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Lack of Awareness in the Detection of Hepatitis B Virus Presence in Patients to Receive Immunosuppressive Therapy: An Experience from a Tertiary Care Hospital

İmmünsupresif Tedavi Verilecek Olan Hastalarda Hapatit B Virüs Varlığı Tespitindeki Farkındalığın Eksikliği: Bir Üçüncü Basamak Hastane Deneyimi

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ABSTRACT

Introduction: *Hepatitis B virus (HBV) reactivation in patients undergoing immunosuppressive therapy can be prevented with antiviral prophylaxis. It is recommended that all patients scheduled to receive immunosuppressive treatment be screened for hepatitis B surface antigen (HBsAg), hepatitis B core antibody (anti-HBcIgG), antibody against hepatitis B surface antigen (anti-HBs), hepatitis C virus antibody (anti-HCV), and human immunodeficiency virus antibody (anti-HIV) before the initiation of therapy. In this study, we aimed to evaluate the screening rates for HBV and the rates of appropriate preemptive treatment and prophylaxis among patients receiving immunosuppressive therapy.*

Materials and Methods: *This study included patients over the age of 18 who received immunosuppressive treatment for various reasons between January 1, 2017, and December 31, 2024, and whose data were fully accessible. Prior to the initiation of immunosuppressive therapy, patients were retrospectively evaluated for HBsAg, anti-HBs, and anti-HBc IgG screening, and whether they were appropriately referred for prophylactic or preemptive treatment based on the results.*

Results: *Data from 81 patients were fully accessible. It was determined that 48 patients were screened for all three HBV markers (HBsAg, anti-HBs, and anti-HBcIgG) before immunosuppressive therapy, while 18 patients had not undergone any HBV serological testing. In 15 patients, only HBsAg and anti-HBs were tested. All patients who were either not screened or partially screened were those receiving cytotoxic chemotherapy for solid organ malignancies. In contrast, patients receiving immunosuppressive or cytotoxic chemotherapy due to hematological malignancies, rheumatological diseases, or vasculitis had all undergone complete HBV serological testing prior to treatment. All of these patients received appropriate prophylactic treatment for HBV. Among the 18 patients with solid organ malignancies who were not screened before chemotherapy, two developed acute HBV reactivation. Entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide were used for prophylactic treatment. None of the patients who received prophylaxis experienced HBV reactivation.*

Conclusion: *While rheumatologists and hematologists demonstrated high awareness of the risk of hepatitis B reactivation, there remains a need to enhance interdisciplinary educational efforts to improve awareness among oncologists on this issue.*

Key Words: *Hepatitis B; Immunosuppressive therapy; Serological screening; Prophylactic treatment*

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ÖZ

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Giriş: *İmmün sistemi baskılayan tedavi altındaki hastalarda hepatit B virüs reaktivasyonu antiviral profilaksiyle engellenebilir. İmmünsupresif tedavi uygulanacak tüm hastalara, immünsupresif tedavi başlanmadan önce hepatit B yüzey antijeni (HBsAg), hepatit B core protein antikoru (anti-HBcIgG), hepatit B yüzey antijenine karşı oluşan antikor (anti-HBs), hepatit C virüs antikoru (anti-HCV) ve insan edinilmiş immün yetmezlik virüs antikoru (anti-HIV) taraması yapılması önerilmektedir. Sunulan çalışmada immünsupresif tedavi alan hastalarda hepatit B virüsü yönünden taranma oranlarıyla uygun preemptif tedavi ve profilaksi verilme oranlarının değerlendirilmesi amaçlandı.*

Materyal ve Metod: *Bu çalışmada 1 Ocak 2017 - 31 Aralık 2024 tarihleri arasında çeşitli sebeplerle immünsupresif tedavi alan ve verilerine tam olarak ulaşılan, 18 yaş üstü hastalar tarandı. Hastalara immünsupresif tedavi başlanmadan önce hastaların HbsAg, anti-HBs ve anti-HBcIgG açısından taranma oranları ve tarama sonuçlarına göre profilaksi veya preemptif tedaviye yönlendirilme oranları geriye dönük olarak değerlendirildi.*

