ORIGINAL ARTICLE

Frequency of hepatitis B virus infection among patients with rheumatoid arthritis: a study from a tertiary care centre in Peshawar

Abdul Jabbar[1], Salim Badshah[2*], Muhammad Abbas[3], Ahmad Ali[4], Numan Khan[5], Naveedullah[6]

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ABSTRACT

Background and Objective: Understanding the prevalence is essential for developing guidelines for screening and managing hepatitis B virus in rheumatoid arthritis patients, particularly in settings like Peshawar, where the burden of both diseases is likely to be high and viral infectivity may rise because of immunosuppression induced by anti-rheumatoid therapy. Therefore, this study was conducted to determine the frequency of Hepatitis B virus (HBV) infection among patients with rheumatoid arthritis presenting at a tertiary care hospital in Peshawar.

Methods: A cross-sectional study was conducted on 231 patients diagnosed with RA. Diagnosis was confirmed using clinical assessment and laboratory investigations, including rheumatoid factor and anti-cyclic citrullinated peptide. All laboratory tests were performed in a single hospital laboratory under the supervision of a senior pathologist. HBV infection was confirmed using a third-generation enzyme-linked immunosorbent assay for hepatitis B surface antigen with a cut-off value of 2.0. An independent *t*-test was applied, keeping $p < 0.05$ as statistically significant.

Results: The age range of patients was 18-60 years, with 43% males and 57% females. Use of disease-modifying antirheumatic drugs was reported by 58% patients while steroid alone was used by 66% patients. HBV testing revealed that only 4% patients had positive and active hepatitis B virus infection. No statistical significance ($p > 0.05$) was observed between HBV infection and age, gender, or type of treatment.

Conclusion: The frequency of rheumatoid arthritis patients infected with Hepatitis B was very low in the population from Peshawar. However, there is a need to screen hepatitis B virus in all patients undergoing anti-arthritic therapy for improving early diagnosis and management in such cases.

Keywords: Hepatitis B, rheumatoid arthritis, immune-suppression, therapy, DMARDs.

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Correspondence to: Salim Badshah
*Medical Specialist, DHQ Hospital Timergara, Khyber Pakhtunkhwa, Pakistan.
Email: mr.salimbadshah@gmail.com
Full list of author information is available at the end of the article.

Introduction

Hepatitis B virus (HBV) is a major global public health concern, responsible for a spectrum of liver disorders ranging from acute hepatitis to chronic conditions such as hepatic fibrosis, cirrhosis, and hepatocellular carcinoma.[1] The World Health Organization (WHO) estimates that 254 million people were living with chronic hepatitis B infection in the year 2022, with 1.2 million new infections each year.[2] This alarming increase underscores the urgent need for early diagnosis and effective management strategies to prevent progressive liver damage and reduce HBV-related mortality.[3]

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease that primarily affects the joints but may also present with significant extra-articular manifestations .[4] Its pathophysiology involves complex immune dysregulation, leading to persistent synovial inflammation and progressive destruction of cartilage and bone .[5] If not adequately treated, RA can result in considerable morbidity, functional disability, and an elevated risk of mortality due to its systemic involvement.[6]

Immune dysregulation in RA increases patients' susceptibility to various bacterial and viral infections, including HBV.[7] This risk is further heightened by the use of immunosuppressive therapies, particularly biological agents, which are commonly employed in RA management.[8] Reactivation of HBV in such patients may result in severe

complications, including acute liver failure, posing a significant clinical challenge during immunomodulatory treatment.[9]

Despite the well-documented risk of HBV reactivation associated with immunosuppressive therapies such as corticosteroids, disease-modifying antirheumatic drugs (DMARDs), and other biological agents, there remains a scarcity of published literature on the prevalence of HBV infection among RA patients who are not receiving these treatments.[10] Several studies have reported that people with RA combined with HBV infection, especially those with occult HBV infection or resolved carriers, may reactivate HBV during treatment with anti-rheumatic drugs .[7,9,11]

The exact pathophysiology of RA remains incompletely understood; however, external triggers such as infections, smoking, and trauma may initiate autoimmune responses in genetically susceptible individuals, leading to synovial hypertrophy, chronic joint inflammation, and extra-articular manifestations .[12] The standard treatment for RA involves the use of DMARDs. In patients with coexisting chronic HBV infection, Etanercept, a tumor necrosis factor inhibitor, is considered a safer biological option. However, in individuals with advanced HBV-related liver disease, particularly those with Child-Pugh class B or higher, the use of biologic agents is generally contraindicated .[13]

In Pakistan, where HBV is endemic, it is important to investigate the incidence of HBV among patients with rheumatoid arthritis, in addition to its general prevalence in the population .[14] Understanding this prevalence is essential for informing screening strategies and guiding the management of RA patients, particularly in settings such as Peshawar, where the burden of both conditions has historically been high .[15] This study addressed this gap by determining the frequency of HBV infection among RA patients presenting to a tertiary care hospital in Peshawar. The findings were expected to provide evidence to support local clinical guidelines and improve the management of RA patients at risk of HBV.

