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ORIGINAL ARTICLE

Examining the Seroprevalance and Antiviral Prophylaxis Rate of Hepatitis B and C Virus in Rheumatic Patients Treated with Biological and Targeted Synthetic Disease Modifying Anti-rheumatic Drugs: Results from a Tertiary Center in Central Anatolia

Biyolojik ve Hedefe Yönelik Sentetik Hastalık Modifiye Edici Antiromatizmal İlaçlarla Tedavi Edilen Romatizmal Hastalarda Hepatit B ve C virüs Seroprevalansının ve Antiviral Profilaksi Oranlarının İncelenmesi: Orta Anadolu'daki Üçüncü Basamak Bir Merkezden Sonuçlar

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ABSTRACT

Objective: To evaluate the epidemiological characteristics of hepatitis B virus (HBV) and hepatitis C virus (HCV) in rheumatic patients treated with biological and targeted synthetic disease modifying anti-rheumatic drugs (DMARDs).
Methods: This cross-sectional study was carried out between September 2021 and April 2022 at the Rheumatology Outpatient Clinic of Erciyes University Faculty of Medicine, and it included 200 patients [113 with axial spondyloarthritis (axSpA), 18 with psoriatic arthritis (PsA) and 69 with rheumatoid arthritis (RA)]. The demographic and clinical characteristics, treatment details and viral hepatitis serology of the patients were recorded. Those not receiving biological and/or targeted synthetic DMARDs (b/tsDMARDs) were excluded.
Results: The median age of the patients was 47 (39-58) years, and the median disease duration was 10 (7-15) years. Of the patients, 117 (58.5%) were female and 83 (41.5%) were male. The median duration of treatment with b/tsDMARDs was 6 (2-9) years. In the viral serological examinations, 1.5% of the patients were positive for HBsAg, 64.5% for anti-HBs, 23.5% for anti-HBc IgG, and 0.5% for anti-HCV. The anti-HBc IgG positivity rate was significantly higher in RA (34.8%) than axSpA patients (16.8%) and was similar to PsA patients (22.2%) ($p = 0.023$). Yet HBsAg, anti-HBs, and anti-HCV serologies were similar across patient subgroups ($p > 0.05$). A total of 44 (22%) patients were undergoing oral antiviral prophylaxis. Three (1.5%) patients who were anti-HBc positive and HBV DNA negative were followed without antiviral treatment. There was no viral reactivation in any patient.
Conclusion: Approximately one in four patients in our cohort showed anti-Hbc positivity, and almost all of them were using antiviral prophylaxis. Anti-HCV prevalence was much lower. Studies addressing viral hepatitis in rheumatic patients and/or patient subgroups, both at the national and local level, will enable rheumatologists to be more effective in managing HBV and HCV.

Keywords: Axial spondyloarthritis, HBV, HCV, Psoriatic arthritis, Rheumatoid arthritis.

