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Study of risk factors of Metabolic Associated Fatty Liver Disease (MAFLD) in Fayoum Governorate

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ABSTRACT

Background and aim; Metabolic associated fatty liver disease (MAFLD) is a new definition in 2020. MAFLD is extremely away concept from criteria for non-alcoholic fatty liver disease (NAFLD). The most significant differences between MAFLD and NAFLD are diagnosis of MAFLD not need alcohol exclusion, chronic liver diseases and the existence of metabolic dysregulation is substantial for MAFLD diagnosis. The current study aimed to distinguish risk factors of MAFLD in Fayoum Governorate. Subjects and methods; In total 1061 subjects of simple random samples from Fayoum University Hospital were selected to perform the current cross-sectional study. The selected subjects were clinically assessed and investigated by laboratory tests including Liver enzymes, serum lipid profile, and imaging i.e., abdominal ultrasound and transient elastography(fibroscan). Results; Level of blood cholesterol and triglycerides were a statistically significantly higher in patients with MAFLD than those without MAFLD. Multiple forward stepwise logistic regression analysis identified female sex. High cholesterol level, and high triglycerides level to be statistically significant predictors for MAFLD. Conclusions; According to our research, patients with MAFLD had a statistically significant higher BMI than those without MAFLD. Blood triglyceride and cholesterol levels were statistically substantially higher in MAFLD patients than in non-MAFLD individuals. High numbers of individualswith MAFLD were diabetics and hypertensives.

1. Introduction

It is known thathighbody mass index (BMI) and waist circumference havean important role in the appearance of metabolic associated fatty liver disease (MAFLD), and their relationwith MAFLD [1–3]. Multiple logistic regression analysis, with controls for body weight, exercise, and sleep, revealed that the severity of MAFLD was positively and independently linked with the levels of hemoglobin (HGB), platelets (PLT), triglyceride (TG), and fasting plasma glucose (FPG) [4]. The liver plays a central role in metabolism of lipids and glucose [5]. Patients with MAFLD have been shown to have lower high-density lipoprotein cholesterol (HDL-C) levels and higher levels of serum total cholesterol (TC), TG, and low-density lipoprotein cholesterol (LDL-C), according to numerous research [6–9]. Metabolic syndrome and MAFLD were significantly correlated with elevated alanine aminotransferase (ALT) levels as elevated ALT levels are indicative [10].

The changing from steatosis to metabolic associated steatohepatitis(MASH) and liver fibrosis may be multi-etiological factors [11]. Changeable microbiota and permeability of the gut, significant severity of metabolic changes,pro-inflammatory imbalances, and oxidative stress may all be identified; with genetic factors haveimportant role [12,13]. MAFLD is diagnosed based on clinical history, laboratory and radiographic studies which are further complemented by histologic information. Abdominal imaging revealing hepatic steatosis may be sufficient for diagnosis of MAFLD and liver biopsy may not be required if clinical and laboratory data have ruled out other causes of liver disease [14,15]. Therefore, the study's objective was to determine the Fayoum Governorate's metabolic associated fatty liver disease (MAFLD) risk factors.

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2. Materials and methods

A cross sectional study was conducted on 1061 subjects of simple random samples from Fayoum University Hospital, the study was conducted from September 2020 to September 2022. The Ethics Review Committee of the Faculty of Medicine at Fayoum University granted ethical permission for the study. Written informed consent was acquired from every individual involved.

2.1. Inclusion and exclusion criteria:

Inclusion criteria were (a) male or female patients and (b) patients with age more than 18 years old. While exclusion criteria were (a)patients with end stage liver disease, (b) patients aged less than 18years, and (c)refusal of consent informs.

All patients were subjected tohistory taking and thorough medical examination stressing onfatigue, malaise, and vague right upper abdominal discomfort. A survey with an emphasis on behavioral variables, family history, pharmaceutical history, disease history, and demographics (such as sex, age, and education). Anthropometric measurements, included height, weight, waist circumference, hip circumference, systolic and diastolic blood pressures, and heart rate. BMI was also calculated.

