Characteristics of Metabolically Dysfunctional Associated Fatty Liver Disease (MAFLD) patients in Al Rajhi Hospital Nutrition Clinic: A Cross-sectional Study

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Abstract:

Objective: Fatty liver disease has become the most frequent chronic liver disease and the fastest-growing reason for liver transplant among waiting list registrants. Egypt is one of the top 10 nations with the prevalence of fatty liver disease. We assessed the prevalence of Metabolically Dysfunctional Associated Fatty Liver Disease (MAFLD) among patients presenting to the nutrition clinic in our hospital between June 2022 and June 2023.

Design: In this cross-sectional study, we collected a group of patients attending to Al Rajhi hospital nutrition clinic in Assiut. Our primary outcome was screening for MAFLD among those patients. Secondary objectives included assessing the degree of fibrosis and steatosis using FibroScan with CAP, the rate of obesity, diabetes, and hyperlipidaemia, and the proportion of patients with other related chronic liver disease (CLD).

Results: Of 1120 patients evaluated, 365 (32.6%) had MAFLD. The mean age of MAFLD patients was 45. (53.3%) were females. Mean fibrosis reading was 6.52 (kPa), and (≥F2) was noted in (23.5%) of MAFLD patients. Mean CAP measurement was 263.45 (dB/m), and S3 (severe steatosis) was reported in 88 (24.1%) MAFLD patients. DM was noted in 17 (4.5%) of MAFLD patients, obesity was noted in 326 (89.3%), and hypertriglyceridemia was reported in 95 (26%). Hepatitis B surface antigen was positive in 20 (5.5%), and Hepatitis C antibodies were positive in 123 (33.7%) of MAFLD patients.

Conclusion: In this cohort of patients, MAFLD was noted in 1 in every 3 patients. Most of those were obese female patients. This is nearly similar to the previous data with the previous nomenclature, NAFLD.

Keywords: Fatty liver; MAFLD; FibroScan; Nafld; Obesity.

Introduction:

Nonalcoholic fatty liver disease (NAFLD) is defined as the presence of macrovesicular steatosis in ≥ 5% of hepatocytes in individuals who consume little or no alcohol (1). NAFLD has become the most common chronic liver disease, with an estimated global prevalence of 25-30% of adults, and is now considered a public health issue (2-5). It is also the most rapidly growing reason for liver transplant among waiting list registrants (6, 7).

NAFLD has a close association with obesity, DM, hyperlipidemia, and metabolic syndrome. It is also known that the prevalence of NAFLD increases with increasing body mass index (BMI). (8, 9). Egypt, a Middle Eastern country with a population of ~100 million people, 60% of whom are under 30 years old (10), ranks in the top ten countries in terms of obesity prevalence (11). The prevalence rate of

NAFLD in the Middle East and North Africa (MENA) reaches up to 31.8% of all adults, which is considered one of the highest NAFLD prevalence rates (2).

NAFLD is divided into two major subtypes: nonalcoholic fatty liver (NAFL) and nonalcoholic steatohepatitis (NASH) (1). Eslam et al., in a consensus expert statement, proposed the new nomenclature (metabolic dysfunction-associated fatty liver disease, MAFLD) and the new criteria for diagnosing MAFLD (4). They also proposed criteria for the diagnosis of MAFLD-related cirrhosis and concomitant MAFLD, and other liver disease (4). They considered MAFLD a separate disease entity caused by metabolic dysregulation and required criteria for the diagnosis, not just a disease of exclusion (4).

Aim

Screening for MAFLD among patients attending Al Rajhi Hospital Nutrition Clinic, assessing the degree of fibrosis and steatosis in MAFLD patients using FibroScan with CAP, the rate of obesity, diabetes, and hyperlipidaemia, and the proportion of patients with other related chronic liver disease (CLD).