Bulgular: *Çalışmada 81 hastanın verilerine tam olarak ulaşıldı. Hastaların 48'inde immünsupresif tedavi öncesi HbsAg, antiHBs ve anti-HBcIgG değerlerinin hepsine bakıldığı, 18 hastanın ise hiçbir hepatit B serolojik göstergesinin taranmadığı saptandı. On beş hastada ise yalnızca HBsAg ve anti-HBs bakılmış olduğu tespit edildi. Hiç tarama yapılmayan ve eksik tarama yapılan hastaların tamamı solid organ malignitesi nedeniyle sitotoksik kemoterapi alan hastalardı. Hematolojik malignite, romatolojik hastalık ve vaskülit nedeniyle immünsupresif tedavi ve sitotoksik kemoterapi verilen tüm hastalarda tedavi öncesi hepatit B'ye ait serolojik göstergeler tam olarak çalışılmıştı. Bu hastaların tamamı hepatit B için uygun endikasyonda koruyucu tedavi almaktaydı. Solid organ malignitesi nedeni ile sitotoksik kemoterapi verilen 18 hastada kemoterapi öncesi tarama yapılmamış olup, bu hastalardan ikisinde akut HBV alevlenme tablosu geliştiği görüldü. Profilakside entekavir, tenofovir disoproksil fumarat, ve tenofovir alafenamid kullanıldı. Profilaksi verilen hiçbir hastada HBV alevlenme tablosu gelişmedi.*

Sonuç: *Romatoloji ve hematoloji uzmanlarının hepatit B reaktivasyonu riski konusundaki farkındalıkları yüksek iken; onkologların farkındalıklarını artırmaya yönelik disiplinler arası eğitim faaliyetlerinin sıklığının artırılması gündeme gelmelidir.*

Anahtar Kelimeler: *Hepatit B; İmmünsüpresif tedavi; Serolojik tarama; Koruyucu tedavi*

INTRODUCTION

Hepatitis B virus (HBV) reactivation is associated with significant morbidity and mortality in patients receiving immunosuppressive therapy. It is well known that HBV reactivation caused by immunosuppression is a preventable condition. The definition of HBV reactivation varies in the literature. The aim of preventing HBV reactivation is to prevent life-threatening clinical outcomes such as hepatic decompensation or acute liver failure. A spectrum of serologic markers indicates ongoing or resolved HBV infection. The risk of HBV flare in patients with these patterns varies depending on the type of immunosuppressive therapy. Several issues regarding the prevention of HBV reactivation have not been fully resolved. These uncertainties include identifying the most appropriate population for screening, determining which individuals should receive prophylaxis with therapeutic agents for HBV, selecting the best antiviral agent to use, defining the duration of prophylaxis, and establishing the appropriate method and length for at-risk patients who do not receive prophylaxis[1]. Patients who will receive immunosuppressive therapy must be screened for HBsAg, anti-HBc IgG, and anti-HBs. If HBsAg and/or anti-HBc IgG are positive, it is recommended to perform HBV deoxyribonucleic acid (DNA) testing and determine the viral load. A risk assessment should be conducted based on the patient's HBV infection status and the degree of immunosuppression associated with the planned treatment. Accordingly, either prophylactic oral antiviral therapy or a preemptive monitoring approach should be selected. When prophylactic therapy is indicated, one of the following agents

is recommended: tenofovir disoproxil fumarate (TDF), entecavir (ETV), or tenofovir alafenamide (TAF). The treatment selection should be made by considering the underlying disease and the effects of the intended therapy on liver and kidney functions. In patients who are HBsAg positive, treatment should be initiated as soon as possible[2-4]. Despite the well-recognized importance of serological screening prior to initiating immunosuppressive therapy, deficiencies persist in clinical practice. The aim of this study was to assess the rate of HBV screening in patients receiving immunosuppressive treatment at our hospital, to evaluate the associated risk of reactivation, to determine the rate of appropriate prophylactic antiviral use, and to analyze the corresponding treatment outcomes.