2.2. Laboratory investigations

Some laboratory investigations were performed includecomplete blood count, fasting blood glucose,serum lipid profile, HBA1C, HOMA IR CRP,measurement of liver enzymes, serumaspartate aminotransferase (AST), and ALT.

2.3. Statistical analysis

Values were presented as mean ± standard deviation, median, and interquartile range for descriptive statistics, where applicable. The non-parametric Mann-Whitney test was employed to determine significance. P-values and frequency (%) were used to display data for categorical variables.

3. Results

This cross-sectional study has included 1061 persons. Compared to patients without MAFLD, those with MAFLD were older (mean ± SD= 49.5 ± 13.7 vs. 47.5 ± 14.8), which was a statistically significant, p=0.033. Prevalence rate of MAFLD was found to be higher in females (72.5 %) than males (63.2%) (OR =1.537, 95% CI =1.183–1.997, p=0.001) as demonstrated in Table (1).

Table 1: Relation between socio-demographics and prevalence of MAFLD.

	MAFLD (N=715)		No MAFLD (N=346)		Mean Difference (95% CI)	P-value
	Mean	SD	Mean	SD		
Age	49.5	13.7	47.5	14.8	2.022 (0.167-3.877)	0.033*
	N	%	N	%	Odds ratio (95% CI)	P-value
Sex						
Male	367	63.2%	214	36.8%	R	
Female	348	72.5%	132	27.5%	1.537 (1.183-1.997)	0.001*

MAFLD; Metabolic associated fatty liver disease and SD; standard deviation.

Table (2) indicated that patients with MAFLD had a statistically significant higher BMI ,waist circumference than patients without MAFLD (mean ± SD= 28.4 ± 3.7 vs. 25.3 ± 2.5), p<0.001, (mean ± SD=102.2 ± 13.7),p- value 0.17.Cutoff values of BMI were: normal weight - BMI greater than or equal to 18.5 to 24.9 kg/m^2, and overweight – BMI greater than or equal to 25 to 29.9 kg/m^2. While, obesity – BMI greater than or equal to 30 kg/m^2.

Table 2: Difference in BMI ,waist circumference according to MAFLD.

	MAFLD (N=715)		No MAFLD (N=346)		Mean Difference (95% CI)	P-value
	Mean	SD	Mean	SD		
BMI	28.4	3.7	25.3	2.5	3.060 (2.684-3.436)	<0.001*
	N	%	N	%	Odds ratio (95% CI)	P-value
BMI						
Normal	121	37.9%	198	62.1%	R	
Overweight	336	73.5%	121	26.5%	4.544 (3.342-6.178)	<0.001*
Obese	258	90.5%	27	9.5%	15.636 (9.906-24.681)	<0.001*
Waist circumference (cm)	102.2	13.7	103.3	11.4		0.17

BMI; Body mass index, SD; standard deviation, MAFLD; Metabolic associated fatty liver disease, and values of waist circumference comparison are mean ±SD .

Compared with normal body weight, increasing levels of obesity was associated with increasing odds of MAFLD: for overweight, OR = 4.544 (95% CI: 3.342-6.178, with a statistical significant p<0.001) and for obese, OR = 15.636 (95% CI: 9.906-24.681, p<0.001) as presented in Table (3).

Table 3: Co-morbidities in relation to MAFLD

	MAFLD (N=715)		No MAFLD (N=346)		Odds ratio (95% CI)	P-value
	N	%	N	%		
D.M						
Not present	390	65.3%	207	34.7%	R	
Present	325	70.0%	139	30.0%	1.241 (0.956-1.610)	0.104
HTN						
Not present	372	65.4%	197	34.6%	R	
Present	343	69.7%	149	30.3%	1.219 (0.941-1.579)	0.133

MAFLD; Metabolic associated fatty liver disease and SD; standard deviation.

