Research Article

Doi: 10.4274/Vhd.97269
Viral Hepatitis Journal 2014; 20(1): 28-31

Correlation Between Hepatitis B and C Positivity and Rheumatoid Factor Levels in Patients with Rheumatoid Arthritis

Romatoid Artritli Hastalarda Hepatit B ve C Pozitifliğinin Romatoid Faktör Düzeyleri ile İlişkisi

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ABSTRACT

Objective: Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder characterized by joint damage and destruction. The role of genetic factors, immunological disorders, gender, hormonal causes and infections, trauma and stress on the etiology of the disease has been investigated. Although hepatitis B and C are included among the infections that have been implicated in the etiology of the disease, there is no evidence to support this hypothesis. We aimed to examine both the prevalence of hepatitis B and C virus infections and the correlation between hepatitis B and C virus infections and rheumatoid factor levels in patients with RA.

Materials and Methods: 114 patients with rheumatoid arthritis had undergone serologic testing for hepatitis and data were recorded for these patients. The patients were divided into two groups according to their test result for rheumatoid factor as seropositive and seronegative patients. The control group included 100 subjects who had no rheumatoid arthritis and received no immunosuppresive therapy.

Results: HBsAg was positive in 5 patients (4.3%), in the group with rheumatoid arthritis. In the control group out of 100 patients, 3 had positive HBsAg (3%). Anti-HCV positivity was found in 4 patients (3.5%) in the RA group compared to 2 subjects in the control group (2%).

Conclusion: No significant difference was observed in HBsAg and Anti-HCV positivity between the RA patient group and the control group. *(Viral Hepatitis Journal 2014; 20(1): 28-31)*

Key words: Hepatitis B, hepatitis C, rheumatoid arthritis

ÖZET

Amaç: Romatoid artrit (RA), eklem hasarı ve destrüksiyonu ile karakterize kronik inflamatuar otoimmün bir hastalıktır. Etiyolojide genetik faktörler, cinsiyet, hormonlar, enfeksiyonlar, travma ve stresin rolü olduğu düşünülmektedir. Etiyolojide suçlanan enfeksiyonlar içerisinde hepatit B ve C enfeksiyonları da yer almakla birlikte bu hipotezi destekleyecek kanıtlar mevcut değildir. Bu çalışmada, RA'lı hastalarda hem hepatit B ve C virüs enfeksiyon sıklığını hem de romatoid faktör düzeyleri ile ilişkisini araştırmayı amaçladık.

Gereç ve Yöntemler: Romatoid artritli 114 hastanın hepatit açısından serolojik testleri çalışılarak kayda alındı. Bu hastalar romatoid faktör düzeylerine göre seropozitif ve seronegatif olmak üzere iki guruba ayrıldı. Kontrol gurubu olarak romatoid artrit hastalığı bulunmayan ve immünsüpresif tedavi almayan 100 kişi çalışmaya alındı.

Bulgular: Romatoid artritli hasta gurubunda 5 hastada (%4,3) HBsAg pozitifliği saptandı. Kontrol gurubunda 3 hastada(%3) HBsAg pozitifliği saptandı. Anti-HCV romatoid artritli hasta gurubunda 4 hastada (%3,5) pozitifken, kontrol gurubunda 2 hastada (%2) pozitif saptandı.

Sonuç: HBsAg ve Anti-HCV pozitifliği açısından romatoid artritli hasta gurubu ve kontrol gurubu arasında anlamlı bir fark gözlenmedi. *(Viral Hepatit Dergisi 2014; 20(1): 28-31)*

Anahtar Kelimeler: Hepatit B, hepatit C, romatoid artrit

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disorder characterized by joint damage and destruction. It is also associated with extra-articular signs and symptoms such as cardiovascular diseases, infections, treatment-related renal failure and death, which evidently affect morbidity and mortality (1,2,3). The prevalence of the disease is around 1%. The role of genetic factors, immunological disorders, gender, hormonal causes, infections, trauma and stress on the etiology of the disease has been investigated (4,5). The rheumatoid factor (RF) is positive in 70%-80% of patients with RA, demonstrating a correlation with the severity of nodular and extra-articular manifestations (6).

