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Romatoid Artritli Hastalarda Alkol Dışı Yağlı Karaciğer Hastalığı Sıklığı
Frequency of Non-Alcoholic Fatty Liver Disease in Patients with Rheumatoid Arthritis

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Özet

Amaç: Romatoid Artrit anılı hastalarda alkol dışı yağlı karaciğer sıklığını araştırmayı amaçladık.

Gereç ve Yöntem: Ocak 2018 ile Aralık 2019 yılları arasında fizik tedavi kliniğince takip edilen RA hastaları çalışmaya dahil edildi. Bu hastaların dosyaları taranarak demografik verileri, biyokimyasal, radyolojik verileri kaydedildi. Kontrol grubu olarak dispepsi nedeniyle gastroenteroloji polikliniğine başvuran hastalar alındı.

Bulgular: Çalışmaya 59 RA hastası 59 kontrol grubu hastası dahil edildi. Kontrol ve hasta grubunun yaş ortalaması ve cinsiyet dağılımı açısında fark yoktu. Cinsiyet dağılımı hasta grubunda kadın erkek dağılımı 51:8, kontrol grubunda ise 50:9 idi (p=0,79). Yaş ortalaması hasta grubunda 52±10 yıl, kontrol grubunda ise 48±12 yıl idi (p=0,23). Alkol dışı yağlı karaciğer sıklığı Romatoid Artrit grubunda 16 (27.1%), kontrol grubunda ise 21(35.6%) idi (p: 0.32).

Sonuç: Bu çalışmada beklenilenin aksine RA'da kontrol grubunda göre NAFLD sıklığının artmadığı görülmüştür.

Anahtar Kelimeler: Romatoid Artrit, Alkol Dışı Yağlı Karaciğer Hastalığı, Kronik Karaciğer Hastalığı

Abstract

Objective: To determine the frequency of non-alcoholic fatty liver disease in patients with rheumatoid arthritis.
Methods: Patients with rheumatoid arthritis who were followed up by the physical therapy clinic between January 2018 and December 2019 were included in this study. The demographic and biochemical data of these patients were recorded by scanning their files. The presence of non-alcoholic fatty liver was investigated by scanning ultrasonography and computed tomography documents. Patients who applied to the gastroenterology outpatient clinic due to dyspepsia were included as the control group.
Results: Fifty-nine rheumatoid arthritis patients and 59 control group patients were included in the study. There was no difference between the control and patient groups in terms of mean age and gender distribution. The gender distribution was 51: 8 in the patient group and 50: 9 in the control group (p = 0.79). The mean age was 52 ± 10 years in the patient group and 48 ± 12 years in the control group (p = 0.23). The frequency of non-alcoholic fatty liver disease was 16 (27.1%) in patients with rheumatoid arthritis and 21 (35.6%) in the control group (p: 0.32).
Conclusion: Nonalcoholic fatty liver disease is not more frequent in patients with rheumatoid arthritis.

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disorder which is the most common inflammatory arthritis affecting 0.5 to 1% of general population worldwide (1). Rheumatoid arthritis has several extra-articular feature and liver injury one of these, increased levels of transaminases have been seen in 18 to 50% cases (2). A retrospective study on 188 autopsy cases of RA found, 65% of patients had abnormal liver biopsies one-half having mild portal chronic inflammatory infiltrate of the portal tract and small foci of necrosis, and one in four having fatty liver changes (3).

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease, which can cause cirrhosis and hepatocellulary carcinoma. Nonalcoholic fatty liver disease is defined as the abnormal accumulation of fats (liver fat >5- 10% of liver weight), primarily in the form of triglycerides in those with daily use of alcohol (≤ 20 g ethanol/d) with worldwide prevalence of (10-40%) (4).
While investigating the reason for the increased transminit in RA, it has been determined that one of the reasons may be fatty change in liver, many years ago. These fatty changes may be due to the both diseases may have common inflammatory pathogenesis (5-8).