ÖZ

Amaç: Biyolojik ve hedefe yönelik sentetik hastalık modifiye edici antiromatizmal ilaçlar (DMARD) ile tedavi edilen romatizmal hastalarda hepatit B virüsü (HBV) ve hepatit C virüsü (HCV)'nün epidemiyolojik özelliklerini değerlendirmek.
Gereç ve Yöntem: Bu kesitsel çalışma Eylül 2021 ile Nisan 2022 tarihleri arasında Erciyes Üniversitesi Tıp Fakültesi Romatoloji Polikliniği'nde gerçekleştirildi ve 200 hasta [113'ü aksiyal spondiloartrit (akSpA), 18'i psöriyatik artrit (PsA) ve 69'u romatoid artrit (RA)]] dahil edildi. Hastaların demografik ve klinik özellikleri, tedavi detayları ve viral hepatit serolojileri kaydedildi. Biyolojik ve/veya hedefe yönelik sentetik DMARD (b/tsDMARD) almayanlar çalışmadan dışlandı.
Bulgular: Hastaların medyan yaşı 47 (39-58) yıl, medyan hastalık süresi ise 10 (7-15) yıldı. 117'si (%58,5) kadın, 83'ü (%41,5) erkekti. B/tsDMARD ile medyan tedavi süresi 6 (2-9) yıldı. Viral serolojik incelemelerde hastaların %1,5'inde HBsAg, %64,5'inde anti-HBs, %23,5'inde anti-HBc IgG ve %0,5'inde anti-HCV pozitifliği tespit edildi. Anti-HBc IgG pozitifliği oranı RA hastalarında (%34,8) axSpA hastalarına (%16,8) göre anlamlı derecede yüksekti ve PsA hastalarına (%22,2) benzerdi ($p = 0,023$). Ancak HBsAg, anti-HBs ve anti-HCV serolojileri hasta alt grupları arasında benzerdi ($p > 0,05$). Toplam 44 (%22) hasta oral antiviral profilaksi tedavisi altındaydı. Anti-HBc pozitif ve HBV DNA negatif olan 3 (%1,5) hasta antiviral tedavi uygulanmadan takip edildi. Hiçbir hastada viral reaktivasyon görülmedi.
Sonuç: Kohortumuzdaki yaklaşık dört hastadan biri anti-Hbc pozitifliği gösterdi ve neredeyse tamamı antiviral profilaksi kullanıyordu. Anti-HCV prevalansı çok daha düşüktü. Romatizmal hastalarda ve/veya hasta alt gruplarında viral hepatitleri ele alan hem ulusal hem de yerel düzeydeki çalışmalar, romatologların HBV ve HCV'yi yönetmede daha etkin olmalarını sağlayacaktır.

Anahtar kelimeler: Aksiyal spondiloartrit, HBV, HCV, psöriyatik artrit, romatoid artrit.

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Introduction

Conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) have been used for many years in the treatment of inflammatory rheumatic diseases (1). Over the past two decades, millions of rheumatic patients have been treated with anti-tumor necrosis factor inhibitors (anti-TNFs). These were the first of the biologic DMARDs (bDMARDs) targeting pro-inflammatory cytokines [interleukin (IL)-1, IL-6, tumor necrosis factor (TNF), IL-17, etc.] in the inflammatory pathway and were introduced in the 2000s (2, 3). More recently, other biological agents and targeted synthetic DMARDs (tsDMARDs) that act by mechanisms different from anti-TNFs have been developed (4). Today, both bDMARDs and tsDMARDs are widely used to treat various immune-mediated inflammatory diseases, particularly the major rheumatological diseases such as axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), and rheumatoid arthritis (RA), which are commonly seen in clinical practice (5-8).

In terms of inflammatory diseases, infections are important in two ways. First, some infections can be the cause of musculoskeletal symptoms and/or systemic inflammatory conditions. Second, infections may worsen or reactivate as a result of immunosuppression in the treatment of inflammatory rheumatic diseases (9). Viral hepatitis is one of the most important infections to consider in terms of risk of reactivation during immunosuppressive therapy. For this reason, it is essential to evaluate the serologies of the hepatitis B virus (HBV) and the hepatitis C virus (HCV) in patients when planning the treatment with DMARDs and to apply the principles of protection according to test results (10, 11). HBV and HCV are estimated to affect more than 300 million people worldwide (12). In Turkiye, at least one third of the adult population encounters HBV; the overall prevalence of hepatitis B surface antigen (HBsAg) positivity is 4%, and anti-HCV positivity is 1% (13). The rate of HBV reactivation in the rheumatic population receiving immunosuppressive therapy ranges from 0.3% to 9%, depending on the underlying disease and treatment used (12).

Previously, various studies have examined HBV and HCV, both in the general population and in various rheumatic diseases (10, 12-16). However, the regional differences in the results obtained have also been highlighted (13). In this study, we aimed to evaluate the seroprevalence and prophylaxis rate of viral hepatitis (HBV and HCV) in the three most common rheumatic diseases (axSpA, PsA, and RA) encountered the rheumatology outpatient clinic of a tertiary hospital in Central Anatolia.

