Prevalence and chemotherapy-induced reactivation of occult hepatitis B virus among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma: Significance of hepatitis B core antibodies screening

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Keywords
Hepatitis B virus; HBsAg; HBV-DNA; Anti-HBc; Occult HBV reactivation; Diffuse large B-cell lymphoma

Abstract  Background: Occult hepatitis B infection (OBI) is characterized by negative hepatitis B surface antigen (HBsAg) and detectable hepatitis B virus (HBV)-DNA in the liver and/or serum, with or without hepatitis B core antibody (anti-HBc). Anti-HBc is the most sensitive marker of previous HBV. HBV reactivation in patients under immunosuppressive treatment is life-threatening, occurring in both overt and occult HBV especially in hematological malignancies.

Aim of the work: To evaluate the prevalence and chemotherapy-induced reactivation of OBI among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma (DLBCL) patients and to determine the significance of anti-HBc screening among this group of patients before receiving chemotherapy.

Patients and methods: This cross-sectional study included 72 DLBCL patients negative for HBsAg, HBsAb and hepatitis C virus antibodies (anti-HCV). Patients were subjected to investigations including anti-HBc. All patients underwent alanine transaminase (ALT) monitoring before each cycle of chemotherapy and monthly for 12 months after the end of chemotherapy. Patients with suspected OBI were tested for HBV-DNA using real-time polymerase chain reaction (PCR).

Results: Anti-HBc was detected in 10 of 72 HBsAg negative sera (13.89%) (95% confidence interval 6.9–22.2%). Five of the 10 anti-HBc positive patients in this study had OBI reactivation.
Introduction

Hepatitis B virus (HBV) infection is a major health problem, affecting about 2 billion people worldwide despite of the effective vaccination. There are 350 million HBV carriers worldwide and about one million die annually from HBV-related liver disease [1]. The prevalence of HBV infection varies in different parts of the world (<1–15%) [2]. Intermediate endemicity of HBV infection had been recorded in Egypt [3].

Occult HBV infection (OBI) is characterized by negative serum hepatitis B surface antigen (HBsAg) and detectable HBV-DNA in the liver and/or serum, with or without hepatitis B core antibody (anti-HBc) [4]. Anti-HBc is the most sensitive marker of previous HBV infection [5]. Anti-HBc is the first antibody to appear and present in all different phases of HBV. Anti-HBc may persist longer than hepatitis B surface antibody (anti-HBs) or hepatitis B envelope antibody (anti-HBe); however, it is not protective. Anti-HBc IgM may help in the diagnosis of the acute HBV and also during flares [6].

HBV reactivation in patients under immunosuppressive treatment is life-threatening occurring in both overt and occult HBV infection [7,8]. The risk of HBV reactivation is high with marked immunosuppression, especially in hematological malignancies chemotherapy (21–67%), bone marrow transplantation and monoclonal antibody therapy [9,10]. Under these conditions, HBV reactivation is associated with a mortality rate close to 20%, due to hepatic failure [11].

Diffuse large B-cell lymphoma (DLBCL) is the most common non-Hodgkin’s lymphoma (NHL). Standard treatment for newly diagnosed DLBCL is anthracycline-based chemotherapy regimen, usually cyclophosphamide, doxorubicin, vincristine, and prednisone with or without rituximab [12].

Hence, the aim of this study was to evaluate the prevalence and chemotherapy-induced reactivation of OBI among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma (DLBCL) patients and to determine the significance of anti-HBc screening among this group of patients before receiving chemotherapy.

Patients and methods

This cross-sectional study included 72 patients with diffuse large B-cell lymphoma (DLBCL) before receiving chemotherapy. Patients of this study were selected from the Hematology Unit, Internal Medicine Department, Faculty of Medicine, Tanta University and Tanta Cancer Center from May 2012 to October 2014. All patients included were negative for HBsAg, HBsAb and antibody for hepatitis C (anti-HCV). This study was conducted in accordance with the guidelines of the declaration of Helsinki 1975 and its subsequent amendments (1983). Participation in the study was voluntary after an informed written consent was obtained from the patients prior to the study.

All the patients were asked questions regarding age, sex, blood transfusion, past surgical procedures, intravenous drug abuse, jaundice, admission to fever hospital, and history of HBV vaccination.

