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Transitioning from NAFLD to MAFLD to MASLD in the Mexican population

Transicionando de NAFLD a MAFLD y a MASLD en la población mexicana

Recently, the nomenclature for nonalcoholic fatty liver disease has significantly evolved. Originally known as NAFLD, the term was updated to MAFLD (metabolic dysfunction-associated fatty liver disease), and more recently, to MASLD (metabolic dysfunction-associated steatotic liver disease), whose Spanish equivalent is *esteatosis hepática metabólica* (metabolic hepatic steatosis).[1] This evolution reflects a broader and more accurate approach that is in accordance with the understanding of the pathophysiology of the disease.

In this context, we have read the Letters to the Editor of Hagström et al.,[2] Song et al.,[3] and Ratziu et al.[4] with great interest. Those authors argue that the differences between NAFLD and MASLD are minimal, and thus maintain that applying the findings of previous studies on NAFLD to the new definition of MASLD is a reasonable proposition. Likewise, they propose that there is no need to conduct new confirmatory studies during the transition from NAFLD to MASLD.

NAFLD is defined as an accumulation of fat in the liver, in the absence of significant alcohol use, as well as of apparent secondary causes, such as viral hepatitis or lipogenic medication use. This diagnosis is based mainly on ruling out other causes.[5,6] In contrast, MAFLD is characterized by the presence of hepatic steatosis accompanied by one or more criteria, including overweight, obesity, type 2 diabetes mellitus, or at least 2 additional metabolic factors, such as

Table 1 Correlations between NAFLD, MAFLD, and MASLD

Variable	NAFLD n = 255	MAFLD n = 242	MASLD n = 249
Sociodemographic data			
Prevalence	43.7%	41.4%	42.6%
Age	51 (41-58)	51 (41-58)	51 (41.5-58)
Sex			
Women	166 (65.1%)	158 (65.3%)	163 (65.5%)
BMI	31.6 (28.8-35.4)	31.9 (29.3-35.9)	31.8 (29.1-35.4)
Visceral fat	3.5 (2.8-4.5)	3.5 (2.8-4.6)	3.5 (2.8-4.6)
Obesity	163 (63.9%)	163 (67.4%)	163 (65.5%)
Type 2 diabetes mellitus	52 (20.4%)	52 (21.5%)	52 (20.9%)
Systemic arterial hypertension	93 (36.5%)	90 (37.2%)	93 (37.3%)
Hypercholesterolemia	58 (22.7%)	57 (23.6%)	58 (23.3%)
Hypertriglyceridemia	159 (62.4%)	155 (64%)	159 (63.9%)
Biochemical data			
Glucose	94 (87-106)	95 (87-107)	94 (87-106.5)
Platelets	238 (198-289)	239.5 (198.7-289.2)	239 (199-289)
Creatinine	0.80 (0.70-1)	0.80 (0.70-1)	0.80 (0.70-1)
Uric acid	6 (5-7)	6.05 (5.1-7)	6 (5-7)
Total cholesterol	197 (172-220)	197 (173.5-219.2)	197 (174-220)
Triglycerides	164 (124-220)	167.5 (127-222.2)	167 (126-221)
AST	31 (25-40)	32 (25-41)	32 (25-40.5)
ALT	33 (25-48)	34 (26-49)	34 (26-48.5)
HDL	49 (41-29.9)	48.8 (40.9-132.6)	49 (41-59.7)
LDL	109 (87.7-132.6)	109.4 (87.8-132.6)	109.2 (88.3-132.6)
Albumin	4.1 (3.9-4.3)	4.1 (3.9-4.3)	4.1 (3.9-4.3)
FIB-4	1. (0.77-1.62)	1.1 (0.77-1.59)	1.1 (0.77-1.62)

