METABOLIC DYSFUNCTION-ASSOCIATED FATTY LIVER DISEASE IN OVERWEIGHT AND OBESE VIETNAMESE

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ABSTRACT

Introduction: Metabolic dysfunction-associated fatty liver disease (MAFLD) is gradually becoming the leading cause of chronic liver disease worldwide, with its prevalence increasing due to the widespread incidence of obesity and metabolic syndrome. MAFLD has been proposed to replace the term non-alcoholic fatty liver disease (NAFLD), emphasizing the role of metabolic factors such as type 2 diabetes, hypertension, and dyslipidemia in the development and progression of liver disease. **Objectives**: To investigate the correlation between the degree of liver steatosis and fibrosis with BMI in patients with MAFLD. To identify the risk factors for significant liver fibrosis (F ≥ 2) in overweight and obese patients with MAFLD. **Methods**: The study was conducted on 192 overweight and obese patients visiting 115 People's Hospital in Vietnam from January to December 2023. Patients were evaluated using abdominal ultrasound and FibroScan to determine the degree of liver steatosis and fibrosis. Data were analyzed using SPSS software with descriptive, correlation, and regression analyses to identify risk factors. **Results**: The prevalence of MAFLD in the overweight and obese group was 72.92%, higher than in previous studies. There was a positive correlation between BMI and liver steatosis as well as liver fibrosis. The main risk factors for significant liver fibrosis included a high BMI (BMI ≥ 25 kg/m²) and the presence of MAFLD comorbid with other liver conditions such as chronic hepatitis B, chronic hepatitis C, and alcoholic liver disease. **Conclusion**: This study highlights the close correlation between BMI and the degree of liver steatosis and fibrosis in overweight and obese patients with MAFLD. The results indicate the importance of weight management and control of comorbid liver conditions to prevent the progression of liver disease in this population.

***Keywords**: Metabolic dysfunction-associated fatty liver disease; MAFLD, Liver fibrosis; Liver steatosis, Overweight and obesity; FibroScan.*

I. INTRODUCTION

Metabolic dysfunction-associated fatty liver disease (MAFLD) is gradually becoming the leading cause of chronic liver disease worldwide, with a rapidly increasing prevalence due to the widespread incidence of obesity and metabolic syndrome. MAFLD represents a combination of fatty liver disease and metabolic factors such as type 2 diabetes, hypertension, and dyslipidemia [1]. According to the study by Younossi et al. (2016), the prevalence of MAFLD in the overweight and obese population can reach up to 50.7% [2].

MAFLD has been proposed to replace the previous term, non-alcoholic fatty liver disease (NAFLD). The rationale behind this change is that NAFLD focused solely on excluding alcohol-related causes, overlooking the role of metabolic factors.

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Date of receipt: 24/2/2025
Date of scientific judgment: 24/3/2025
Reviewed date: 7/4/2025

MAFLD is no longer an exclusion-based diagnosis but includes metabolic factors, thereby increasing its accuracy and clinical applicability in patient evaluation [3].

According to MAFLD criteria, a patient is diagnosed with MAFLD when there is evidence of liver steatosis (through imaging or biomarkers) along with at least one of the following three factors: overweight/obesity, type 2 diabetes, or at least two criteria of metabolic syndrome [4]. This approach not only helps in more clearly identifying risk factors but also facilitates better disease monitoring and management, especially in the context of the rising global prevalence of this condition [5].

Compared to NAFLD, MAFLD has several distinct advantages. Firstly, MAFLD emphasizes the role of metabolic factors in the development and progression of liver disease, rather than merely focusing on excluding alcohol as a cause like NAFLD. Secondly, the MAFLD criteria encompass patients who do not have alcoholic hepatitis but are at high risk of liver damage due to other factors such as diabetes and obesity [6]. Finally, this change aids in better patient management, particularly in high-risk groups, thereby improving prognosis and treatment outcomes [7].

Currently, in Vietnam, although the number of overweight and obese cases is increasing rapidly, studies on the prevalence of MAFLD and the degree of liver fibrosis in the overweight and obese population remain limited. This study was conducted to investigate the prevalence of MAFLD, the correlation between liver steatosis and fibrosis levels with body mass index (BMI), and the risk factors for significant liver fibrosis in overweight and obese patients [8]. Our study aims to determine the rate of MALSD in overweight and obese people and to identify the risk factors for significant liver fibrosis.

II. METHODS

Study Subjects: Overweight and obese patients (BMI ≥ 25 kg/m²) who visited and were treated at 115 People's Hospital from January to December 2023, diagnosed with metabolic dysfunction-associated fatty liver disease (MAFLD).