Methods

This study was a prospective cross-sectional study conducted in Al Rajhi Hospital Nutrition Clinic, Department of Tropical Medicine and Gastroenterology, that included outpatient subjects presenting to the clinic between June 2022 and June 2023, Assiut, Egypt. The inclusion criteria were age (18- 60 years), both sexes, and a BMI > 18 kg/m^2. Exclusion criteria were pregnant females, BMI < 18 kg/m^2, and patients who refused to participate in the study.

The Institutional Review Board (IRB) of the Faculty of Medicine at Assiut University approved the study protocol with the number **17101472**.

Patients and their relatives were invited to undergo screening for fatty liver by undergoing a conventional abdominal ultrasound by the nutrition clinic team members to assess liver echopattern. Patients with detected bright liver by US suggestive of fatty liver have undergone an evaluation for the BMI and tests to detect metabolic dysregulation, which included waist circumference ≥102/88 cm in men and women, blood pressure ≥ 130/85 mmHg or specific drug treatment, plasma triglycerides ≥150 mg/dl or specific drug treatment, plasma HDL-cholesterol <40 mg/dl for men and <50 mg/dl for women or specific drug treatment, prediabetes: HbA1c 5.7% to 6.4% and plasma high-sensitivity C-reactive protein level (CRP) >2 mg/L.

The diagnosis of MAFLD was made when a patient had a BMI >25 kg/m2, DM, or at least two metabolic risk abnormalities in lean patients.

All patients diagnosed with MAFLD have undergone detailed history-taking (age, sex, comorbid disease, etc.), clinical examination (pulse, blood pressure, BMI, etc.), and laboratory work that included liver function tests (ALT, AST, albumin, and bilirubin), INR, CBC, HCV antibody (HCV Ab), HBV surface antigen (HBsAg), thyroid stimulating hormone (TSH), free T3 (FT3), free T4 (FT4), and CRP.

FibroScan with CAP (Echosens FibroScan® Compact 530) was used to evaluate steatosis and fibrosis; 10 correct readings were taken for every patient. The IQR-to-median ratio had to be <30% for the whole scan to be correct. The M probe was routinely used in all patients except those with deep liver; the XL probe was used as suggested by the device. Fasting for at least 3 hours before the procedure was a prerequisite (12). A cut-off value of 238 for significant hepatic steatosis was used (13).

Results

A total of 1120 patients were evaluated for the presence of MAFLD in the current study. Out of those patients, 365/1120 (32.6%) patients had MAFLD, as shown in **Figure 1**

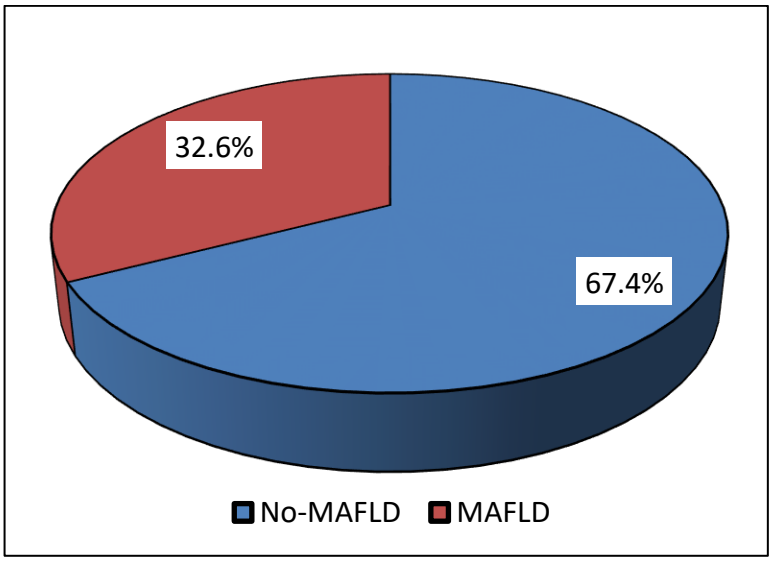

Fig. (1): Frequency of MAFLD among the study group

Baseline data among those patients with MAFLD:

The mean age of patients was 45.15 years, ranging between 18 and 45 years old. The majority (53.3%) of patients were females, and 170 (46.6%) patients were males. Mean body mass index was 29.87 (kg/m^2) while mean waist circumference was 103.25 (cm). Only 17 (4.7%) patients had diabetes, as shown in Table 1.

