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Risk of the Development of Fibrosis in Metabolic Dysfunction-Associated Fatty Liver Disease in Patients with Rheumatoid Arthritis

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ABSTRACT

Introduction: Individuals diagnosed with rheumatoid arthritis (RA) face a heightened risk of developing metabolic dysfunction-associated fatty liver disease (MAFLD). The primary objective of this study was to examine the progression of hepatic fibrosis through non-invasive tests in patients with MAFLD, both those with RA and those without RA.

Methods: In our retrospective study, a total of 120 MAFLD patients aged between 18 and 65 years, excluding those with juvenile RA, were included. Patients were divided into two main groups as patients with (n=60) and without (control group, n=60) RA. Fibrosis-4 (FIB-4) and NAFLD Fibrosis Score (NFS) (NAFLD/MAFLD fibrosis) scores were used to determine the risk of hepatic fibrosis in patients with MAFLD. These scores were compared between the two groups. The relationship between FIB-4 and NFS scores and other parameters was evaluated. SPSS 25.0 software was used for statistical analysis, and significance was accepted as $p<0.05$.

Results: The RA group exhibited a higher NFS value than the control group ($p<0.05$). Receiver operating characteristic analysis indicated that NFS, although relatively weak, could be considered a viable variable for diagnosis ($p<0.05$). Notably, a statistically significant correlation was identified between the FIB-4 score and several other factors, including age, estimated-glomerular filtration rate, platelet (PLT) count, and aspartate aminotransferase values ($p<0.001$; $r=0.860$). Similarly, a statistically significant correlation was found between the NFS score and factors such as age ($p<0.001$), albumin ($p<0.001$), PLT count ($p<0.001$), and alanine aminotransferase values ($p<0.05$) ($r=0.956$).

Conclusion: Our study highlights that patients with both MAFLD and RA face a heightened risk of fibrosis progression compared with those without RA. While existing literature acknowledges MAFLD's association with liver fibrosis, there is a scarcity of research on RA's influence in this context. Our findings emphasize RA as an additional risk factor for liver fibrosis, particularly among patients with MAFLD. Consequently, liver fibrosis is more prevalent in patients with MAFLD and RA.

Keywords: Fibrosis, MAFLD, rheumatoid arthritis

Introduction

Persistent inflammation and excessive buildup of collagen in the extracellular matrix, primarily driven by chronic inflammation and damage to hepatocytes, play a pivotal role in the development of chronic liver disease. Over time, this fibrosis can progress to cirrhosis, portal hypertension, and liver failure. The etiological factors contributing to this condition include obesity, viral infections, systemic diseases, alcohol consumption, and metabolic-associated fatty liver disease (MAFLD). Despite liver biopsy being considered the gold standard for diagnosis, its invasiveness and limitations in fibrosis assessment have spurred interest in non-invasive alternatives. Notably, patients with rheumatoid arthritis (RA) are at an increased risk of developing MAFLD and subsequent liver fibrosis. Early detection of hepatic fibrosis in patients with RA is paramount for preventing complications, improving their quality of life, and mitigating healthcare costs. Unfortunately, there is a dearth of research investigating the influence of RA on fibrosis in individuals with MAFLD.

Although liver biopsy is regarded as the "gold standard" for diagnosis, it comes with limitations in evaluating fibrosis, potentially leading to heterogeneity within the liver parenchyma. Furthermore, it is an invasive procedure that may not be practical for frequent follow-up and monitoring. Consequently, there is a growing trend toward non-invasive tests that can serve as viable alternatives to biopsy. Patients with RA are susceptible to MAFLD and, consequently, liver fibrosis. Timely detection of hepatic fibrosis in patients with RA plays a pivotal role in averting fibrosis-related complications, enhancing their quality of life,

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and reducing overall healthcare expenses. Remarkably, no study has investigated the influence of RA on fibrosis in individuals with MAFLD.

The definition of MAFLD was validated using data from the "Third National Health and Nutrition Examination Surveys" (1988-1994) database, leading to the conclusion that MAFLD offers a more practical and precise framework for identifying patients compared with NAFLD/NASH (1).

