Effect of COVID-19 lockdown on the prevalence of metabolic dysfunction-associated steatotic liver disease

Efecto del confinamiento por COVID-19 en la prevalencia de la enfermedad hepática esteatósica asociada a disfuncion metabólica

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Abstract

Introduction. Metabolic dysfunction-associated steatotic liver disease (MASLD) is a common clinical condition, associated with overweight, dyslipidemia and diabetes. As these risk factors are in turn associated with sedentary lifestyle and weight gain, an impact would be expected as a result of the COVID-19 lockdown on the prevalence of MASLD. **Methodology.** Retrospective longitudinal study in a data panel of 132 patients from 2017 to 2022. Patients with a liver ultrasound and a medical and paraclinical assessment 1.5 years before and after the confinement period (March 25, 2020 to February 28, 2021) were included. The primary outcome was a significant change in the prevalence of MASLD, and an exploratory fixed-effects logistic regression model with panel data was used to find predictors of change in the prevalence of MASLD from 2017 to 2022. **Results.** In a total of 132 patients analyzed, the overall prevalence of MASLD before (31%, 95%CI: 23-39) and after (35.6%, 95%CI: 27.4-43.8) lockdown by COVID-19 did not change significantly, however, in women there was a significant increase (RR: 4, 95%CI: 1.0004-16). A marked difference in prevalence was found between sexes (17% in women and 46% in men; p=0.001). Lockdown was associated with increases in body mass (difference: +1 kg, 95%CI: 0.1-1.9), LDL cholesterol (difference: +9.7 mg/dL, 95%CI: 4.9-14.4) and the diagnosis of prediabetes (RR: 2.1, 95%CI: 1.4-3.1). MASLD was positively associated with nutritional preference for fast food (p=0.047). Only body mass index was an independent predictor of MASLD (RR: 1.49, 95%CI: 1.07-1.93). **Conclusion.** The overall prevalence of MASLD did not change after the COVID-19 lockdown, but it did increase in women, and some of its risk factors also increased significantly. Numerical equivalence was found between MASLD and the previous definition of the disease. A larger local study is required to develop and validate a better predictor model of MASLD change over time.

Keywords: non-alcoholic fatty liver disease, prevalence, COVID-19, risk factors, lifestyle factors, lockdown.

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Resumen

Introducción. La enfermedad hepática esteatósica asociada a disfunción metabólica (MASLD) es una condición clínica frecuente, relacionada con el sobrepeso, la dislipidemia y la diabetes. Como estos factores de riesgo están a su vez asociados al sedentarismo y la ganancia de peso, se esperaría un impacto como resultado del confinamiento por COVID-19 en la prevalencia de dicha condición. **Metodología.** Estudio longitudinal retrospectivo en un panel de datos de 132 pacientes de 2017 a 2022, en donde fueron incluidos pacientes con una ecografía hepática y una valoración médica y paraclínica 1,5 años antes y después del período de confinamiento (25 de marzo de 2020 a 28 de febrero de 2021). El desenlace primario fue un cambio significativo en la prevalencia de la MASLD, y se utilizó un modelo exploratorio de regresión logística de efectos fijos con panel de datos para hallar predictores de cambio. **Resultados.** En un total de 132 pacientes analizados, la prevalencia global de la MASLD antes (31 %; IC95%: 23-39) y después (35,6 %; IC95%: 27,4-43,8) del confinamiento por COVID-19 no cambió significativamente, sin embargo, en las mujeres sí hubo un aumento significativo (RR: 4; IC95%: 1,0004-16). Se encontró una marcada diferencia de prevalencia entre sexos (17 % en mujeres y 46 % en hombres; *p*=0,001). El confinamiento se asoció a incrementos en la masa corporal (diferencia: +1 kg; IC95%: 0,1-1,9), el colesterol LDL (diferencia: +9,7 mg/dL; IC95:% 4,9-14,4) y al diagnóstico de prediabetes (RR: 2,1; IC95%: 1,4-3,1). La MASLD se asoció positivamente a la preferencia nutricional por la comida rápida (*p*=0,047). Solo el índice de masa corporal resultó predictor independiente de la MASLD (RR: 1,49; IC95%: 1,07-1,93). **Conclusión.** La prevalencia global de la MASLD no varió después del confinamiento por COVID-19, pero sí se incrementó en mujeres, y algunos de sus factores de riesgo también aumentaron significativamente. Se encontró equivalencia numérica entre la MASLD y la definición previa de la enfermedad. Se requiere un estudio local más grande para desarrollar y validar un mejor modelo predictor del cambio de la MASLD a través del tiempo.