Material and Methods

This cross-sectional study was performed between September 2021 and April 2022 in Rheumatology outpatient clinic of Erciyes University Faculty of Medicine. Local ethics committee approval was obtained (Date: 22 September 2021, Approval Number:2021/612). We followed the principles of the Declaration of Helsinki and obtained written informed consent from all patients. Patients were included if they were over the age of 18, were undergoing b/tsDMARDs treatment, and met one of the following classification schemes: Assessment of SpondyloArthritis International Society (for axSpA) (17), ClASsification Criteria for Psoriatic Arthritis (for PsA) (18), and the American College of Rheumatology/European Alliance of Associations for Rheumatology (for RA) (19). Demographic and clinical characteristics as well as treatment-related data of the patients were recorded (i.e., name of last b/tsDMARDs used, total duration of b/tsDMARDs used, concomitant csDMARDs, and antivirals for viral hepatitis prophylaxis, if available). Disease activity was assessed, as previously described, with BASDAI (20) in axSpA, DAPSA (21) in PsA, and DAS28CRP (22) in RA. The exclusion criteria were the following: age ≤ 18 and rheumatic diseases except axSpA, PsA, and RA.

The results of laboratory tests [Hemogram, biochemistry, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), viral hepatitis serology, etc.] requested during the routine outpatient clinic applications of the patients were noted. In our department, HbsAg, anti-HBs, hepatitis B core antibody (Anti-HBc) tests for HBV serology and anti-HCV for HCV serology were requested in accordance with the guideline recommendations before starting bDMARDs and tsDMARDs. If HbsAg and/or anti-HBc positivity was detected, HBV DNA test was ordered, and if anti-HCV positivity is detected, HCV RNA was asked, and the relevant patient was consulted with hepatology (11). Definitions of reactivation for HBV and HCV were made according to the HBV DNA and HCV RNA levels at follow-ups (11, 23).

Statistical analyses

The normality of the distribution of the data was analyzes using the Shapiro-Wilk test. Descriptive statistics for continuous data are expressed as mean ± standard deviation (SD) or median (interquartile range [IQR]), while those for categorical data are expressed as number (%). For numerical variables, more than two group comparisons were made with the one-way analysis of variance test (post hoc test: Tukey's honestly significant difference) or with the Kruskal-Wallis test (post hoc test: Dunn) according to the normality. Pearson's chi-square test or Fisher's exact test was used to compare the categorical variables. Bonferroni's correction was applied to adjust for multiple comparisons. The TURCOSA program (Turcosa Analytics Ltd Co, Turkiye, www.turcosa.com.tr) was used for graphics. IBM SPSS Statistics for Windows, Version 22.0 (IBM Corp., Armonk, NY, USA) was used for all other statistical analysis. All $p < 0.05$ results were considered statistically significant.

Results

A total of 200 patients (113 axSpA, 18 PsA, and 69 RA) who met the inclusion criteria were enrolled in the study (Figure 1). The median age of the patients was 47 (39-58) years, the mean body mass index (BMI) was 29.6 ± 5,4 kg/m2, and the median disease duration

was 10 (7-15) years. Among the patients, 117 (58.5%) were female and 83 (41.5) were male.

Age, female sex, and disease duration were significantly higher in RA patients than in axSpA and PsA patients (for all, $p < 0.001$). Smoking was significantly higher in axSpA patients compared with PsA and RA patients ($p = 0.003$). In the laboratory evaluation, ESR was higher in RA than axSpA patients but did not differ from PsA patients significantly($p = 0.002$). We found that human leukocyte antigen B27 (HLAB27) positivity was higher in the axSpA group compared to the PsA group ($p < 0.001$). While the use of methotrexate and corticosteroids was higher in RA patients than in axSpA and PsA patients ($p < 0.001$ and $p < 0.001$, respectively), the rate of those using sulphasalazine was higher in RA patients than axSpA patients and was similar to PsA patients ($p = 0.023$). We did not find any difference between the patient groups in terms of other demographic and clinical characteristics, laboratory data, and treatment-related variables ($p > 0.05$) (Table 1).