MATERIALS and METHODS

Patients over 18 years of age who received immunosuppressive or cytotoxic chemotherapy at our hospital between January 1, 2017, and December 31, 2024, for rheumatic or autoimmune diseases, solid organ malignancies, or hematological malignancies were included in the study. Study data were obtained through a retrospective review of electronic medical records. Ethics approval for the study was obtained from the Amasya University Non-Interventional Clinical Research Ethics Committee (Approval No: E-76988455-050.01-263437; Date: 23.05.2025). Patients' age, gender, diagnosis, screening with HBsAg, anti-HBs, anti-HBcIgG, polymerase chain reaction HBV-DNA, and follow-up durations were evaluated. The records of patients who were HBsAg and/or anti-HBcIgG positive were examined to determine whether antiviral prophylaxis was administered.

HBV reactivation was defined according to the following criteria:

- In HBsAg positive patients: Conversion from undetectable to detectable HBV DNA; an increase of at least one log in HBV DNA levels in patients with previously detectable HBV DNA; or a three-fold elevation in alanine transaminase (ALT) or ALT ≥100 IU/mL in patients with increasing HBV DNA levels.
- In patients who were HBsAg-negative but anti-HBcIgG-positive: seroconversion resulting in HBsAg becoming positive, detection of HBV DNA in the serum, and/or biochemical evidence of hepatitis due to HBV reactivation[5].

Patients who were screened for HBsAg, anti-HBs, and anti-HBcIgG were considered fully screened; those who were screened for only HBsAg and anti-HBs but not anti-HBcIgG were considered partially screened; and those who were not screened with any HBV marker were considered unscreened[6].

Statistical analysis was performed using IBM SPSS version 21. HBV screening, antiviral prophylaxis use, and reactivation rates were reported as frequencies and percentages.

RESULTS

A total of 81 patients were included in the study. The mean age of these patients was 64.6 ± 21.1 years, and the female/male ratio was 45/36. The overall rate of complete screening for hepatitis B reactivation risk was 59.25%. The proportion of unscreened patients in our cohort was 22.2% (n= 18).

The distribution of patients across serologically defined groups (Group 1-Group 7) is summarized in Table 1. Notably, all patients in Group 1, Group 2, and Group 3 received prophylactic antiviral therapy, and no cases of HBV reactivation were observed in these groups. Two patients in Group 4, both diagnosed with lymphoma and undergoing intensive immunosuppressive therapy due to bone marrow transplantation, received prophylactic antiviral treatment. No HBV reactivation occurred in either of these patients. The other two patients in Group 4 were receiving tumor necrosis factor-α (TNF-α) inhibitor (etanercept) therapy for rheumatoid arthritis and were followed up without prophylaxis. HBV reactivation was not observed in these two patients. No patients in Groups 5, 6, or 7 received prophylaxis (Table 1).

Of the patients, 24 had rheumatologic or autoimmune diseases, 49 had solid organ malignancies, and eight had hematological malignancies and received immunosuppressive or cytotoxic

Table 1. Number of patients in groups according to serological markers

Group; viral markers	Number	Number of patients receiving prophylaxis	Rate of HBV reactivation n (%)
Group 1; HBsAg positive, HBV-DNA positive	6	6	0 (0)
Group 2; HBsAg negative, Anti-HBs positive, Anti-HBc IgG positive, HBV-DNA positive	1	1	0 (0)
Group 3; HBsAg negative, Anti-HBs positive, Anti-HBc IgG positive, HBV-DNA negative	9	9	0 (0)
Group 4; HBsAg negative, Anti-HBs negative, Anti-HBc IgG positive, HBV-DNA negative	4	2	0 (0)
Group 5; HBsAg negative, Anti-HBs positive, Anti-HBc IgG negative, HBV-DNA negative	12	0	0 (0)
Group 6; HBsAg negative, Anti-HBs negative, Anti-HBc IgG negative	31	0	0 (0)
Group 7; No viral marker screening performed	18	0	2 (11.1)

chemotherapy. All patients followed for hematological malignancy, rheumatologic, and autoimmune diseases were fully screened for hepatitis B reactivation risk. Among patients who received cytotoxic chemotherapy for solid organ malignancies, the rate of full HBV screening was 32.7%, while 36.7% were not screened at all (Table 2).

