Original Article

Prevalence and Characteristics of Metabolic-Associated Fatty Liver Disease: A Cross-Sectional Study

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ABSTRACT

Background

Metabolic-associated fatty liver disease (MAFLD) is the concurrent presence of fatty liver disease (FLD) with overweight or obesity and/or type 2 diabetes mellitus. We aimed to determine the frequency and characteristics of MAFLD in patients with FLD.

Materials and Methods

This cross-sectional study was conducted on 143 patients with FLD referred to the gastrointestinal clinic of Shahid Rahimi Hospital in Khorramabad, Iran in 2021-2022. After obtaining a detailed medical history and in case of clinical suspicion of FLD, the levels of functional liver enzymes, fasting blood sugar (FBS), and lipid profile were measured. Furthermore, an ultrasound study of the liver was performed. The degree of insulin resistance was determined by the Homeostasis Model Assessment (HOMA) index. The data were gathered in a checklist and analyzed using SPSS software version 22.

Results

The mean FBS was 93.15±16.21 mg/dL, and the mean serum insulin levels were 7.88±15.81 mmol/L. The mean triglyceride level was 82.13±172.13 mg/dL, and the mean high-density lipoprotein was 37.27±7.15 mg/dL. In this study, 105 patients (73.4%) had high HOMA indexes. Serum alkaline phosphatase, alanine transaminase, and cholesterol levels were significantly higher in patients with high HOMA index than in those with normal index (P values=0.004, 0.047, and 0.039, respectively).

Conclusion

There appears to be a strong relationship between insulin resistance and impaired liver function in patients with FLD, indicating the necessity for managing insulin resistance in these patients.

Keywords: Metabolic-associated fatty liver disease, Non-alcoholic fatty liver disease, Insulin, Insulin resistance, Metabolic syndrome

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) includes a wide range of pathological liver damage, from steatohepatitis and non-alcoholic steatohepatitis (NASH) to fibrosis, cirrhosis, and even hepatocellular carcinoma (1). This disease is an abnormal or excessive increase of fat in hepatocyte cells, leading to chronic liver inflammation, cirrhosis, liver cancer, and death (2).

The prevalence of NAFLD in Iran is reportedly at 43.8%, 42.2%, and 45.8% overall, and in male and female groups, respectively (3). The pathogenesis of fatty liver disease is unclear. However, the possibility of insulin resistance as the pathogenesis of this disease has been explained (4). Abdominal obesity seems to be an essential risk factor for fatty liver. A study demonstrated that about half of the patients with hyperlipidemia had fatty liver based on sonography (5). In fact, the association of high blood pressure, hyperlipidemia, obesity, and diabetes, and all components of metabolic syndrome, with fatty liver disease has been observed. Hence, some researchers consider fatty liver disease as a liver manifestation of insulin resistance or metabolic syndrome. In this regard, the term metabolic-associated fatty liver disease (MAFLD) has been recently suggested to describe the simultaneous presence of fatty liver disease (FLD) with overweight or obesity and/or type 2 diabetes mellitus (6). The prevalence of MAFLD is estimated to be 22.8% in Iran (7).

Although most patients are asymptomatic, fatigue, weakness, and discomfort in the right upper abdomen prompt patients to seek medical attention. The most common manifestation of this disease is an increase in liver transaminases. In 19% of patients, an increase in alanine transaminase (ALT) and aspartate transaminase (AST) is seen (8, 9). Ultrasonography is the selective diagnostic method, and liver biopsy is the most accurate and sensitive method for definitively diagnosing fatty liver (10). Gradually, metabolic diseases have become more critical to improving health and controlling diseases. Also, the prevalence of fatty liver and metabolic syndromes has increased with changes in nutrition and social habits (11, 12).

Since insulin resistance has side effects on the body's vital organs, such as the heart and blood vessels, kidneys, brain, peripheral nerves, and liver, early diagnosis and proper treatment will prevent not only the damage to liver cells but also its critical cardiovascular complications (13). Today, the homeostasis model for evaluating insulin resistance or HOMA index is used in epidemiological and clinical studies to estimate insulin resistance and is calculated based on the serum concentration of insulin and glucose (14, 15).