Table 1. Demographic, clinical, laboratory, and treatment data of the patients

	axSpA (n=113)	PsA (n=18)	RA (n=69)	p
Age, years	45 (37.5-52)[a]	47.5 (34.8-57.8)[a]	57 (47-63)[b]	<0.001
Female, n (%)	40 (42.5)[a]	10 (55.6)[a]	59 (85.5)[b]	<0.001
BMI, kg/m^2	29.1 ± 5.1	29.8 ± 5.5	30.5 ± 5.7	0.261
Disease duration, years	10 (6-12)[a]	7 (3-13.3)[a]	13 (9.5-20)[b]	<0.001
Smoking, n (%)	37 (32.7)[a]	2 (11.1)[a, b]	9 (13)[b]	0.003
Comorbidities, n (%)				
Hypertension	20 (17.7)	2 (11.1)	20 (9)	0.108
Diabetes mellitus	12 (10.6)	4 (22.2)	8 (11.6)	0.429
Thyroid disorders	3 (2.7)	1 (5.6)	4 (5.8)	0.545
Pulmonary disease	8 (7.1)	1 (5.6)	12 (17.4)	0. 078
Cerebrovascular disease	1 (0.9)	0 (0)	1 (1.4)	0.778
Cardiac disease	4 (3.5)	1 (5.6)	5 (7.2)	0.543
Renal disease	5 (4.4)	0 (0)	1 (1.4)	0.288
History of malignancy	0 (0)	0 (0)	1 (1.4)	0.343
BASDAI	2.7 (1.8-4.2)	-	-	-
DAPSA	-	16.5 (6.3-23.3)	-	-
DAS28-CRP	-	-	3.2 (2.7-3.9)	-
ESR, mm/h	8 (5-21)[a]	10 (5.3-22.5)[a, b]	15 (6.5-30.5)[b]	0.002
CRP, mg/L	2.8 (1.4-7.1)	2.7 (1.2-6.1)	4.5 (1.2-9.8)	0.693
HLAB27 positivity, n (%)	57 (50.4)[a]	1 (5.6)[b]	-	<0.001
RF positivity, n (%)	-	-	55 (79.7)	-
Anti-CCP positivity, n (%)	-	-	52 (75.4)	-
Methotrexate, n (%)	3 (2.7)[a]	2 (11.1)[a]	37 (53.6)[b]	<0.001
Sulphasalazine, n (%)	4 (3.5)[a]	1 (5.6)[a, b]	10 (14.5)[b]	0.023
Leflunomide, n (%)	-	1 (5.6)	8 (11.6)	0.678
Hydroxychloroquine, n (%)	-	-	7 (10.1)	-
Corticosteroid, n (%)	1 (0.9)[a]	1 (5.6)[a]	25 (36.2)[b]	<0.001

Continuous variables are presented as mean ± standard deviation or median (interquartile range) according to normality tests.

A statistically significant difference between groups is indicated by different lower-case letters in one row.

axSpA, axial spondyloarthritis; BASDAI, bath ankylosing spondylitis disease activity index; BMI, body mass index; CCP, cyclic citrullinated peptide; CRP, C-reactive protein; DAPSA, disease activity index for psoriatic arthritis; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HLA, human leukocyte antigen; PsA, psoriatic arthritis; RA, rheumatoid arthritis; RF, rheumatoid factor.

Table 2. Evaluation of data on viral serology and antiviral treatments

	axSpA (n=113)	PsA (n=18)	RA (n=69)	p
HBsAg positivity	1 (0.9)	0 (0)	2 (2.9)	0.449
Anti-HBs positivity	75 (66.4)	12 (66.7)	42 (60.9)	0.740
Anti-HBc IgM positivity	0 (0)	0 (0)	0 (0)	-
Anti-HBc IgG positivity	19 (16.8)[a]	4 (22.2)[a, b]	24 (34.8)[b]	0.023
Anti-HCV positivity	0 (0)	0 (0)	1 (1.4)	0.343
HBV DNA positivity before DMARD(s) treatment	0 (0)	0 (0)	1 (1.4)	0.343
HCV RNA positivity	0 (0)	0 (0)	0 (0)	-
Viral reactivation	0 (0)	0 (0)	0 (0)	-
Prophylaxis of viral hepatitis	19 (16.8)	3 (16.7)	22 (31.9)	0.055
Entecavir	11 (9.7)	1 (5.6)	15 (21.7)	
Tenofovir	8 (7.1)	2 (11.1)	7 (10.1)	

Data are presented as n (%).

