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Observational Study

Chronic Hepatitis B and Occult Infection in Chemotherapy Patients - Evaluation in Oncology and Hemato-Oncology Settings- The CHOICE study

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Abstract

BACKGROUND

Reactivation of HBV infection is a known threat that can occur spontaneously or following immunosuppressive therapies, including cancer chemotherapy. This adds to morbidity and mortality, which is preventable if at- risk individuals are identified through screening and started on antiviral prophylaxis.

AIM

To determine the prevalence of chronic HBV & occult HBV infection, among oncology and Hematology-oncology patients undergoing chemotherapy

METHODS

In this observational study, the prevalence of chronic HBV & occult HBV infection was assessed among patients receiving chemotherapy. Serological markers of HBV infection (HBsAg/anti-HBc/anti-HBs) were evaluated for all participants. Those who tested negative for HBsAg but positive for total anti-HBc were tested for HBV DNA levels.

RESULTS

In our study, the prevalence of Chronic Hepatitis B (CHB) within the study cohort was determined to be 2.3% (95%CI: 1.0-4.2). Additionally, the prevalence of Occult Hepatitis B infection (OBI) among the study participants was found to be 0.8% (95%CI: 0.2–2.3).

CONCLUSION

The findings of this study highlight the importance of screening for Hepatitis B infection in oncology and hematology-oncology patients undergoing chemotherapy. Identifying individuals with CHB and OBI is crucial for implementing appropriate antiviral prophylaxis to prevent the reactivation of HBV infection, which can lead to increased morbidity and mortality.

INTRODUCTION

Reactivation of Hepatitis B virus (HBV) infection is a well-known threat that can occur spontaneously or following immunosuppressive therapies, including cancer chemotherapy [1]. This reactivation adds to the morbidity and mortality burden, which is preventable if at-risk individuals are identified through screening and started on antiviral prophylaxis[1]. The prevalence of chronic Hepatitis B (CHB) infection and occult Hepatitis B infection (OBI) among oncology and hemato-oncology patients receiving chemotherapy is an important area of study. CHB refers to persistent HBV infection characterized by the presence of Hepatitis B surface antigen (HBsAg) for more than six months. OBI, on the other hand, is defined as the presence of HBV DNA in the absence of detectable HBsAg [2]. Understanding the prevalence of CHB and OBI in this patient population is crucial for implementing appropriate preventive measures and antiviral prophylaxis to prevent HBV reactivation. Previous studies have reported varying prevalence rates of CHB and OBI among cancer patients undergoing chemotherapy, highlighting the need for further investigation [3–5]. By determining the prevalence of CHB and OBI in this specific patient population, this study will contribute to the existing knowledge on HBV infection in the context of cancer chemotherapy. The

findings will provide valuable insights into the need for routine screening, antiviral prophylaxis, and infection control measures to prevent HBV reactivation and associated complications in oncology and hematology-oncology patients undergoing chemotherapy.

MATERIALS AND METHODS

Study Design and Population:

This observational study aimed to estimate the prevalence of chronic hepatitis B (CHB) and occult hepatitis B infection (OBI) in newly diagnosed oncological and hematology-oncological patients before starting chemotherapy. The study population included both male and female patients from urban and rural areas, aged 18 years or older, who were seeking treatment at a tertiary care oncology center. Patients with solid organ cancer, leukemia, and lymphoma, as well as those planned for chemotherapy (standard chemotherapy protocols as per cancer type) and hematopoietic stem cell transplant (HSCT), were included in the study. Patients with a history of previous chemotherapy or immunosuppressive therapy, pre-existing chronic HBV or chronic HCV infection, and contraindications for antiviral therapy for chronic hepatitis B were excluded.

Data Collection:

Data was collected from a total of 400 patients over two years. All patients underwent screening for HBsAg and Total Anti HBc. Patients who tested positive for either of these markers were further tested for HBV DNA quantification using polymerase chain reaction (PCR) analysis. All the patients who were identified as CHB or OBI were started on antiviral prophylaxis with Entecavir or Tenofovir and followed up at 6 & 12 months with HBV DNA and Liver function tests. The data collected from the patients was recorded in an Excel spreadsheet for further analysis.

Statistical Analysis

The collected data was analyzed using appropriate statistical methods. Descriptive

statistics were used to summarize the demographic and clinical characteristics of the study population. The prevalence of chronic hepatitis B and occult hepatitis B infection was estimated based on the number of patients testing positive for HBsAg, Total Anti HBc, and HBV DNA. The statistical analysis aimed to determine the prevalence rates and associated confidence intervals for CHB and OBI in the study population.

Ethical Considerations

The study protocol was reviewed and approved by the relevant ethical committee. Informed consent was obtained from all participants before their inclusion in the study. Confidentiality and privacy of patient information were strictly maintained throughout the study.

RESULTS

In this observational study, we investigated the prevalence of chronic hepatitis B (CHB) and occult hepatitis B infection (OBI) in a cohort of 400 patients visiting the oncology and hematology departments with different types of malignancies (Figure 1). Among the 400 subjects studied, 129 (32.3%) were females and 271 (67.8%) were males. The mean age of the study group was 51.34 years (95%CI: 49.83-52.85). Most of the participants were oncology patients 339 (84.8%), with only 61 (15.3%) patients with hematolymphoid malignancies (Figure 2).