According to the high importance of insulin resistance, we aimed to investigate the prevalence and characteristics of MAFLD in patients with FLD.

MATERIALS AND METHODS

Study design and participants

This descriptive-analytical cross-sectional study was conducted to assess the frequency of insulin resistance in patients with FLD referred to the gastroenterology clinic of Shahid Rahimi Hospital in Khorramabad, Iran in 2021-2022. The inclusion criteria were as follows: the presence of FLD, the presence of ultrasonography and tests in the patient's medical record, and informed consent to enter the study. Exclusion criteria were as follows: lack of consent to enter the study, evidence of cirrhosis (clinical, biochemical, or ultrasonographic findings), hepatitis (viral, autoimmune, and medicinal), and history of taking any hepatotoxic drug of known causes, secondary fatty liver (jejunoileal bypass surgery, wide resection of the small intestine, surgery to treat obesity, severe and extensive weight loss), morbid obesity [BMI (body mass index)>40], proven alcoholic fatty liver disease and suffering from any malignancy. Finally, 143 people who met the inclusion criteria were studied.

Data collection

A complete medical history was taken from all patients. In case of clinical suspicion of suffering from FLD, first, the level of liver transaminases, alkaline phosphatase, and bilirubin (Parsazmon, Iran), FBS (*fasting blood sugar*) (Parsazmoon, Iran), and serum levels of TG (triglycerides), cholesterol, HDL (high-density lipoprotein), LDL (low-density lipoprotein) (Parsazmoon, Iran) was requested. At the same time, an ultrasonography of the liver was performed by a radiologist to confirm the presence of NAFLD. If people had impaired liver enzymes, serological tests of HBs-Ag, HBc-Ab, HCV-Ab, antinuclear

antibodies, total iron-binding capacity, serum iron, and ceruloplasmin were requested. Patients with a negative serological test and a typical appearance of fatty liver reported in ultrasonography were included in the study. Patients were excluded from the study if they met the exclusion criteria. After fasting for twelve hours, 10 mL of blood was collected from each person in the laboratory. Also, the insulin level (Tosoh, Japan) was checked to evaluate insulin resistance, and then they were checked for insulin resistance using the HOMA index (16).

Data analysis

After collecting the required information, descriptive statistics were used to describe the data, calculate central and dispersion indices for quantitative variables, and frequency and percentage for qualitative variables. Chi-square and Fisher's exact tests were used to analyze the data. All statistical tests were performed using SPSS software version 22. For comparison and correlation between variables, the obtained results were compared with a significance level of 0.05.

Ethical considerations

This study was conducted with the permission of the Research Ethics Committee of Lorestan University of Medical Sciences with the ethical code IR.LUMS.REC.1400.196. Written, informed, and voluntary consent was obtained from all patients. The checklists were designed anonymously, and patients' personal information remained confidential. The principles of ethics in medicine, the Helsinki Declaration, were observed.

RESULTS

In the present study, 61.5% (88 people) of patients were≤40 years old, and 38.5% of patients (55 people) were older than 40 years. Regarding sex distribution, 50.3% (72 people) were men and 49.7% (71 patients) were women. Also, the average BMI of the study subjects was 27.29±3.56 Kg/m^2. See Table 1 for more demographic information.

The ultrasonographic findings showed that 32.2% of patients (46 people) had grade I, 53.1% (76 people) had grade II, and 14.7% (21 people) had grade III FLD.

The mean and standard deviation of laboratory tests were as follows: TG 82.13±172.13 mg/dL, cholesterol (Chol) 179.38±36.01 mg/dL, HDL 37.27±7.15 mg/dL, and LDL 27.44±99.48 mg/dL. Also, the mean and standard deviation of liver enzyme function levels in people with NAFLD was 30.43±19.53 U/L for AST, 46.11±36.67 U/L for ALT, 166.23±44.73 U/L for ALK, 0.76±0.33 mg/dL for total bilirubin, and 0.23±0.09 mg/dL for direct bilirubin. The mean FBS in people with NAFLD was 93.15±16.21 mg/dL, and mean insulin levels were 15.81±7.88 mmol/L. The mean HOMA index was reported to be 2.44±3.79. In this study, 26.6% (n=38) of patients had a negative HOMA index, and 73.4% (n=105) had a positive HOMA index (Table 2).

