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The Frequency of Nonalcoholic Fatty Liver Disease in Non-Diabetic Patients and Evaluation of CRP, Coagulation and Lipid Parameters in These Cases

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ABSTRACT

***Objective:** Nonalcoholic fatty liver disease (NAFLD) is common in all over the world; Obesity, type 2 diabetes mellitus and hyperlipidemia are often associated with the common practice in daily practice. The aim of this study was to evaluate the incidence of NAFLD in patients without alcohol use and diabetes mellitus (DM) in our clinic and to evaluate the inflammation, coagulation and lipid parameters in these cases.*

***Materials Methods:** Patients who were admitted to our outpatient clinic with a history of alcohol use and those with known DM were not included in the study. 75 grams of oral glucose tolerance test (OGTT) was performed to study patients and DM was excluded. A total of 67 patients complied with the study criteria. After the venous blood was taken for the necessary laboratory tests, liver fat was investigated by abdominal ultrasonography.*

***Results:** Of the 67 patients, 32 (47.7%) were female and 35 (52.3%) were male. Thirthy-one (46.2%) of the patients had NAFLD. NAFLD was higher in women than in men (67.7%, 32.3%, respectively). In patients with NAFLD, hypertension was significantly higher than those without hypertension (48.4%, 22.2%, respectively). HDL / LDL ratio was low and CRP values were higher in NAFLD.*

***Discussion:** NAFLD is a liver specific finding of metabolic syndrome. Therefore, patients with NAFLD are at risk for DM and consequently coronary artery disease. Patients with NAFLD should be followed up more closely and should be motivated in terms of healthy life.*

Keywords: *NAFLD, CRP, metabolic syndrome*

INTRODUCTION

The liver lubrication is more than 5% of the liver weight of lipids or histopathological examination of the presence of fat vacuoles in more than 5% of hepatocytes (1). NAFLD; It has become a public health problem in which the prevalence of obesity in modern societies is increasing and its progress in the diagnosis and pathophysiology of the last 20 years has been recorded (2). The more frequent use of imaging modalities in NAFLD has been observed in clinical practice in the last 20 years (3). Obesity, type 2 DM, hyperlipidemia, hypertension, waist / hip ratio increase and risk factors for the development of advanced age NAFLD are (4). The incidence of NAFLD is higher in women (5,3). NAFLD was found in 76% of obese, 50% (12) in type 2 DM, and 21-83% (5) in hyperlipdemics patients. NAFLD is generally asymptomatic (5), but symptomatic patients do not have any signs except pain and fullness in the right upper quadrant (6). Physical examination generally does not reveal any other findings than hepatomegaly (7). The most common condition in the laboratory is the elevation of aminotransferase, which can be 2-5 times higher than normal (7). The AST / ALT ratio is less than 1 (as opposed to alcoholic liver disease) (8). There is no correlation between the level of KC enzymes and KC histology (6). Transferrin saturation may increase in 5-10% of patients and ferritin may increase in 20-50% of patients (9,10). Antinukleer antibody (ANA) and anti smooth muscle antibody (ASMA) from autoantibodies can be shown in 23-36% of patients (11,12). Diagnosis of liver lubrication is made by imaging methods. Ultrasonography has 89% sensitivity and 93% specificity in diagnosis (13). NAFLD is largely benign. However, for unknown reasons, some patients progress to

steatohepatitis, resulting in cirrhosis and liver failure (3). Advanced age, obesity, DM and AST / ALT ratio above 1 were found to be independent predictive factors for liver fibrosis (5). Weight loss diet and exercise NAFLD is also the most effective treatment. A relatively small amount of weight loss reduces liver fat and improves hepatic insulin resistance (14).