Patients with recent jaundice, recent hospitalization due to fever, pregnancy, recent delivery less than 12 weeks or close contact with a patient suffering from hepatitis in the last 6 months were excluded. Exclusion criteria also included acute or chronic HBV infection as marked by positive HBsAg. Patients with HCV, human immunodeficiency virus (HIV), any hematological malignancy other than DLBCL or previous immunosuppressive treatments of any kind were also excluded.

Prior to start of the DLBCL treatment every patient underwent full history talking, complete physical examination, routine biochemistry assays including alanine transaminase (ALT) and aspartate transaminase (AST).

Diffuse large B-cell lymphoma (DLBCL) was diagnosed based on histopathological examination of lymph nodes and/or extranodal tissue biopsy specimen according to the Revised European-American Lymphoma (REAL) classification criteria revised by Harris [13]. Patients were staged according to the Ann Arbor staging system with Cotswolds modifications [14]. Ann Arbor staging was determined for all patients at the onset of DLBCL by physical examination, computed tomography scan (abdomen & pelvis, chest and neck) and bone marrow examination. The International Prognostic Index (IPI) was used for determining the prognosis of DLBCL [15]. Cheson’s criteria were used to define the response to chemotherapy [16].

The standard protocol chemotherapy for DLBCL used in this study was CHOP [intravenous cyclophosphamide 750 mg/m², doxorubicin 50 mg/m², and vincristine 1.4 mg/m² (maximum dose: 2 mg) on day 1 and oral prednisone 100 mg/day on days 1–5] every 3 weeks for (6–8) cycles [17]. For patients with relapsed or progressed disease second line therapy ICE [24 h intravenous infusion ifosfamide 5000 mg/m² on day 2, intravenous carboplatin using the Calvert formula with maximum 800 mg on day 2 and intravenous etoposide 100 mg/m² on day 1–3] every 14 days or CEOP [intravenous cyclophosphamide 750 mg/m² on day 1, intravenous etoposide 50 mg/m² on day 1 and 100 mg/m² orally on day 2 and 3, intravenous vincristine 1.4 mg/m² IV (maximum dose: 2 mg) on day 1 and orally prednisone 100 mg/m² on day 1–10] every 3 weeks for patients candidate and non candidate for high dose therapy respectively [18,19].

All patients underwent total bilirubin and ALT monitoring during therapy before each cycle of chemotherapy and monthly for 12 months after the end of chemotherapy. If the patient experienced an ALT elevation more than threefold above the upper normal value, complete investigations including HBsAg, HBV-DNA levels, anti-HBc IgM, IgM hepatitis A virus antibody (anti-HAV) and HCV-RNA were performed to prove

Conclusion: The study concluded that anti-HBc screening is mandatory before chemotherapy. HBsAg-negative/anti-HBc-positive patients should be closely observed for signs of HBV reactivation through the regular monitoring of ALT. Prophylaxis lamivudine is recommended for anti-HBc positive patients before chemotherapy.
OBI reactivation and exclude other causes of hepatitis. When OBI reactivation occurred, lamivudine therapy was promptly started at the standard dosage (100 mg orally once daily). ALT monitoring was performed every 2 weeks and complete liver functional tests including HBV-DNA quantitative assay were performed monthly.

Definition of OBI reactivation

Hepatitis was defined as a threefold or greater increase in serum ALT levels that exceeded the reference range (normal value, < 42 IU/L) or an absolute increase of ALT to more than 100 IU/L. Hepatitis was attributed to OBI reactivation when there was evidence of HBsAg seroreversion (the reappearance of HBsAg) with an increase in HBV-DNA levels when compared with baseline HBV-DNA levels (> 2000 IU/mL), in the absence of history, clinical or laboratory features of all other possible etiological factors of hepatitis [20].

Serological assays

Ten milliliters of blood were collected from each patient in a sterile, capped tube (before chemotherapy and after OBI reactivation). Blood was centrifuged and serum stored at −80 °C until it was needed for testing.

Another portion of blood was collected in vacutainer tubes containing citrate to separate plasma used for the assay of prothrombin time and activity.