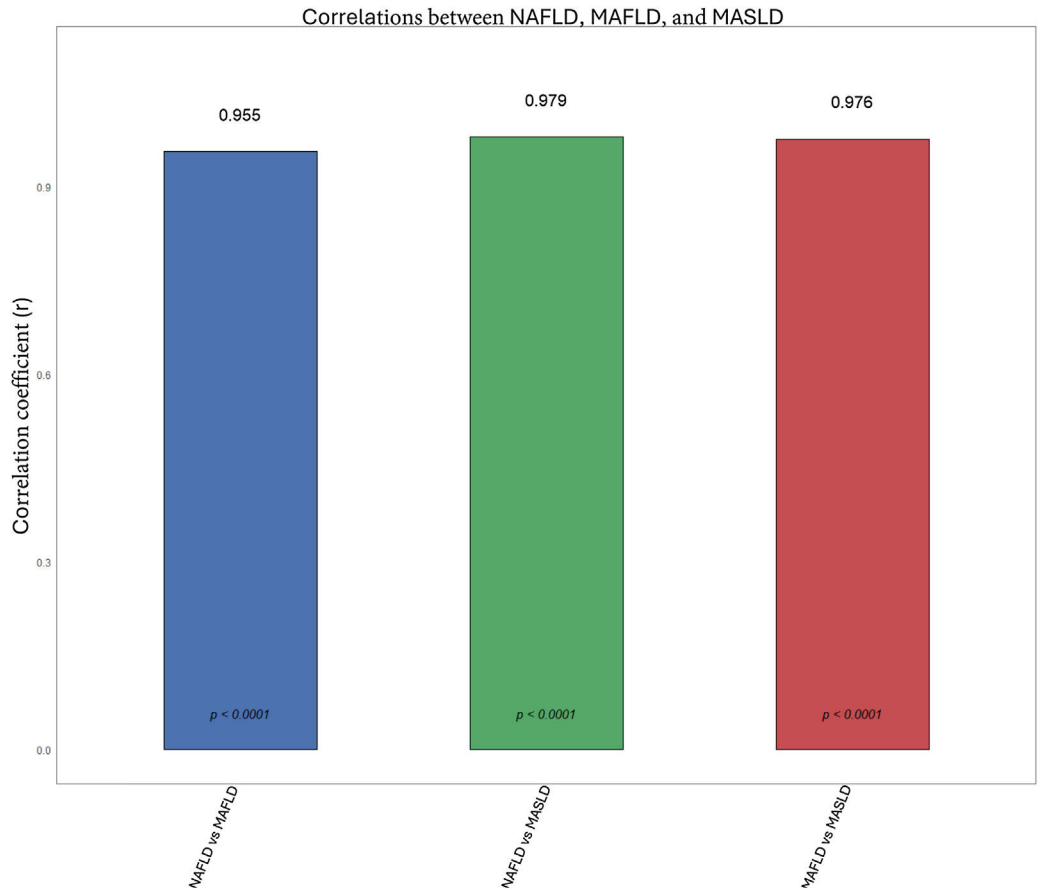

Figure 1 Similarities between NAFLD, MAFLD, and MASLD. The Spearman's Rho was used for the correlations.
NAFLD: nonalcoholic fatty liver disease; MAFLD: metabolic dysfunction-associated fatty liver disease; MASLD: metabolic dysfunction-associated steatotic liver disease (named *esteatosis hepática metabólica* in Spanish).

dyslipidemia or high blood pressure, among others.[7] This change in terminology reflects the consideration of hepatic steatosis as a component of metabolic syndrome, moving from a rule-out diagnosis to a rule-in one.

For its part, MASLD requires the presence of hepatic steatosis and at least one cardiometabolic criterion.[8,9] With respect to MAFLD, the main modification is the reduction in the number of cardiometabolic criteria necessary for the diagnosis, enabling an earlier identification of the individuals affected, as well as replacing the word ''fatty'' with ''steatotic'', which could contribute to reducing the stigma associated with the disease.