MAFLD affects approximately one-quarter of the global adult population, imposing a significant healthcare and economic burden on societies worldwide. It is anticipated that the affected population will increase by up to 56% over the next decade (2). A recent meta-analysis reported the global prevalence of MAFLD at 25.2%. MAFLD exhibits higher prevalence rates in the Middle East (32%) and South America (31%), whereas Africa demonstrates a lower prevalence at 14%. Prevalence is 27% in Asia, 24% in North America, and 23% in Europe (3). Assessing liver damage is an important step in the management of individuals with chronic liver disease. Although liver biopsy is considered the gold standard for evaluating necrosis, inflammation, and fibrosis, its invasiveness and difficulty in repetition have led to the development of several non-invasive methods as alternatives to liver biopsy. Some non-invasive tests used for assessing hepatic fibrosis include fibrosis-4 (FIB-4), NAFLD Fibrosis Score (NFS), the AST to Platelet Ratio Index (APRI), and AST/ALT Ratio and Diabetes (BARD) (4).

Recent studies on the incidence and prevalence of RA have revealed significant variations in disease occurrence across different populations (5). The prevalence of RA varies from 0.5% to 1.0% in many populations, with higher rates observed in specific groups such as Pima Indians (5.3%) and Chippewa Indians (6.8%), while lower prevalence is noted in Chinese and Japanese populations (6).

RA is a progressive and chronic inflammatory disease characterized by uncontrolled proliferation of synovial tissue and the development of multisystemic comorbidities. Its pathogenesis results from a combination of genetic and environmental factors, with a higher incidence in women than in men. Without proper treatment, 20% to 30% of patients may experience permanent disability within 2 to 3 years after diagnosis (7). Extra-articular manifestations of RA can manifest at any age following its onset, affecting various organs such as the skin, eyes, heart, lungs, kidneys, nerves, and gastrointestinal system (8). Gastrointestinal and hepatological complications in RA are primarily iatrogenic and often stem from medication use (9). The most common non-iatrogenic gastrointestinal and hepatological comorbidity involves liver dysfunction, which is characterized by elevated liver function test results in 18% to 50% of patients. Other associated findings include intrahepatic bleeding, hepatosplenomegaly, cirrhosis, and necrotic pancreatitis (10).

Methods

This retrospective study was conducted at the Clinic of Internal Medicine and Rheumatology, University of Health Sciences Turkey, Ümraniye Training and Research Hospital from February 2020 to February 2022. The study included a total of 120 patients aged 18 to 65 who had been diagnosed with MAFLD. Ethical approval was obtained from University of Health Sciences Turkey, Ümraniye Training and Research Hospital Ethics Committee (approval number: B.10.1TKH.4.34.H.GP.0.01/41, date: 10.02.2022), and all participants provided informed consent. The patients were categorized into two primary groups: those with a diagnosis of RA and those without RA (the control group).

Both groups comprised patients with similar age and gender characteristics. In the RA group, special attention was paid to confirm the presence of abdominal imaging performed within the last year in patients who were not in the active phase of their disease and to assess the consistent use of antirheumatic drugs. Exclusion criteria for the study included patients with a history of cancer within the past 5 years, individuals with obesity, diabetes, hypertension, those undergoing chronic renal replacement therapy (such as hemodialysis, peritoneal dialysis, or renal transplantation), pregnant patients, as well as those with a history of chronic viral hepatitis or HIV infection.

In this study, individuals diagnosed with abnormal fat accumulation in liver cells, known as hepatic steatosis, were included in the non-RA MAFLD group. The diagnosis was based on findings from imaging, biomarkers, or histological assessments. To be eligible for inclusion, these patients needed to meet at least two of the following criteria: being overweight or obese or having metabolic dysfunction. These criteria included waist circumference measurements of ≥102 cm for men and ≥88 cm for women, blood pressure readings ≥135/85 mmHg or receiving treatment for hypertension, plasma triglyceride levels ≥150 mg/dL, high-density lipoprotein cholesterol levels <40/50 mg/dL for men/women, prediabetes, a Homeostatic Model Assessment for Insulin Resistance score ≥2.5, and plasma high-sensitivity C-reactive protein levels exceeding 2 mg/dL.