Materials and Methods

The study was performed with random sampling method in Cardiology outpatient clinic of İzmir Atatürk Training and Research Hospital. Alcohol users (confirmed by first-degree relatives) and those with known DM were not included in the study. Blood samples were taken from the antecubital vein in the sitting position after fasting for 12 hours. Fasting blood glucose (FBG), HBsAg and anti-HCV were obtained from venous blood. Patients with HBsAg and anti-HCV positivity were excluded from the study. The remaining subjects were fed with 300 grams of carbohydrate in 3 days and 75 grams of glucose were dissolved in 300 ml of water and oral glucose tolerance test (OGTT) was performed. Patients with blood glucose levels above 200 mg / dl were excluded from the study and 67 cases were included in the study. After resting for 5 minutes, blood pressure was measured with sphygmomanometer from right arm. Total cholesterol, triglyceride, LDL-cholesterol, HDL-cholesterol, VLDL, ALT, AST, GGT, prothrombin time, protein C, protein S and fibrinogen parameters were studied in the biochemistry laboratory and CRP in the microbiology laboratory. Hepatobiliary ultrasound (USG) was performed by the same radiologist after blood collection. The cases with KC lubrication were determined as USG (+) and KC lubrication cases were determined as USG(-). Chi-square Test and Fisher ves Exact Test were used to compare categorical variables while statistical analysis of the data was performed using Independent samples t Test statistical analysis. Categorical variables were summarized as number and percentage, numerical values as mean and standard deviation. All analyzes were performed with 95% confidence in SPSS 10.0 for Windows statistical package program. P <0.05 was considered statistically significant.

Results

Of the 67 patients included in the study, 32 (47.7%) were female and 35 (52.3%) were male (Table1). There was no statistically significant difference between the mean age of male and female cases (respectively 58.5 ± 10.33, 56.86 ± 12.96). 18 cases (26.8%) were obese (BMI 30 kg / m2), 33 (49.2%) were overweight (25≤ BMI <30), 15 (22.3%) were normal weight (20 kg ≤ BMI<25) and one case was tnin (15≤V BMI <20). Of obese patients, 13 (72.2%) were female and 5 (27.8%) were male. Hyperlipidemia was present in 35 cases (55.2%). Fifteen (40.5%) of the hyperlipidemic cases were obese. Fatty liver was detected in USG in 31 (67.2%) of 67 cases. Nine patients (21.7%) were female and 10 (32.3%) were male. NAFLD was significantly higher in women than men (p <0.05) (Figure 1).

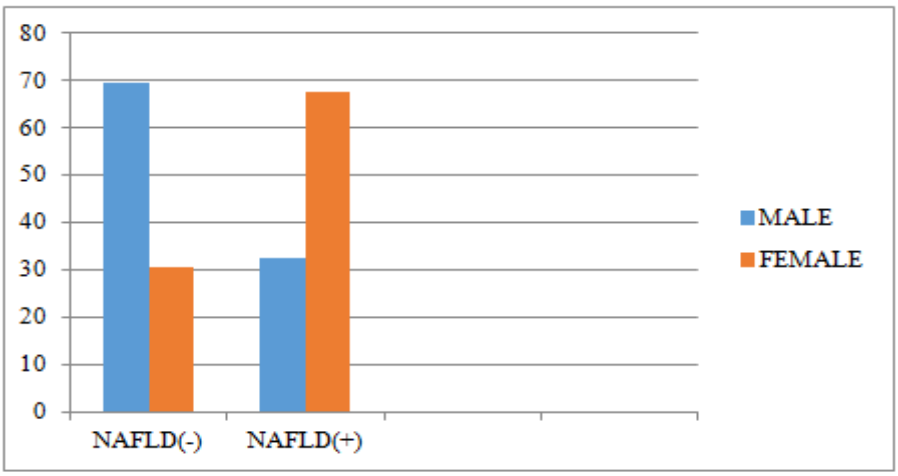

Figure1. *Comparison between gender and NAFLD*

There was no significant difference in smoking use between patients with and without NAFLD (p> 0.05). When the cases were compared in terms of NAFLD hypertension (HT) association, HT was 48.4% in patients with NAFLD and 22.2% in non-NAFLD patients (p <0.05) (Figure 2).