All patients who had an indication for hepatitis B prophylaxis or preemptive treatment-among those receiving immunosuppressive therapy (including steroids, TNF-α inhibitors, and cytotoxic chemotherapy) for rheumatologic/autoimmune diseases or hematological malignancies-were administered appropriate antiviral therapy. None of these patients experienced hepatitis B reactivation. Among patients with solid organ malignancies who were fully screened for hepatitis B reactivation risk, eight had an indication for prophylactic antiviral therapy; of these, six received treatment, with a prophylaxis compliance rate of 75% (Table 3). The two patients who did not receive prophylaxis were undergoing cytotoxic

Table 2. Screening rates for hepatitis B reactivation risk according to primary diseases in immunosuppressed patients

Primary Disease	Full Screening Performed n (%)	Partial Screening Performed n (%)	No Screening Performed n (%)	Total n
Rheumatologic or autoimmune disease	24 (100)	0 (0)	0 (0)	24
Solid organ malignancy	16 (32.7)	15 (30.6)	18 (36.7)	49
Hematologic malignancy	8 (100)	0 (0)	0 (0)	8

Table 3. Rates of appropriate preemptive treatment or prophylaxis administration and reactivation rates according to treatment subgroups in patients receiving immunosuppressive therapy

Administered Treatment	Patients Indicated for Preemptive Treatment or Prophylaxis for HBV (n)	Patients Receiving Appropriate Preemptive Treatment or Prophylaxis n (%)	Reactivation Rate in Patients Receiving Prophylaxis n (%)
Cytotoxic chemotherapy	8	6 (75)	0 (0)
TNF-α inhibitors	4	4 (100)	0 (0)
Steroids	6	6 (100)	0 (0)
Total	18	16 (88.8)	0 (0)

TNF-α: Tumor necrosis factor-alpha.

chemotherapy for breast and lung cancer, and their serologic markers were similar to those in Group 4. Despite not receiving prophylaxis, no HBV reactivation occurred in these patients.

In two patients who underwent cytotoxic chemotherapy for solid organ malignancy, no hepatitis B screening was performed prior to treatment. Following the initiation of chemotherapy, both patients developed elevated liver enzymes and bilirubin levels. Subsequent serologic testing revealed positivity for HBsAg, anti-HBcIgG, and HBV-DNA. The characteristics of these patients who developed HBV reactivation are detailed in Table 4.

Case 1

The first patient with suspected HBV reactivation was a 76-year-old woman with colon adenocarcinoma. Due to hepatic metastases, she received FOLFIRI combination chemotherapy (irinotecan 180 mg/m^2 (211 mg), leucovorin 400 mg/m^2 (486 mg), fluorouracil 400 mg/m^2 (486 mg) + bevacizumab 5 mg/kg (320 mg). After four cycles of chemotherapy (one month after the initiation of chemotherapy), serological test results were as follows: ALT= 376 U/L, aspartate aminotransferase (AST)= 211 U/L, international normalized ratio= 1.72, total bilirubin= 11.3 mg/dL, HBsAg positive, anti-HBs negative, anti-HBe positive, anti-HBcIgG positive, anti-HBcIgM negative, anti-HAV-IgM negative, anti-HCV and HCV-RNA negative, and HBV-DNA 122.700.000 IU/mL. It was determined that the patient had not been screened for HBV before chemotherapy. This condition was interpreted as chronic hepatitis B reactivation, and treatment with TDF 245 mg was initiated. Chemotherapy was continued with dose reductions. By the third month of antiviral therapy, ALT and bilirubin levels had normalized, and HBV-DNA levels became undetectable. HBsAg positivity persisted. TDF treatment was maintained. The patient died in the 14th month of antiviral therapy due to multiple organ metastases of colon adenocarcinoma.