The frequency of NAFLD in RA is expected to increase due to this common pathogenesis, but there are few studies on this subject and these studies do not include a control group. With this study, we aimed to investigate the frequency of NAFLD in RA.

Methods

Rheumatoid arthritis patients followed by the Physical Therapy and Rehabilitation Department of Gaziosmanpasa University Hospital between January 2018 and December 2019 were included in the study.

We performed a retrospective review of the medical records of patients.

The exclusion criteria were patients who abuse alcohol, presence of any other chronic liver disease such as chronic hepatitis B, chronic hepatitis C, autoimmune hepatitis, primary biliary cholanghitis, any cause of cirrhosis, Wilson disease, hemochromatosis.

Details regarding the demographic characteristics, such as, age, sex, smoking habits, laboratory records were available from a computer database, medications were recorded.

The demographic and clinical characteristics of the above patients were compiled and compared with age- and gender-matched controls who were admitted to our gastroenterology department for dyspepsia complain. The ratio of cases to controls was fixed at 1:1.

Nonalcoholic fatty liver disease was diagnosed based on characteristic ultrasonographic features which include Bright hepatic echoes, increased hepato-renal echogenicity and vascular blurring of portal or hepatic vein have been classified as unique sonographic features of NAFLD (9). Liver biopsy for histological evidence of hepatic steatosis was not required.

Statistical Analysis.

All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) package for Windows version 21. Continuous variables were expressed as mean ± SD. Differences between the two groups (the cases and the controls) were analysed using the chi square test and Fisher's exact test for categorical data, and the Mann-Whitney test and independent t-test were used for continuous variables. For all tests, probability values (p values) < 0.05 were considered to indicate statistical significance.

Results

Ninety rheumatoid arthritis patients were evaluated and 59 rheumatoid arthritis patients and 59 control group patients were included in the study.

Female gender was 51 (86%) and 50 (84%) in RA group and control group, respectively. The gender distribution was 51: 8 in the patient group and 50: 9 in the control group (p = 0.79). The mean age was 52 ± 10 years in the RA group and 48 ± 12 years in the control group (p = 0.23). There was no difference between the control and patient groups in terms of mean age and gender distribution (Table 1).

The frequency of non-alcoholic fatty liver disease was 16 (27.1%) in patients with rheumatoid arthritis and 21 (35.6%) in the control group (p: 0.32)(Table 1).

When comparing the mean AST and ALT averages were compared in patients with NAFLD and without NAFLD, ALT and AST were found to be significantly higher in the presence of NAFLD (AST was 24 ± 11, 19.7 ± 6, group with and without NAFLD, respectively, p = 0.04, ALT was 25 , 9 ± 15, 19 ± 12 group with and without NAFLD, respectively, p = 0.01) (Table 2).

A difference was found between the patients with fatty liver and those without fatty liver in terms of female gender in the whole study group and the patient group with RA (p = 0.03) (Table 2).

Table 1. Characteristics of all groups.

	RA	Control	p
Age	54 ± 10	49 ± 12	>0.05
Sex Female	51 (86%)	50(84%)	>0.05
Male	8 (14%)	9 (16%)	
Smoking	6 (12%)	5 (8%)	>0.05
Diabetes Mellitus	2 (3%)	1 (1%)	>0.05
Hypertension	2 (3%)	2 (3%)	>0.05
NAFLD	16 (27.1%)	21 (35.6%)	>0.05

RA: Rheumatoid arthritis, NAFLD: Non alcholoic fatty liver disease

Table 2. Characteristics of patients with or without NAFLD.