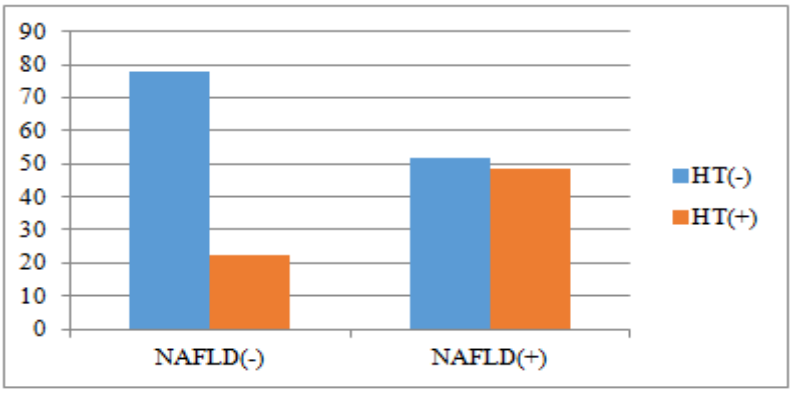

Figure2. *Comparison of NAFLD and HT*

When BMI was compared in terms of NAFLD relationship, BMI was significantly higher in patients with NAFLD than in non-NAFLD cases ($p < 0.05$). The mean BMI was 30.51 ± 2.94 kg / m2 in patients with NAFLD. In cases without NAFLD, it was 25.25 ± 3.03 kg / m2. When the cases were compared in terms of lipid parameters; Total cholesterol (CHOL), triglyceride (TG) and LDL values were higher in patients with NAFLD than in patients without NAFLD ($p < 0.05$). NAFLD was found to be 70.2% in patients with hyperlipidemia. CHOL, TG and LDL-arm averages were 216.55 ± 32.67, 153.32 ± 49.93 and 148.84 ± 29.74 in patients with NAFLD and 174.08 ± 28.08, 1114.06, and 114.97 ± 26.08 respectively. When the patients were compared in terms of ALT / AST ratio, ALT / AST ratios were significantly higher in patients with NAFLD compared to those without NAFLD ($p < 0.05$) (1.17 ± 0.14, 0.97 ± 0.10, respectively) (Figure 3).

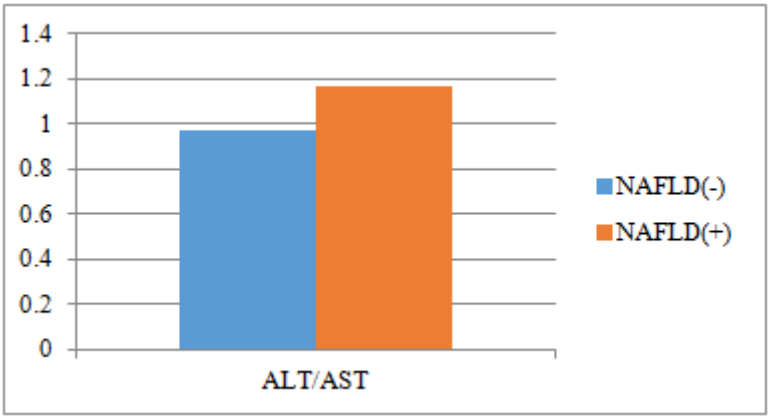

Figure3. *Comparison of ALT / AST and NAFLD*

When HDL / LDL ratio was compared, the HDL / LDL ratio was significantly lower in patients with NAFLD compared to the cases without NAFLD (0.29, 0.33, respectively) ($p < 0.05$) (Figure 4).