All serum samples were tested for serum alanine transaminase (ALT; upper normal limit UNL 42 IU/L), aspartate transaminase (AST; upper normal limit UNL 37 IU/L) and total bilirubin (UNL 1 mg/dl) using chemistry autoanalyzer (Synchron CX5, Beckman Instrument Inc., Scientific Instrument Division, Fullerton, CA).

Hepatitis B markers (hepatitis B core antibodies, hepatitis B surface antigen and hepatitis B surface antibody) were detected by electrochemiluminescence immunoassay on Roche Elecsys 201014. Antibodies to HCV (anti-HCV) were detected using a standard third generation ELISA test (Murex anti-HCV, version 4.0). HAV was detected by commercial enzyme immunoassays (Cobas Core Anti-HAV IgM EIA, Roche Diagnostics GmbH, Mannheim, Germany). All procedures were performed according to the manufacturers’ instructions.

Detection of HBV-DNA and HCV-RNA: [21]

DNA was extracted from patient’s serum with OBI reactivation and stored serum for these patients. Samples from each patient were tested for HBV-DNA using highly sensitive and specific real-time PCR. HBV-DNA was extracted from 850 µL of plasma by the Cobas AmpliPrep instrument. The Cobas TaqMan 48 analyzer was used for automated real-time PCR amplification and detection of PCR products. HBV-DNA levels were expressed in IU/mL. The HBV detection limit was 12 IU/mL.

Patients with OBI reactivation, HCV-DNA was extracted from patient's serum with OBI reactivation and stored serum for these patients. Samples from each patient were tested for HBV-DNA using highly sensitive and specific real-time PCR. HBV-DNA was extracted from 850 µL of plasma by the Cobas AmpliPrep instrument. The Cobas TaqMan 48 analyzer was used for automated real-time PCR amplification and detection of PCR products. HBV-DNA levels were expressed in IU/mL. The HBV detection limit was 12 IU/mL.

Statistical analysis

The collected data were analyzed using SPSS version 17 software (SPSS Inc, Chicago, ILL Company). Comparison of continuous data between two groups was made by using Mann–Whitney test for non-parametric data. Fisher’s exact test was used for comparison between categorical data. Survival analysis was done using Kaplan–Meier method and comparison between two survival curves was done using log-rank test. The accepted level of significance in this work was stated at 0.05 (P < 0.05 was considered significant).

Results

Patient characteristics

This study included 72 patients with diffuse large B-cell lymphoma (DLBCL) before receiving chemotherapy; their ages ranged from 23 to 67 years (mean 50.79 ± 9.381 years), 51 were males (70.83%) while the other 21 were females (29.17%). All patients did not receive HBV vaccination before. Fifteen patients (20.83%) had history of blood transfusion and 24 patients (33.33%) had history of surgical operations. Other demographical characteristics of the study population are shown in Table 1.

All patients were followed up for 18 months from the start of chemotherapy with median 18 months (range 7–18 months) due to death of 2 patients due to OBI reactivation at the 10th and 11th months from the start of chemotherapy and death of 6 patients due to tumor progression at the 7th, 8th, 9th, 12th, 13th and 15th months from the start of chemotherapy.

HBV serology before receiving chemotherapy

Among the 72 HBsAg negative sera, anti-HBc was detected in 10 of 72 (13.89%) (95% confidence interval 6.9–22.2%). All the anti-HBc positive sera were anti-HBs negative.

Consequences of HBV serology after chemotherapy

After the initiation of systemic chemotherapy, examination of the HBV serology revealed that 5 of the 10 anti-HBc-positive patients (50%) (6.94% as regarding all patients) became seroconverted. Serological factors of hepatitis [20].

<table>
<thead>
<tr>
<th>Table 1 Demographical characteristics of the study population.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variables</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma stages</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>IV</td>
</tr>
<tr>
<td>International Prognostic Index</td>
</tr>
<tr>
<td>Low</td>
</tr>
<tr>
<td>Low/Intermediate</td>
</tr>
<tr>
<td>Intermediate/high</td>
</tr>
<tr>
<td>High</td>
</tr>
<tr>
<td>Cheson’s criteria for response</td>
</tr>
<tr>
<td>Complete Remission</td>
</tr>
<tr>
<td>Partial remission</td>
</tr>
<tr>
<td>Relapse or progression</td>
</tr>
<tr>
<td>Fate of all patients</td>
</tr>
<tr>
<td>Alive</td>
</tr>
<tr>
<td>Died</td>
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</tbody>
</table>
detectable for the HBV-DNA (OBI reactivation) as shown in Table 2.