It should be pointed out that individuals with NAFLD are distinguished from those with MAFLD because NAFLD describes a more general condition that does not necessarily involve metabolic disorders, whereas MAFLD requires the presence of steatosis, together with specific metabolic factors, without taking other secondary causes of steatosis into consideration. In addition, due to the number of metabolic criteria necessary, not all individuals with MASLD meet the criteria for being diagnosed with MAFLD, whereas by requiring 2 metabolic criteria for MAFLD, 100% of individuals with normal range alcohol use should meet the criteria for MASLD.

Recent studies have shown that up to 99% of individuals with NAFLD also meet the criteria for MASLD,[2] but this relation has yet to be studied in the Mexican population.

In 2020, our group studied the prevalence of MAFLD in a Mexican population with no significant alcohol use and found a prevalence of 41.3% in a representative sample of 585 individuals.[10]

We conducted a new analysis, in which we categorized and compared individuals, according to the criteria of NAFLD, MAFLD, and MASLD. The results indicated that 94.9% of the individuals identified as having NAFLD (n = 255) also met the criteria for MAFLD (n = 242), and 97.6% (n = 249) of the individuals with NAFLD met the criteria for MASLD, whereas 100% of the individuals classified as having MAFLD met the criteria for MASLD, with no significant sociodemographic or biochemical differences between nomenclatures. The prevalence of MASLD in our population was 42.6%. Table 1 shows the descriptive statistics between the 3 classifications.

Regarding the correlations observed, strong correlations were identified between NAFLD and MAFLD ($r = 0.955$, $p < 0.0001$), NAFLD and MASLD ($r = 0.979$, $p < 0.0001$), and MAFLD and MASLD ($r = 0.970$, $p < 0.0001$), as shown in Fig. 1. Excellent concordance was also observed between NAFLD and MAFLD (kappa index = 0.954), NAFLD and MASLD (kappa index = 0.974), and MAFLD and MASLD (kappa index = 0.975).

In conclusion, 97.6% of the individuals with NAFLD met the criteria for MASLD and all the individuals classified as having MAFLD met the criteria for MASLD. Based on these data, and as occurs in other populations, we suggest that the information of previous studies on NAFLD and MAFLD in the Mexican population can be extrapolated to the nomenclature of MASLD. Said findings could have important implications for the diagnosis and management of these diseases in similar clinical contexts.

CRediT author statement

BAPP: conceptualization, investigation, and writing of the original draft. RBR: reviewing, editing, supervision. MEIC: reviewing and editing. SEMR: reviewing and editing. JMRT: reviewing, editing and supervision. All authors reviewed and/or edited the final version of the manuscript.

Statement on the use of generative AI and AI-assisted technologies

The authors declare that no artificial intelligence was utilized at any stage of the writing or investigation process or in the data analysis.

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Conflict of interest

The authors declare that there is no conflict of interest.

Data availability

The data supporting the findings of this study are available upon reasonable request from the corresponding author, B.A. Priego-Parra.

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Fontan-associated liver disease: A case report and literature review

Enfermedad hepática asociada a Fontan: reporte de caso y revisión de la literatura

Fontan surgery, originally described in 1971, is a surgical procedure to correct univentricular congenital heart defects. It consists of creating an anastomosis between the systemic venous return from the inferior vena cava and superior vena cava and the branches of the pulmonary artery, thus achieving passive ventricular filling. This disposition eliminates the mixing of intracardiac blood (oxygenated and deoxygenated) and increases arterial oxygen saturations in the blood, while at the same time reducing volume overload in the single ventricle. The aim is to alleviate hypoxemia and prolong patient survival, but the procedure elevates central venous pressure.[1,2]