Table 1. Demographic characteristics of patients

Variables		Frequency (%)	Min	Mix	Mean±SD
Age (years)	≤40	88 (61.5)	25	65	41.19±9.56
	>40	55 (38.5)			
Height (cm)		143 (100)	150	190	169.93±10.84
Weight (kg)		143 (100)	55	104	78.68±11.09
BMI (kg/m^2)		143 (100)	20.89	35.98	27.29±3.56
Sex	Men	72 (50.3)	-	-	-
	Women	71 (49.7)			

Table 2. Laboratory test results of the patients

Variables	Min	Max	Mean±SD
TG (mg/dL)	44	408	172.13±82.13
Chol (mg/dL)	120	289	179.38±36.01
HDL (mg/dL)	25	63	37.27±7.15
LDL (mg/dL)	11	169	99.48±27.44
FBS (mg/dL)	69.37	161.44	93.15±16.21
INS (mmol/l)	2.6	40.4	15.81±7.88
AST (U/L)	13	128	30.43±36.67
ALT (U/L)	12	165	46.11±36.67
ALK (U/L)	85	263	166.23±44.73
Total bilirubin (mg/dL)	0.3	1.6	0.76±0.33
Direct bilirubin (mg/dL)	0.1	0.6	0.23±0.09
HOMA scale	0.120	14.8	3.79±2.44

Abbreviations: TG=trigelyceride; Chol=cholesterol; HDL=high-density lipoprotein ; LDL=low-density lipoprotein; FBS=fasting blood sugar; INS=insulin; AST=aspartate aminotransferase; ALT=alanine aminotransferase; ALK=alkaline phosphatase; HOMA=Homeostasis Model Assessment.

There was a statistically significant relationship between age and insulin resistance in the patients (P=0.019). Also, Fisher's exact test showed no statistically significant relationship between sex and insulin resistance (P=0.260, Table 3). The independent *t* test showed that there was a statistically significant relationship between insulin resistance and ALT (P=0.047), and ALK (P=0.004). There was no statistically significant relationship between insulin resistance and AST (P=0.090), total bilirubin (P>0.999), and direct bilirubin levels (P=0.613). Also, there was no significant relationship between insulin resistance and TG levels (P=0.106). There was a significant relationship between insulin resistance and Chol levels (P=0.039, Table 4). Regarding lipid profile, there was no statistically significant relationship between insulin resistance and HDL (P=0.112) or LDL (P=0.200, Table 4). In terms of BMI, there was no statistically significant relationship between BMI and insulin resistance in the studied population (P=0.116, Table 4).

Table 3. Comparison of frequency distribution of insulin resistance in patients according to age and sex

Variables		HOMA		Total	P value*
		Positive Frequency (%)	Negative Frequency (%)		
Sex	Male	16 (22.20)	56 (77.80)	72	0.260
	Female	22 (31.00)	49 (96.00)	71	
Age (years)	≤40	17 (19.30)	71 (80.70)	88	0.019
	>40	21 (38.20)	34 (61.80)	55	

*Fisher's exact test.

DISCUSSION

The pathogenesis of FLD has not been determined definitively, but the most widely supported theory is the insulin resistance mechanism. The increase in defects in glucose metabolism, as one of the most fundamental causes of the disease, is related to the progression of the disease and the development of fibrosis, and the correction of these conditions is an essential part of the treatment (17). Most of the studies conducted in this regard have expressed that patients with diabetes are more likely to suffer from liver disease than other people,

Table 4. The relationship between the level of liver function tests, lipid profile level, age, height, and weight with insulin resistance