In contrast, the RA group consisted of patients diagnosed with RA.

FIB-4 score= [age x aspartate aminotransferase (AST)]/platelet (PLT) value x [alanine aminotransferase (ALT)] 1/2 was calculated using the formula. NFS= (-1.675 + 0.037 x age (yr) + 0.094 x body mass index (BMI) (kg/m^2) + 1.13 x impaired fasting glycaemia/diabetes (yes= 1, no= 0) + 0.99 x AST/ALT ratio - 0.013 x PLT count ($x10^9/L$) - 0.66 x albumin [g/dL)] was calculated using the formula.

To assess the risk of hepatic fibrosis in patients diagnosed with MAFLD, non-invasive tests were employed, including FIB-4 and NFS. FIB-4 was evaluated based on age, AST, ALT, and PLT values, with low risk indicated if <1.45 (F0-1), intermediate risk if 1.45/3.25 (F2-3), and high risk if >3.25 (F4-6). NFS, on the other hand, was assessed using age, BMI, diabetes mellitus, AST, ALT, ALB, and PLT values, categorizing individuals as low risk if <-1.455, intermediate risk if -1.455/0.675, and high risk if >0.675 for hepatic fibrosis.

Furthermore, the patients' BMI was calculated, and various laboratory tests were conducted during their diagnostic and treatment visits, encompassing fasting glucose, hemoglobin A1C (HbA1C), urea, creatinine, AST, ALT, glomerular filtration rate (GFR), lipid profile, complete blood count, and albumin levels. In addition, the results of liver imaging, including ultrasound, computed tomography, and magnetic resonance imaging, were verified and recorded through the hospital system.

Statistical Analysis

The data were analyzed using the SPSS 25.0 software package. To assess the data distribution, the Kolmogorov-Smirnov test was applied. Descriptive statistical techniques, including measures such as mean, standard deviation, median, interquartile range, frequency, and ratio, were employed to evaluate the study dataset.

To compare the two groups exhibiting a parametric distribution, the independent t-test was used. In cases where two groups demonstrated a non-parametric distribution, the Mann-Whitney U test was employed.

For the purpose of elucidating the variation in dependent variables, linear regression analysis was conducted. In addition, receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of FIB-4 and NFS values. In all analyses, statistical significance was considered $p<0.05$.

Results

The study enrolled a total of 120 participants, evenly divided into two groups: 60 patients diagnosed with RA, comprising 30 females and 30 males, and 60 patients diagnosed with non-RA, with an equal gender distribution. The patients' average age was 53.34±9.46 years, and their mean BMI was 25.73±1.15 kg/m2.

Descriptive statistics, encompassing measures such as mean, standard deviation, median, minimum, and maximum values, were computed for the laboratory parameters, FIB-4, and NFS scores, along with an assessment of liver fibrosis risk based on FIB-4 and NFS scores, as presented in Table 1.

To determine disparities in demographic and laboratory parameters between the groups, the independent t-test and Mann-Whitney U test were employed. The results, outlined in Table 2, revealed a statistically significant contrast in the median values of HbA1C and albumin ($p<0.05$). Specifically, the RA group exhibited higher HbA1C levels, whereas the non-RA group demonstrated elevated albumin levels.