**Characteristics of occult HBV reactivated patients**

Five of the 72 patients (6.94%) treated for DLBCL manifested with OBI reactivation. All of the five patients had OBI reactivation after the completion of all their chemotherapy cycles with mean time $9.4 \pm 1.517$ months; range 7–11 months after chemotherapy was started. Patients with OBI had mean baseline ALT (35 ± 6.595; range 29–45 U/L), mean ALT after reactivation (1092.2 ± 533.2; range 450–1776 U/L), mean HBV-DNA after reactivation (84.6 ± 26.7; range 48–121 $\times 10^4$ IU/mL), mean total bilirubin after reactivation (5.42 ± 3.419; range 2.2–9.4 mg/dl), and mean prothrombin activity after reactivation (52.8 ± 15.531; range 36–72%). All of the five patients had negative result of Anti-HAV-IgM and HCV-RNA. All of them received lamivudine therapy but 2 of them died due to liver failure and the other three patients had been recovered. Characteristics of occult HBV reactivated patients are shown in Table 2.

Comparison between patients with OBI reactivation and patients without OBI reactivation in Anti-HBc positive patients as regard different variables were shown in Table 3.

Survival analysis was done using Kaplan–Meier method and comparison between two survival curves was done using log-rank test which revealed insignificant difference between patients with negative anti-HBc and patients with positive anti-HBc, also insignificant difference between patients with or without OBI reactivation as regard survival rate (Table 4 and Figs. 1, 2).

**Discussion**

The natural course of HBV infection is determined by the interplay between virus replication and host’s immune response [22]. Chemotherapy may lead to an increase in virus replication and infection of more hepatocytes in the absence of an active host immune response [23].

Chemotherapy decreases the host’s immune response, so a period of time is necessary for the immune system to begin attacking the hepatocytes, where a massive replication of HBV has taken place [24]. For this reason, HBV reactivation often manifests between cycles of chemotherapy or at the end of therapy after the recovery of the host immune system [25]. The reported interval ranges from 1 to 9 months from initiation of chemotherapy. HBV reactivation can easily be missed, particularly in early stages, when salvage anti-viral therapy could be lifesaving [26]. Since OBI reactivation is asymptomatic and transient, regular frequent monitoring of ALT is essential although there is no guideline regarding frequency of testing [27].

Prophylaxis of HBsAg-negative/anti-HBc-positive patients undergoing highly immunosuppressive treatment for hematological malignancies is not conclusive and not routinely recommended [28,29]. Although the data of a recent meta-analysis recommended prophylaxis therapy for patients receiving rituximab-based chemotherapy due to increases the risk of OBI reactivation [30].

In Egypt, testing for the presence of HBsAg is the initial diagnostic examination used to determine HBV infection.
Anti-HBc was not used to as screening test to determine previous exposure to the hepatitis B virus. Hence, the aim of this study was to evaluate the prevalence and chemotherapy-induced reactivation of OBI among hepatitis B surface antigen negative patients with diffuse large B-cell lymphoma (DLBCL) patients and to determine the significance of anti-HBc.

### Table 3
Comparison between patients with OBI reactivation and patients without OBI reactivation in anti-HBc positive patients as regards different variables.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients with OBI reactivation ($N = 5$)</th>
<th>Patients without OBI reactivation ($N = 5$)</th>
<th>$P$-value (significance)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>53 ± 9.06</td>
<td>51.2 ± 8.11</td>
<td>0.75 (NS)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male (N) (%)</td>
<td>Female (N) (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 (80%)</td>
<td>1 (20%)</td>
<td>1.00 (NS)</td>
</tr>
<tr>
<td>Stage</td>
<td>II (N) (%)</td>
<td>III (N) (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>1.00 (NS)</td>
</tr>
<tr>
<td>IPI</td>
<td>L/I (N) (%)</td>
<td>I/H (N) (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (20%)</td>
<td>4 (80%)</td>
<td>1.00 (NS)</td>
</tr>
<tr>
<td>Response</td>
<td>CR (N) (%)</td>
<td>PR (N) (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 (100%)</td>
<td>4 (80%)</td>
<td></td>
</tr>
<tr>
<td>Fate</td>
<td>Alive (N) (%)</td>
<td>Dead (N) (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 (60%)</td>
<td>2 (40%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>5 (100%)</td>
<td>Zero (0%)</td>
<td>0.44 (NS)</td>
</tr>
</tbody>
</table>

