International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

ORIGINAL ARTICLE

The Prevalence of Metabolic Syndrome in Patients with Non-Alcoholic Fatty Liver Disease in Ahvaz, Iran

Alireza Jahanshahi*, Homeira Rashidi, Arian Ezzatpanah, Saeed Hessam, Eskandar Hajiani, Fatemeh Amiri

Diabetes Research Center, Health Research Institute, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

ARTICLE INFO

Keywords:
Non-alcoholic fatty liver disease
Metabolic syndrome
Liver steatosis
Iran

**Corresponding author:*
Alireza Jahanshahi, MD;
Diabetes Research Center,
Health Research Institute,
Ahvaz Jundishapur University of Medical Sciences,
Ahvaz, Iran.
Tel: +98-9188742080
Email: dr.a.jahanshahi@gmail.com
Received: August 4, 2023
Revised: November 2, 2023
Accepted: November 9, 2023

ABSTRACT

Background: Previous studies have shown that there may be a link between metabolic syndrome (MetS) and non-alcoholic fatty liver disease (NAFLD). Therefore, the present study was designed with the aim of investigating the prevalence of metabolic syndrome in patients with NAFLD.

Methods: One hundred and fourteen patients with NAFLD were recruited to the study in Ahvaz, Iran. The Metabolic Syndrome Severity Score (MSSS) was used in an online calculator from available information. The NAFLD determined based on clinical or laboratory symptoms, and liver ultrasonography. The determination of its severity was made using liver elastography. Univariate and multivariate analyses were used to correlate the collected parameters. Receiver operating characteristic (ROC) curve was used to evaluate the cutoff value of fibrograde and steagrade that predicts fibrosis and steatosis.

Results: Totally, 69 patients (60.5%) had MetS. The chance of higher grade of steatosis in patients with MetS was 3.76 times higher than that of patients without MetS (p=0.003). Moreover, the correlation coefficient between MSSS and osteoscore was 0.274 (p=0.023). MSSS had the predictive power to detect steagrade (0:1, 2, 3) with 83.78% sensitivity and 59.38% specificity (p=0.005) and a cutoff point of 0.45.

Conclusion: MSSS was shown to have the predictive power to detect steatosis grades. However, further studies are required to determine whether fibrosis has a relationship with severity of MetS.

Please cite this article as: Jahanshahi AR, Rashidi H, Ezzatpanah A, Hessam S, Hajiani E, Amiri F. The Prevalence of Metabolic Syndrome in Patients with Non-Alcoholic Fatty Liver Disease in Ahvaz, Iran. Int J Nutr Sci. 2023;8(4): 207-215. doi: 10.30476/IJNS.2023.99502.1245.

Introduction

Non-alcoholic fatty liver disease (NAFLD) includes a disease range varying from simple steatosis to steatohepatitis, with different degrees of inflammation and fibrosis, which can progress to end-stage liver disease with cirrhosis and hepatocellular carcinoma (1). NAFLD is now more common than alcoholic liver disease owing to the quick rise in the prevalence of obesity, and NAFLD is the most common cause of abnormal liver function tests (2, 3). Also, it has been shown that NAFLD and non-alcoholic osteohepatitis (NASH) are common and may lead to serious clinical consequences (4). One possible risk factor of NAFLD is metabolic syndrome (MetS), which is becoming increasingly common (5, 6). NAFLD

affects 30% of the general population and up to 60-70% of obese and diabetes mellitus patients (7). MetS is one of the dangerous syndromes that increases the risk of developing cardiovascular diseases, diabetes, NAFLD or NASH, liver fibrosis, liver cirrhosis, Hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma, Chronic kidney disease (CKD) and all-causes of mortality (8).

Patients with NAFLD have hepatic steatosis with or without inflammation and fibrosis. NAFLD is divided into two categories of NAFLD and NASH. In NAFL, there is hepatic steatosis without evidence of inflammation; whereas in NASH, there is hepatic steatosis with liver inflammation that may be histologically indistinguishable from alcoholic osteohepatitis (9, 10). A total of 90% of patients with NAFLD have at least one MetS risk factor, and 33% of them have all MetS risk factors. In patients with MetS, compared to people without this syndrome, liver fat content increases significantly and independently of age, sex, and body mass index (BMI) (11, 12). The importance of the issue and the possibility of early prevention of NAFLD and MetS which have almost the same physiopathology have been emphasized. As these diagnostic and comparative methods have not been done in Iran so far and based on very few global studies, the present study was designed to use the MSSS (Metabolic syndrome severity score) index to study MetS for patients who were more likely to have steatosis or liver fibrosis, and to speed up diagnostic and therapeutic measures.

Materials and Methods

A cross-sectional study was conducted at the Out-Patient Department (OPD) of Imam Khomeni Hospital in Ahvaz, Iran from November 2022 to April 2023 to determine the prevalence of MetS in patients with NAFLD who attended this hospital. A total of 114 (using G*Power of 3.1.9.4 statistical software, two tailed, 0.5 effect size, 0.05 alpha error probability, and 0.8 power) conveniently selected NAFLD patients were recruited for this study upon passing the required inclusion (6). Patients aged between 18 and 65 years old, with NAFLD with initial diagnosis by ultrasound and liver tests and definitive diagnosis of steatosis or fibrosis by Fibro Touch elastography (FT100 model) were included.