Palabras clave: enfermedad del hígado graso no alcohólico, prevalencia, COVID-19, factores de riesgo, factores de estilo de vida, confinamiento, aislamiento.

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is nowadays defined by hepatic steatosis in >5% of hepatocytes, plus one additional cardiometabolic risk criteria: either hyperglycemia, body mass index (BMI) ≥25 kg/m^2, central adiposity, arterial blood pressure ≥130/85 mmHg, low HDL cholesterol or hypertriglyceridemia [1]. MASLD is estimated to affect about one quarter of the worldwide population [2], with an estimated annual medical cost of around US$100 billion in the United States and €35 billion in Europe [3]. The spectrum of this disease goes from simple steatosis to metabolic dysfunction-associated steatohepatitis (MASH) and cirrhosis, and up to one half of patients with MASH may develop hepatocellular carcinoma, even in the absence of cirrhosis [4]. MASH is currently ranked as the second leading cause for liver transplants in the United States, and it has been estimated that by 2030, it might become the leading cause of liver transplantation in that country [5]. In Colombia, prevalence of non-alcoholic fatty liver disease (previously known as NAFLD) was estimated to be 26.6% of a non-high risk population of males before COVID-19 pandemic [6], which is comparable to a mean of 23.3% of subjects in 5 similar studies from Mexico, Brazil and Chile [7]; but the definition of the disease has changed [8] and more than a decade has passed since the publication of that research works.

On June of 2023 the most recent disease nomenclature change took place [1], in order to keep avoiding exclusion criteria in the definition, as already done with the change from NAFLD to MAFLD [8], but additionally to avoid using potentially stigmatizing language. Despite this nomenclature change, neither the natural history, nor biomarker development, nor clinical trial evidence were affected due to the retention of the term steatohepatitis (MASH). It was found that 98% of the patients with NAFLD in the NAFLD European Registry would meet the new MASLD criteria [1,9]. This suggests a conceptual equivalence when applying the term in medical practice and clinical research.

On the other hand, in response to COVID-19 global outbreak, many countries established mandatory lockdown as one of the most effective public health measures to reduce coronavirus transmission [10]. Lockdown itself has been found to be associated to sedentariness, through an increase in sitting time [11] and a decrease in physical activity level [12]; which in turn may be responsible for weight gain detected during confinement in several studies [13,14]. As it is known that selected lifestyle risk factors have been strongly associated to the incidence of MASLD, such as sitting times of at least 5 hours/day [15] and weight gains as small as 5% [16], it would be expected that lockdown-induced change in lifestyle during COVID-19 pandemic would lead to an increase in MASLD prevalence. The objective of this work was to estimate the effect of lockdown on MASLD prevalence and to explore predictors for change in prevalence of MASLD from 2017 to 2022.

Methodology

Observational, retrospective study, with a panel data of 132 patients attending to the outpatient visit of an executive medical checkup program at Clínica Universitaria Colombia in Bogotá, Colombia, during a 6-year period from 2017 to 2022, excluding the year corresponding to lockdown from march 25th of 2020 to February 28th of 2021, as the program outpatient visit was closed from April of 2020 to April of 2021. Every patient with at least one hepatic echography and a medical and paraclinical assessment 1,5 years before and 1,5 years after the lockdown was included and the exclusion criteria was having missing data on the main variables of the study, namely, liver ultrasonography result, weight, height and selected paraclinical variables such as blood glucose and lipids. Clinical records of internal medicine and nutritional evaluation were reviewed in search for anthropometrical variables and physical activity relevant information. Given that the present work was designed and developed before the last disease nomenclature change [1], MASLD was diagnosed according to previously published criteria (MAFLD) [8]. Central adiposity was defined as a waist circumference (WC) ≥91 cm in men or ≥89 cm in women, according to a validated local study [17]. Primary outcome was a significant change in MASLD prevalence estimate before and after the lockdown period, and secondary outcome was the finding of significant predictors for MASLD prevalence change from 2017 to 2022, through an exploratory panel data logistic regression model. To ascertain the conceptual equivalence between diagnostic criteria used in this study (MAFLD) and recently published new nomenclature (MASLD), primary outcome was statistically processed with both definitions, and the proportion of patients with MAFLD who would meet MASLD definition was estimated.