Table 3 displays the outcomes of the Mann-Whitney U test, which investigated potential differences in FIB-4 and NFS scores between the groups. The findings indicated a statistically significant variance in NFS scores ($p<0.05$), signifying that NFS values diverged between the

Table 1. Descriptive statistics of patients' demographic and laboratory measurements

	Average ± SD	**Median (minimum-maximum)**
Age	53.34±9.46	54 (28-65)
Height (cm)	166.56±7.61	167 (152-192)
Weight (kg)	71.6±7.19	70.5 (56-100)
BMI (kg/m^2)	25.73±1.15	25.9 (22.2-27.4)
Glucose	94.23±7.18	94 (74-107)
HbA1C (%)	5.29±0.3	5.4 (4.6-6)
BUN	26.27±5.73	26 (15-45)
Creatinine	0.74±0.15	0.7 (0.4-1.1)
GFR	98.25±14.3	99 (63-135)
AST	22.02±10.82	19 (10-82)
ALT	23.75±15.48	19 (5-88)
PLT	270.24±79.56	262.5 (108-535)
Albumin	4.37±0.41	4.4 (2.6-5)
Total cholesterol	187.82±39.01	191 (102-299)
HDL cholesterol	46.18±11.57	44 (19-83)
LDL cholesterol	115.27±31.75	116 (46-211)
Triglyceride	133.05±66.16	114 (41-353)
FIB-4	1.02±0.62	0.88 (0.2-4.52)
NFS	-2.65±1.30	-2.54 (-6.62-0.74)
	n	**%**
FIB-4		
Low risk	100	83.3
Medium risk	18	15.0
High risk	2	1.7
NFS		
Low risk	101	84.2%
Medium risk	18	15.0%
High risk	1	0.8%

SD: Standard deviation, BMI: Body mass index, HbA1C: Hemoglobin A1C, BUN: Blood urea nitrogen, GFR: Glomerular filtration rate, AST: Aspartate aminotransferase platelet, ALT: Alanine aminotransferase, PLT: Platelet, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, FIB-4: Fibrosis-4, NFS: NAFLD Fibrosis Score

groups. In contrast, the FIB-4 scores displayed no statistically significant disparity. Notably, NFS measurements were notably higher in the RA group.

Regression Analysis of the Effects of Risk Factors on FIB-4 Measurements in Patients with RA

The regression analysis outcomes revealed significant impacts of age, GFR, and PLT parameters on the model. Age emerged as the most influential factor, followed by PLT and GFR. Notably, the effects of age were statistically significant at $p<0.05$, while both PLT and GFR exhibited significant effects at the more stringent $p<0.001$ level within the model.

Regression Analysis of the Effects of Risk Factors on NFS Measurements in Patients with RA

In the univariate analysis of key variables such as age, BMI, and identified risk factors, which encompassed HbA1C, creatinine, GFR, ALT, PLT, albumin, and triglyceride levels, each of them demonstrated noteworthy individual impacts on NFS. To assess their combined effects, a linear regression (backward) analysis was conducted.

The results of the regression analysis indicated that all these parameters exerted significant influences on the model. Albumin emerged as the most influential, closely followed by age and PLT values. Notably, the effects of albumin, age, and PLT were deemed statistically significant at the $p<0.001$ level in the model.

Regression Analysis of the Effects of Risk Factors on FIB-4 Measurements in Non-RA Patients

In the univariate analysis of characteristic variables such as age, BMI, and identified risk factors including glucose, HbA1C, creatinine, AST, GFR, and PLT values, it was observed that they individually had significant effects on FIB-4. To demonstrate their multivariate effects, a linear regression (backward) analysis was conducted.

Regression Analysis of the Effects of Risk Factors on NFS Measurements in Non-RA Patients

The results of the regression analysis indicated that, with the exception of ALT, the other parameters did not have a significant impact on the model. However, the effect of ALT was deemed statistically significant at the $p<0.05$ level within the model.

In Table 4 and Figure 1, the ROC analysis outcomes revealed an area under the curve (AUC) of 59.0% for the FIB-4 variable, suggesting that FIB-4 is not statistically appropriate for diagnosis ($p>0.05$). Conversely,

Table 2. Comparison of demographic data and laboratory measurements between the groups