Patients with diabetes, use of various drugs (methotrexate, amiodarion, corticosteroid, tamoxifen, aspirin, active treatment with antiretroviral drugs, diltiazem, blood lipid-lowering drugs), alcohol consumption in any amount, viral and autoimmune hepatitis, history of gastrointestinal surgeries (liposuction, sleeve or gastric bypass or jejunum bypass, small intestine resection surgery), history of chemotherapy or presence of cancer, history of chronic kidney disease, history of metabolic genetic diseases, pregnancy and breastfeeding were excluded from the study. Participation of patients was voluntary. Informed consent was obtained from each of the patients after a thorough explanation of the study in a language (Farsi) they understood. Ethical approval for the study was obtained from the Research Ethics Committee of the Ahvaz Jundishapour University of Medical Sciences with Ethical Clearance Certificate Number number of IR.AJUMS.HGOLESTAN.REC.1401.149.

A semi-structured questionnaire was utilized for the patients to ascertain their sociodemographic details. After 20 minutes resting time on comfortable seat, the blood pressure (BP) was measured by a fully automated blood pressure monitor (Omron Automated Blood Pressure Monitor, HEM-71217, Japan) twice on the left arm supported at heart level, and mean diastolic and systolic blood pressures were recorded. A multipurpose weight and height scale (Yongkang Zhezhong Weighing Apparatus, China) was used to measure body weight of the participants to the nearest accuracy of 0.1 kg and height to the nearest of 0.1 cm, with participants in standing erect position, back straight, heels together, barefooted, and in light weighted clothing.

BMI was calculated as weight (kg) divided by height squared (m^2). Waist circumference (WC) (cm) was assessed at the end of expiration, with a Gulick II spring-loaded measuring tape (Gay Mills, WI) midway between the inferior angle of the ribs and the suprailiac crest just below the level of the umbilicus. BMI ($kg\,m^{-2}$) was categorized according to Centers for Disease Control and Prevention (CDC), underweight (BMI<18.5), normal weight (BMI=18.5-24.9), overweight (BMI=25.0-29.9), and obese (BMI≥30) (13, 14). A total of 5 mL of the venous blood sample was collected from the participant's median cubital vein after overnight fasting (12-16 hours) between 8 am to 10 am and was dispensed into a serum separator tube, while 1 mL was transferred into a fluoride oxalate tube. Serum and plasma were obtained by centrifuging of the samples at 2500 rpm for 5 minutes, while pipetted into cryotubes, and stored at -20°C until analysis. Alkaline Phosphatase (ALP), fasting plasma glucose (FPG), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) concentrations were evaluated using a Selectra ProS chemistry analyzer, adhering to the reagent manufacturer's instructions (ELITech Clinical Systems).

MetS was defined in this study according to

National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria; where MetS was present in an individual if three out of the five parameters below were present in the patients as abdominal obesity (waist circumference>88 cm for women), high concentration of TG (TG≥1.7 mmol/L), low HDL-C (HDL-C<1.0 mmol/L for women), high BP (systolic BP≥130 mmHg or diastolic BP≥85 mmHg or treatment of hypertension), and increased FPG (FPG≥6.1 mmol/L) (15). MSSS was used to determine the severity of MetS. The equations for calculation of MSSS were based on the National Health and Nutrition Examination Survey (NHANES) study in the USA with the following arguments including age, race, gender, WC, TG, HDL-C, low-density lipoprotein cholesterol (LDL-C), systolic BP and blood glucose levels (16).

Vibration-controlled transient elastography (VCTE) was performed using Fibroscan® 502 Touch, which were provided by Echosens (Paris, France) to all the NASH Clinical Research Network (NASH-CRN) sites through a Clinical Trial Agreement with the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Trained study coordinators or principal investigators were performed all VCTE examinations using a standardized protocol (16). Participants were placed in supine position with the right arm in maximal abduction and measurements were taken over the right hepatic lobe through an intercostal space (16). All studies were started using the M probe with transition to the XL probe; only if prompted by the device's automatic probe selection tool. Only cases with ≥10 valid acquisitions were enrolled, while either the same or a different certified technician repeated the VCTE exam at the same session. The mean of the two VCTE exams was used to obtain higher statistical power due to lower variability when using mean as opposed to a single measurement. To evaluate the impact of using the first reading compared to the mean of the two VCTE examination, summary statistics between the first and second examination were compared. Unreliability of liver stiffness measure (LSM) was defined as interquartile range (IQR)/Median>30%, while the success rate was less than 60% and technical failure was defined by the inability to obtain 10 valid measurements. The LSM and controlled attenuation parameter (CAP) measurements used for this analysis were the mean of the medians obtained with the 2 exams. If one exam was missing or had unreliable data, the data from the completed exam was utilized (17).