- **Inclusion Criteria**: Patients aged 18 years or older, with a BMI ≥ 23 kg/m² [1] and with evidence of liver steatosis via FibroScan [2]
- **Exclusion Criteria**: Unreliable FibroScan results, including cases of patients with ascites, excessive abdominal fat (skin-to-liver distance over 25 mm affecting the measurement with the FibroScan M probe), or patients with heart failure and portal hypertension [3].

Clinical Data Collection:

- Measure patients' BMI, waist circumference, and blood pressure.
- Blood sampling to measure relevant biochemical markers: fasting glucose, triglycerides, HDL-c, LDL-c, liver enzymes (AST, ALT), and HbA1c.
- Type 2 diabetes (according to ADA 2020 criteria).
- Metabolic syndrome: patients must have at least two criteria of metabolic syndrome as defined by the World Health Organization (WHO), including: waist circumference greater than 90 cm for men and 80 cm for women, hypertension (≥ 130/85 mmHg), triglycerides ≥ 150 mg/dL, low HDL-c, or currently on medication for these conditions [2].

Assessment of Liver Steatosis and Fibrosis:

- **FibroScan** used to evaluate liver fibrosis through liver stiffness measurement (LSM)

and controlled attenuation parameter (CAP) to assess liver steatosis.

- Liver fibrosis classified according to stages F0-F1 (no fibrosis or mild fibrosis), F2 (significant fibrosis), F3 (advanced fibrosis), and F4 (cirrhosis).

- Threshold values for fibrosis stages: ≥ 7 kPa for significant fibrosis (F2), ≥ 9.6 kPa for advanced fibrosis (F3), and ≥ 12.5 kPa for cirrhosis (F4) [5].

- CAP value > 248 dB/m is considered indicative of liver steatosis starting from grade S1 [6].

Data Analysis Methods:

- **Data encoding and entry**: All collected data were entered into SPSS software version 26.0 for analysis.

-**Descriptive analysis**:

- Frequency and percentage were used to describe the clinical and subclinical characteristics of the patient group.

- Mean and standard deviation (SD) were calculated for quantitative variables such as BMI, liver fibrosis (kPa), liver steatosis (dB/m), and biochemical markers.

- **Correlation analysis**:

- Pearson or Spearman correlation coefficients (depending on data distribution) were used to assess the correlation between liver fibrosis, liver steatosis, and BMI.

- **Regression analysis:** Multivariate linear regression was used to identify risk factors for significant liver fibrosis (F ≥ 2). Independent variables included: BMI, age, gender, diabetes, hypertension, dyslipidemia, and relevant biochemical markers. The multivariate regression model calculated the odds ratio (OR) and 95% confidence interval (CI) to determine the impact of each risk factor on significant liver fibrosis.

Study Duration and Location: From January to December 2023 at 115 People's Hospital, Ho Chi Minh City, Vietnam.

III. RESULTS

Characteristics of the Study Population

In this study, a total of 192 overweight and obese patients with metabolic dysfunction-associated fatty liver disease (MAFLD) were surveyed. The main clinical and subclinical characteristics of the study population are summarized in the table below.

Table 1: **This table summarizes the demographic and clinical characteristics of the study population**

Characteristics	Mean ± SD	n (%)
Age (years)	48.5 ± 12.4	192 (100)
Male		100 (52.1)
BMI (kg/m²)	29.7 ± 3.1	192 (100)
Waist circumference (cm)	98.2 ± 12.5	192 (100)
≥ 90 cm men and ≥ 80 cm women		
Hypertension		82 (42.7)
Type 2 diabetes		74 (38.5)
Dyslipidemia		109 (56.8)
Metabolic syndrome		86 (44.8)
ALT level (U/L)	47.3 ± 16.5	
AST level (U/L)	35.9 ± 12.8	
MAFLD with other liver diseases		
Chronic hepatitis B		39 (20.3)
Chronic hepatitis C		9 (4.7)
Alcoholic liver disease		17 (8.9)

The study population has a mean age of 48.5 years, with a slight male predominance (52.1%). The majority of patients are obese (mean BMI 29.7 kg/m²) and have central obesity (100%), with high prevalence of dyslipidemia (56.8%), hypertension (42.7%), and type 2 diabetes (38.5%). Additionally, 44.8% have metabolic syndrome, and 20.3% have concurrent chronic hepatitis B.