Table (1): Baseline data among those patients with MAFLD

	N= 365
Mean age (years)	45.15 ± 27.16
Range	18-45
Sex	
Male	170 (46.6%)
Female	195 (53.3%)
Mean body mass index (kg/m^2)	29.87 ± 4.78
Mean systolic blood pressure (mmHg)	123.58 ± 12.78
Mean diastolic blood pressure (mmHg)	82.09 ± 4.33
Waist circumference (cm)	103.35 ± 13.32
Diabetes mellitus	17 (4.5%)

Data expressed as frequency (percentage), mean (SD), and range. MAFLD: metabolic dysfunction-associated fatty liver disease.

Baseline laboratory data among the studied patients:

Baseline laboratory data are summarized in Table 2. It was found that 20 (5.5%) and 123 (33.7%) patients had positive HBsAg and HCV Ab, respectively.

Table (2): Baseline laboratory data among the studied patients

	N= 365
Complete blood count	
Hemoglobin (mg/dl)	13.27 ± 1.78
Leucocytes (10^3/ul)	6.95 ± 2.29
Platelets (10^3/ul)	257.02 ± 66.38
Lipid profile	
Triglycerides (mg/dl)	133.84 ± 74.52
Low density lipoproteins (mg/dl)	93.94 ± 19.36
High density lipoproteins (mg/dl)	38.77 ± 7.63
Cholesterol (mg/dl)	189.45 ± 12.87
Liver function tests	
Total bilirubin (mg/dl)	0.63 ± 0.36
Direct bilirubin (mg/dl)	0.16 ± 0.11
Total proteins (g/l)	8.35 ± 3.7
Albumin (g/l)	4.62 ± 2.40
Aspartate transaminase (u/l)	27.64 ± 17.39
Alanine transaminase (u/l)	29.08 ± 18.23
Alkaline phosphatase (u/l)	96.08 ± 28.48
Coagulation profile	
International randomized ratio	0.96 ± 0.13
Prothrombin time (sec)	11.09 ± 0.18
Prothrombin concentration (%)	97.98 ± 0.50
Thyroid function tests	
Thyroid-stimulating hormone (mIU/l)	1.78 ± 0.62
Triiodothyronine (ng/dl)	24.28 ± 9.84
Thyroxin (μg/dl)	1.69 ± 0.70
Inflammatory markers	
C-reactive proteins (mg/dl)	5.73 ± 2.20
Viral markers	
Hepatitis B surface antigen	20 (5.5%)
Hepatitis C antibodies	123 (33.7%)

Data expressed as frequency (percentage), mean (SD)

Distribution of patients based on classes of body mass index:

We found that a total of 166 (45.5%) patients had a BMI between 25-30 kg/m^2, 109 (29.8%) patients had a BMI between 30-35 kg/m^{2,} while the other 51 (14%) patients had a BMI exceeding 35 kg/m^2. There were only 39 (10.7%) patients who had a normal body mass index (between 18-24.9 kg/m^2) as shown in Figure 2.

