Results: Fifty-two patients (94 % female, 57 ± 11 years, BMI 25 ± 6 kg m^{-2}, histological stages 1(n23)/2(n16/3(n13) completed follow-up. ALP normalised in 36 % with UDCA, 78 % with UDCA +BZF 400 mg and 100 % with UDCA+BZF 800 mg ($\chi^2 < 0.01$). Mean ALP (× ULN) at six months was 1.5±0.7 (UDCA), 0.98±0.2 (UDCA+BZF 400 mg), and 0.8±0.2 (UDCA+BZF 800 mg) (ANOVA p<0.001). Linear mixed-effects analysis showed significant time-dependent ALP declines in all groups; BZF intensified these monthly slopes ($\beta = -0.34$ for 400 mg, −0.44 for 800 mg vs UDCA, both Tukey-adjusted p<0.01). Pruritus persisted in 14 % of UDCA recipients but in none on BZF, and renal function and creatine kinase were unchanged across groups.

Conclusions: Up-front UDCA+BZF achieves dose-dependent, near-universal six-month ALP normalisation and accelerates biochemical improvement without early safety concerns. These interim data support initiating combination therapy at diagnosis, particularly in symptomatic PBC.

Conflict of interest: None

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#97

STEATOTIC HEPATOCYTES SHOWN REDUCED CYP450 EXPRESSION AND IN VITRO RESISTANCE TO DRUG-INDUCED TOXICITYSTEATOTIC HEPATOCYTES SHOWN REDUCED CYP450 EXPRESSION AND IN VITRO RESISTANCE TO DRUG-INDUCED TOXICITY

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Introduction and Objectives: Metabolic dysfunction-associated steatotic liver disease (MASLD), has been associated with dysregulation of CYP450 enzymes, resulting in an altered drug-metabolizing profile. It has been suggested that lipid droplets (LDs) might influence CYP450 expression and function. Diclofenac (DF) and acetaminophen (APAP) are common analgesics that can cause drug-induced liver injury (DILI), due to their toxic metabolites produced by CYP450 dependent reactions. The aim of this study was to characterize the effect of lipid droplets present in hepatocytes on drug-induced toxicity.

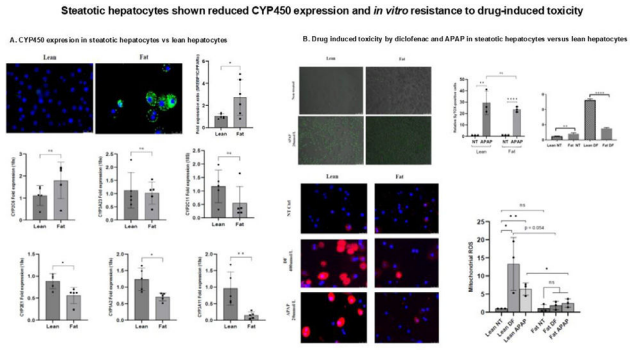
Materials and Methods: Steatotic Zucker rat hepatocytes (Fa/Fa) (chronic lipid accumulation) or free fatty acid (FFA)-treated Wistar rat hepatocytes (acute lipid accumulation) were treated with DF (400 μmol/L) or APAP (20 mmol/L). Caspase-3 activity, necrotic cell death and mitochondrial ROS production were determined. mRNA levels of different CYP450 related with diclofenac and APAP metabolism, were quantified by RT-qPCR. Lipid droplets quantity and distribution were assessed by BODIPY staining. To compare our results with the human data available we performed in silico analysis using tanscriptomic databases from patients with hepatic steatosis.

Results: Decreased expression of CYP2E1 and CYP3A11(CYP3A4 human homologue) was observed in steatotic Zucker rat hepatocytes. No regulation of CYP450 expression was observed in FFA-treated Wistar hepatocytes (acute lipid accumulation). Lipid droplets reduced mitochondrial ROS production and prevented apoptotic and necrotic cell death induced by DF and APAP, respectively. Changes in lipid droplet distribution were also observed in DF and APAP treated hepatocytes. In Silico analysis using transcriptomic human data available are now in progress to compare these findings and their relevance in the context of MASLD.

Conclusions: Lipid droplets are associated with protective mechanisms during drug-induced toxicity due to the downregulation of CYP450 gene expression and prevention of ROS production. Further studies are needed to understand the exact mechanisms and molecular targets regulated by LDs that influence drug-induced toxicity.

Conflict of interest: None

Graphical Abstract_Steatotic hepatocytes shown reduced CYP450 expression and in vitro resistance to drug-induced toxicity



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#99

PROJECTED CLINICAL AND ECONOMIC BURDEN OF METABOLIC DYSFUNCTION–ASSOCIATED STEATOHEPATITIS IN BRAZIL: A 20-YEAR FORECAST ACROSS TYPE 2 DIABETES STATUS

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Introduction and Objectives: Type 2 diabetes (T2D) is an important risk factor for metabolic dysfunction–associated steatohepatitis (MASH) and its complications.

Explore long-term impact economic burden of MASH among adults by T2D status.

Patients and Methods: Markov model simulated the natural history of patients with MASH in Brazil over a 20-year horizon (2021–2040).