Case 2

The second patient with suspected HBV reactivation was a 57-year-old man with pancreatic cancer. After pancreatic surgery, adjuvant gemcitabine 1000 mg/m^2 (1700 mg) chemotherapy

Table 4. Characteristics and Clinical Outcomes of Patients with HBV Reactivation

Case	1	2
Age (years)	76	57
Gender	Female	Male
Diagnosis	Colon adenocarcinoma	Pancreatic cancer
Chemotherapy regimen	FOLFIRI	Gemcitabine
Baseline ALT (U/L)	42	39
Baseline HBV DNA (IU/mL)	Unknown	Unknown
Baseline HBV serology HBsAg/anti-HBs/anti-HBc IgG	Unknown	Unknown
Time to HBV reactivation (months)	1	2
HBV serology at reactivation HBsAg/anti-HBs/anti-HBc IgG/anti-HBc IgM	+/-/+/-	+/-/+/-
HBV-DNA level at reactivation (IU/mL)	122.700.000	23.600
ALT level during HBV reactivation (U/L)	376	845
Antiviral agent used during hepatitis B reactivation	Tenofovir disoproxil fumarate (TDF)	Tenofovir alafenamide fumarate (TAF)
Hepatic failure	Did not develop	Did not develop
Outcome	Death due to progression of primary disease	Death due to progression of primary disease

HBV: Hepatitis B virus, HbsAg: Hepatitis B surface antigen, Anti-HBs: Hepatitis B surface antibody, Anti-HBc: Hepatitis B core antibody, ALT: Serum alanine aminotransferase, FOLFIRI: Fluorouracil + irinotecan.

Table 5. Comparison of HBV reactivation rates based on pre-treatment screening status in patients receiving immunosuppressive therapy (Chi-square test)

	Reactivation (+)	Reactivation (-)	P (χ^2)
Screening performed (n= 63)	0	63	
No screening performed (n= 18)	2	16	<0.001
Total (n= 81)	2	79	

was initiated. After five cycles of chemotherapy (two months after initiation), laboratory tests revealed the following findings: ALT= 845 U/L, AST= 1012 U/L, total bilirubin= 7.5 mg/dL, HBsAg positive, anti-HBs negative, anti-HBe positive, anti-HBcIgG positive, anti-HBcIgM negative, anti-HAV-IgM negative, anti-HCV and HCV-RNA negative, and HBV-DNA= 23.600 IU/mL. This patient also had not been screened for HBV prior to chemotherapy. The case was interpreted as chronic hepatitis B reactivation, and treatment with TAF 25 mg was initiated. Chemotherapy was discontinued. By the third month of antiviral therapy, the patient's laboratory results showed HBsAg positivity, anti-HBs negativity, and undetectable HBV-DNA levels. Aminotransferase and bilirubin levels normalized; however, the patient died two months after receiving four cycles of chemotherapy due to progression of pancreatic cancer.

According to the screening results, compliance with preemptive treatment or prophylaxis was 100% among patients with rheumatologic and hematologic malignancies, whereas it was 75% in patients receiving cytotoxic chemotherapy for solid organ malignancies (Table 3). Of the 18 patients who received preemptive or prophylactic antiviral therapy, seven were treated with ETV, five with TDF, and six with TAF; none experienced HBV reactivation.

In all patients from Group 1 and Group 2, antiviral therapy was continued after discontinuation of immunosuppressive therapy. In contrast, for patients in Groups 3 and 4, prophylactic therapy was maintained for an additional year following the cessation of immunosuppressive therapy.