It should be noted that most patients with NAFLD were asymptomatic, although some NASH patients might complain of fatigue, weakness, and discomfort on the right side of the abdomen, and they may also have hepatomegaly during physical examination due to the presence of fat in the liver, while it was highly variable in NAFLD patients. NAFLD patients might have mild to moderate elevations in AST, ALT; although normal liver function tests (LFT) levels did not rule out NAFLD. The true prevalence of abnormal LFT in NAFLD patients was unclear. AST and ALT when elevated were usually 2 or 5 times the upper limit of normal (With the ratio of AST and ALT less than one), while the degree of LFT increase did not predict the degree of liver inflammation and fibrosis.

Data were analyzed using the SPSS statistical software (Version 22.00, Chicago, IL, USA), GraphPad Prism statistical software (version 6), and Microsoft Excel (Version 2016). Unique codes were assigned to each participant in order to ensure data security and confidentiality. Normality of all continuous variables was tested. Continuous parametric variables were expressed as their mean±standard deviation (SD); continuous nonparametric variables were expressed as median (minimum and maximum) while categorical variables were expressed as frequencies and percentages. Comparisons of parameters were performed using the unpaired t-tests, Mann–Whitney U test, Chi-squared (χ^2) test, or Fisher's exact test. Kruskal-Wallis test and Spearman's correlation coefficient were employed for univariate data analysis and rank regression was utilized for multivariate data analysis. Receiver operating characteristic (ROC) analysis was used to check the predictive power of the data. Also, appropriate cut points were selected based on appropriate sensitivity and specificity. A $p<0.05$ was considered statistically significant for all analyses.

Results

Among 114 enrolled patients, 69 individuals (60.5%) suffered from MetS. According to the information in Table 1, the mean age of the patients was 42.87±11.69 years. In addition, 68 patients equal to 59.6% were male. A total of 16.7% of patients had smoking history, and 27.2% had a previous history of physical activity. There was no significant difference between the two groups with and without MetS in terms of age ($p=0.12$), gender ($p=0.15$), history of smoking ($p=0.50$) and physical activity ($p=0.16$). According to Table 1, in patients with and without MetS, the prevalence of abdominal obesity was 81.2% vs. 31.1% ($p<0.001$), high TG was 81.2% vs. 33.3% ($p<0.001$), high fasting blood sugar (FBS) was 50.7% vs. 15.6% ($p<0.001$), high BP was 62.0% vs. 31.1% ($p=0.002$) and low HDL-C was 65.2% vs. 53.3% ($p=0.14$) were significantly different. In addition, only 7%

Table 1: Demographic characteristics and frequency of components of metabolic syndrome.

Variable		With MetS	Without MetS	Total	P value
Age, Year		40.8±10.94	44.22±12.04	42.87±11.69	0.12
Gender, No (%)	Male	30 (44.1)	38 (55.9)	68 (59.6)	0.15
	Female	15 (33.6)	31 (67.4)	46 (40.4)	
Regular exercise, No (%)		15 (33.3)	16 (23.2)	31 (27.2)	0.16
Abdominal obesity		56 (81.2)	14 (31.1)	70 (61.4)	<0.001
Elevated TG		56 (81.2)	15 (33.3)	71 (62.3)	<0.001
Hyperglycemia		35 (50.7)	7 (15.6)	41 (36.0)	<0.001
High blood pressure		43 (62.3)	14 (31.1)	57 (49.1)	0.002
Low HDL		45 (65.2)	24 (53.3)	69 (60.5)	0.14

MetS: Metabolic syndrome; TG: Triglycerides; HDL: High-density lipoprotein Mean±SD for quantitative and frequency, (%) for qualitative variables. Using Mann-Whitney U or Independent t test or Chi-square as appropriate.

Table 2: Univariate and multivariate regression of metabolic syndrome and its components with grade of fibrosis.

Variable		1	2	3	4	P value[1]	Multivariate		
							OR	95% CI	P value[2]
Metabolic syndrome	No	15 (33.3)	21 (46.7)	2 (4.4)	7 (15.6)	0.051	1.76	0.87-3.56	0.116
	Yes	17 (24.7)	23 (34.3)	15 (21.7)	14 (20.3)				
Diastolic BP		79.06±8.93	80.23±9.02	75.88±7.12	77.14±7.17	0.199	0.80	1.20 – 0.54	0.286
Systolic BP		124.84±13.04	126.36±10.58	127.6±12.52	124.29±11.21	0.765	1.05	1.41 – 0.77	0.816
FBS		96.25±9.51	95.66±11.46	99.47±10.83	98.95±10.96	0.495	1.21	0.88 - 1.66	0.242
HDL		41.16±9.67	40.77±9.36	40.71±8.74	41.05±7.77	0.997	0.98	0.80 – 1.18	0.813
TG		181.81±72.19	185.20±58.17	175.94±80.08	163.24±42.74	0.928	0.94	0.85 – 1.04	0.281
Weight		78.7±11.96	85.46±18.34	86.59±15.94	81.55±19.92	0.022	1.12	0.97 – 1.29	0.125
WC		95.8±10.74	102.09±13.67	105.18±10.6	95.09±16.58	0.035	1.25	1.67 – 0.94	0.125
MSSS		0.66±0.39	0.89±0.48	0.78±0.43	0.76±0.29	0.326	1.07	1.19 – 0.96	0.224

BP: Blood pressure; FBS: Fasting blood sugar; HDL: High-density lipoprotein; TG: Triglycerides; WC: Waist circumference; MSSS: Metabolic syndrome severity score; Mean±SD for quantitative and frequency, (%) for qualitative variables. [1]P value refers to comparisons of mean differences between patients with different grade of fibrosis (Kruskal-Wallis test or ANOVA as appropriate). [2]P value refers to association between grade of fibrosis and other variables (univariate and multivariate regression test).

of patients did not have evidence of fatty liver in sonographic examination. Totally, 43%, 38.6% and 11.4% of patients had grade 1, 2 and 3 of fatty liver based on ultrasound sonography, respectively.