Variables	HOMA		P value*
	Negative Frequency (mean±SD)	Positive Frequency (mean±SD)	
AST (U/L)	38 (25.84±11.84)	105 (32.10±21.46)	0.090
ALT (U/L)	38 (36.03±25.85)	105 (49.76±39.33)	0.047
ALK (U/L)	38 (183.79±64.25)	105 (159.88±33.31)	0.004
Total bilirubin (mg/dL)	38 (0.76±0.35)	105 (0.76±0.33)	>0.999
Direct bilirubin (mg/dL)	38 (0.24±0.11)	105 (0.23±0.09)	0.613
TG (mg/dL)	38 (153.68±66.67)	105 (178.81±86.37)	0.106
Chol (mg/dL)	38 (169.08±46.15)	105 (183.10±30.98)	0.039
HDL (mg/dL)	38 (35.68±6.7)	105 (37.84±7.25)	0.112
LDL (mg/dL)	38 (94.58±25.71)	105 (101.26±27.94)	0.200
FBS (mg/dL)	38 (86.12±7.38)	105 (95.49±17.83)	<0.001
INS (mmol/l)	38 (7.29±2.26)	105 (18.89±6.85)	<0.001
Age (years)	38 (44.45±8.50)	105 (40.01±9.68)	0.014
Height (cm)	38 (166.36±10.45)	105 (171.21±10.74)	0.018
Weight (kg)	38 (77.61±10.56)	105 (79.07±11.30)	0.489
BMI (kg/m^2)	38 (28.07±3.47)	105 (27.01±3.56)	0.116

*Independent *t* test.

Abbreviations: AST=aspartate aminotransferase; ALT=alanine aminotransferase; ALK=alkaline phosphatase; TG=trigelyceride; Chol=cholesterol; HDL=high-density lipoprotein ; LDL=low-density lipoprotein; FBS=fasting blood sugar; INS=insulin; BMI=body mass index.

but in the present study, the prevalence of resistance was investigated, and there were few studies in this field previously.

In this study, 73.4% of patients had a positive HOMA index, which indicates the high prevalence of insulin resistance. The results of this study are in agreement with the results of Willner and colleagues (18) who showed that a large percentage of NASH patients (85%) had insulin resistance.

In the present study, there was a statistically significant relationship between age and insulin resistance. Rad and colleagues showed that with the gradual industrialization of life and the lifestyle change, following age, people are exposed to various chronic diseases such as high blood pressure, high blood fat, obesity, etc., and prone to insulin resistance. These findings are consistent with the results of our study (19).

In the present study, there was a statistically significant relationship between liver function tests (ALT, and ALK) and insulin resistance. The results are along with the results of the study of Sheng and colleagues (20) who investigated the relationship between insulin resistance and metabolic syndrome in patients with NAFLD. The increase in the plasma levels of functional liver enzymes, mainly ALT, indicates fat deposition in the liver. According to the results of the present study, it can be concluded that high levels of liver enzymes can be a predictor of subsequent metabolic problems such as insulin resistance, type 2 diabetes, and heart diseases.

In the present study, there was no statistically significant relationship between BMI and insulin resistance. Our results were not consistent with the results reported by Liu and others (21). This difference can be due to the difference in sample size in these studies. Miao Liu and his colleagues examined 18,507 patients in 5 years, while the current study was conducted over a shorter period and with a more limited statistical population, which can explain the difference in the results obtained from the present study and other studies.

According to the results of the present study, it is crucial to determine the modifiable risk factors for the prevention and treatment of fatty liver to reduce the incidence of chronic diseases such as metabolic syndrome and the subsequent incidence of insulin resistance. Therefore, it is recommended to design and implement educational programs to increase public awareness about MAFLD risk factors so that they can adopt a healthy lifestyle.

Limitations

This study was performed during the COVID-19 pandemic, which could affect the referral pattern of patients to medical centers. Hence, precautions should be taken for interpreting the findings.

CONCLUSION

The prevalence of MAFLD is high, and due to a significant relationship between liver function tests, including AST, ALT, and ALK, with insulin resistance, these tests, especially ALT, can be used to predict future metabolic problems such as insulin resistance, type 2 diabetes, and heart diseases in patients.

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AUTHORS CONTRIBUTION

Dr. Saleh Azadbakht conceptualized and designed the study, Mr. Arian Karimi Rouzbahani contributed to the study design, Mr. Mohammad Amin Khazeei Tabari contributed to drafting, Dr. Golnaz Mahmoudvand reviewed and revised the manuscript, Ms. Salehe Azadbakht contributed to drafting, Dr. Maryam Omidi Majd collected the data, and Dr. Morteza Azadbakht coordinated and supervised the study. All authors read and approved the final manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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