronic liver disease and liver cancer even after the loss of surface antigen and undetectable HBV DNA by PCR in serum. We strongly recommend further multi-centre studies that contribute further data. In the future, a larger prospective, cohort study is recommended in which patients with OBI can be followed and will clarify its role in the liver.

LIMITATIONS

The article may have a limited sample size, which can affect the generalizability of the findings. If the sample size is too small, it may not accurately represent the broader population of patients with decompensated chronic liver disease in Peshawar or other regions.

CONCLUSIONS

This study has shown that a significant proportion of decompensated cirrhotic patients had occult hepatitis B. PCR testing and Anti-HBc testing shall be integrated into the routine health care system, and robust investigation for diagnosing occult hepatitis B should be done in Cirrhotic patients in Hepatitis B endemic regions to minimize the Hepatitis B Virus infection risk of transmission, reactivation and complications.

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