HBV screening status was evaluated in patients scheduled to receive immunosuppressive therapy. Among the 81 patients included in the analysis, 63 (77.8%) were screened prior to treatment, while 18 (22.2%) were not. HBV reactivation occurred in two (11.1%) of the unscreened patients and in none of the screened patients. The difference in reactivation rates between the groups was statistically significant, suggesting that a lack of HBV screening prior to immunosuppressive therapy is associated with a higher risk of reactivation (Table 5).

DISCUSSION

HBV reactivation can manifest across a broad clinical spectrum, ranging from asymptomatic cases to severe and potentially fatal outcomes. It may also necessitate the discontinuation of immunosuppressive therapy or chemotherapy. Early discontinuation of treatment increases morbidity and mortality associated with the primary disease. Therefore, patients requiring immunosuppressive therapy should be screened for HBV reactivation risk using HBsAg, anti-HBs, anti-HBc, HBeAg, and HBV-DNA tests[7]. Bozkurt et al. reported an appropriate screening rate of 63.7% for HBV reactivation risk among patients receiving anti-TNF-α therapy [8]. In the study by Engin et al., only 23.1% of patients scheduled to receive immunosuppressive therapy underwent full HBV screening, while 49.7% were not screened at all[9]. In the present study, the full screening rate in 81 patients receiving immunosuppressive treatment was 59.3%, and the rate of no screening was 22.2%. These results reveal deficiencies in identifying patient groups at risk of HBV reactivation in our center. This issue appears more pronounced among patients with solid organ malignancies. Specifically, among 18 patients with solid organ malignancies who received cytotoxic chemotherapy without prior HBV screening, two (11.1%) developed HBV reactivation. This may be attributed to the higher incidence of solid organ malignancies compared

to hematological malignancies and the resulting heavier workload of medical oncologists under local healthcare conditions. Furthermore, the absence of absolute prophylaxis indications for every chemotherapy regimen used in solid tumors - or the lack of standardized protocols for viral screening associated with each chemotherapeutic agent -may reduce medical oncologists' vigilance in assessing viral serology prior to treatment.

The risk of hepatitis B reactivation associated with immunosuppressive therapy is closely linked to the presence of serological and virological HBV markers in a patient. The strongest risk factor is elevated HBV DNA levels (>2000 IU/mL)[10,11]. In our study, six patients (7.4%) screened prior to immunosuppressive treatment had overt hepatitis B infection (HBsAg positive, HBV-DNA positive), and all received antiviral prophylaxis. None of these patients experienced HBV reactivation. Among patients positive for HBsAg and/or anti-HBc IgG, reactivation risk is higher in those with detectable or high HBV DNA levels compared to those with negative or low HBV DNA levels. The risk of reactivation in HBsAg-positive patients is eight times higher than in those with isolated anti-HBc IgG positivity[12]. A consensus report from Türkiye recommends that in HBsAg(-)/anti-HBc(+) patients with negative HBV DNA, HBV DNA monitoring at three-month intervals should be performed without prophylaxis[7]. In our cohort, the rate of isolated anti-HBc IgG positivity was 4.94% (four patients). All four patients received cytotoxic chemotherapy for solid organ malignancy; two were administered HBV prophylaxis, while the other two were not. Prophylaxis was initiated in these two patients due to anticipated irregular follow-up, stemming from sociocultural and economic challenges. None of the patients developed HBV reactivation. Consistent with our findings, previous literature indicates that patients with isolated anti-HBc IgG positivity rarely experience HBV reactivation even in the absence of prophylactic treatment[13,14]. In a study by Fidan et al. involving 645 patients with solid organ malignancies who were HBsAg-negative and anti-HBc-positive, 602 patients did not receive antiviral prophylaxis, while 43 patients did. HBV reactivation occurred in none of the patients who received prophylaxis, whereas three cases of reactivation were observed in the non-prophylaxis group, corresponding to a reactivation rate of 0.49%[15].

The risk of HBV reactivation is higher in HBeAg-positive patients compared to those who are HBeAg-negative[16]. In our study population, all HBsAg-positive patients were also screened for HBeAg, and all were HBeAg-negative. We believe that the absence of HBV reactivation in patients positive for HBsAg and HBV-DNA, despite immunosuppression, was due to both antiviral prophylaxis and their HBeAg-negative status.