According to Table (4) patients with MAFLD had statistically substantially higher levels of AST and ALT than patients without MAFLD (mean ± SD= 48.9 ± 11.7 vs. 35.7 ± 10.4 for AST and 49.1 ± 11.6 vs. 36.0 ± 10.6 for ALT, p<0.001).

Table 4: Difference between patients with MAFLD and those without as regards Liver enzymes

	MAFLD (N=715)		No MAFLD (N=346)		Mean Difference (95% CI)	P-value
	Mean	SD	Mean	SD		
AST	48.9	11.7	35.7	10.4	13.178 (11.788-14.569)	<0.001*
ALT	49.1	11.6	36	10.6	13.072 (11.662-14.482)	<0.001*

MAFLD; Metabolic associated fatty liver disease, SD; standard deviation.

According to Table (5), individuals with MAFLD had statistically substantially higher blood levels of triglycerides and cholesterol (HDL, LDL) than patients without MAFLD (mean ± SD= 219 ± 23.5 vs. 200 ± 14.5 for cholesterol and 214.7 ± 44.7 vs. 153.9 ± 22.9 for triglycerides, p<0.001).

Table 5: Association between Lipid profile and MAFLD

	MAFLD (N=715)		No MAFLD (N=346)		Mean Difference (95% CI)	P-value
	Mean	SD	Mean	SD		
Cholesterol	219.9	23.5	200	14.5	19.838 (17.531-22.144)	<0.001*
TAG	214.7	44.7	153.9	22.9	60.791 (56.719-64.863)	<0.001*
	N	%	N	%	Odds ratio (95% CI)	P-value
Hypercholesterolemia						
Desirable	185	46.5%	213	53.5%	R	
Borderline	339	72.7%	127	27.3%	3.073 (2.315-4.081)	<0.001*
High	191	97.0%	6	3.0%	36.651 (15.884-84.572)	<0.001*
Hypertriglyceridemia						
Normal	28	10.3%	243	89.7%	R	
Borderline	170	70.0%	73	30.0%	20.210 (12.634-32.587)	<0.001*
High	517	94.5%	30	5.5%	149.650 (87.409-255.905)	<0.001*
HDL-cholesterol (mg/dL)	44	11	45	11		0.4
LDL-cholesterol (mg/dL)	122	68	149	73		0

MAFLD; Metabolic associated fatty liver disease, SD; standard deviation.

As compared to desirable level of blood cholesterol, increasing levels was a statistically significantly associated with increasing risk of MAFLD: for borderline level, OR = 3.073 (95% CI: 2.315-4.081, p<0.001) and for high level, OR = 36.651 (95% CI: 15.884-84.572, p<0.001). Cutoff values of blood cholesterol are: Normal: Less than 200 mg/dL. Borderline high: 200 to 239 mg/dL. High: At or above 240 mg/dL.

Likewise, increasing levels of blood triglycerides was a statistically significantly associated with increasing risk of MAFLD as follow; for borderline level, OR = 20.210 (95% CI: 12.634-32.587, p<0.001) and for high level, OR = 149.650 (95% CI: 87.409-255.905, p<0.001).Cutoff values of blood triglycerides are: Normal — Less than 150 milligrams per deciliter (mg/dL), or less than 1.7 millimoles per liter (mmol/L) Borderline high — 150 to 199 mg/dL (1.8 to 2.2 mmol/L) High — 200 to 499 mg/dL (2.3 to 5.6 mmol/L).

Multiple forward stepwise logistic regression analysis identified that female sex {OR = 1.486 (95% CI: 1.073-2.059, p=0.017)}, high cholesterol level {OR = 4.667(95% CI: 1.910-11.401, p<0.001)}, and high triglycerides level {OR = 19.798 (95% CI: 12.972-30.216, p<0.001)} to be statistically significant predictors for MAFLD, as shown in Table (6).

Table 6: Multiple logistic regression.