Sample size was estimated based on the presumption that MASLD prevalence before and after the lockdown would have a difference of at least 15%. The minimally important difference selection was chosen based on the assumption that any difference smaller

than 15% would have no clinical relevance. Because the main analysis of the paired data is planned with McNemar marginal homogeneity test, effect size was calculated based on results of a previous local study [6], according to which 26.6% of subjects had NAFLD (nowadays known as MASLD) diagnosed with liver ultrasound. Based on this data, the minimally significant difference selected, and maintaining a statistical power of 80%, the required sample size was adjusted to a total of 131 patients using the G*Power 3.1.9.2 (Universität Düsseldorf, Düseldorf, Germany) software [18,19].

Patients identity was protected with a unique alpha-numerical code for each participant in the database. Statistical processing was done with STATA 13.0 MP Parallel Edition for Windows (StataCorp LP, Texas, USA). For null hypothesis evaluation, a McNemar marginal homogeneity test was applied. McNemar mid-p was used for discordant pairs sum smaller than 25 [20]. Differences with a one-tailed $p<0.05$ were accepted as statistically significant. Additionally, an exploratory analysis of panel data with logistic regression was done, to search for predictors of MASLD prevalence change from 2017 to 2022. A random effects model was discarded since a systematic difference in coefficients between random- and fixed-effects models was found (Hausman test $\chi^2=48.5$; $p<0.0001$). To avoid multicollinearity problems, only one variable representing body mass (e. g., BMI, WC, central adiposity), one variable representing blood lipids (e. g., HDL cholesterol, triglycerides, dyslipidemia), one variable representing blood glucose (e.g., prediabetes, blood glucose, glycated hemoglobin) and one variable representing energy expenditure (e. g., sedentariness, physical activity time) was tested at a time in the model. Due to the impossibility to obtain prevalence ratios directly from a logistic regression, a post-estimation of predictive margins was implemented to obtain adjusted prevalences, and from that point, calculate hazard ratios. To estimate the impact of missing data on logistic regression, multiple imputation was done with 20 repetitions, based on a maximum fraction of missing information of 19.4%. As this research posed no risk for recruited patients, no informed consent was obtained from investigation subjects and data retrieved from clinical records were protected with privacy and confidentiality. The institutional Ethics Review Board supervised the process.

Results

Out of 374 clinical records only 137 met the inclusion criteria and five patients were excluded because of missing data, for a total of 132 patients included in this work. In **table 1**, basal features (last medical pre-lockdown visit) of recruited patients are shown. Only 1 of 132 patients had harmful alcohol intake (0.8%, 95%CI: 0.1-4.2), 5 were receiving lipid lowering drugs (3.8%, 95%CI: 1.6-8.6), and 2 were receiving glucose lowering medications (1.5%, 95%CI: 0.4-5.4). No variable describing race and ethnic origin of patients was found on clinical records.

As shown in **table 2**, the prevalence of MASLD after the lockdown did not change significantly, but the prevalence of prediabetes, as defined by the World Health Organization [21], increased twice. Body weight increased 1 kg (95%CI: 0.1-1.9; p=0.014) and BMI increased 0.37 kg/m^2 (95%CI: 0.05-0.68; p=0.011) (data not shown but available). Likewise, an elevation of both LDL ($p<0.001$) and HDL (p=0.001) cholesterol after the lockdown period was also found (data not shown but available), but the above mentioned increments did not lead to a change in the clinical diagnosis of neither overweight/obesity nor dyslipidemia (**table 2**). As shown in **figure 1**, there was a predominance of MASLD diagnosis

Table 1. Baseline features of recruited patients.