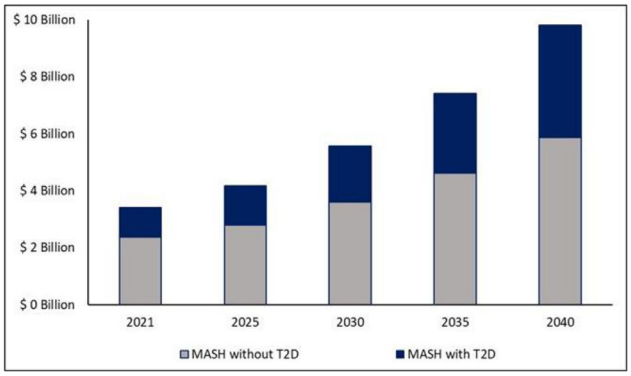
Transition probabilities were calibrated to align with Brazil's national data for cirrhosis, hepatocellular carcinoma (HCC), liver transplantation (LT), obesity, and T2D. The model incorporated competing mortality risks (liver-related, cardiovascular, and other causes). Baseline estimates of direct medical costs (outpatient care, diagnostics, hospitalizations, procedures, medications) were estimated by disease stage using national sources, including the Fiocruz Observatory database and Brazil's health system profile. Costs are reported in 2020 USD, adjusted using IMF inflation projections.

Results: From 2021 to 2040, MASH prevalence among adults in Brazil is projected to rise from 7.19% to 7.52%. In the general population, the prevalence of MASH-related cirrhosis will increase from 0.63% to 0.99%, while MASH-related HCC, -LT and -liver deaths will increase from 0.50 to 1.02, 0.17 to 0.38 and 10.08 to 13.46 per 100,000. The proportion of MASH cases with T2D will increase from 25.3% to 30.8%. Among MASH-cirrhosis patients, this proportion will increase from 23.9% to 27.8%. Annual MASH-related direct medical costs will rise from $3.41 billion in 2021 to $9.81 billion by 2040, with the proportion attributable to T2D increasing from 30.7% to 40.1% (Figure).

Conclusions: Clinical and economic burden of MASH in Brazil is expected to rise with increasing share attributable to T2D.

Conflict of interest: None

Figure



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#103

STUDY OF METABOLIC DYSFUNCTION ASSOCIATED WITH ESTABLISHED LIVER DISEASE USING FLI AND HSI INDICES IN THE ADULT POPULATION OF CUQUÍO, JALISCO, MEXICO

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Introduction and Objectives: The frequency of fatty liver disease is very high in Mexico. However, its prevalence is unknown in many regions of the country, which is why in this study we analyzed a region of the state of Jalisco

How can hepatic steatosis indices be used to detect metabolic-associated fatty liver disease (MAFLD) in adults from Cuquío, Jalisco, considering their risk factors?

Materials and Methods: Descriptive study conducted in the population of Cuquio, Jalisco, through open invitation. A total of 235 individuals participated, of whom 71 met the inclusion criteria. Participants signed an informed consent form in accordance with the Declaration of Helsinki. During medical consultation, anthropometric measurements were taken and blood samples were collected for comprehensive biochemical analysis using an automated system. The FLI and HSI indices were calculated. Multivariate and cluster statistical analyses were performed using StarGraphics and SPSS software.

Results: A total of 81.7% were women, mean age of 47.4 ± 12.5 years, 12.5% were diabetic. The components of the FLI were mainly associated with liver enzymes and lipid profile, while the HSI was linked to central adiposity and low HDL levels. Factor and cluster analyses allowed the identification of three metabolic profiles: high hepatic risk (dyslipidemia and cellular damage), low risk (good metabolic control), and intermediate risk, possibly functional or cholestatic.

Conclusions: These findings support that the FLI is more closely related to general lipid metabolism, whereas the HSI more accurately reflects central fat accumulation and functional liver alterations. The results underscore the importance of using multivariate approaches to characterize complex diseases such as MAFLD.

Conflict of interest: None

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#105

HIGH PREVALENCE OF DILI/HILI IN A CENTER PARTICIPATING IN A MULTICENTER STUDY FOR DIAGNOSING ACUTE HEPATITIS IN BRAZIL

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Introduction and Objectives: Hepatotoxicity caused by drugs and herbs (DILI/HILI) can cause mild to severe lesions. The diagnosis is based on exclusion, and it is essential to investigate the use of drugs and herbal remedies.

To assess the prevalence of DILI/HILI in a multicenter study on acute hepatitis.

Materials and Methods: A cross-sectional, descriptive, and analytical study conducted at a university hospital in Bahia, as part of a national multicenter screening project for acute hepatitis. Patients with clinical suspicion of acute hepatitis were included.

Results: The sample included 50 patients: 17 (34%) with DILI/HILI and 33 (66%) with other etiologies. These included: autoimmune hepatitis 4 (8%), cholestatic syndrome 1(2%), late transplant rejection 1 (2%), Chikungunya and Dengue 2(4%), alcoholic hepatitis 1(2%), Caroli syndrome 1 (2%), and biliary cholangiopathy 1(2%). Viral etiologies: hepatitis B 6 (12%), including one case of chronic HBV reactivated by herbal use, hepatitis C 3 (6%), Epstein-Barr virus IgM 5 (10%), and