Prevalence of MAFLD in overweight and obese patients

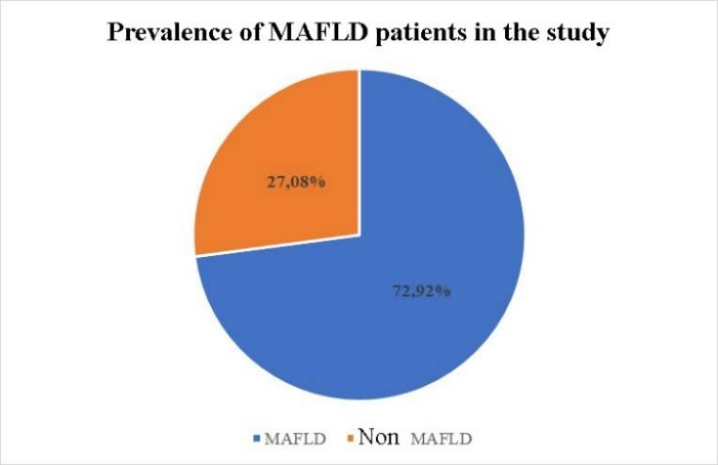

Figure 1: **Prevalence of MAFLD among overweight and obese individuals (n=192).** The majority of the study population (72.92%) has MAFLD

Table 2: **Comparison of clinical and paraclinical characteristics between patients with and without MAFLD**

Variable	MAFLD Mean ± SD	n (%)	Non-MAFLD Mean ± SD	n (%)	p-value*
Age (years)	53.18 (14.14)		49.54 (11.70)		0.099
Male, n (%)		70 (50.0%)		31 (59.62%)	0.236
BMI (kg/m²)	25.00 (2.07)		24.20 (1.28)		<0.001
Waist circumference (cm)	86.50 (9.00)		85.50 (11.75)		0.062
Glucose (mmol/l)	5.97 (0.91)		4.78 (0.68)		<0.001
Cholesterol (mmol/l)	4.63 (0.72)		4.39 (0.59)		0.002
HDL-c (mmol/l)	1.33 (0.19)		1.33 (0.19)		0.987
LDL-c (mmol/l)	2.52 (0.56)		1.76 (0.44)		<0.001
Triglyceride (mmol/l)	1.68 (0.15)		1.43 (0.14)		<0.001
CAP (dB/m)	287.24 (36.85)		190.60 (31.76)		<0.001
LSM (kPa)	5.60 (2.90)		4.30 (1.45)		<0.001
Type 2 diabetes		42 (30.00)		4 (7.69)	0.001
Dyslipidemia		90 (64.29)		15 (28.85)	<0.001
Hypertension		68 (48.57)		13 (25.00)	0.003
Metabolic syndrome		79 (56.43)		7 (13.46)	<0.001
Central obesity		90 (64.29)		21 (40.38)	0.003
Hypercholesterolemia		26 (18.57)		5 (9.62)	0.134
Low HDL-c		32 (22.86)		10 (19.23)	0.589

Variable	MAFLD Mean ± SD	n (%)	Non-MAFLD Mean ± SD	n (%)	p-value*
Elevated LDL-c		58 (41.43)		3 (5.77)	<0.001
Elevated triglycerides		65 (46.43)		6 (11.54)	<0.001
ALT/AST ratio > 1		54 (38.57)		21 (40.38)	0.819
BMI ≥ 25		72 (51.43)		11 (21.15)	<0.001
Chronic hepatitis B		32 (22.86)		7 (13.46)	0.150
Chronic hepatitis C		7 (5.00)		2 (3.85)	0.541
Alcoholic liver disease		14 (10.00)		3 (5.77)	0.272

Patients with MAFLD show significantly higher levels of BMI, glucose, LDL-c, triglycerides, and liver stiffness (LSM) compared to non-MAFLD, with p-values < 0.001. Additionally, there is a higher prevalence of dyslipidemia, metabolic syndrome, and central obesity in the MAFLD group (all p < 0.001).

Correlation between BMI and liver steatosis and fibrosis in overweight and obese patients with MAFLD

Table 3: **Correlation analysis of BMI with liver steatosis and fibrosis indicators**

Variable	Pearson Correlation Coefficient (r)	p
BMI and liver steatosis	0.45	< 0.001
BMI and liver fibrosis	0.34	< 0.05

BMI is moderately correlated with both liver steatosis and fibrosis, with stronger association seen for steatosis.