	B	P-value	Odds ratio	95% CI for odds ratio	
				Lower	Upper
Sex (female vs. male)	0.396	0.017	1.486	1.073	2.059
Blood cholesterol(High cholesterol vs. normal and borderline)	1.54	<0.001	4.667	1.910	11.401
Blood triglycerides (High triglycerides vs. normal and borderline)	2.986	<0.001	19.798	12.972	30.216
Constant	-0.665	<0.001	0.514		

As regards FIB-4,patients with level less than 1.45 were 47.9%,patients with level between 1.45and 3.25 were 19.9%and patients with level more than 3.25 were 5.1% (Table 7). Patients with MAFLD have higher level of FIB4 than non MAFLD patients (mean ± SD=1.370 ± 1.026) .p-value 0.14. Using a lower cutoff value of 1.45, a FIB-4 score <1.45 had a negative predictive value of 90% for advanced fibrosis (Ishak fibrosis score 4-6 which includes early bridging fibrosis to cirrhosis). In contrast, a FIB-4 >3.25 would have a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Table 7: FIB-4, Association between FIB -4 and MAFLD

FIB-4	N	%
<1.45	795	74.9%
1.45-3.25	212	19.9%
>3.25	54	5.1%
Association between FIB -4 and MAFLD		
MAFLD	No MAFLD	P-value
1.370 ± 1.026	1.145 ± 0.828	0.14

MAFLD Metabolic associated fatty liver disease. Values of FIB 4 comparison are mean ± SD.

Table (8) demonstrated the U/S and fibro-scan findings. In about one third of study participants 346/1061 (32.6%), U.S was normal. While in near half 525/1061 (49.5%), U.S showed mild steatosis. Moderate and severe steatosis was found in 150/1061 (14.1%) and 40/1061 (3.8%), respectively. By the same manner, about one third of study participants 344/1061 (32.4%), had S0 by fibro-scan. While in less than half 509/1061 (48.0%), fibro-scan revealed S1. S3, S4 were found in 163/1061 (15.4%) and 45/1061 (4.2%), respectively. According to Table (9) the HOMA-IR, HBA1C and FPG were found to be are significantly higher in patients with MAFLD.

Table 8: U/S and fibro-scan findings

	N	%
Ultrasound		
Normal	346	32.6%
Mild	525	49.5%
Moderate	150	14.1%
Severe	40	3.8%
Fibro-scan		
S0	344	32.4%
S1	509	48.0%
S2	163	15.4%
S3	45	4.2%

Table 9 : Association between labs and MAFLD

	MAFLD (N=715)		No MAFLD (N=346)		P-value
	Mean	SD	Mean	SD	
Platelet count (109/L)	259	76	278	83	0.04
Hemoglobin (g/dL)	13	1.8	13	1.7	0.9
HBA1c, %	9	1.4	7.2	1.4	0.71
FPG,	73	18	97	23	0.02
HOMA-IR score	8.64	9.48	27	9.5%	0.1

MAFLD Metabolic associated fatty liver disease,SD standard deviation.

4. Discussion

MAFLD is diagnosed based on a radiologically diagnosed hepatic steatosis and the presence of any one of the following three conditions, namely overweight/obesity, presence of diabetes mellitus (DM), or evidence of metabolic dysregulation. Increased cardiometabolic and MAFLD risk defined as the presence of at least two ofthe following at-risk criteria: (a) Waist circumference ≥102/88 cm in Caucasian men and women or ≥90/80 cm in Asian men and women). (b) Blood pressure ≥130/85 mmHg or specific drug treatment. (c) Plasma triglycerides ≥150 mg/dl (≥1.70 mmol/L) or specific drug treatment. (d) Plasma HDL-cholesterol <40 mg/dl (<1.0 mmol/L) for men and <50 mg/dl (<1.3 mmol/L) for women or specific drug treatment. (e) Prediabetes (i.e., fasting glucose levels 100 to 125 mg/dl [5.6 to 6.9 mmol/L], or 2-hourpost-load glucose levels 140 to 199 mg/dl [7.8 to 11.0 mmol] or HbA1c 5.7% to 6.4% [39 to47 mmol/mol]). (f) Homeostasis model assessment of insulin resistance score ≥2.5. (g) Plasma high-sensitivity C-reactive protein level >2 mg/L.