Variable	Total (n=132)
Sex*	
Male	85 (64.4)
Female	47 (35.6)
Age §	39.1 (8.2)
Age category*	
≤30 years	19 (14.4)
30-39 years	54 (40.9)
40-49 years	46 (34.8)
≥50 years	13 (9.8)
Weight (kg) ¥	74.9 (13.6)
Height (cm) §	169.7 (15.8)
BMI (kg/m^2) ¥	26.2 (3.4)
<25*	50 (38.5)
25-29,9*	65 (50)
≥30*	15 (11.5)
Waist circumference (cm) ¥	89.9 (10.3)
Marital status*	
Single	33 (25.6)
Married	71 (55)
Cohabiting	25 (19.4)
Aerobic physical activity (minutes/week) §	120 (240)
Absence of comorbidities*	32 (24.2)
Dyslipidemia	38 (28.8)
Obesity	22 (16.7)
Gastroesophageal reflux disease	21 (15.9)
Hypothyroidism	15 (11.4)
Hypertension	10 (7.6)
Sleep apnea syndrome	5 (3.8)
Type 2 diabetes	3 (2.3)
Other	71 (53.8)
Paraclinical data (mg/dL) §	
Total cholesterol	188 (47)
HDL cholesterol	47.2 (15.5)
LDL cholesterol	110.6 (45)
Triglycerides	117 (73.2)
Alanine aminotransferase (U/L)	25.9 (22.4)
Aspartate aminotransferase (U/L)	20.7 (8)
Glucose	88.4 (10)
Glycated hemoglobin (%)	5.37 (0.38)

n: number of subjects; BMI: body mass index; §: median (ICR); ¥: mean (SD); *: frequency (%).

among males (p=0.001), and post-lockdown MASLD prevalence increment among women was significant. Some of the risk factors for MASLD were also found to significantly differ by sex category (**figure 2**). FIB-4 score had a modest, although significant post-lockdown increment (difference: +0.08, 95%CI: 0.03-0.14; p=0.002); nonetheless, that increment did not lead to a change in the proportion of patients classified as indeterminate risk for fibrosis (pre-lockdown: 3.9%; post-lockdown 7.6%; p=0.06) (data not shown but available). No patients were classified as high risk for fibrosis. Having a post-lockdown MASLD diagnosis was positively associated to nutritional preferences for fast food (p=0.047), but this association was not found for pre-lockdown diagnosis of MASLD.

In order to ascertain conceptual equivalence between diagnostic criteria used in this study (MAFLD) [8] and recently published new nomenclature (MASLD) [1], it was found that 40 out of 41 (98%) patients with pre-lockdown MAFLD and 43 out of 44 patients (98%) with post-lockdown MAFLD, met MASLD definition. The remaining patient,

Table 2. COVID-19 pandemic lockdown effect on different clinical outcomes.

	Pre-lockdown	Post-lockdown	ARR (95%CI)	HR (95%CI)	*p* (one tail)
Prevalence % (95%CI)					
MASLD (n=132)	31.1 (23.2-39)	35.6 (27.4-43.8)	4.5 (-2.8-11.9)	1.1 (0.9-1.4)	0.189*
Women (n=47)	4.3 (0-10)	17 (6.3-27.8)	12.8 (-0.6-26.1)	4 (1.0004-16)	0.016*
Men (n=85)	45.9 (35.3-56.5)	45.9 (35.3-56.5)	0 (-9.2-9.2)	1 (0.84-1.19)	0.774*
BMI ≥25 kg/m^2 (n=130)	6.5 (53.2-69.9)	64.4 (56.2-72.6)	2.3 (-5-9.6)	1 (0.9-1.2)	0.503*
Central adiposity § (n=111)	47.5 (38.6-56.4)	48 (39.1-56.8)	1.8 (-6.6-10.2)	1 (0.9 -1.2)	0.648*
Sedentariness (n=111)	33.8 (25.6-42.1)	35.3 (26.6-44)	2.7 (-8.6-14)	1.1 (0.8-1.5)	0.736
Prediabetes ¥ (n=132)	18 (11.6-24.7)	38.6 (30.3-46.9)	20.4 (10.4-30.5)	2.1 (1.4-3.1)	0.0001
LDL colesterol ≥130 mg/dL (n=132)	34.1 (26-42.2)	40.2 (31.8-48.5)	6 (-1.9-14)	1.2 (1-1.4)	0.108*
Low HDL cholesterol £ and/or triglycerides ≥150 mg/dL (n=132)	45.4 (37-53.9)	52.3 (43.8-60.8)	6.8 (-3.1-16.8)	1.2 (1-1.4)	0.200

§: abdominal circumference ≥91 cm in men and ≥89 cm in women; ¥: serum glucose ≥100 mg/dL and glycated hemoglobin ≥5,7%; £: HDL cholesterol ≤50 mg/dL in women or ≤40 mg/dL in men; ARR: absolute risk reduction; HR: hazard ratio; MASLD: metabolic dysfunction-associated steatotic liver disease; BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; n: number of observations. *A mid-p value of McNemar test was used, because the number of discordant pairs was lower than 25.

whose steatotic liver disease could not be classified as MASLD, was classified as metabolic dysfunction-associated alcoholic liver disease (MetALD) because of harmful alcohol intake.