	RA		Non-RA			
	Median	IQR	Median	IQR	Z/t	p
Age	55.7	11.5	54.8	12.5	-0.762	0.415**
Height (cm)	166.0	10.0	167.0	12.0	-0.527	0.598**
Weight (kg)	70.0	9.0	72.0	11.0	-0.860	0.390**
BMI	26.0	1.6	25.9	2.0	-0.313	0.755**
Glucose	93.0	12.0	96.0	10.0	-1.934	0.053**
HbA1C	5.4	0.5	5.2	0.5	-2.192	**0.028****
BUN	26.0	4.0	26.0	10.0	0.063	0.950**
Creatinine	0.7	0.2	0.8	0.3	-1.194	0.232**
GFR	97.0	15.0	102.0	23.0	-1.345	0.181*
AST	18.0	9.0	20.0	11.0	-0.691	0.489**
ALT	19.0	13.0	22.0	17.0	-1.072	0.284**
PLT	255.0	103.0	270.0	89.0	-0.052	0.958**
Albumin	4.2	0.6	4.5	0.4	-4.058	**0.001****
Total cholesterol	193.0	49.0	190.0	49.0	-0.273	0.785*
HDL cholesterol	46.0	17.0	44.0	10.0	-10.69	0.285**
LDL cholesterol	112.0	36.0	119.0	42.0	-0.524	0.602*
Triglyceride	104.0	84.0	119.0	82.0	-0.258	0.796**

*Independent t-test, **Mann-Whitney U test, RA: Rheumatoid arthritis, IQR: Interquartile range, BMI: Body mass index, HbA1C: Hemoglobin A1C, BUN: Blood urea nitrogen, GFR: Glomerular filtration rate, AST: Aspartate aminotransferase platelet, ALT: Alanine aminotransferase, PLT: Platelet, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Table 3. Comparison of demographic data and laboratory measurements between the groups

	RA		Non-RA			
	Median	IQR	Median	IQR	Z	p
FIB-4	0.91	0.58	0.81	0.64	-1.709	0.087**
NFS	-2.32	1.8	-2.87	1.76	-2.357	**0.018****

**Mann-Whitney U test, RA: Rheumatoid arthritis, IQR: Interquartile range, FIB-4: Fibrosis-4, NFS: NAFLD Fibrosis Score

Table 4. ROC analysis was conducted for the FIB-4 and NFS values

	AUC (95%)	Cut-off	Standard error	p	Sensitivity (%)	Specifity (%)
FIB-4	0.590 (0.488-0.693)	0.910	0.052	0.088	0.550	0.550
NFS	0.625 (0.525-0.724)	-2.505	0.051	**0.018**	0.567	0.583

*ROC curve, ROC: Receiver operating characteristic, FIB-4: Fibrosis-4, NFS: NAFLD Fibrosis Score, AUC: Area under the curve

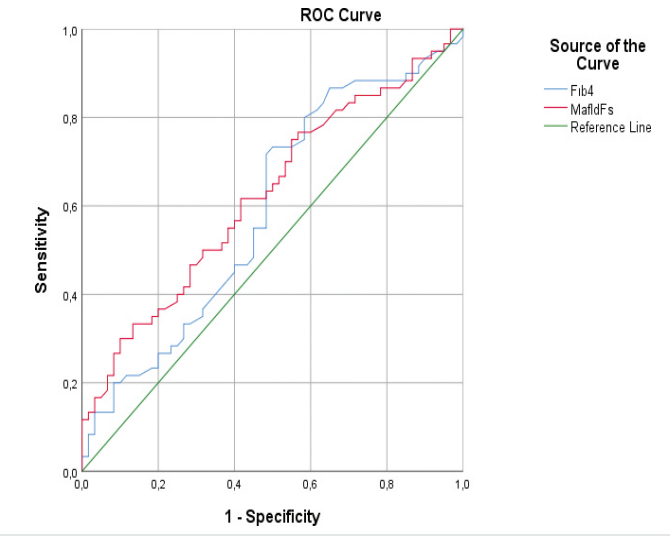

Figure 1. ROC curve for the FIB-4 and NFS values

ROC: Receiver operating characteristic, FIB-4: Fibrosis-4, NFS: NAFLD Fibrosis Score

the ROC analysis of the NFS variable yielded an AUC of 62.5%. The NFS value could be considered statistically suitable for diagnosis, although it demonstrates a relatively weak diagnostic capability ($p<0.05$).