Anti-HBc, hepatitis B core antibody; CR, complete remission; I/H, intermediate/high; IPI, International Prognostic Index; L/I, intermediate/high; $N$, number; NS, non-significant; OBI, occult hepatitis B infection; PR, partial remission.

### Table 4
Overall survival probability for different groups of patients.

<table>
<thead>
<tr>
<th></th>
<th>Number of patients</th>
<th>Events ($N$)</th>
<th>Censored ($N$) (%)</th>
<th>Median survival (years)</th>
<th>Range (years)</th>
<th>Statistic test for equality of survival distributions (Log Rank)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>Statistic df $P$-value (significance)</td>
</tr>
<tr>
<td>Patients with negative anti-HBc</td>
<td>62</td>
<td>6</td>
<td>56 (90.32%)</td>
<td>18</td>
<td>7–18</td>
<td>0.95 1 0.329 (NS)</td>
</tr>
<tr>
<td>Patients with positive anti-HBc</td>
<td>10</td>
<td>2</td>
<td>8 (80%)</td>
<td>18</td>
<td>10–18</td>
<td>2.24 1 0.134 (NS)</td>
</tr>
<tr>
<td>Patients with OBI reactivation</td>
<td>5</td>
<td>2</td>
<td>3 (60%)</td>
<td>18</td>
<td>10–18</td>
<td></td>
</tr>
<tr>
<td>Patients without OBI reactivation</td>
<td>5</td>
<td>0</td>
<td>5 (100%)</td>
<td>Can’t be computed since all patients are censored</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Anti-HBc, hepatitis B core antibody; $N$, number; NS, non-significant; OBI, occult hepatitis B infection.

Figure 1  Kaplan–Meier analysis of the overall survival probability in patients with positive and negative hepatitis B core antibody (anti-HBc).
screening among this group of patients before receiving chemotherapy.

Our study revealed that, among the 72 HBsAg negative sera of patients with DLBCL, anti-HBc was detected in 10 of 72 (13.89%) (95% confidence interval 6.9–22.2%). All the anti-HBc positive sera were anti-HBs negative. After the initiation of systemic chemotherapy, examination of the HBV serology revealed that 5 of the 10 anti-HBc-positive patients (50%) (6.94% as regarding all patients) became serologically positive for the HBsAg with a marked increase in ALT levels exceeding threefold which was molecularly detectable for the HBV-DNA (OBI reactivation). All of the 5 patients had OBI reactivation after the completion of all their chemotherapy cycles with mean time 9.4 ± 1.517 months after chemotherapy start (range 7–11 months). All of them received lamivudine therapy but 2 of them died due liver cell failure and the other three patients had been recovered.

Different studies had been done in patients with lymphoma and other hematological malignancies for the incidence of OBI and reactivation of OBI during and after different regimens of chemotherapy. Different figures in OBI and reactivation of OBI were reported, some were with our results and the others were different.

In China, Hui et al. [31] estimated HBV reactivation incidence in 244 HBsAg-negative lymphoma patients receiving chemotherapy was 3.3% (8/244). All the 8 patients were sero-positive for either anti-HBc or anti-HBs antibody. Also in China, Yeo et al. [10] who made their study among 104 CD20+ DLBCL patients, found that 80 out of 104 were HBsAg negative, 46 patients out of 104 (44.2%) were HBsAg negative/anti-HBc positive; 25 of these patients were treated with CHOP without HBV reactivation but among the other 21 patients who were treated with R-CHOP, five developed HBV reactivation, including one patient who died of hepatic failure.