Univariate significant predictors for MASLD prevalence change from 2017 to 2022 were included in a multivariable fixed effects-model. As shown in **table 3**, the statistical significance of the predictors decreased because of missing data and therefore, multiple imputation was used to complete full sets of data. After that procedure, only BMI was found to be independently associated with MASLD prevalence change. Notably, not even after multiple imputation a post-lockdown state was found to be predictor of MASLD (data not shown but available). In order to address the multiplicity problem of secondary analysis, p values were not formally adjusted because they were considered exploratory, but instead, it was estimated that up to 16 statistically significant interactions ($p<0.05$) were found merely by chance, based on predetermined significance level and the number of analyses done.

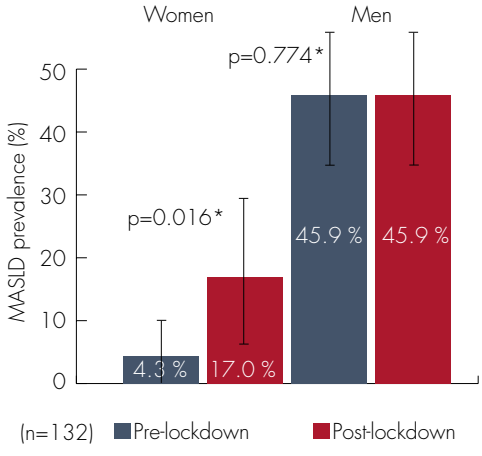

Figure 1. Prevalence of MASLD by sex and time. Bars represent proportions with 95% confidence intervals. MASLD: Metabolic dysfunction-associated steatotic liver disease; n: number of pairs of observations. *A mid-p value of McNemar test was used because the number of discordant pairs was <25.

Discussion

In this study, overall MASLD prevalence did not change significantly after the COVID-19 lockdown, despite significant increases in body weight and prediabetes. From the design of this work, the sample size was calculated to detect a change of at least 15% in MASLD prevalence; thus, significant smaller differences could have been found with a higher number of patients. Additionally, the present data might suggest a worrisome increment in NAFLD prevalence in Colombia from 26.6% [6] to 47.1% (proportion of NAFLD in this study among only men; data not shown but available) in a decade; having into account that the only local prevalence study was done exclusively with male participants and there was no definition of MASLD back then in 2011, but rather of NAFLD. An overall MASLD prevalence of 35.9% in the study population (**table 2**) is also higher than reported for America [7]. The 98% concordance between MAFLD and MASLD diagnoses found in the present work was identical to the one found in the large cohort of NAFLD European Registry [1,9] and suggests a conceptual equivalence of both terms. Recently, there has been an attempt to quantify MASLD pre and post COVID-19 pandemic, but that work is not comparable to the present study because definition of NAFLD was based on scores and not on ultrasonography [22]. Another study quantified mean fatty content by magnetic resonance, pre and post lockdown, in 59 patients with confirmed NAFLD and metabolic syndrome. It was found that many patients (66.1%, 95%CI: 52.6-77.9) had an increased intrahepatic fat content ≥6.4% with respect to basal content [23]. Nonetheless, none of the cited studies offered an estimation of MASLD prevalence in a low-risk population. A recent review also highlighted a predominance of MASLD diagnosis among males as shown in this work, which was explained by the protective role of estrogen against hepatic steatosis, as well as other non-hormonal chromosomic influences in women [24]. Known anthropometrical differences by sex such as a greater WC in males also may provide more risk of MASLD to men, because gynoid gluteo-femoral adipose tissue has a lower lipolytic response to catecholamines and deliver less fatty acids to the liver in women [25]. Consistently, in this study, men were found to have not only more central adiposity than women (**figure 2A**), but also more overweight/obesity (data not shown but available) despite a smaller prevalence of sedentariness (**figure 2B**). Surprisingly, post-lockdown MASLD prevalence increase in women was significant (**figure 1**), which seems paradoxical considering the already mentioned biological protective factors women have against steatosis. Given that the present work was not designed to analyze extensively gender dif-