Discussion

In this study, we demonstrated that RA increases the risk of liver fibrosis in individuals diagnosed with MAFLD. The uniqueness of MAFLD as a novel definition and the scarcity of research exploring its impact on liver fibrosis in patients with RA using non-invasive tests contribute to the value of our study.

Given the limitations associated with the gold standard method of liver biopsy for diagnosing liver fibrosis, various non-invasive methods have been developed. Primary among these methods are FIB-4, NFS, APRI, and BARD (11). A study conducted by Lee et al. (12) on non-invasive tests found significant AUC values for predicting liver-related events for NFS, FIB-4, and APRI. In another study by Roh et al. (13), FIB-4 was identified as having low sensitivity but high specificity in the diagnosis of liver fibrosis. In line with the existing literature, our study also found NFS to be a useful albeit weak diagnostic tool, while the same cannot be said for FIB-4.

A study by Yun Hao Xun et al., involving 152 NAFLD patients to assess the effectiveness of non-invasive tests in detecting fibrosis, reported FIB-4 and NFS scores similar to our study involving 120 patients. In Yun Hao Xun's study, FIB-4 exhibited low sensitivity but high specificity, and NFS also displayed low sensitivity but high specificity. Considering the body of literature, both tests can be considered specific in diagnosing liver fibrosis although they may have lower sensitivity. Correspondingly, in a study by McPherson et al. (14) in 2010, which included 145 patients with fatty liver, the effectiveness of non-invasive tests was evaluated. The results demonstrated that non-invasive tests could be safely employed in patients without advanced fibrosis. Our study similarly identified patients without advanced-stage fibrosis on the basis of their FIB-4 and NFS scores, further enhancing the meaningfulness of the findings.

Methotrexate (MTX) is a commonly prescribed medication for the treatment of specific malignancies, psoriasis, and rheumatoid diseases. Although hepatotoxicity is not a leading cause of death in RA patients undergoing MTX treatment, it represents the most frequently encountered side effect. Research has indicated that approximately 50% of Japanese patients with RA exhibit elevated serum AST and ALT levels. Typically, these elevations are mild and either self-correct or can be managed with additional folate supplementation. However, even when transaminase levels remain within the normal range, prolonged MTX use can lead to liver conditions such as steatosis, steatohepatitis, and fibrosis, which can ultimately progress to cirrhosis (15-17).

A study by Miyata et al. (18) examined the relationship between cumulative MTX dosage and FIB-4 scores in patients with RA using MTX. Notably, the average age of their study group was significantly higher compared to the average age of the patients in our study. Their exclusion criteria encompassed factors such as alcoholism, viral hepatitis, and autoimmune hepatitis. Interestingly, the control group in their study exhibited higher FIB-4 scores compared with our study (18).

In our study, we had a smaller number of patients with RA, all of whom were using MTX, and the average age of the RA group was lower. Our exclusion criteria covered a wide range of secondary causes of liver damage, including alcoholism, viral hepatitis, autoimmune hepatitis, advanced age, pregnancy, diabetes, obesity, hypertension, malignancy, and chronic renal replacement therapy. In our study, the FIB-4 score for patients with RA was low. Although the limited number of patients in our study should be acknowledged, the lower FIB-4 score can be attributed to the younger average age of our patients and the lower prevalence of comorbidities.

In our research, we discovered that age, GFR, and PLT count had significant effects on the FIB-4 score. While the effects of age and PLT were expected because they are already part of the scoring system, the influence of GFR was an unexpected finding, and this effect was not present in the non-RA group. This finding suggests that renal function may contribute to the progression of liver fibrosis in patients with RA. A study by Mima (19) involving 179 patients diagnosed with NAFLD and chronic kidney disease also found a significant effect of GFR on the FIB-4 score. Another study by Ishiba et al. (20) with patients diagnosed with NAFLD demonstrated that the FIB-4 score increased with age. Our study's findings align with the literature, showing a correlation between the FIB-4 score, age, and GFR.