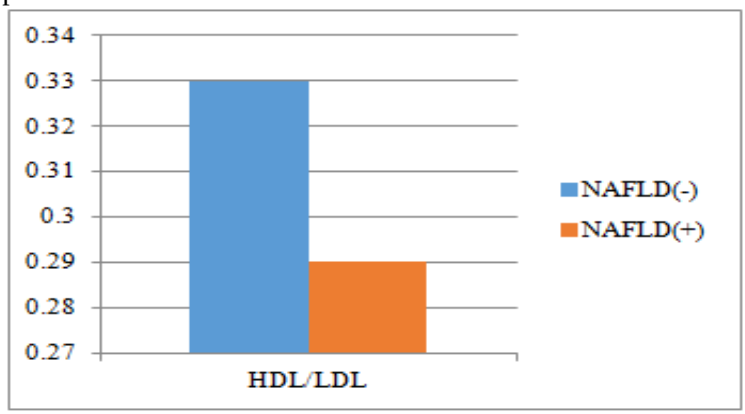

Figure4. *Comparison of NAFLD and HDL / LDL*

CRP values were significantly higher in patients with NAFLD than those without NAFLD (6.69 ± 4.03, 4.71 ± 4.03, respectively) (p <0.05) (Figure 5).

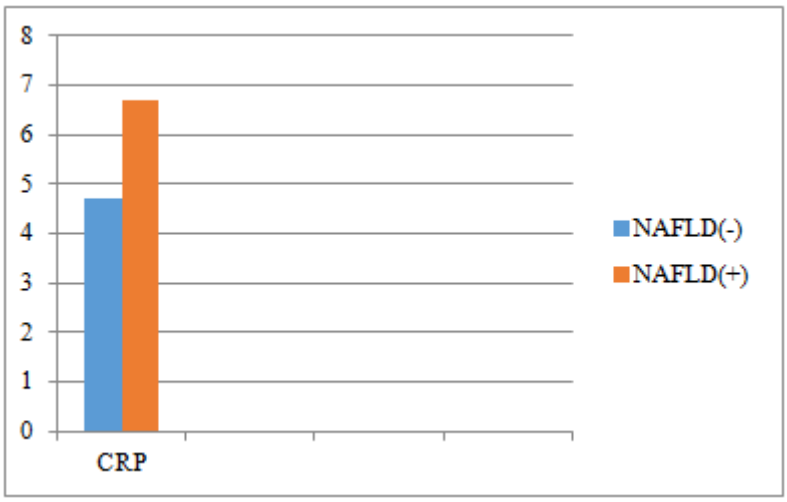

Figure5. *Comparison of CRP and NAFLD*

There was no statistically significant difference between the patients with and without NAFLD when compared with Fibrinogen, protein C, protein S, prothrombin time (PTZ) and VLDL-cholesterol parameters (p> 0.05).

Table1. *Comparison of NAFLD (+) and NAFLD (-) patients parameters.*

	NAFLD(-) Mean±SD	NAFLD(+) Mean±SD	*P*
Age	55.11±11.99	60.58±10.85	0.056
Weight	71.28±11.27	81,33±10.30	0.000*
Height	1.68±0.09	1.63±0.09	0.051
BMİ	25.25±3.03	30.51±2.94	0.000*
CHOLESTROL	174.08±28.08	216.55±32.67	0.000*
TG	114.06±46.69	153.32±49.93	0.001*
LDL	114.97±26.08	148.84±29.74	0.000*
HDL	37.08±8.65	42.09±10.79	0.039*
VLDL	25.0±13.5	28.45±10.77	0.257
HDL/LDL	0.33±0.08	0.29±0.09	0.049*
Fibrinogen	448.17±417.76	400.65±87.31	0.537
Protein-C	10.04±25.51	118.18±18.95	0.149
Protein-S	101.72±22.42	96.46±13.67	0.260
PTZ	12.98±1.34	13.25±3.27	0.647
ALT	30.36±5.05	45.03±6.50	0.000*
AST	31.44±4.78	38.84±5.93	0.000*
ALP	87.97±8.09	101.84±11.96	0.000*
GGT	27.64±4.01	31.61±3.78	0.000*
ALT/AST	0.97±0.10	1.17±0.14	0.000*
CRP	4.71±3.41	6.69±4.03	0.032*