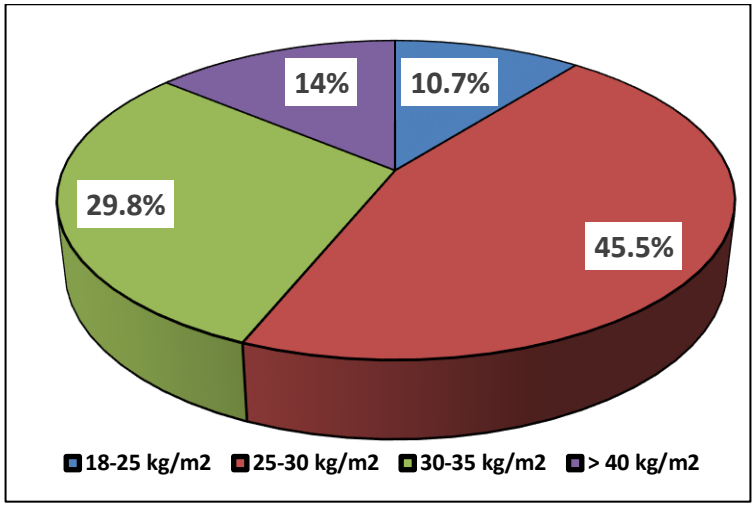

Fig. (2): Classification of patients based on body mass index

Frequency of males' and females' patients that exceeded normal waist circumference (WC): A total of 49/170 (28.8%) male patients had WC > 102 cm, and 183/195 (93.8%) female patients had WC > 88 cm, as shown in Figure 3.

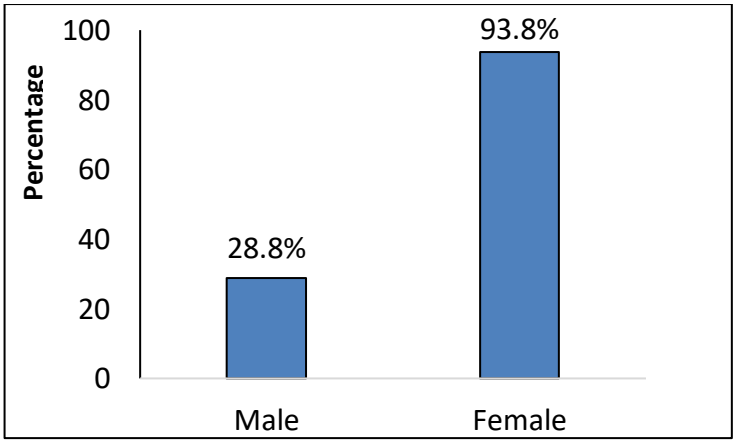

Fig. (3): Frequency of males' and females' patients that exceeded normal WC

FibroScan and CAP assessment among the studied patients:

It was found that the mean fibrosis reading was 6.52 (kPa). 198 (54.2%) of patients had F0, while 81 (22.2%), 56 (15.3%), 18 (4.9%), and 12 (3.3%) patients had F1, F2, F3, and F4, respectively, as shown in Table 3 and Figure 6.

Table (3): FibroScan and CAP measurement among the studied patients

	N= 365
Fibrosis reading	
Mean ± SD	6.52 ± 2.35
Category	
F0	198 (54.2%)
F1	81 (22.2%)
F2	56 (15.3%)
F3	18 (4.9%)
F4	12 (3.3%)

	N= 365
CAP assessment	
Mean ± SD	263.45 ± 54.86
Category	
S0	93 (25.5%)
S1	87 (23.8%)
S2	97 (26.6%)
S3	88 (24.1%)

Data is expressed as frequency (percentage) and mean (SD).

Discussion

In our study, we adopted the criteria proposed by the aforementioned international expert consensus (4) to detect cases of MAFLD.

MAFLD was detected in 365 out of 1120 precipitants (32.6%). Those results were consistent with previous studies addressing the prevalence of NAFLD. Younossi et al. performed a meta-analytic assessment for the global epidemiology of NAFLD, searching PubMed/MEDLINE from 1989 to 2015 for terms involving epidemiology and progression of NAFLD. They found that the prevalence of NAFLD varies from 13.5% in Africa to 31.8% in the Middle East (2).

Similar to our study, they excluded the pediatric population (<18 years old) and patients diagnosed only by blood tests. They included only patients in whom imaging studies were done in addition to blood tests and/or liver biopsy. However, unlike our study, they excluded patients with viral hepatitis B or C, which could explain the slightly higher number we found, along with the worldwide increasing prevalence of obesity and its impact on the increasing prevalence of fatty liver disease (14).