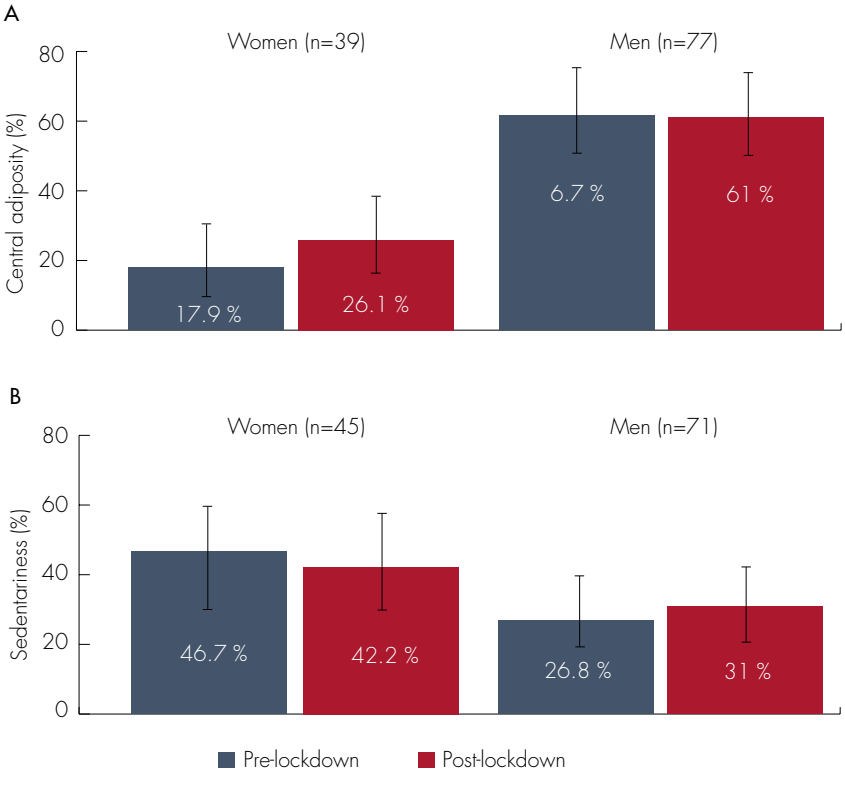

Figure 2. Selected risk factors for MASLD by sex and lockdown status. Changes in prevalence of central adiposity (A) and sedentariness (B) before and after lockdown period. Bars represent proportions with 95% confidence intervals. n: number of pairs of observations.

ferences, future studies could explore the hypothesis of an influence of differential lifestyle changes attributed to the social role of women on this result.

Not every patient in the present work had a longitudinal nutritional assessment (n=49) which may be responsible for the weak although significant association of MASLD with preference for fast food. The above mentioned result could be consistent with those of a case-control study from Iran, which found a positive association between fast food consumption two or more times a month and the development of MASLD (OR: 2.7, IC95%: 1.4-5.4), although this association was not present if patients with central obesity were excluded [26].

Most published studies about weight gain during lockdown have large methodological differences with the present work (e. g., self-reported weight gain through on-line survey), making a direct comparison difficult. For instance, body weight increase during lockdown period (median difference: +1.34 kg) was reported by a recent Brazilian online survey where 58.8% of participants reported weight increases >0.1 kg [13]. In the present work, the absolute weight gain was similar and the proportion of patients with weight gain >0.1 kg was also comparable (59.2%, 95%CI: 50.8-

Table 3. Multivariable analysis of significant predictors of MASLD prevalence change from 2017 to 2022.

	Odds ratio	95%CI	HR*	95%CI
Original data fixed-effects model (n=59; g=23)				
BMI (kg/m^2)	1.53	0.92-2.54	1.32	0.94-1.74
Prediabetes §	3.36	0.66-17.1	1.97	0.73-2.93
Sedentariness	2.32	0.42-12.7	1.66	0.51-2.82
Multiple imputation fixed-effects model (n=81; g=26)				
BMI (kg/m^2)	1.89	1.11-3.21	1.49	1.07-1.93
Prediabetes §	2.31	0.63-8.42	1.66	0.71-2.61
Sedentariness	2.66	0.5-14.2	1.78	0.59-2.86

Logistic regression model with panel data and MASLD as dependent variable. §: blood glucose ≥100 mg/dL and/or glycated hemoglobin ≥5,7%. *Hazard ratio computed by post-estimation of predictive margins to obtain adjusted prevalences. MASLD: metabolic dysfunction-associated steatotic liver disease; BMI: body mass index; n: number of individual observations; g: number of groups of observations (patients).