*Independent samples t test, * p< 0.05*

DISCUSSION

Although the prevalence of NAFLD is geographically different, it is a common pathology worldwide (3). The estimated prevalence is around 20% (6). In our study, the NAFLD rate was 46.2%. Although it is higher than reported in the literature, the reason for this condition is probably due to the high average age of the patients (60.58 ± 1.85), hyperlipidemia (55.2%) and obesity (26.8%). Although the prevalence of the disease was increasing as NAFLD increased in age (2.6% in children, 26% in 40-59 years of age) (16,17), there was no significant difference in age between the cases with NAFLD (p> 0.05). Although there was no significant age difference between the groups, the presence of more NAFLD in a group was not an independent risk factor but rather a contributing factor to other

etiological factors. In our study, the incidence of NAFLD was higher in women than in men and this result was consistent with the literature (5,3). Obesity can be explained by the higher prevalence of obesity in females (72.2% (n = 13) and 27.8% (n = 5) in males. There was no significant relationship between smoking and NAFLD (p> 0.05). The same results were obtained in the literature (18,19). In our study, the incidence of NAFLD increased as BMI increased. Even in our obese patients (BMI ≥ 30 kg / m2) the incidence of NAFLD was 88.8%. This rate was consistent with the literature. In the literature, it was reported that the association of obesity with NAFLD was 76% (20). The incidence of hypertension was higher in patients with NAFLD than in those without NAFLD (p <0.05) (18,19). Hypertension is a component of the metabolic syndrome (3). NAFLD is accepted as the reflection of metabolic syndrome in liver (21). This may explain the association of NAFLD with hypertension. There was no significant difference in terms of protein C, protein S and prothrombin time (PTZ) as the coagulation parameters (p> 0.05). Fibrinogen and CRP were used as inflamation markers. There was no significant difference between the groups in terms of fibrinogen (p> 0.05). In the study of Völzke et al., It was found that there was a significant difference when compared with the control group when compared with the control group when the levels of fibrinogen were compared in the patients with KC lubrication, but when the fibrinogen values were corrected according to age and sex, it was shown that there was no statistically significant difference (18). When CRP levels were compared, CRP levels were significantly higher in patients with NAFLD than those without NAFLD (p <0.05). In their study by Brea et al., CRP levels were found to be higher in patients with NAFLD compared to the control group. Reported that CRP is strongly associated with adipose tissue measurements and insulin resistance, and CRP is a good serum marker of hepatic inflammation (18). Lemieux et al. Reported that there was a high correlation between high sensitivity CRP (hs-CRP) levels and visceral fat in their postmenopausal women and higher prevalence of hs-CRP levels and metabolic syndrome. In the same study, hs-CRP levels increased as the number of metabolic syndrome components increased (22). These results indicate that visceral fat tissue is the site of inflammation and cytokine production. It has been reported that CRP levels have been reduced with the decrease in weight loss and visceral lubrication provided by diet, exercise and drugs in different studies (23,24). This confirms the association between CRP and visceral lubrication.

CONCLUSION

In our study, it was found that increased incidence of obesity, hyperlipidemia and hypertension compared to the group without NAFLD in the patients with NAFLD detected in the sonographic examination, supports the idea that NAFLD is a reflection of the metabolic syndrome specific to KC. In the light of these results, we believe that NAFLD is a risk factor for the development of DM and it may be a risk factor for the development of coronary artery disease. Therefore, we believe that screening of the other components of the metabolic syndrome in the cases with NAFLD will be appropriate and it is appropriate to follow up with appropriate lifestyle changes in these cases.

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