A statistically significant difference between groups is indicated by different lower-case letters in one row.

Anti-HBc, hepatitis B core antibody; Anti-HBs, hepatitis B surface antibody; Anti-HCV, antibody against hepatitis C virus; axSpA, axial spondyloarthritis; HBsAg, hepatitis B surface antigen; HBV DNA, hepatitis B virus DNA; PsA, psoriatic arthritis; RA, rheumatoid arthritis.

Detailed information about the b/tsDMARD treatments used by patients is shown in Figure 2 and the most used drug was etanercept (23%). On the other hand, MTX (21%) was the most common csDMARD used concomitantly with b/tsDMARDs in our patient cohort (Table 1). In addition, the median duration of b/tsDMARDs treatment was 6 (2-9) years. The median duration of b/tsDMARDs treatment use in AxSpA, PsA, and RA patients was 6 (3-9), 4 (1-7.3), and 6 (1.3-9) years respectively, and there was no statistically significant difference between the groups ($p = 0.125$).

In HBV-related serological examinations, three (1.5%) of the patients were positive for HBsAg, 129 (64.5%) for anti-HBs, and 47 (23.5%) for anti-HBc IgG (Figure 3). Forty-four patients (22%) had HBsAg negative/anti-HBc IgG positive serology. While the rate of anti-HBc IgG positivity was significantly higher in RA patients than axSpA patients, it was similar to PsA patients ($p = 0.023$). Moreover, one (0.5%) patient was anti-HCV positive serology, but their HCV RNA was negative. Yet HBsAg, anti-HBs, and anti-HCV were similar across patient subgroups ($p > 0.05$). A total of 44 (22%) patients were undergoing oral antiviral prophylaxis. A total of three (1.5%) patients, including two RA patients and one PsA patient, who were anti-HBc positive and HBV DNA negative were followed without antiviral treatment. The antiviral treatment distribution was

27 (61.4%) entecavir and 17 (38.6%) tenofovir. There was no difference in the rate of antiviral treatment between patients with AxSpA, PsA, and RA (p = 0.055). In addition, viral hepatitis reactivation was not observed in any patient. Detailed laboratory analyzes of HBV and HCV are shown in Table 2.

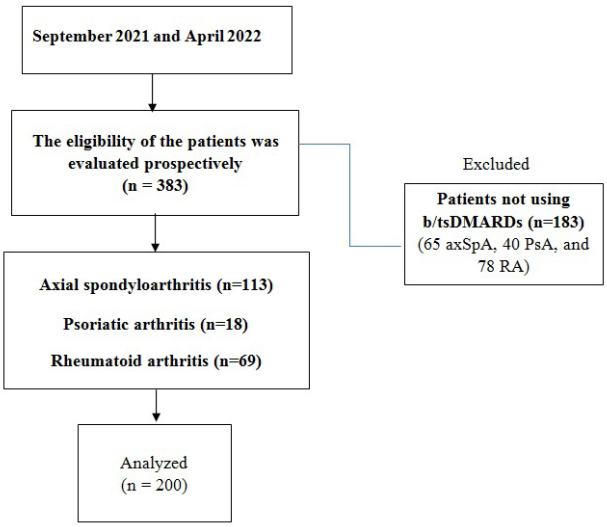

Figure 1. The flowchart diagram for the participants.