67.7) (data not shown but available). In contrast, a longitudinal retrospective study from Saudi Arabia, whose weight variable was measured and registered by clinicians, found that 23.1% of patients had a ≥5% weight gain during lockdown, while the absolute increase in body weight was small (+0.33 kg; 95%CI: 0.29-0.36) [27]. In the present study, a weight increase ≥5% was detected in 26.9% (95%CI: 19.3-34.5) (data not shown but available) of patients and the confidence interval of the absolute increase in weight was wide (95%CI: 0.1-1.9), which make those findings consistent with the cited report.

As shown in **figure 2B**, prevalence of sedentariness was higher in women than in men before lockdown (p=0.031; n=127), but this difference nullified post-lockdown. Although this could be explained by a decrease in physical activity in men during lockdown, equaling that of women, it may also be secondary to a loss of power because of post-lockdown missing data in this variable (post-lockdown n=116). A systematic review of 40 studies with a larger number of patients reported post-lockdown increases in total daily sedentary time irrespective of sex [28], but the present study was not designed to detect such differences.

Regarding the remarkable post-lockdown increase in the diagnosis of prediabetes found in the present work, other recent studies report a significant post-lockdown increase in both fasting plasma glucose and glycated hemoglobin, but not in the proportion of participants diagnosed with prediabetes [29,30]. The cited studies also reported significant parallel increases in LDL cholesterol levels. Those findings altogether highlight the adverse metabolic impact of COVID-19 pandemic lockdown in non-high risk population for MASLD, through a worsening of metabolic syndrome.

The exploratory logistic regression model with panel data (2017-2022) found only BMI as an independent predictor of MASLD occurrence through time. Collinearity prob-

lems with the intercept for some continuous variables led to the exclusion of some promising variables as candidates for the prediction model (e. g., WC, HDL cholesterol, triglycerides). On the other hand, a high risk of endogenous variables within the potential predictors led to the use of a fixed-effects model which further reduced sample size, as time-invariant groups of binomial observations were dropped from the model. Moreover, the observed time-invariant sex variable was also automatically dropped from the model, and it was not possible to estimate its effect. However, in a fixed effects model, those variables that are unobserved and constant over time (intrinsic factors of individuals such as genetics, long-life nutritional habits and cultural factors) are not ignored, but instead become controlled variables, which may be seen as a key advantage over a random effects-model [31]. Interestingly, a large nested case-control study from Iran reported recently that also BMI was the main independent predictor of MASLD in a multivariable logistic regression model [32], and another large cross-sectional Chinese study also found BMI within the two most important multivariable independent predictors of MASLD [33]. Another retrospective cross-sectional study based on National Health and Nutrition Examination Survey (NHANES) data, developed a nomogram to predict MASLD from nine predictors, among which BMI was selected [34]. It is to be noted that, despite a smaller sample size, the present work is longitudinal in nature and so it better approximates causality than the cited studies. Moreover, this is a good starting point for future local studies, as until now, no other study in Colombia has attempted previously to characterize predictors for MASLD by these statistical methods.

Several limitations have to be mentioned, first, MASLD prevalence found in the study population cannot be extrapolated to all of Colombia, because of the sampling method used. Additionally, as a retrospective longitudinal study, information bias is a possibility, although paraclinical information was corroborated directly in the clinical laboratory database. Missing data for physical activity and PC variables could have affected results for secondary analyses but there were no missing data in variables related to the primary outcome. To deal with this bias in the regression model, multiple imputation was done. Confusion bias was minimized with multivariable analysis. The sample calculation on this study confers power only for the primary endpoint, so secondary findings must be interpreted with caution. Finally, the present work was designed and developed before the last change in disease nomenclature, for that reason, primary outcome analysis was computed again with the new definition of MASLD and the equivalence between MAFLD and MASLD was stablished, and resulted high and consistent with the one found in a large European registry [1,9].

In conclusion, although no significant change due to lockdown was found for overall MASLD prevalence in the study population, some associated metabolic risk factors did increase, suggesting a negative metabolic impact of COVID-19 lockdown. This work also highlights the conceptual equivalence of the new nomenclature with respect to previously used disease definition in Colombian patients. A larger local study is needed to develop and validate a better model to predict MASLD change through time, and to explore a possible explanation for post-lockdown MASLD prevalence increase found only in women.

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