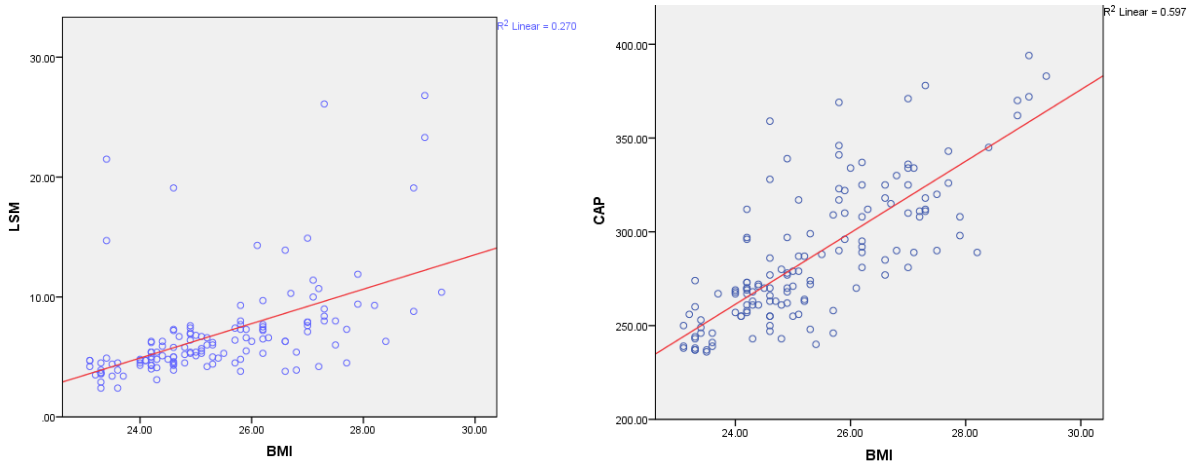

Figure 2: **Scatter plots showing correlations of BMI with liver fibrosis and liver steatosis**

The risk factors for significant liver fibrosis (F ≥ 2) in overweight and obese patients with MAFLD

Table 4: **Prevalence of significant liver fibrosis (F ≥ 2) among overweight and obese patients with MAFLD and non-MAFLD.**

Significant Fibrosis	MAFLD (n=140)	Non-MAFLD (n=52)	p-value
Yes, n (%)	45 (32.14)	3 (5.77)	<0.001
No, n (%)	95 (67.86)	49 (94.23)	

Patients with MAFLD have a significantly higher prevalence of significant fibrosis compared to non-MAFLD patients, with a p-value < 0.001.

Table 5: **The risk factors for significant liver fibrosis (F ≥ 2) in overweight and obese patients with MAFLD**

Variables	Univariate Analysis	p-value	Multivariate Analysis	p-value
	OR (95% CI)		OR (95% CI)	
Age	1.02 (0.99-1.04)	0.215		
Gender	0.63 (0.31-1.29)	0.207		
BMI ≥ 25	7.93 (3.32-18.94)	<0.001	4.17 (1.34-13.01)	0.014
Central obesity	4.49 (1.82-11.06)	0.001		
Hypertension	4.71 (2.16-10.30)	<0.001		
Type 2 diabetes	4.89 (2.24-10.65)	<0.001		
Dyslipidemia	4.49 (1.82-11.06)	0.001		
Metabolic syndrome	7.15 (2.90-17.63)	<0.001		
Low HDL-c	1.36 (0.60-3.11)	0.461		
High LDL-c	2.35 (1.14-4.84)	0.021		
High Triglycerides	2.97 (1.42-6.21)	0.004		
ALT/AST ratio >1	1.25 (0.61-2.58)	0.542		
Comorbid MAFLD	5.36 (2.49-11.53)	<0.001	4.74 (1.82-12.32)	0.001

In univariate analysis, BMI ≥ 25, central obesity, hypertension, type 2 diabetes, dyslipidemia, metabolic syndrome, and comorbid MAFLD were all significantly associated with the outcome. In multivariate analysis, BMI ≥ 25 (OR 4.17, p = 0.014) and comorbid MAFLD (OR 4.74, p = 0.001) remained independent predictors.

IV. DISCUSSION

Characteristics of the Study Population

The mean age of the study participants was 48.5 ± 12.4 years, similar to other studies on MAFLD, such as Yamamura et al. (54 years) [9]. The percentage of males was 52.1%, while females accounted for 47.9%, aligning closely with the study by Yuan et al. (males 46%, females 54%) [10]. The average BMI was 29.7 ± 3.1 kg/m², consistent with the study by Yamamura et al., which reported an average BMI of 25 kg/m² [9]. The mean waist circumference was 98.2 ± 12.5 cm, with an abnormal waist circumference rate of 100%. The hypertension rate was 42.7%, close to the results of Yuan et al., which reported a hypertension rate of 43.7% in the MAFLD group [10]. The dyslipidemia rate in our study was 56.8%, These findings indicate that the characteristics of our study population are consistent with previous studies on MAFLD, especially in terms of age, gender, BMI, waist circumference, and metabolic risk factors such as hypertension, type 2 diabetes, and dyslipidemia. This supports the strong association between overweight, obesity, and metabolic disorders and highlights the importance of screening and managing these risk factors to prevent complications related to liver and cardiovascular diseases.