	RA with NAFLD	RA without NAFLD	p
Age	54.4±9.4	54.6±10.9	>0.05
Sex Female	16	36	**0.03**
Male	0	7	
Smoking	2	6	>0.05
Diabetes Mellitus	2	4	>0.05
Hypertension	4	7	>0.05
AST	24 ± 11	19.7 ± 6	**0.04**
ALT	25.9 ± 15	19 ± 12	**0.01**

RA: Rheumatoid arthritis, NAFLD: Non alcholoic fatty liver disease, ALT: Alanin transaminase, AST: Aspartat transaminase

Discussion

It has been suggested that NAFLD association with RA may increase due to common pathophysiological mechanisms such as increased inflammatory activity, increased TNF alpha, increased cell turnover, therefore NAFLD frequency in RA may also increase, too. However, the number of studies on this topic is scarce, and the results are contradictory. In this study, which we conducted to investigate the evidence of this theoretically acceptable view, we showed that NAFLD did not increase in patients with RA compared to the control group.

In this study, we found frequency of NAFLD in patients with RA as 27.1% and in the control group as 35.6%. Although not statistically significant, the frequency seemed to be less than in the control group. Unfortunately, Turkey is one of the world's leading countries regarding NAFLD frequency; our control group data also supports this. A study conducted in Pakistan found that NAFLD's frequency in RA patients was 20.3% (n=39) (10). Rajalingham et al. and Mori et al. investigated the NAFLD with abdominal ultrasonography only in RA patients with increased enzyme levels; NAFLD was identified in 46 of 112 patients (4.7% of all

cohort) and 45 out of 51 patients with increased transaminase, respectively. Although it may seem like a low frequency compared to the entire group of patients with RA, as is known, an increased transaminase level is not a diagnostic criterion for NAFLD. Therefore, it is expected that the frequency of NAFLD in the entire study group would be higher; however, in both of these working groups, NAFLD frequency of the whole group has not been investigated, nor is there a control group (13,14). In this study, there was no difference between the patient and control groups in terms of frequency. The aim of these two studies, which evaluated RA patients with increased transaminase, was to investigate the hypothesis that there may be an association between fatty liver and MTX use. The authors compared the frequency of MTX use in patients with RA and patients with fatty liver and RA and found more hepatic steatosis in patients using MTX (11,12). However, several subsequent studies have shown that MTX use is not associated with an increase in NAFLD frequency (13,14).

A study conducted by Ursini et al. (15), which investigated the C3 complement as a predictor for NAFLD in patients with RA, identified NAFLD in 41 (25%) of 164 RA patients, which supports our study. Ursini et al. (15) also revealed that the C3 complement could be used as a biomarker in NAFLD diagnosis.

It is thought that TNF alpha may play a key role in the pathogenesis of NAFLD, so TNF may be a treatment target in this disease, which has not yet had adequate treatment. Anti-TNFs are used in RA as well as in many inflammatory diseases. Contrary to this expectation, which is in line with being therapeutically effective in treating fatty liver in RA, there were reports of NAFLD cases that developed with treatment and regressed with discontinuation of the treatment (16). These findings have also been a warner in that NAFLD in RA patients can be seen more, even though its frequency is expected to be decreased, with anti-TNF therapy.

Our study has several limitations while providing some strength, such as involving a sufficient number of patients in the study and having a control group. First, due to retrospective design, the persons who assess the fatty liver were not always the same person. (This could cause interpersonal variability bias.) Second, the NAFLD diagnosis was based on imaging studies, not biopsy. However, it should be kept in mind that the EASL and AASLD guidelines do not recommend biopsies for all NAFL patients diagnosed with imaging studies (17,18).

Conclusion

As the frequency of NAFLD increases throughout the community, it also increases in patients with RA. As in EULAR's recommendations, all RA patients should be investigated for NAFLD. Early diagnosis and treatment of NAFLD are essential for RA patients' overall survival and quality of life.

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Ethics:

Ethics committee approval was not obtained due to the retrospective planning of the study which had done before 2020 .

Therefore, this study has no **Ethical Review Board and number**

Informed consent was not obtained due to the retrospective planning of the study

Conflict of Interest Statement

The authors have no conflicts of interest to declare

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Kefeli A collected data, provided and cared for study patients, participated in writing or technical editing of the manuscript.

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