Although hepatitis B and C are included among the infections that have been implicated in the etiology of the disease, there is no evidence to support this hypothesis (7,8,9,10). However, due to the immunosuppressive agents used for treatment, hepatitis B virus (HBV) and, hepatitis C virus (HCV) reactivation may lead to observable and substantially important clinical signs and symptoms (11,12).

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Viral Hepatitis Journal, published by Galenos Publishing.

Approximately one third of the world's population have been exposed to or are currently infected with HBV. There are 350 million people with chronic HBV infection all over the world, where 75% are from Southeast Asia and the Western Pacific region (13). Chronic hepatitis B includes a wide range of infections from inactive hepatitis B surface antigen carrier to progressive chronic hepatitis including hepatocellular carcinoma (14). Every year 500 000-700 000 people die of HBV related cirrhosis and hepatocellular carcinoma (15). Studies have shown that the prevalence of HBsAg in Turkey is between 2 and 7% although it varies from region to region (16).

Similarly, some 3% of the world's population are infected with HCV. The mean anti-HCV positivity rate was found to be 0.3%-1.7% in our country (16,17,18).

The presence of HBV and HCV infections is important in patients with RA because of both its implications in the etiopathogenesis of RA and potential for reactivation with immunosuppressive therapies used. In the present study, we aimed to examine both the prevalence of HBV and HCV infections and the correlation between HBV and HCV infections and RF levels, which are important in the prognosis of patients with RA.

Material and Methods

Data from 130 patients who were diagnosed with RA according to the ACR 1987 criteria, and followed by the Immunology and Rheumatology Polyclinic of Adnan Menderes University were retrospectively evaluated. Among all, 114 patients had undergone serologic testing for hepatitis, and data were recorded for these patients. The patients were divided into two groups according to their test result for RF as seropositive and seronegative patients. The control group included 100 subjects who had no RA and received no immunosuppresive therapy, but underwent endoscopy for any reason at the gastroenterology clinic, and their files were reviewed, and their serologic test results for hepatitis were recorded.

Results

All of the patients with RA were using at least 2 disease-modifying-drugs while the subjects in control group had no chronic disease, and received no immunosuppressive therapy.

Among a total of 114 patients, HBsAg was positive in 5 (4.3%) patients, and negative in 109 (95.7%) patients in the group with RA. In the control group, out of 100 patients, 3 had positive (3%), and 97 had negative HBsAg (97%). No statistically significant difference was found in HBsAg positivity between the two groups (p=0.726). Anti-HBs antibodies were positive in 20 patients in RA group (17.5%) compared to 17 subjects in control group (17%), and there was no significant difference between the two groups (p=1,000). Anti-HCV positivity was found in 4 (3.5%) patients in the RA group compared to 2 subjects in the control group (2%). No statistically significant difference was found in anti-HCV antibody positivity between the two groups (p=0,687). In conclusion, no significant difference was observed in HBsAg, anti-HBs, and anti-HCV positivity between the RA patient group and the control group (Table 1).

When patients with RA were classified according to their RF positivity, 68 (59.6%) patients were found to be seropositive and 46 (40.4%) patients seronegative. In the RF positive group, HBsAg positivity was 5.8% and anti-HBs antibody positivity was 20.5% while in the RF negative group, HBsAg positivity was 2.17% and anti-HBs positivity was 3.04%. Anti-HCV positivity was 2.94% in the RF-positive group, and 4.34% in the RF-negative group. No statistically significant difference was observed in HBsAg positivity, anti-HBs positivity and anti-HCV positivity between the RF-positive and RF-negative patient groups (p=0.647, 0.329, and 1 000, respectively) (Table 2).

Discussion

Studies indicate that the prevalence of HBsAg varies from 2% to 7% in our country (16). The prevalence of hepatitis B seems to show various rates in different regions, however, it appears that the prevalence has a tendency to increase roughly from west to east (19,20,21,22). The highest rate of HBsAg positivity was observed in Eskişehir, Antalya, Diyarbakir, Adana, Elazig, Sivas and Erzurum with local differences. The highest endemic region of HBsAg was, as expected, the Diyarbakir region, with a rate of up to 10% (23).