As Table 2 shows, the frequency (%) of fibrograde 1, 2, 3 and 4 in patients with MetS was 17 (24.6%), 23 (34.3%), 15 (21.7%) and 14 (20.3%), respectively. In patients without MetS, the frequency (%) of fibrograde 1, 2, 3 and 4 was 15 (33.3%), 21 (46.7%), 2 (4.4%) and 7 (15.6%), respectively. The relationship between MetS and fibrograde was not significant (p=0.051), however, it showed a borderline correlation. Also, in the presence of other variables, the chance of fibrograde with a higher grade in patients with MetS was 1.76 times (p=0.051) that of patients without MetS, but this difference was not statistically significant (p=0.116). There was no significant relationship between mean of diastolic BP, systolic BP, FBS, HDL, TG and MSSS and fibrogrades 1, 2, 3 and 4. However, the mean of weight and WC in fibrogrades 1, 2, 3, and 4 were statistically different (p=0.022 and p=0.035, respectively). Moreover, by controlling other variables, for every 5 unit increase in the weight and WC, the chance of higher grades became 1.12 and 1.25, which were not statistically significant (p=0.125).

As Table 3 demonstrates, the frequency (%) of steagrade 0, 1, 2 and 3 in patients with MetS was 32 (46.4%), 17 (24.6%), 13 (18.8%) and 7 (10.1%), respectively. In patients without MetS, the frequency (%) of steagrade 0, 1, 2 and 3 was 32 (71.1%), 7 (15.6%), 2 (4.4%) and 4 (8.9%), respectively. The relationship between MetS and steagrade was significant in univariate analysis (p=0.039) which means that patients with MetS had the higher level of steatosis. Moreover, in the presence of other variables, the chance of higher grade of steatosis in patients with MetS was 3.76 times higher than that of patients without MetS, which this difference was statistically significant (p=0.003).

Moreover, there was significant relationship between mean of diastolic BP, systolic BP, FBS, weight, WC and steagrade 1, 2, 3 and 4 (p=0.030, p=0.005, p=0.017, p=0.002, p=0.001, respectively). It means that the average BP was higher in higher grades of steatosis. Also, by controlling other

Table 3: Univariate and multivariate regression of metabolic syndrome and its components with grade of steatosis.

Variable		Univariate					Multivariate		
		0	1	2	3	P value[1]	OR	95% CI	P Value[2]
Metabolic	No	32 (71.1)	7 (15.6)	2 (4.4)	4 (8.9)	0.039	3.76	1.58-8.97	0.003
syndrome	Yes	32 (46.2)	17 (24.6)	13 (18.8)	7 (10.1)				
Diastolic BP		77.34±6.23	76.67±7.02	86.67±13.45	80±8.94	0.030	1.46	0.97-2.21	0.071
Systolic BP		123.13±9.24	124.79±10.37	133.3317.18±	132.73±11.91	0.005	1.60	2.24-1.14	0.006
FBS		94.22±8.54	101.83±11.97	100.33±12.93	99.64±12.8	0.017	1.77	2.56-1.22	0.003
HDL		40.30±8.33	41.83±92.8	40.3±8.88	42.55±13.12	0.825	1.16	1.43-0.94	0.180
TG		166.08±62.42	198.58±106.8	199.87±57.51	181.18±62.6	0.070	1.06	1.18-0.94	0.293
Weight		76.61±14.10	87.5±12.8	95.27±19.85	73.93±18.94	0.002	1.19	0.38-1.03	0.019
WC		95.48±12.43	103.33±12.95	98.76±15.96	105.18±7.45	0.001	1.4	1.06-1.91	0.019
MSSS		0.65±0.35	0.91±0.41	0.92±0.51	0.82±0.42	0.075	1.08	0.96-1.21	0.215

BP: Blood pressure, FBS: Fasting blood sugar; HDL: High-density lipoprotein; TG: Triglycerides; WC: Waist circumference, MSSS: Metabolic syndrome severity score; Mean±SD for quantitative and frequency, (%) for qualitative variables. [1]P value refers to comparisons of mean differences between patients with different grade of fibrosis (Kruskal-Wallis test or ANOVA as appropriate). [2]P value refers to association between grade of steatosis and other variables (univariate and multivariate regression test).

Table 4: Multivariate regression between metabolic syndrome and its components with fibroscore.