Mean ± SD of blood cholesterol and triglycerides were 213.4 ± 23 and 194.9 ± 48.3, respectively. Level of blood Cholesterol and triglycerides were a statistically significantly higher in patients with MAFLD than those without MAFLD (mean ± SD= 219 ± 23.5 vs. 200 ± 14.5 for cholesterol and 214.7 ± 44.7 vs. 153.9 ± 22.9 for triglycerides, p<0.001). As compared to desirable level of blood cholesterol, increasing levelswas a statistically significantly associated with increasing risk of MAFLD: for borderline level, OR = 3.073 (95% CI: 2.315-4.081, p<0.001) and for high level, OR = 36.651 (95% CI: 15.884-84.572, p<0.001). Likewise, increasing levels of blood triglycerides was a statistically significantly associated with increasing risk of MAFLD as follow; for borderline level, OR = 20.210 (95% CI: 12.634-32.587, p<0.001) and for high level, OR = 149.650 (95% CI: 87.409-255.905, p<0.001).

This was in line with the findings of Al Omary et al. [1], who stated that two putative sub-types of MAFLD have significantly different lipid compositions in their livers, according to a recent study. Patients with subtype 2 based on carrying the PNPLA3 risk genotype at rs738409 have polyunsaturated triacylglycerols (TAG), whereas subtype 1 based on insulin resistance patients typically have monounsaturated TAGs and free fatty acids loaded with ceramides in the liver.This also was in agreement with Jongraksak et al. [16] who reported that TG (mmol/L) in patients with MAFLD was 2.16+ 1.62, while TG in Non MAFLD patients was1.46+ 1.08, LDL-C (mmol/L) in patients with MAFLD was 3.13+ 0.86,while LDL in Non MAFLD patients was 2.93+0.85,HDL-C (mmol/L) in patients with MAFLD was 1.15+ 0.26,while HDL in non MAFLD patients 1.33+ 0.31.

In about one third of study participants 346/1061 (32.6%), U.S was normal. While in near half 525/1061 (49.5%), U.S showed mild steatosis. Moderate and severe steatosis was found in 150/1061 (14.1%) and 40/1061 (3.8%), respectively. By the same manner, about one third of study participants 344/1061 (32.4%), had S0 by fibro-scan. While in less than half 509/1061 (48.0%), fibro-scan revealed S1. S3, S4 fibrosis was found in 163/1061 (15.4%) and 45/1061 (4.2%), respectively.

This was in line with the findings of Eslam, et al. [17] who stated that non-invasive fibrosis scores should be used to rule out severe fibrosis in

hepatic steatosis patients. The emergence of non-invasive scores and the liver stiffness cutoffs from Transient Elastography in various demographics, with a focus on obese and diabetic individuals as specific subpopulations.

This was also consistent with the findings of Boursier, et al. [18] who stated that abdominal ultrasonography (USG), which measures the liver's increased echogenicity, is a coincidental method of diagnosing hepatic steatosis. USG has a sensitivity range of 60 to 94%, specificity of 84 to 95%, and a sensitivity of more than 90% when a liver biopsy reveals more than 20% steatosis in the liver.

Also this was in agreement with Eslam, et al. [17] whostated that research shows a strong correlation between CAP score and steatosis grades in actual clinical settings. For estimating hepatic steatosis grades like S1, S2, and S3, the ideal CAP cut-off values are > 263 dB/m, ≥ 281 dB/m, and ≥ 283 dB/m, respectively. Hepatic steatosis was similarly graded in another study according to CAP value: S1 > 238 dB/m, S2 ≥ 260 dB/m, and S3 ≥ 293 dB/m.