HBV reactivation is common during systemic chemotherapy. This is related not only to the chemotherapeutic agents used but also to the origin of the cancer (hematologic vs. solid organ). Patients with hematologic malignancies have a higher risk of HBV reactivation compared to those with solid organ malignancies and are considered high-risk. In HBsAg-positive patients undergoing treatment for hematologic malignancies, reactivation risk ranges between 40%-50%[17,18]. This risk is further increased with regimens containing high-dose steroids or rituximab (immunotherapy). In our study, eight patients with hematologic malignancies received cytotoxic chemotherapy and high-dose steroids; all were fully screened for HBV serology. Since none of the patients exhibited viral serological profiles indicating reactivation risk, antiviral prophylaxis was not administered. This result reflects the high level of awareness among hematology specialists regarding the risk of HBV reactivation.

TNF-α plays an important role in host defense, and patients treated with anti-TNF agents are more susceptible to infections. TNF-α suppresses HBV replication and stimulates HBV-specific cytotoxic T-cell responses, which are important for clearing HBV. Blocking TNF-α allows HBV to evade immune control and facilitates viral replication. While antiviral prophylaxis is recommended for HBsAg-positive patients, routine prophylaxis is not recommended for patients who are positive only for anti-HBc[19].

Lee et al. recommended screening for occult HBV infection before starting anti-TNF therapy in rheumatologic patients. They reported a 1.7% risk of HBV reactivation in patients with occult HBV infection treated with anti-TNF agents[20]. In our study, all patients treated with anti-TNF agents for rheumatologic or autoimmune diseases were fully screened for HBV serology. Four patients received antiviral prophylaxis; none developed reactivation (one patient in Group 1, one in Group 2, two in Group 4). Although routine prophylaxis is not recommended for isolated anti-HBc positivity, prophylaxis was given to two patients in Group 4 due to the non-zero risk of reactivation. Our findings demonstrate the careful approach of rheumatology specialists regarding the risk of HBV reactivation.

In a study comparing TAF and ETV for HBV prophylaxis in cancer patients undergoing chemotherapy, the risk of HBV relapse was reported to be higher with TAF[21]. However, other studies have shown TAF to be a safe and effective agent in preventing HBV reactivation[22]. TAF, TDF, and ETV are preferred over lamivudine, telbivudine, and adefovir due to their higher barrier to resistance in preventing HBV reactivation during cancer chemotherapy[23]. In our study, among 18 patients receiving preemptive or prophylactic antiviral therapy, seven received ETV, five received TDF, and six received TAF. None developed HBV reactivation. Our results indicate these three agents are highly effective in preventing HBV reactivation, with no superiority among them.

In conclusion, all patients scheduled to receive immunosuppressive agents for cancer, rheumatologic, or autoimmune diseases should undergo full screening for HBV reactivation risk before treatment initiation. Our study demonstrates that hematology and rheumatology specialists are meticulous in HBV reactivation screening, whereas a lack of awareness persists among oncology specialists. Strengthening interdisciplinary communication and educational initiatives may effectively raise awareness among oncologists and help bridge this gap.

Limitations

This study has several limitations, including its single-center design, retrospective nature, lack of immunosuppressive drug risk classification, and relatively small sample size.

ETHICS COMMITTEE APPROVAL

The study was conducted in accordance with the ethical standards outlined in the Declaration of Helsinki, revised in 2013, and was approved by the Amasya University Non-Interventional Clinical Research Ethics Committee (decision no: E-76988455-050.01-263437; date: 23.05.2025).

CONFLICT of INTEREST

The authors have no conflicts of interest to declare that are relevant to the content of this article.

AUTHORSHIP CONTRIBUTIONS

Concept and Design: MA

Analysis/Interpretation: MA, AMC

Data Collection or Processing: MA, AMC

Writing: MA, AMC

Review and Correction: MA, AMC

Final Approval: MA, AMC

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