Methods

This cross-sectional observational study was conducted in the Department of General Medicine at Lady Reading Hospital, Peshawar, over a 6-month period from August 5, 2019, to February 5, 2020. A total of 231 patients who met the inclusion criteria and presented during the study period were enrolled using consecutive sampling. This approach allowed us to capture the maximum number of available cases, minimize selection bias, and provide a representative sample of RA patients from the hospital population.

The inclusion criteria were adults aged ≥18 years of both genders, with a diagnosis of rheumatoid arthritis established through standard guidelines by the treating physician and documented in hospital records. Patients with known and documented prior HBV infection, preexisting chronic liver disease of any etiology as confirmed through medical records, patients on current or prior treatment with steroids or biologic immunomodulatory agents, patients having known bleeding disorders or other significant immunodeficiency states, evidence of recent (within 6 months) blood transfusion or organ transplant, or having a current pregnancy were excluded.

All patients were enrolled in the study after taking written informed consent.

The diagnosis of RA was established by the treating rheumatologist or physician after clinical evaluation and laboratory findings, including rheumatoid factor and anti-cyclic citrullinated peptide, as documented in hospital medical records.

For HBV screening, venous blood samples were collected and analyzed in the hospital laboratory. HBV infection was determined using a third-generation enzyme-linked immunosorbent assay (ELISA) for hepatitis B surface antigen (HBsAg), with a cut-off value of 2.0 defining a positive result. All laboratory procedures were conducted under the supervision of a senior pathologist with more than 5 years of experience.

Demographic and clinical data, including age, sex, body mass index (BMI), and vaccination status, were recorded for each patient. Ethical approval for this study was obtained from the Institutional Review Board of Lady Reading Hospital, Peshawar, prior to data collection.

Statistical analysis

Data were entered and analyzed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were presented as frequencies and percentages. Associations between HBV infection and demographic/clinical variables were assessed using chi-square tests for categorical variables and independent *t*-tests for continuous variables, with a p-value < 0.05 considered statistically significant.

Results

The study included 231 patients diagnosed with rheumatoid arthritis. Of these, 99 (42.9%) were male and 132 (57.1%) were female. Regarding age distribution, 72 patients (31.2%) were between 18 and 30 years, while 159 (68.8%) were between 31 and 60 years. A majority of patients, 164 (71.0%), had a BMI ≤25 kg/m², whereas 67 (29.0%) had a BMI >25 kg/m². A total of 134 patients (58.0%) were receiving disease-modifying antirheumatic drugs (DMARDs), and 152 (65.8%) were on corticosteroid therapy (Table 1). Nine patients (4%) tested positive for HBsAg, indicating HBV infection (Figure 1).

Table 1. *Baseline demographic data of enrolled patients (n = 231).*

Variables		Frequency	%
Age (years)	18-30	72	31%
	31-60	159	69%
Gender	Male	99	43%
	Female	132	57%
BMI (kg/m^2)	<25	164	71%
	>25	67	29%
Use of DMARDs	Yes	134	58%
	No	97	42%
Use of steroids	Yes	152	66%
	No	79	34%

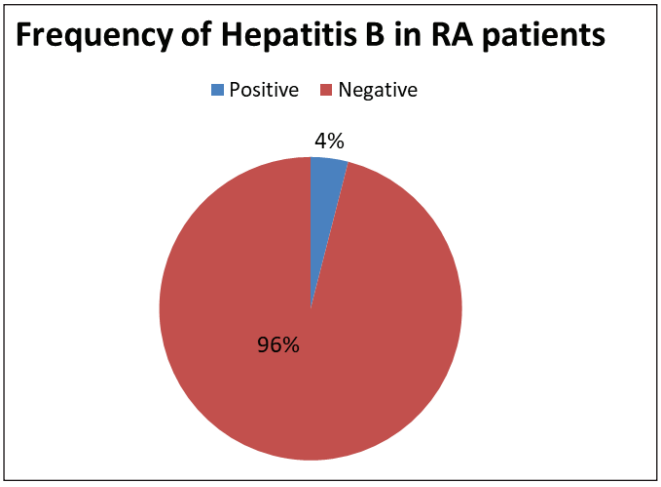

Figure 1. *Frequency of Hepatitis B among RA patients included in the study (n = 231).*

Stratified analysis of HBV infection among RA patients is presented in Table 2 which describes that out of the 231 patients, nine (4%) were positive for HBsAg. Fisher's Exact Test did not reveal any statistically significant associations between HBV infection and use of DMARDs or corticosteroid therapy (p = 0.99, each).