Variable	R	B	95% CI	P value
Diastolic BP	-0.112	0.001	(-0.016-0.003)	0.155
Systolic BP	0.035	0.006	(-0.007-0.008)	0.895
FBS	0.121	-0.002	(-0.002-0.013)	0.138
HDL	0.001	-0.002	(0.007-0.011)	0.658
TG	0.009	0.001	(-0.002-0.001)	0.498
Weight	-0.024	0.004	(-0.002-0.011)	0.216
WC	0.168	0.004	(-0.002-0.01)	0.216
MSSS	0.121	0.12	(-0.16-0.41)	0.403

BP: Blood pressure; FBS: Fasting blood sugar; HDL: High-density lipoprotein; TG: Triglycerides; WC: Waist circumference; MSSS: Metabolic syndrome severity score; B: Unstandardized regression coefficients; CI: Confidence interval; P value refers to association between fibroscore and other variables (multivariate regression test).

Table 5: Multivariate regression between metabolic syndrome and its components with osteoscore.

Variable	R	B	95% CI	P value
Diastolic BP	0.058	0.69	(-0.39-1.78)	0.206
Systolic BP	0.229	0.80	(-0.01-1.61)	0.052
FBS	0.275	1.25	(0.40-2.10)	0.004
HDL	0.082	0.74	(-0.29-1.77)	0.158
TG	0.264	0.08	(-0.06-0.21)	0.26
Weight	0.364	1.04	(0.33-1.74)	0.004
WC	0.364	1.04	(0.33-1.74)	0.004
MSSS	0.274	24.63	(-54.69-5.43)	0.106

BP: Blood pressure; FBS: Fasting blood sugar; HDL: High-density lipoprotein; TG: Triglycerides; WC: Waist circumference; MSSS: Metabolic syndrome severity score; B: Unstandardized regression coefficients; CI: Confidence interval; P value refers to association between osteoscore and other variables (multivariate regression test).

variables, for every 10 unit increase in diastolic BP and systolic BP, the chance of higher grades became 1.46 and 1.60, which was statistically significant for systolic BP (p=0.006). Moreover, by controlling other variables, for every 10 unit increase for FBS variable, the chance of higher grades became 1.77, which was also statistically significant (p=0.003). Also, in term of weight and WC, by controlling other variables, for every 5 unit increase in weight, the chance of higher grades became 1.19 and 1.4, respectively, which were also statistically significant (p=0.019 and p=0.019, respectively).

As Table 4 illustrates, the mean of fibroscore in patients with MetS was 9.93±5.46 and in patients without MetS was 8.06±3.51, respectively. This difference was statistically significant (p=0.037). Also, by controlling other variables, the relationship between MetS and fibroscore was not statistically

significant (p=0.068). The correlation coefficient between diastolic BP, systolic BP, FBS, HDL-C, TG and MSSS were not statistically significant (p>0.05). Also, by controlling other variables, the relationships between these variables with fibroscore were not significant (p>0.05).

As Table 5 displays, the mean of osteoscore in patients with MetS was 197.24±51.80 and in patients without MetS was 224.09±52.01, respectively. This difference was statistically significant (p=0.002). With the control of other variables, the relationship between MetS and osteoscore was statistically significant (p<0.001). The relationships between systolic BP, FBS, TG, weight, WC and MSSS with osteoscore were statistically significant (p=0.05), that is, with the increase of these parameters, the osteoscore increased. Also, by controlling other variables, the relationship between FBS, weight, WC and osteoscore was significant (p<0.05).

As Figure 1 (a, b and c) reveals, the area under the Receiver operating characteristic (ROC) curve of the MSSS variable for diagnosis of fibrogrades (1:2,3,4), (1,2:3,4) and (4:1,2,3), respectively were equal to 0.631, 0.500 and 0.516, while these parameters did not have predictive power for diagnosing fibrogrades (p>0.05). According to Figure 2 (a), the area under the ROC curve of the MSSS variable to detect steagrades (0:1,2,3) was equal to 0.682. This variable had the predictive power to detect steagrade (0:1,2,3) with a sensitivity of 83.78% and a specificity of 59.38% and a cutoff point equal to 0.45 (p=0.005). As Figure 2 (b and c) exhibits, the area under the ROC curve of the MSSS variable for diagnosing steagrades (0.1:2.3) and (3:0,1,2), respectively were equal to 0.592 and 0.555 that means this parameter did not have predictive power for diagnosing steagrades (p>0.05).

Discussion

In the present study, the prevalence of MetS in patients with NAFLD was equal to 60.5%. In a study conducted by Fatahi *et al.* (6) in 2016, the frequency of MetS in patients with NAFLD was between 61% and 65% based on different diagnostic criteria of clinical diagnosis of metabolic syndrome in Iranian adults (CCDMIA) and NCEP/ATPIII; while the results of this study were close to our study. In a study conducted by Chen *et al.* (18) in 2011, the prevalence of MetS in patients with NAFLD was reported 87.76%, which is higher than our study. Also, in the study of Uchil *et al.* in 2009, the frequency of MetS in this category of patients was reported 47%, which is lower than our study (19).