In our study,individuals who were not obese exhibited a more favorable metabolic profile compared to obese individuals, as evidenced by their reduced BMI, waist circumference, fasting blood sugar, lipid profile, and liver enzymes.

This was consistent with a study by Fouad, et al. [19] that found non-obese MAFLD patients had a favorable metabolic profile because, by definition, they had lower BMI, waist circumference, fasting blood sugar, and HOMA-IR, but not significantly lower lipid profiles or other characteristics when compared to their obese counterparts.

5. Conclusion

In Fayoum governorate, our findings showed that higher body mass index, waist circumference, triglyceride, cholesterol, fasting plasma glucose, were risk factors for MAFLD. Level of blood Cholesterol and triglycerides were a statistically significantly higher in patients with MAFLD than those without MAFLD. High percentages of patients with MAFLD were diabetics and hypertensives. Multiple forward stepwise logistic regression analysis identifies female sex, high cholesterol level, and high triglycerides level to be statistically significant predictors for MAFLD. With the recent consensus, this is the ideal moment to solidify the increasing momentum for change and, going forward, to priorities efforts by redefining the illness.

Author Contributions

Conceptualization, A. A. Gomaa , E. A. Hassan and M. Tawfic; Methodology, Y. Fouad and A. A. Gomaa ; Validation, E. A. Hassan; Formal analysis, M. Massoud; Investigation, A. A. Gomaa, Y. Fouad; Data curation, A. A. Gomaa, E. A. Hassan and Y. Fouad; Writing—original draft preparation, E.G.Fouad, M. Tawfic, Y. Fouad, and A. A. Gomaa; Writing—review and editing, E. G. Fouad, M. Tawfic, Y. Fouad, and A. A. Gomaa; Visualization, E. A. Hassan and E. Fares; Supervision, A. A. Gomaa, E. A. Hassan, M. Tawfic, and M. Massoud; Project administration, A. A. Gomaa, E. A. Hassan, Y. Fouad and M. Massoud; Funding acquisition, A. A. Gomaa, E. G. Fouad, and M. Massoud. All authors have read and agreed to the published version of the manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] A. Al Omary, K. Byth, M. Weltman, J. George, M. Eslam, Metabolic-associated fatty liver disease increases fibrosis severity in patients with chronic hepatitis C, in: J. Gastroenterol. Hepatol., WILEY 111 RIVER ST, HOBOKEN 07030-5774, NJ USA, 2020: pp. 44–45.

[2] S. Oh, K. Tanaka, T. Tsujimoto, R. So, T. Shida, J. Shoda, Regular exercise coupled to diet regimen accelerates reduction of hepatic steatosis and associated pathological conditions in nonalcoholic fatty liver disease, Metab. Syndr. Relat. Disord., 12 (2014) 290–298.

[3] D.J. Van der Windt, V. Sud, H. Zhang, A. Tsung, H. Huang, The effects of physical exercise on fatty liver disease, Gene Expr., 18 (2018) 89.

[4] H. Li, M. Guo, Z. An, J. Meng, J. Jiang, J. Song, W. Wu, Prevalence and risk factors of metabolic associated fatty liver disease in Xinxiang, China, Int. J. Environ. Res. Public Health, 17 (2020) 1818.

[5] M.F. Abdelmalek, E.D. Charles, A.J. Sanyal, S.A. Harrison, B.A. Neuschwander-Tetri, Z. Goodman, R.A. Ehman, M. Karsdal, A. Nakajima, S. Du, The FALCON program: Two phase 2b randomized, double-blind, placebo-controlled studies to assess the efficacy and safety of pegbelfermin in the treatment of patients with nonalcoholic steatohepatitis and bridging fibrosis or compensated cirrhosis, Contemp. Clin. Trials, 104 (2021) 106335.

[6] K. Hosoyamada, H. Uto, Y. Imamura, Y. Hiramine, E. Toyokura, Y. Hidaka, T. Kuwahara, K. Kusano, K. Saito, M. Oketani, Fatty liver in men is associated with high serum levels of small, dense low-density lipoprotein cholesterol, Diabetol. Metab. Syndr., 4 (2012) 1–7.