Discussion

The present study shows contrasting low results in terms of frequency of HBV positive cases (4%) in our cohort of RA patients, as compared to international studies. For instance, a retrospective cohort study from Taiwan reported a prevalence of approximately 7% among RA patients.[16] Similarly, a study from Japan highlighted distinct transmission dynamics, with approximately 20% or more of patients with rheumatic diseases are infected with HBV.[17] It may also be influenced by methodological factors, such as the exclusion criteria applied, the diagnostic assays used, and differences in healthcare infrastructure. Furthermore, the persistence and potential

Table 2. *Stratification of Hepatitis B with various demographic factors (n = 231).*

Variables		Hepatitis B		*p*-value*
		Yes	No	
Age (years)	18-30	03	69	0.99
	31-60	06	153	
Gender	Male	04	95	0.99
	Female	05	127	
BMI (kg/m^2)	<25	06	158	0.72
	>25	03	64	
	No	05	141	
Use of DMARDs	Yes	05	129	0.99
	No	04	93	
Use of steroids	Yes	06	146	0.99
	No	03	76	

**Fisher Exact Test, p-value < 0.05 as significant.*

reactivation of HBV remain important considerations in RA patients receiving immunosuppressive therapy, underscoring the need for careful screening and monitoring.[18,19]

Several studies from different regions have reported varying prevalence rates of HBV among patients with RA and related rheumatologic conditions. For example, in a cohort of 268 RA patients from Iran, predominantly female (82.2%) with a mean age of 46 ± 14 years, HBsAg was detected in 4 patients (1.49%).[20] A multicenter study from Turkiye evaluating both RA and ankylosing spondylitis (AS) reported mean ages of 49.0 ± 13.2 years in RA and 37.3 ± 10.5 years in AS, with HBsAg positivity observed in 35 RA patients (2.3%) and 27 AS patients (3%).[21] Similarly, another study from Bulgaria assessing 23 AS and 24 RA patients found HBsAg positivity in 2 RA patients (8%) and anti-HBc positivity in 7 (29%). Among the AS group, 2 patients (8%) were HBsAg positive and 9 (39%) were anti-HBc positive.[22] Similarly, a study from China including 30 patients of RA having co-infection with HBV reports that HBV co-infection significantly aggravates the disease in patients with RA resulting in an increased disease activity, a loss of body immune status, an altered normal state of immunoglobulin and T-lymphocyte subsets, and a loss of organism immune function, and an increased degree of inflammatory response.[23]

The frequency of HBV positivity observed in this study (4%) aligns with the lower end of the range reported in previous studies from different populations .[16,19-21] One possible explanation for this finding is the exclusion of patients receiving biological therapies, who are known to have an increased risk of HBV reactivation.[23] Despite these limitations, the results highlight the ongoing clinical relevance of HBV screening in RA patients, particularly in HBV-endemic regions such as Pakistan, and provide a basis

for further research to inform evidence-based screening and management guidelines. The findings of this study indicate the importance of early detection and appropriate management of HBV in patients with RA. Preventing HBV-related liver complications is particularly relevant in this population, as RA itself imposes a considerable systemic burden and a significant adverse biological change in the course of RA disease occurs with concomitant HBV infection. [24] These results also support the need for clinical guidelines that emphasize routine HBV screening and the consideration of prophylactic antiviral therapy in RA patients receiving or preparing to receive immunosuppressive treatment.

Limitations of the study

This study, however, has several limitations. The cross-sectional design restricts causal inferences, and the small number of HBV-positive cases (*n* = 9) limited the statistical power to detect associations between HBV infection and demographic or clinical factors. Consequently, the absence of significant associations in stratified analyses should be interpreted with caution. Further selection bias by excluding patients receiving therapy may have contributed to the lower prevalence observed in our cohort. Therefore, future studies with larger, multicenter cohorts and longitudinal follow-up are required to better understand the relationship between RA and HBV.

Conclusion

Although the frequency of Hepatitis B virus infection is relatively low in patients with rheumatoid arthritis, the findings highlight the importance of incorporating routine HBV screening into the management of RA patients, particularly in endemic regions such as Peshawar. Such screening is essential to ensure patient safety, prevent HBV-related complications, and guide the appropriate use of immunosuppressive therapies during the management of rheumatoid arthritis.

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List of Abbreviations

anti-CCP	Anti-cyclic citrullinated peptide
BMI	Body mass index
DMARDs	Disease-modifying antirheumatic drugs
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
RA	Rheumatoid arthritis
RF	Rheumatoid factor
WHO	World Health Organization

Conflicts of interest

None to declare.

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None to disclose.

Ethical approval

The study was approved by the Institutional Ethics Committee of Lady Reading Hospital Peshawar vide Letter No: LRHMTH/0094 dated 14-03-2019.

Authors' contributions

AJ, SB: Conception and design of study, data collection, drafting, and critical review of manuscript.

MA, AA, NK, N: Data collection, analysis and drafting, and interpreting the results section with critical intellectual input.

ALL AUTHORS: Approval and full responsibility of the final version of the manuscript to be published.

Authors' Details

Abdul Jabbar[1], Salim Badshah[2], Muhammad Abbas[3], Ahmad Ali[4], Numan Khan[5], Naveedullah[6]

1. Assistant Professor, Department of Medicine, Qazi Hussain Ahmed Medical Complex, Nowshera, Pakistan
2. Medical Specialist, DHQ Hospital Timergara, Pakistan
3. Medical Officer, Category D Hospital Wari, Pakistan
4. Medical Officer, Department of Internal Medicine, Lady Reading Hospital Peshawar, Pakistan
5. Medical Officer, DHQ Hospital Lakki Marwat, Pakistan
6. Medical Officer, Medical A Ward, DHQ Hospital Timergara, Pakistan

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