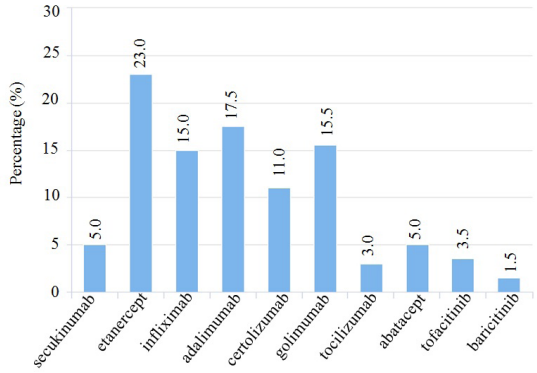

Figure 2. Distribution of bDMARDs and tsDMARDs used by patients.

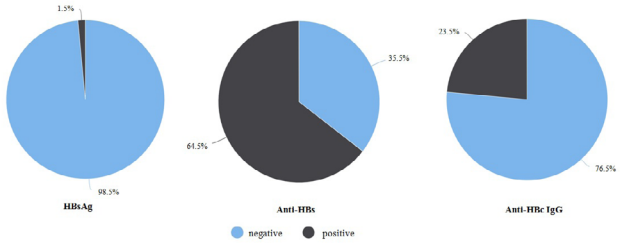

Figure 3. Distribution of HBsAg, Anti-HBs, and Anti-HBc IgG serologies among all patients.

Discussion

Our study examining the serology of viral hepatitis in three different major rheumatological diseases showed that HBsAg positivity was 1.5%, anti-HBs positivity 64.5%, anti-HBc positivity 23.5%, and anti-HCV positivity was 0.5% in patients (AxSpA, PsA, and RA) using b/tsDMARDs. In addition, the rate of those receiving viral hepatitis prophylaxis was 22%, and the rate of prophylaxis use was 93.6% of patients who needed to be assessed for prophylaxis according to their viral serology. No patients developed viral reactivation for a median of 6 years on b/tsDMARDs.

Biologic therapies treating AxSpA, PsA, and/or RA can be broadly divided into anti-TNF biologics and non-TNF biologics (4). The anti-TNF group includes the following: a fusion protein formed by the fusion of the human TNF receptor 2 with the Fc portion of human IgG1 (etanercept); three monoclonal antibodies (infliximab, adalimumab, and golimumab), and a monoclonal antibody fragment (certolizumab) (4, 24). Non-TNF biologics include such drugs as T cell costimulatory inhibitors (abatacept), IL-6 inhibitors (tocilizumab), IL-17 inhibitors (secukinumab and ixekizumab), and B-cell depleters (rituximab) (25). Janus kinase (JAK) inhibitors (tofacitinib and baricitinib) are classified under the heading of tsDMARDs and are recommended to be used as an equivalent or alternative to bDMARDs in phase II of RA and axSpA and at varying stages for PsA, according to different disease domains (4, 6-8).

When HBV enters the body, it multiplies in hepatocytes, and in the following periods, it can result in the following forms: 1) HBsAg positivity with or without anti-HBc positivity (chronic HBV infection); 2) HBsAg negativity and anti-HBc positivity (past HBV infection); 3) HBsAg negativity and anti-HBc positivity together with normal ALT and undetectable serum HBV-DNA (resolved HBV infection); and 4) HBsAg negativity and anti-HBc positivity with detectable but usually low levels of serum HBV-DNA (occult HBV infection). The HBsAg-negative/anti-HBc-positive form(s) is clinically insignificant if there is no immunosuppression. However, such factors as the type and dosage of drugs used in patients undergoing immunosuppressive treatment, the underlying disease, the viral load, and the use of antiviral prophylaxis affect the rate of HBV reactivation, which varies between 0.3% and 9% depending on these conditions (12, 26). For example, Su et al. (27) have reported that rituximab-based treatments and anti-HBs negativity constitute the most important risk factors for HBV reactivation in patients using chemotherapy and immunosuppressives (including bDMARDs). Lin et al. (28) emphasized that HBV reactivation rates in rheumatic patients undergoing DMARDs treatment were lower in resolved HBV than in chronic HBV infection and in those using antiviral therapy compared to those not using it. However, in a multicenter retrospective study in which 4060 rheumatic patients undergoing b/tsDMARDs treatment were analyzed in our country, Çapkın et al. (12) found no relationship between reactivation rates and disease subtypes. They also reported that all the reactivations consisted of those who should be followed up in terms of antiviral treatment according to viral hepatitis serologies but who did not use antiviral. In another study evaluating 3147 RA and 6071 SpA biological users, one RA patient undergoing rituximab therapy