NFS, another non-invasive test designed as an alternative to liver biopsy, evaluates age, BMI, insulin resistance/diabetes, AST, ALT, PLT, and albumin levels. According to a study by Wai-Sun et al. (21) in the Chinese population, implementing NFS would have rendered approximately four-fifths of liver biopsies unnecessary. Hsieh et al. (22) also established a relationship between NFS, age, and ALT in their study. Similarly, Gisondi et al. (23) identified a connection between NFS, age, and BMI. In accordance with the existing literature, our study also revealed correlations between age, ALT, and NFS. Furthermore, in our study, unlike the literature, we observed associations between PLT, albumin, and NFS in the RA group. These associations may be attributed to RA itself and the anti-rheumatic drugs employed. In contrast to the literature, we did not find a correlation between BMI and NFS scores in our study. This discrepancy could be attributed to the relatively similar BMI values among the patients included in our study, who were non-obese and non-cachectic.

While debates persist concerning the classification of liver damage as an extra-articular manifestation of RA, it is widely acknowledged that liver injury occurs in a range of 6-74% of RA patients. The primary factors contributing to liver damage in patients with RA include autoimmunity, infections, metabolic factors, alcohol consumption, and the adverse effects of medications (24). An autopsy study discovered abnormal liver histology in 92% of patients with RA, with clinical studies reporting similar abnormalities in 65% of cases. Predominant histological findings included periportal fibrosis, fatty liver, obstruction, and portal system inflammation (25). Patients with RA are susceptible to developing fatty liver disease because of their unfavorable metabolic profiles, adverse cardiovascular profiles, systemic inflammation, and chronic exposure to teratogenic drugs such as glucocorticoids and MTX (26). Research conducted by Ogdie et al. (27) revealed a higher prevalence and incidence of various liver diseases, including fatty liver and cirrhosis risk, in patients with RA compared with a control group. In our study, in line with the existing literature, both FIB-4 and NFS scores, which serve as predictors of liver damage, were elevated in the RA group. However, the disparity between the two groups was only statistically significant for NFS scores, likely because NFS evaluates a broader range of parameters. Additionally, our study's ROC analysis indicated that NFS is a more valuable tool than the FIB-4 score for diagnosing liver damage.

Indeed, the precise cause of liver damage in RA remains unclear, whether it results from the disease itself, medication use, or a combination of both factors. In our study, we tried to include patients with RA who were taking similar medications for comparable durations. However, concerns persist regarding the consistent and timely use of these medications by patients and whether they were exposed to additional hepatotoxic drugs (similar concerns apply to the control group as well).

Study Limitations

Several limitations characterize our study, including its single-center and retrospective nature. Assessments aimed at identifying liver hepatosteatosis were operator-dependent and qualitative. Furthermore, we employed only two tests to assess liver fibrosis, and there may be a relatively limited body of literature related to MAFLD because of its recent emergence as a diagnostic entity. These limitations are crucial to acknowledge when interpreting our study findings.

Conclusion

Our study employed two non-invasive tests for diagnosing liver fibrosis, with ROC analysis highlighting the utility of NFS as a diagnostic variable, despite its relative weakness. In line with the existing literature, our study revealed that age and GFR impacted the FIB-4 score, whereas age and ALT influenced the NFS score. In addition, we identified AST and PLT values as significant contributors to the FIB-4 score, and albumin and PLT values as significant determinants of the NFS score. Nevertheless, we believe that further comprehensive studies in this domain will offer valuable insights.

MAFLD is a recently adopted and more encompassing term for fatty liver disease linked to metabolic dysfunction. In our study, we observed higher NFS values in the RA group, implying that patients with RA diagnosed with MAFLD face an elevated risk of developing liver fibrosis.

Ethics Committee Approval: Ethical approval was obtained from University of Health Sciences Turkey, Ümraniye Training and Research Hospital Ethics Committee (approval number: B.10.1 TKH.4.34.H.GP.0.01/41, date: 10.02.2022).

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