In the present study, HBsAg positivity rate was 3% in the control group compared to 4.3% in the RA group. In the patient group with RA, the rate of HBsAg positivity was higher compared to the general population in Aydin. The mean anti-HCV positivity rate was found to be 0.3%-1.7% in our country (17,18).

Table 1. The relationship between HBsAg, anti-HBs and anti-HCV positivity in the RA patient group and the control group

	Patients n=114	Controls n=100	p
HBsAg (+)	5	3	0,726
HBsAg (-)	109	97	
Anti-HBs (+)	20	17	1,000
Anti-HBs (-)	94	83	
Anti-HCV (+)	4	2	0,687
Anti-HCV (-)	110	98	

Table 2. The relationship between HBsAg, anti-HBs and anti-HCV positivity in the RF-positive and RF-negative patient groups

	RF(+)	RF(-)	Total	p
HBsAg (+)	4	1	5	0.647
HBsAg (-)	64	45	109	
Anti-HBs (+)	14	6	20	0.329
Anti-HBs (-)	54	40	94	
Anti-HCV (+)	2	2	4	1.0
Anti-HCV (-)	66	44	110	

RF: Rheumatoid factor

However, we found a higher rate of anti-HCV positivity such as 2% in the control group and 3.5% in the RA patients group.

In a study by Cefle et al. in the Kocaeli region, RA patients had a HBsAg positivity of 5.3%, and and anti-HCV positivity of 1.6% (23). Our rates were 4.3% and 3.5%, respectively. The prevalence of HBsAg was similar to the one reported for Turkey in both studies. But, when prevalence of HCV positivity is considered to be around 0.3%-1.7%, there is a higher risk of 3.5% in patients with RA in the Aydin region. However, it should also be noted that this region had a 2% of HCV positivity in general population, which was higher than the mean rate in Turkey. Barbosa et al. found an anti-HCV positivity rate of 3.4% in patients with RA, while it was reported to be 0.65% by Maillefert et al (24,25). The study by Permin et al. found that HBsAg was 4% in patients with RA, and reported that this rate was 20 times higher than in the general Danish population (26). In the present study, both HBsAg and anti-HCV positivity were higher in patients with RA compared to the control group, however there was no statistically significant difference between the two groups.

Based on the RF levels, HBsAg positivity was 5.8%, and anti-HCV positivity was 2.94% in seropositive patients compared to 2.17 and 4.34%, respectively in seronegative patients. HBsAg positivity was higher in the group of seropositive patients, whereas anti-HCV positivity was higher in the group of seronegative patients. Similarly, anti-HBs positivity was 20.5% in the seropositive group compared to 13.4% in the seronegative group. Anti-HBs positivity was also higher in the seropositive group. These results suggest that HBV may be involved in the etiology in the seropositive group of RA patients, and HCV in the seronegative group of RA patients.

Hepatitis B and C reactivation can be seen during immunosuppressive therapies used in rheumatic diseases (11,12). Studies show that HBV reactivation usually occurs within 15 to 60 days of therapy as well as any other time throughout the treatment period. Although many cases are asymptomatic, there are also reports of decompensated hepatic failure and death. No consensus exists about any treatment strategy to prevent HBV reactivation in patients with rheumatic disease receiving immunosuppressive therapy. However, it has been suggested that all HBsAg (+) patients should start with prophylactic antiviral drugs before they receive immunosuppressive therapy; HBsAg (-), anti-HBsAg (-), and anti-HBc (-) patients should be vaccinated; and HBV-DNA and ALT levels should be closely monitored for reactivation of HBV in HBsAg (-), anti-HBsAg (-/+), and anti-HBc (+) patients (27).

Conclusion

Although our study did not observe a significant relationship it is at least known that hepatitis B and hepatitis C infections whose roles in the etiopathogenesis of RA remain to be elucidated may result in reactivation with immunosuppressive therapies. Thus, patients should undergo appropriate serological testing before initiation of an immunosuppressive therapy, and receive prophylaxis if required.

Conflict of interest: None declared.

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