Despite the differences in various studies and our study in terms of the frequency of MetS in patients with NAFLD, all the reported findings indicated that MetS was higher in this category of patients compared to the normal population (18%). Among the causes of differences between studies, we can

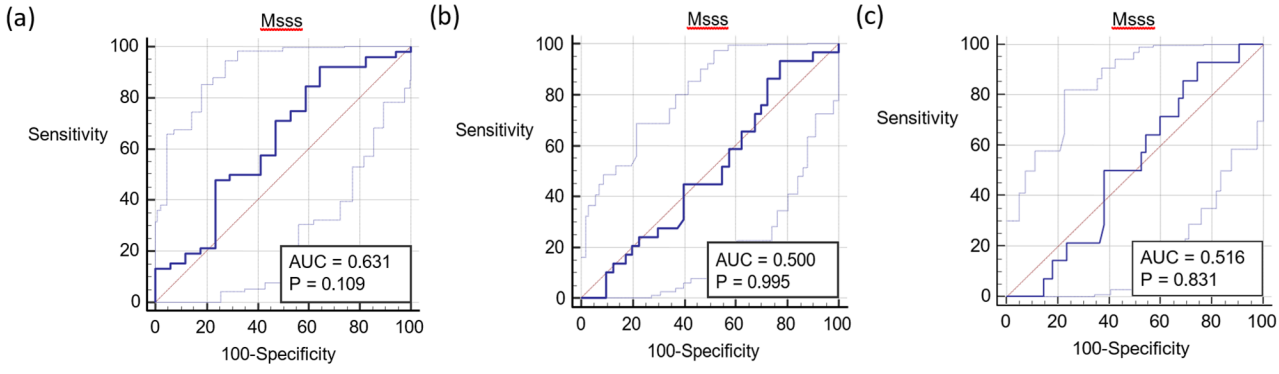

Figure 1: ROC curve of MSSS variable for fibrosis score detection (4, 3, 2:1), (4, 3: 2, 1) and (3, 2, 1:4).

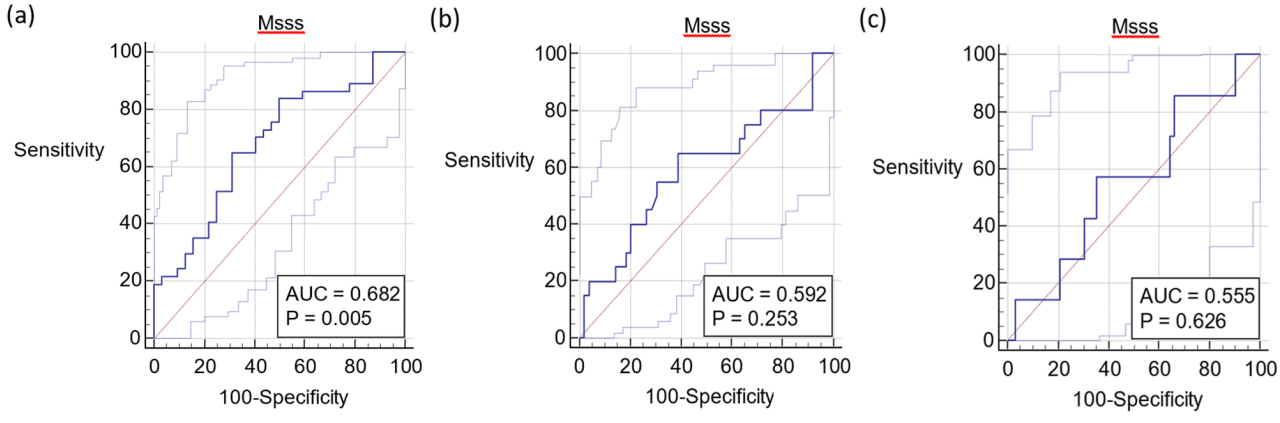

Figure 2: ROC curve of MSSS variable for steatosis score detection (3, 2, 1:0), (3, 2:1, 0) and (2, 1, 0:3).

mention the difference in the diagnostic criteria used in various studies as well as regional differences. The results of the present study showed that MSSS had the predictive power to diagnose steagrade (0:1,2,3) with a sensitivity of 83.78% and a specificity of 59.38% and with a cut-off point of 0.45. But it did not have the predictive power to detect other grades of steatosis as well as different grades of fibrosis.

In the study of Mohamed *et al.* (20), which was conducted with the aim of evaluating the predictive power of MetS severity in NAFLD mortality, it was found that the severity of MetS (MetS severity score) was significantly higher in NAFLD patients. Also, the findings of this study revealed that with increasing severity of MetS (actually with increasing MetS severity score), the risk of cardiovascular diseases (CVDs), insulin resistance, abnormal lipid profile and liver and kidney problems increased directly and linearly. In addition, the results of this study showed that MetS severity score was a strong predictor for all causes of mortality and specific causes of mortality caused by NAFLD. Although the previous studies (20-22) were conducted with a different purpose and implementation method, it showed the importance of grading the severity of MetS to predict its possible complications.