developed reactivation despite antiviral prophylaxis (14). In the current study, there were no patients with HBV reactivation, and also HCV reactivation, which is clinical entity less frequently expected than HBV reactivation (26). This result may be due to the fact that the rates of antiviral use among patients requiring follow-up for prophylaxis in viral serology were higher in our study compared to the study of Çapkın et al. (12) (93.6% vs. 49%). In addition, there was no patient in our cohort using rituximab, a bDMARD that is thought to be more related to reactivation (29). Moreover, we think that to prevent reactivation in these patients, compliance with antiviral therapy is important, and there is a need for objective tests to monitor antiviral therapy.

In addition to the studies on viral hepatitis serology in the general population, this topic has been discussed in terms of the different aspects of different rheumatic diseases (10, 13, 16). Dağlı et al. (10) found 4.5% HBsAg positivity, 22.4% anti-HBs positivity, 1.5% anti-HCV positivity, and 23.8% anti-HBc positivity in patients with ankylosing spondylitis. Yılmaz et al. (30) reported that the prevalence of HBsAg was 2.3%, and the prevalence of anti-HCV was 1.1% in RA patients, and these two viral serological tests were 3% and 1.1%, respectively, in patients with ankylosing spondylitis. In a multicenter study examining the epidemiological features of HBV and HCV in biologic therapy users, it was determined that HBsAg positivity was 2% and 2.6%, anti-HBs positivity was 34% and 32.3%, anti-HBc positivity 12.5% and 20.3%, anti-HCV positivity 0.3% and 0.8%, and HBV DNA positivity was 12.5% and 3.5% in SpA and RA patients, respectively (14). In our study, 1.5% of the patients were positive for HBsAg, 35.5% for anti-HBs, 23.5% for anti-HBc, and 0.5% for anti-HCV. Our results showed partial similarity with the results of a large cohort study (12) conducted in Turkiye, which includes treatments and patient subgroups similar to our study in some aspects, such as the rate of HBsAg positivity, the rate of anti-HCV positivity, and anti-HBc positivity being higher in RA patients than axSPA patients. Yet, the different viral hepatitis serology results we obtained in patient subgroups may be attributed to regional differences highlighted in previous studies (13) and/or the smaller sample size of our study.

The strength of our study is that such studies from different centers make an additional contribution to the literature due to the regional variation in viral hepatitis serology (13). However, this study had some limitations. First, it does not include healthy controls that would enable the viral hepatitis serology to be comparable to the general population. Second, it has a relatively small sample size. Lastly, our results cannot be generalized to the whole population as the study include data obtained from only one center.

Conclusion

Our results showed that approximately one in four rheumatic patients using b/tsDMARDs had anti-Hbc positivity, and almost all of them were using antiviral prophylaxis. In addition, HBsAg positivity was 1.5%, anti-HBs positivity 64.5%, and anti-HCV positivity was 0.5% in these patient cohorts. The fact that viral hepatitis seropositivity rates in rheumatic patients and/or patient subgroups vary between studies suggests the need for more comprehensive national and local evaluations. Knowledge of actual HBV and HCV seroprevalence in patients undergoing b/tsDMARDs treatment in their local area would allow rheumatologists to manage patients more effectively and to reduce viral reactivation.

Conflict of interest

The authors have no conflicts of interest to declare.

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Statement of Ethics

This study was approved by the Erciyes University Clinical Research Ethics Committee (Date:22 September 2021, Approval Number:2021/612). This study was conducted in accordance with the Declaration of Helsinki and written informed consent was obtained from all patients.

Author contributions

HK, GC, and SŞ designed the study. HK, GC, SŞ, and HK acquired the data. HK and HK analyzed and interpreted the data. All authors were involved in writing of the manuscript. The manuscript has been approved by all authors for publication.

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