[7] T. Du, X. Sun, X. Yu, Non-HDL cholesterol and LDL cholesterol in the dyslipidemic classification in patients with nonalcoholic fatty liver disease, Lipids Health Dis., 16 (2017) 1–7.

[8] G. Feng, L. Feng, Y. Zhao, Association between ratio of γ-glutamyl transpeptidase to high-density lipoprotein cholesterol and prevalence of nonalcoholic fatty liver disease and metabolic syndrome: a cross-sectional study, Ann. Transl. Med., 8 (2020).

[9] X.Y. Ren, D. Shi, J. Ding, Z.Y. Cheng, H.Y. Li, J.S. Li, H.Q. Pu, A.M. Yang, C.L. He, J.P. Zhang, Total cholesterol to high-density lipoprotein cholesterol ratio is a significant predictor of nonalcoholic fatty liver: Jinchang cohort study, Lipids Health Dis., 18 (2019) 1–7.

[10] Q.M. Anstee, G. Targher, C.P. Day, Progression of NAFLD to diabetes mellitus, cardiovascular disease or cirrhosis, Nat. Rev. Gastroenterol. Hepatol., 10 (2013) 330–344.

[11] A. Lozano, H. Carrillo-Ng, C. Castro, Z. Lozano, L. Saavedra, G. Salinas, Normal transaminases in obese patients with metabolic associated steatohepatitis (MASH): a cohort of Peruvian patients, Rev. Gastroenterol. Del Perú, 42 (2022) 99–105.

[12] Z. Chen, R. Tian, Z. She, J. Cai, H. Li, Role of oxidative stress in the pathogenesis of nonalcoholic fatty liver disease, Free Radic. Biol. Med., 152 (2020) 116–141.

[13] R.G. Cutler, Oxidative stress profiling: part I Its potential importance in the optimization of human health, Ann. N. Y. Acad. Sci., 1055 (2005) 93–

135.
[14] G. Baffy, Is the name 'NAFLD'too big to fail? Let's keep it for 'nutrition-associated fatty liver disease,' J. Hepatol., 74 (2021) 988.
[15] Y. Sunami, A. Rebelo, J. Kleeff, Lipid droplet-associated factors, PNPLA3, TM6SF2, and HSD17B proteins in hepatopancreatobiliary cancer, Cancers (Basel)., 13 (2021) 4391.
[16] T. Jongraksak, A. Sobhonslidsuk, J. Jatchavala, D. Warodomwichit, P. Kaewduang, S. Sungkanuparph, Prevalence and predicting factors of metabolic-associated fatty liver disease diagnosed by transient elastography with controlled attenuation parameters in HIV-positive people, Int. J. STD AIDS, 32 (2021) 266–275.
[17] M. Eslam, A.J. Sanyal, J. George, A. Sanyal, B. Neuschwander-Tetri, C. Tiribelli, D.E. Kleiner, E. Brunt, E. Bugianesi, H. Yki-Järvinen, MAFLD: a consensus-driven proposed nomenclature for metabolic associated fatty liver disease, Gastroenterology, 158 (2020) 1999–2014.
[18] J. Boursier, R. Anty, L. Vonghia, V. Moal, T. Vanwolleghem, C.M. Canivet, S. Michalak, S. Bonnafous, P. Michielsen, F. Oberti, Screening for therapeutic trials and treatment indication in clinical practice: MACK-3, a new blood test for the diagnosis of fibrotic NASH, Aliment. Pharmacol. Ther., 47 (2018) 1387–1396.
[19] Y. Fouad, Z.M. Saad, E.M. Abdel-Raheem, Y. Abdelghani, N.M. Osman, W. Abdelhameed, A.M. Mostafa, D. Attia, Clinical Validity of the diagnostic criteria for metabolic-associated fatty liver disease: a real-world experience, MedRxiv, (2020) 2008–2020.