In addition, in the study of Dimitrov *et al.* (23), there was a significant relationship between MSSS and the severity of CVDs and related complications (CVD-related outcomes) such as myocardial infarction (MI), previous operation (heart surgery) and bypass surgeries. Moreover, in another study (24), it was found that MSSS was a predictive factor for MetS and type 2 diabetes. It is also mentioned in this study that there was a strong positive relationship between MSSS and the risk of CVDs in a ten-year period. In this study, the importance of grading the severity of MetS in predicting the risk of CVDs and diabetes has been determined. In fact, the increase in the severity score of MetS was correlated with cardiovascular factors, fat profile, and kidney and liver diseases. In a systematic review study of 27 cross-sectional studies, MetS and markers such as atherosclerosis, increased carotid intima thickness showed a correlation. There was a relationship between coronary artery calcification and arterial stiffness too (25).

The results of the present study showed that the mean of fibroscore and osteoscore was significantly higher in patients with MetS. In another study (26), which was conducted with the aim of relating NAFLD with MetS independent of central obesity and insulin resistance, it was found that after adjustment of confounding factors of BMI and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), the odds ratio for MetS was 3.64-fold for participants with mild NAFLD and 9.4-fold for participants with moderate-to-severe NAFLD compared to participants without NAFLD. In another study (6) with the aim of investigating the prevalence of MetS in NAFLD, MetS was identified in 65.9% of patients with NAFLD. The results of this study showed that there was a relationship between NAFLD and MetS. In the present study, all patients had NAFLD and the findings revealed that in patients with MetS, the amount of liver fibrosis and steatosis was higher in patients with NAFLD. In fact, the results of the present study confirmed the previous findings based on relationship between the presence of MetS and the severity of fatty liver.

The results of the present study showed that the average WC was higher in high grades of steatosis and liver fibrosis. By controlling other variables, the chance of higher grades of steatosis became 1.19, which was statistically significant, but by controlling other variables, increasing the chance of higher grades of fibrosis was not significant. In a previous study (26), a significant linear relationship between WC and the severity of NAFLD was observed. The results of the present study indicated that 59.6 of the patients were male. In the study conducted by Fatahi *et al.* (6), similar to the results of our study, men constituted a greater number of patients with NAFLD. In the study conducted by Chen *et al.* (18) in 2011, as in our study, men made up a higher percentage of NAFLD.

It should be noted that the present study had some limitations due to the limited sample size, while the statistical population was limited to NAFLD patients in the absence of a control group (not affected by NAFLD). Considering the lack of more similar studies to compare MSSS with the severity of alcoholic fatty liver and the newness of the recent study, conducting more studies with a larger statistical population is needed to achieve more accurate results.

Conclusion

Our data suggest a relationship between MetS and osteoscore. Moreover, MSSS had the predictive power to detect steagrade with a sensitivity of 83.78% and a specificity of 59.38% and a cutoff point equal to 0.45 in patients with NAFLD. However, further studies are required to determine whether fibrosis has a relationship with severity of metabolic syndrome.

Acknowledgement

The authors would like to thank the staff of Emam Khomeini hospital (Ahvaz, Iran) for their assistance in this project. The present study was supported by a

grant from the Vice chancellor for Research, Ahvaz Jundishapour University of Medical Sciences, Iran (Grant number: 330101166).

Authors' Contribution

Study concept and design: A.J. and E.H.; acquisition of data: A.E., H.R and F.A.; analysis and interpretation of data: S.H.; drafting of the manuscript: A.E. and A.J.; critical revision of the manuscript: A.J., S.H., and E.H; statistical analysis: S.H.; obtained funding: A.J.; administrative, technical, or material support: A.J.; and study supervision: A.J.

Conflict of Interest

None declared.

References

1 Pacifico L, Nobili V, Anania C, et al. Pediatric nonalcoholic fatty liver disease, metabolic syndrome and cardiovascular risk. *World J Gastroenterol*. 2011;17:3082-91. DOI: 10.3748/wjg.v17.i26.3082. PMID: 21912450.

2 Sattar N, Forrest E, Preiss D. Non-alcoholic fatty liver disease. *BMJ*. 2014;349:g4596. DOI: 10.1136/bmj.g4596. PMID: 25239614.

3 Rezaie A, Pashmforosh M, Karamallah MH, et al. Hepatoprotective effect of caffeine on diethylnitrosamine-induced liver injury in rats. *Bulg J Vet Med*. 2014;17:183-90.

4 Sotoudehmanesh R, Sotoudeh M, Ali-Asgari A, et al. Silent liver diseases in autopsies from forensic medicine of Tehran. *Arch Iran Med*. 2006;9:324-8. PMID: 17061603.

5 Musso G, Gambino R, Tabibian JH, et al. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. *PLoS Med*. 2014;11:e1001680. DOI: 10.1371/journal.pmed.1001680. PMID: 25050550.

6 Fattahi MR, Niknam R, Safarpour A, et al. The Prevalence of Metabolic Syndrome In Non-alcoholic Fatty Liver Disease; A Population-Based Study. *Middle East J Dig Dis*. 2016;8:131-7. DOI: 10.15171/mejdd.2016.18. PMID: 27252820.

7 Chalasani N, Younossi Z, Lavine JE, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. *Hepatology*. 2012;55:2005-23. DOI: 10.1002/hep.25762. PMID: 22488764.

8 Wilson PW, Kannel WB, Silbershatz H, et al. Clustering of metabolic factors and coronary heart disease. *Arch Intern Med*. 1999;159:1104-9. DOI: 10.1001/archinte.159.10.1104. PMID: 10335688.