Lin et al. conducted another study comparing MAFLD and NAFLD using data from the third National Health and Nutrition Examination Surveys of the United States (NHANES III), an impartial survey dataset often utilized for studying fatty liver disease. MAFLD was diagnosed in 4087/13083 (31.24%) participants, while NAFLD was diagnosed in 4347/13083 (33.23%) (15).

Regarding the demographic data of patients diagnosed with MAFLD in our study, female predominance was observed with 195 (53.3%) patients, which was expected given the higher prevalence of overweight and obesity in Egyptian females. More than 71.2% of adult men are overweight, 26.4% are obese, 79.4% of adult women are overweight, and 48.4% are obese (16). This female predominance was consistent with the study done by Lin et al., in which they found 53% of patients to be females (15).

Regarding DM in MAFLD, Lin et al. found 28.65% of MAFLD patients to have diabetes (15). Younossi et al. found 22.51% of NAFLD patients to be diabetic (2).

In our study, DM was observed in 17/365 (4.5%) of MAFLD patients, which is much lower than previous studies, which could be explained by the fact that we used only HbA1C for the diagnosis of DM regardless of the treatment status of patients, as many patients could have been controlled and were not considered as diabetics.

Regarding viral hepatitis in patients with MAFLD, we have found that HCV Ab was positive in 123/365 (33.7%) of MAFLD patients, while HBsAg was positive in 20/356 (5.5 %) Those numbers could be explained under the umbrella of the previous data suggesting an inverse relation between hepatic steatosis and HBV replication (17-19). Although the underlying mechanisms are unclear, some studies have proposed that fat deposition in HBV-infected hepatocytes may impede HBV replication. (20).

Although the global estimated prevalence of liver steatosis in patients with HCV infection varies between 40% and 80% (21), the lower number we observed could be explained by the fact that all the patients we recruited were eligible for and had already received direct acting antivirals (DAAs), which were shown to decrease the severity of hepatic steatosis (22).

Regarding CAP, a cut-off value to detect hepatic steatosis of ≥ 238 (≥ S1) was adopted (13). Results showed that 74.5% of patients had ≥ S1 with a mean CAP of 263.45 ± 54.86 SD, consistent with the mean value of 268±64 obtained in a previous study on a group of patients with metabolic risk factors (23).

Karlas et al. reviewed literature to identify studies containing histology-verified CAP for steatosis grading (S0–S3). They found that optimal cut-offs were 248 (237–261) and 268 (257–284) for those above S0 and S1, respectively(24).

It is important to mention that CAP showed excellent diagnostic performance for differentiating the presence and absence of hepatic steatosis but has limited value in evaluating grades of steatosis (13).

Regarding fibrosis, the cut-off value of <8 kPa has a 94–100% negative predictive value to exclude significant hepatic fibrosis (25), and the cut-off values used to identify stages of hepatic fibrosis are as follows: 7.1 kPa for F ≥ 2, 9.5 kPa for F ≥ 3, and 12.5kPa for F4 (13).

We found the degree of liver stiffness to be 6.52 ± 2.35kPa; in a previous study, they found it to be 4.9 ± 2.7kPa (23). The higher mean value we got could be explained by the fact that 33.7% of our patients had HCV, unlike the other study, which was performed only in patients with metabolic risk factors without a history of chronic liver disease.

Lin et al. used a FIB-4 score >1.3 (not FibroScan) to compare the degree of fibrosis between NAFLD (21.60% of patients) and MAFLD (23.63% of patients). A statistically significant difference was found (p-value =0.027). (Lin et al., 2020).

Conclusion

Our study draws attention to the new method proposed for diagnosing fatty liver disease (MAFLD), making it a diagnosis of inclusion rather than just a diagnosis of exclusion. Given our study's results, the MAFLD frequency is nearly similar to that of the previous nomenclature, NAFLD. It also reinforces the theory that fatty liver disease can coexist with other chronic liver diseases, specifically chronic viral hepatitis B and C.

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