Hepatitis B Virus Reactivation in Patients Receiving Chemotherapy and Immunosuppressive Therapy

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Abstract

Hepatitis B virus (HBV) infection is a serious and common infectious disease of the liver, affecting millions of people throughout the world. The incubation period for HBV is 45-180 days, most commonly 60-90 days. Hepatitis B reactivation is the reappearance or rise of hepatitis B virus (HBV) DNA in the serum of patients with past or chronic HBV infection. Reactivation can occur in a variety of clinical settings, usually in the context of an immunosuppressed state or immunosuppressive therapy. The aim of study is to find out the reasons that lead to reactivation of hepatitis B virus. The study conducted during the period from September 2019 to February 2020 the sample size were 135 individuals include 85 patients and 50 control with 56.47% female and 43.53% male) blood samples. A 42 (49.41%) from patients have reactivated HBV positive results as detected by ELISA assay . A five samples at a rate of 5.88% from these are HBV reactivation by PCR technique.

Keyword: *Hepatitis B virus, Reactivation, Liver function test, ELISA and PCR.*

Introduction

Hepatitis B virus (HBV) is a DNA virus belonging to the Hepadnaviridae family,which includes hepatotropic viruses . The HBV virion consists of an external lipoprotein envelope and an internal protein nucleocapsid with icosahedral symmetry,containing the viral genome and the DNA polymerase. The HBV genome is partially double-stranded circular DNA molecule with four partially overlapping open reading frame encoding structural and non-structural viral proteins [(1)]. It is transmitted through exposure to infectious blood,semen and other body fluids. HBV can be transmitted from infected mothers to infants at the time of birth, or from family members to infants in early childhood. Transmission may also occur through unsafe sexual intercourse, transfusions of HBV-infected blood and blood products, contaminated injections during medical procedures and sharing of needles and syringes among injecting drug users[(2)]. The infection can be diagnosed 30 to 60 days after exposure; the diagnosis is usually confirmed by testing the blood for parts of the virus and for antibodies against the virus . The incubation period ranges from 45–160 days, with an average of 75 days, followed by an insidious onset of acute disease [(3)]. Hepatitis B reactivation is the reappearance or rise of hepatitis B virus (HBV) DNA in the serum of patients with past or chronic HBV infection. Reactivation can occur in a variety of clinical settings, usually in the context of an immunosuppressed state or immunosuppressive therapy. HBV reactivation has been most commonly reported in patients receiving chemotherapy for hematologic malignancies and following hematopoietic stem cell transplants[(4)]. An estimated 2 billion people worldwide have serological evidence of either past or present HBV infection, with around 240 million people chronically infected[(5)]. The prevalence varies globally, ranging between 2% in Europe to over 10% in East Asia; in the UK it is estimated to be between 0.5-1.7%, with areas of greater ethnic diversity such as London having a higher prevalence of approximately 2.4%[(6)].

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Reactivation of hepatitis Bvirus (HBV)is a major problem in patients receiving chemotherapy for malignant diseases or immunosuppression therapies. It has been thought that a reduction in the immune responses might result in the reactivation of HBV replication from covalently closed circular DNA (cccDNA) residing in hepatocytes. However, not only the host's immune status, but also viral mutations have been reported to be associated with reactivation[7].

Materials and Method

The practical side of this study was conducted during the period from September 2019 to February 2020 one hundred and thirty five (135) samples were collected .Two enrolled groups of subjects were involved in this study. A eighty five (85) blood samples . The Patients were piously diagnosed with suspected liver disease by physician, included(48 females and 37 males) with an age range (14-78 years old) they were diagnosed by serological and molecular test, liver function test (LFT), complete blood count (CBC). Plasma and serum samples taken from every patients and control having thoroughly examined Fifty(50) healthy control. After laboratory tests for patients,only 42 patients were HBV positive by ELISA and PCR,using the primers designed for this study at length 482bp (RE2 5-AACCACTGAACAAATGGCAC-3), five cases appeared to have HBV reactivation .

Results and Dissection

The results of this study were shown in tables (1) and (2) five HBV reactivation risk group by PCR, only one without chemotherapy and immunosuppression therapy (renal frailer) but the other four with chemotherapy and immunosuppression therapy,(A cute Leukemia, Kidney Transplantation, Lung cancer and Leukemia) two of them are normal ALT, AST, decrease in PL, and positive HBV,the four other are increase ALT, AST, decrease in PL and positive HBV. All patient are females with different age (52,15,40,71, and 50) years old.

Table(1): The characteristic of reactivation HBV of PCR positively cases in relation to the liver enzymes and liver markers test results.

Anti-HBc	HBsAg	AST	ALT	Disease/Chemo+immune therapy and	Age	Sex
Positive	Positive	Normal	Normal	Renal failer/without	52 years	Female
Positive	Negative	Normal	Normal	Acute Leukemia/with	15 years	Female
Positive	Negative	Increase	Increase	Kidney Transplantation/with	40 years	Female
Positive	Negative	Increase	Increase	Lung cancer/with	71 years	Female
Positive	Negative	Increase	Increase	Leukemia/with	50 years	Female

Table(2):The characteristic of reactivation HBV of PCR positively cases in relation to the platelets.

Anti-HBc	HBsAg	PL	Disease/Chemo+immune therapy and	Age	Sex
Positive	Positive	Decrease	Renal failer/without	52 years	Female
Positive	Negative	Decrease	Acute Leukemia/with	15 years	Female
Positive	Negative	Decrease	Kidney Transplantation/with	40years	Female
Positive	Negative	Decrease	Lung cancer/with	71 years	Female
Positive	Negative	Decrease	Leukemia/with	50 years	Female

The results explained in tables 1 and 2 indicated that the patient who take chemotherapy and immunosuppression therapy with HBsAg negative and Anti-HBc positive, the patients with renal failure, acute leukemia, kidney transplantation, lung cancer leukemia are in danger (most at risk) of HBV reactivation these results consistent with previous study. Through this study it was found that patient with cancer and who have undergone an organ transplant are more likely to reactive hepatitis B virus.

HBV reactivation generally occurs in some cancer patients after chemotherapy, immunosuppressive therapy and biological modifier therapies[8]. especially

when some solid tumors and leukemia patients are using hormones such as prednisolone and rituximab that emerged clinical crisis. It can also occur in some patients with autoimmune diseases, organ transplants (kidney transplants, lung transplants, heart transplants, etc.) and human immunodeficiency virus (HIV), but the most serious cases are often with bone marrow or liver transplants[9]. At the same time, drugs such as some tyrosine kinase inhibitors[10]. the serum ALT rapidly rose above the upper limit of the baseline. If the serum ALT increases by more than 5 times compared with the upper limit of normal value, which could be called hepatitis burst and if it increases by more than 10 times, it could be called deteriorating acute hepatitis. In the course of HBV reactivation, rise of the serum ALT level can be accompanied by that of HBV DNA level and sometimes the HBV DNA can increase firstly, when the HBV DNA falls back and the serum ALT level rises remarkably. Therefore, the serum ALT levels and HBV DNA levels are often used as important indicators to monitor the risk of HBV reactivation in clinical patients[11].

Conclusion

From the present work we can concludes that reactivation of hepatitis B virus (HBV) can be occurred in patients receiving chemotherapy for malignant diseases or immunosuppression drugs. The evidence for such reactivation that the platelets count were decrease while the ALT and AST levels vary and the patient have asymptomatic HBV .

Ethical Clearance: The Research Ethical Committee at scientific research by ethical approval of both MOH and MOHSER in Iraq

Conflict of Interest: Non

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