9 Aghakhani L, Haghighat N, Amini M, et al. The Risk Factors of Nonalcoholic Fatty Liver Disease in Morbidly Obese Patients Undergoing Bariatric Surgery in Iran. *Gastroenterol Res Pract*. 2022;2022:5980390. DOI: 10.1155/2022/5980390. PMID: 35178085.

10 Pacifico L, Nobili V, Anania C, et al. Pediatric nonalcoholic fatty liver disease, metabolic syndrome and cardiovascular risk. *World J Gastroenterol*. 2011;17:3082-91. DOI: 10.3748/wjg.v17.i26.3082. PMID: 21912450.

11 Lankarani KB, Ghaffarpasand F, Mahmoodi M, et al. Non alcoholic fatty liver disease in southern Iran: a population based study. *Hepat Mon*. 2013;13:e9248. DOI: 10.5812/hepatmon.9248. PMID: 23922564.

12 Chen SH, He F, Zhou HL, et al. Relationship between nonalcoholic fatty liver disease and metabolic syndrome. *J Dig Dis*. 2011;12:125-30. DOI: 10.1111/j.1751-2980.2011.00487.x. PMID: 21401898.

13 Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*. 2014;311:806-14. DOI: 10.1001/jama.2014.732. PMID: 24570244.

14 Ahmadi A, Haghighat N, Hakimrabet M, et al. Nutritional evaluation in chronic obstructive pulmonary disease patients. *Pak J Biol Sci*. 2012;15:501-5. DOI: 10.3923/pjbs.2012.501.505. PMID: 24187906.

15 Ford ES. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the U.S. *Diabetes Care*. 2005;28:2745-9. DOI: 10.2337/diacare.28.11.2745. PMID: 16249550.

16 Gurka MJ, Lilly CL, Oliver MN, et al. An examination of sex and racial/ethnic differences in the metabolic syndrome among adults: a confirmatory factor analysis and a resulting continuous severity score. *Metabolism*. 2014;63:218-25. DOI: 10.1016/j.metabol.2013.10.006. PMID: 24290837.

17 Vuppalanchi R, Siddiqui MS, Van Natta ML, et al. Performance characteristics of vibration-controlled transient elastography for evaluation of nonalcoholic fatty liver disease. *Hepatology*. 2018;67:134-144. DOI: 10.1002/hep.29489. PMID: 28859228

18 Chen SH, He F, Zhou HL, et al. Relationship between nonalcoholic fatty liver disease and metabolic syndrome. *J Dig Dis*. 2011;12:125-30. DOI: 10.1111/j.1751-2980.2011.00487.x. PMID:

21401898.

19 Uchil D, Pipalia D, Chawla M, et al. Non-alcoholic fatty liver disease (NAFLD)--the hepatic component of metabolic syndrome. *J Assoc Physicians India*. 2009;57:201-4. PMID: 19588647.

20 Elsaid MI, Bridges JF, Li N, et al. Metabolic syndrome severity predicts mortality in nonalcoholic fatty liver disease. *Gastro Hep Advances*. 2022;1:445-56. DOI:10.1016/j.gastha.2022.02.002.

21 Haghighat N, Ashtari-Larky D, Aghakhani L, et al. How Does Fat Mass Change in the First Year After Bariatric Surgery? A Systemic Review and Meta-Analysis. *Obes Surg*. 2021;31:3799-3821. DOI: 10.1007/s11695-021-05512-9. PMID: 34089442.

22 Haghighat N, Ashtary-Larky D, Bagheri R, et al. Effects of 6 Months of Soy-Enriched High Protein Compared to Eucaloric Low Protein Snack Replacement on Appetite, Dietary Intake, and Body Composition in Normal-Weight Obese Women: A Randomized Controlled Trial. *Nutrients*. 2021;13:2266. DOI: 10.3390/nu13072266. PMID: 34208986.

23 Dimitrov BD, Bahchevanov KM, Atanassova PA, et al. Metabolic syndrome severity score: range and associations with cardiovascular risk factors. *Arch Med Sci Atheroscler Dis*. 2016;1(1):e90-e97. DOI: 10.5114/amsad.2016.62137. PMID: 28905027.

24 Gurka MJ, Lilly CL, Oliver MN, et al. An examination of sex and racial/ethnic differences in the metabolic syndrome among adults: a confirmatory factor analysis and a resulting continuous severity score. *Metabolism*. 2014;63:218-25. DOI: 10.1016/j.metabol.2013.10.006. PMID: 24290837.

25 Oni ET, Agatston AS, Blaha MJ, et al. A systematic review: burden and severity of subclinical cardiovascular disease among those with nonalcoholic fatty liver; should we care? *Atherosclerosis*. 2013;230(2):258-67. DOI: 10.1016/j.atherosclerosis.2013.07.052. PMID: 24075754.

26 Yang KC, Hung HF, Lu CW, et al. Association of Non-alcoholic Fatty Liver Disease with Metabolic Syndrome Independently of Central Obesity and Insulin Resistance. *Sci Rep*. 2016;6:27034. DOI: 10.1038/srep27034. PMID:27246655.