A 19-year-old man had a past medical history of hypoplastic left heart syndrome that was corrected through the Norwood procedure in 2005, the bidirectional Glenn procedure in 2009, and the extracardiac fenestrated Fontan procedure in 2017. He was referred from the *Instituto Nacional de Cardiología* for consultation at the hepatology service, as the approach to portal hypertension due to the presence of postprandial hematemesis. Upper gastrointestinal endoscopy was performed that reported small esophageal varices, with no signs of poor prognosis (Baveno IV), and mild portal hypertensive gastropathy (McCormack). Vibration-controlled transient elastography (VCTE®) was ordered to evaluate liver fibrosis grade and reported 5.9 kPa and a controlled attenuation parameter of 185 dB/m, corresponding to steatosis grade S0 (0-5% steatosis). The lower esophageal varices, ascites, splenomegaly, and thrombocytopenia (VAST) score for this patient was 3 points, indicating probable advanced Fontan-associated liver disease (FALD). Triphasic abdominal tomography was ordered (Fig. 1) to rule out portal vein and suprahepatic vein thromboses. A percutaneous liver biopsy was carried out to confirm the diagnosis (Fig. 2), in which liver fibrosis was reported as stage 2b, Ishak 2b, and modified Metavir F2, according to the congestive hepatic fibrosis score (CHFS), and as stage 2, according to the 3-scale scoring system for changes related to chronic congestion.[2]

FALD, arising from different hemodynamic changes secondary to the Fontan procedure, was first described in 1983. Due to the effect of the connection of the pulmonary circulation with the systemic circulation, patients undergoing this palliative procedure can present with an increase in pulmonary pressure. This causes an increase in pulmonary resistance with a consequently chronic elevation of the central venous pressure, which is associated with reduced cardiac output with ventricular systolic and diastolic dysfunction that produces liver congestion with sinusoidal dilatation.[2–4] Said sinusoidal dilatation with perisinusoidal edema causes oxidative stress activation in the sinusoidal endothelial cells, which decreases nitric oxide production, and also causes stellate cell activation, resulting in liver fibrosis. Sinusoidal dilatation also causes lymphatic congestion that contributes to the depositing of collagen. There is also a decrease in hepatic blood flow due to reduced cardiac output, which causes hypoxic/ischemic damage, altering oxygen diffusion and causing atrophy and the potential apoptosis of centrilobular hepatocytes. All this is associated with the presence of an increase in intestinal permeability due to intestinal lymphatic and venous congestion, contributing to the hepatic and systemic inflammatory process. Likewise, patients with FALD show a decrease in anticoagulant proteins, presenting with a thrombophilic state, with the risk of systemic and sinusoidal thromboses.[2] The above-described situation favors the development of portal hypertension, arterialization of the blood supply to the liver, and as a consequence, chronic liver injury.[3] Liver

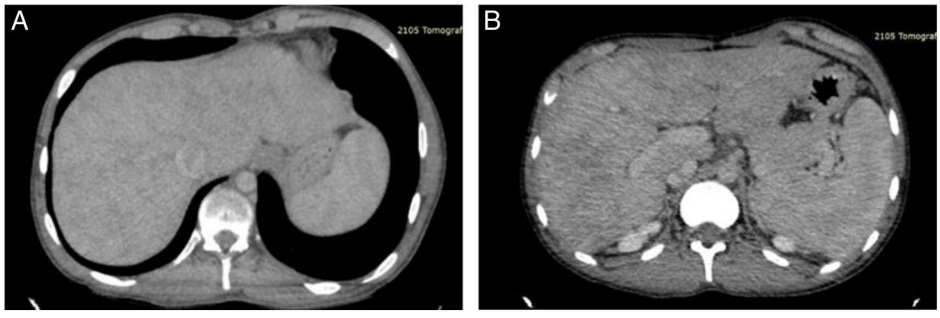

Figure 1 A) Computed tomography with contrast in the portal venous phase, showing an enlarged liver with dilatation of the inferior vena cava and an enhanced reticular pattern that affects the entire liver, with severe congestive changes in the periphery. B) Computed tomography with contrast in the portal venous phase, showing splenomegaly, accompanied by congestive hepatopathy. Portal vein and suprahepatic vein thromboses were ruled out.