In Japan, Matsue et al. [32] conducted a retrospective study on consecutive patients with CD20-positive B cell lymphoma before and after rituximab-containing treatment. Five out of 230 patients negative for HBsAg (2.2%) experienced HBV reactivation, representing an incidence of 8.9% of the anti-HBc-positive patients. In Hong Kong, Cheung et al. [33] included 47 lymphoma patients in their study, 10 out of 47 (21%) had OBI. One of the 10 patients, showed virological reactivation followed by biochemical reactivation without liver cell failure where entecavir treatment was used. Regarding the other nine OBI patients, their serum hepatitis B virus DNA levels fluctuated, but there was no associated biochemical reactivation.

In Italy, a prospective observational study of patients with hematological malignancies, Francisci et al. [34] reported the incidence of HBV reactivation was 18%, which is close to that detected in the present study. Also in Italy, Masarone et al. [35] who study 498 patients with non Hodgkin’s lymphoma 40% of patients were treated with monoclonal antibodies and 60% without. Ninety-six patients (19.28%) were anti-HBc+, HBsAg--; HBV reactivation occurred in ten subjects of this subgroup (10.42%). All of them were successfully treated with lamivudine.

In Egypt, Elkady et al. [36] showed that 18 (34%) out of 53 HBsAg-negative Egyptian patients with hematologic malignancies were found to be positive for anti-HBc. Five of the 53 (9.4%) patients with hematologic malignancies experienced HBV reactivation. In Greece, Zachou et al. [37] retrospectively evaluated the medical records of HBsAg negative patients who suffered HBV reactivation after chemotherapy or immunosuppression and identified 14 patients with occult or resolved infection. Twelve out of 14 patients were males. In 71.4% of them the primary diagnosis was hematologic malignancy; 78.6% had received rituximab as part of the immunosuppressive regimen. The median time from last chemotherapy schedule till HBV reactivation for 10 out of 11 patients who received rituximab was 3 (range 2–17) months. Three patients (21.4%) deteriorated, manifesting ascites and hepatic encephalopathy and 2 (14.3%) of them died due to liver failure.

In Taiwan, Hsu et al. [38] who made their study on 150 newly diagnosed lymphoma patients with resolved HBV infection who received rituximab-CHOP-based chemotherapy and found that the incidence of HBV reactivation and HBV-related hepatitis flares was 10.4 and 6.4 per 100 person-year, respectively and showed that severe HBV-related hepatitis occurred in 4 patients, despite entecavir treatment.

The reasons for the difference in the incidence in OBI reactivation among different studies remain to be elucidated.
However, immunosuppressive regimen, the intensity of treatment, study size, studied population characters, geographic differences in HBV prevalence, HBV genotypes, lack of a clear definition of OBI reactivation and differences in sensitivity of the methods used for detection of the virus genome may account for these differences [39].

Our study is not without limitation; as it lacked examination of liver biopsy to certify that patients with anti-HBc and having negative HBV-DNA had no occult HBV. Indeed, we found it unethical to expose the patient to this aggressive technique without direct benefit to them. Also, our study lacked patients treated with the golden standard regimen (R-CHOP) but we found it unethical to expose the patient to high incidence of OBI reactivation without lamivudine prophylaxis which may affect the result of this study.

Conclusion

The study concluded that anti-HBc screening is mandatory before chemotherapy. HBsAg-negative/anti-HBc-positive patients should be closely observed for signs of HBV reactivation through the regular monitoring of ALT. Prophylaxis lamivudine is recommended for OBI before chemotherapy.

A wider study on large number of patients is recommended. Also, HBV full genome amplification and sequencing are recommended in further research to identify the most susceptible HBV genome for HBV reactivation.

Authors’ contributions

* Concept, design, definition of intellectual content, data analysis, statistical analysis and manuscript preparation: Tamer A. Elbedewy.
* Literature search, manuscript review and manuscript editing: Tamer A. Elbedewy, Hossam Eldin A. Elashtokhy, Enaam S. Rabee, Gamal E. Kheder.
* Data acquisition, Clinical studies: Tamer A. Elbedewy, Hossam Eldin A. Elashtokhy.
* All authors have been read and approved the final version of the manuscript.

Conflict of interest

The authors report no conflict of interest.

References