MAFLD in Overweight and Obese Patients

In our study, patients with MAFLD had a higher BMI than those without MAFLD. A higher BMI is an independent risk factor for fatty liver disease. We also observed that LDL-c, triglycerides, fasting glucose, central obesity, and metabolic syndrome were all higher in the MAFLD group compared to the

non-MAFLD group, consistent with the results of Yuan and [10].

These results demonstrate a strong association between overweight, obesity, metabolic disorders, and MAFLD. Our findings also align with the literature on the connection between overweight, obesity, MAFLD, and cardiovascular diseases through mechanisms like inflammation, insulin resistance, and dyslipidemia.

The prevalence of overweight and obese patients with MAFLD in our study was 72.92%, higher than the meta-analysis of MAFLD prevalence in overweight and obese populations, which was 50.7% [11]. These differences might be attributed to variations in geographical factors, liver fat assessment methods, and demographic characteristics.

A study by Yuan et al. in the general population in China reported a MAFLD prevalence of 67.6%, while Kleef et al. reported a prevalence of 34.3% [10]. This discrepancy may be due to our study's focus on overweight and obese individuals—a group at higher risk for MAFLD—resulting in a higher prevalence compared to studies on the general population. We used FibroScan to assess liver fat, while many other studies use abdominal ultrasound, which has high sensitivity and specificity but is less accurate in mild steatosis cases. FibroScan has been shown to have higher sensitivity and specificity for evaluating mild liver fat accumulation.

Even when using the same assessment technique as Yuan's study, the MAFLD prevalence may differ because our cutoff threshold was ≥ 236 dB/m, lower than Yuan's threshold of ≥ 244 dB/m [10]. This suggests that the cutoff thresholds used in evaluation can significantly impact the results.

Correlation between BMI and Liver Fat and Fibrosis Indices

Overweight and obesity are major risk factors for metabolic-associated fatty liver disease (MAFLD). Our study showed a positive correlation between increased BMI and the degree of steatosis (CAP), with a correlation coefficient of r = 0.77. This result is consistent with Zysk's study, which found a correlation coefficient of r = 0.67 between BMI and the degree of liver fat accumulation [12].

Additionally, our study observed a positive correlation between BMI and liver fibrosis (LSM), with a correlation coefficient of r = 0.52, higher than in other studies like Gopalakrishna's (r = 0.31), due to differences in study populations and the presence of comorbid liver diseases in our cohort [13].

The physiological mechanism indicates that fat accumulation and inflammation in the liver due to obesity contribute to the progression of liver fibrosis. These factors increase liver stiffness and the association between BMI with metabolic disorders and liver fibrosis in MAFLD, aligning with our results and other studies. Thus, patients with MAFLD with higher BMI tend to have more significant liver fat and fibrosis.

Predictive Factors for Significant Fibrosis in Overweight and Obese Patients with MAFLD

Assessing liver fibrosis is a crucial step in managing MAFLD patients because it impacts treatment, monitoring, and prognosis. Patients with higher levels of liver fibrosis have a greater risk of both hepatic

and extrahepatic complications [14]. In our study, obesity grade I (BMI ≥ 25 kg/m²) and MAFLD with comorbid liver conditions like viral hepatitis B, viral hepatitis C, and alcoholic liver disease were identified as risk factors for significant liver fibrosis (F ≥2).

Sachar's study identified three risk factors for advanced liver fibrosis, including increased BMI, central obesity, and hepatitis C [15]. However, our study identified only two risk factors, possibly due to the high rate of treated patients affecting test results.

Significant fibrosis is considered a crucial threshold in MAFLD treatment as this stage is manageable and reversible through lifestyle changes, along with the development of new therapies like resmetirom. Our study emphasizes that early identification of risk factors like obesity and comorbid liver conditions can help clinicians develop optimal monitoring and treatment plans for MAFLD patients.

V. CONCLUSION

This study highlights the strong association between BMI and the degree of steatosis and liver fibrosis in overweight and obese patients with MAFLD. The results underscore the importance of controlling weight and managing comorbid liver conditions to prevent the progression of liver disease in this population.

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