A total of 9 patients (2.3%) tested positive for HBsAg (Figure 3) of which 7 were above the age of 50 years and 2 were below 50 years (Figure 4). The distribution of cancer types among these patients included 5 with hepatocellular carcinoma (HCC), 2 with colon cancer, one with acute lymphoblastic leukemia (ALL), and 1 with pancreatic cancer. Five patients among them had a history of jaundice, of which 3 were documented to have acute Hepatitis B infection (Table 1). Only 2 of them had elevated liver enzymes. Two patients had high HBV DNA levels which on 6 & 12 months follow-ups were undetectable (Table 2). Among all the HBsAg negative cases 03 patients tested positive for total Anti HBc. Among these patients, one had acute myeloid leukemia (AML), one had a non-seminomatous germ cell tumor (NSGCT), and one had colon

cancer (Table 3). Two of these patients had a history of jaundice in the past. None of the patients with occult hepatitis B infection had detectable HBV DNA levels, and their liver enzymes were within the normal range (Table 4). All the patients with CHB and OBI were started on antiviral prophylaxis (Tenofovir or Entecavir) and were followed up at 6 & 12 months. On follow-up, there was clearance of viral load and normalization of liver enzymes (Table 2)

DISCUSSION

This study identified a prevalence of CHB of 2.3% (95%CI: 1.0-4.2) and OBI of 0.8% (95%CI: 0.2-2.3) within the study group. Two patients in the CHB subgroup had high HBV-DNA levels with deranged liver enzymes wherein none of these patients knew their HBV status before our study. This reiterates the importance of such screening tests before immunosuppressive therapies. Anti-viral prophylaxis was initiated in both the CHB & OBI (Moderate to severe risk). These patients were followed up at 6 & 12 months, but no reactivation was noted. For those who had high viral load, 6 & 12-month follow-up revealed clearance of viral load.

These results provide valuable insights into the burden of hepatitis B infection in this specific patient population and have important implications for clinical management and preventive strategies. The prevalence of CHB in the study cohort is consistent with previous studies reporting a wide range of prevalence rates among cancer patients undergoing chemotherapy [3]. Furthermore, the prevalence of OBI in the study group was estimated to be 0.8%. Although OBI is often considered a low-level infection, it can still pose a risk of transmission, especially in immunocompromised individuals [5]. Identifying OBI in this patient population underscores the importance of infection control measures to prevent HBV transmission in healthcare settings. Among the patients who tested positive for HBsAg, the majority were above the age of 50 years. This is in line with previous studies that have shown an increased risk of chronic hepatitis B infection with advancing age [6]. It is noteworthy that none of the patients with occult hepatitis B infection had detectable HBV DNA levels, and their liver

function tests were within the normal range. This suggests that these patients may have resolved their HBV infection or have very low-level viral replication. However, it is important to monitor these individuals closely, as OBI can still pose a risk of reactivation under immunosuppressive conditions. Loss of immune control over the hepatitis B virus (HBV) is a crucial event in HBV reactivation (HBVr), leading to an increase in HBV DNA levels among individuals previously exposed to HBV [7]. The immune system plays a role in partially controlling viral replication in these individuals, and this control can be disrupted by exposure to immunosuppressive therapy [8]. HBVr can occur due to the ability of HBV to remain latent in the liver as covalently closed circular DNA and its capacity to alter the immune system of infected individuals[9]. Weakening of cellular immune responses during immunosuppressive therapy or chemotherapy can increase HBV replication, leading to HBVr [10]. In a study from Hong Kong among 104 patients with diffuse large B-cell lymphoma undergoing treatment 46 were found to be HBsAg negative and anti-HBc positive. Twenty-one of these patients were treated with R-CHOP and 25 were treated with CHOP alone. Of patients treated with R-CHOP, five (25%) developed HBVr. None of the patients treated with CHOP therapy developed HBVr [11].
In another study, 115 Non-Hodgkin's Lymphoma (NHL) patients who were receiving at least one dose of rituximab were examined for the risk of HBVr. Fifteen of these patients were HBsAg-positive, and 10 of them did not receive antiviral prophylaxis during treatment. 80% of patients who were HBsAg-positive and received rituximab therapy without anti-viral prophylaxis experienced HBV-related hepatitis. Of 95 patients with NHL who were HBsAg-negative, four developed HBV-related hepatitis out of which two died due to fulminant hepatic failure [12].

CONCLUSION

+ADw-html+AD4APA-p+AD4-The findings of this study have important clinical implications. Routine screening for hepatitis B infection should be considered in oncology and hematology patients before initiating chemotherapy or

immunosuppressive therapies. Identifying individuals with CHB and OBI allows for appropriate management strategies, including antiviral prophylaxis, to prevent reactivation and associated complications. Additionally, strict adherence to infection control measures is crucial to prevent HBV transmission in healthcare settings. A notable limitation of our study was that it experienced a loss of follow-up for some patients (20 out of 400), potentially introducing bias and impacting prevalence estimates and while the study population of 400 patients was substantial, its single-center nature might limit its application to other healthcare settings, although the data supports the existing guidelines and perhaps gives way to more work in this interesting clinical setting.