

ultrasound, FIB-4 score, liver stiffness measurement (LSM) by vibration-controlled transient elastography, gastric biopsies, and *H. pylori* cagA and NOD1 single nucleotide polymorphism (rs2075820) were evaluated. Associations were analysed with  $\chi^2$ , ANOVA/Tukey and multivariable logistic regression (\* $p < 0.05$ ).

**Results:** Participants were 60 % women; mean age 49 years; BMI  $27.9 \text{ kg/m}^2$ . MASLD was present in 209 (42 %) and Hp in 252 (51 %). Hp positivity coincided with higher BMI and MASLD prevalence (52 % vs 32 %). Among MASLD subgroup, Hp +/cagA + infection was associated with higher AST ( $25 \pm 11$  vs  $33 \pm 14 \text{ U/L}$ ), FIB-4 ( $1.0 \pm 0.5$  vs  $1.5 \pm 0.8$ ), and LSM ( $5.7 \pm 2.8$  vs  $7.8 \pm 5.2 \text{ kPa}$ ) compared with Hp-negative patients ( $p < 0.05$  for all), without significant differences in ALT or GGT. The combined cagA +/NOD1-GG genotype displayed the greatest FIB-4 (1.5) and LSM (8.5 kPa); 41 % of carriers exceeded the  $\geq 8 \text{ kPa}$  threshold for advanced fibrosis, yielding an odds ratio (OR) of 3.99 (95 % CI 1.6–10.0;  $p = 0.003$ ), which remained significant after adjustment for metabolic comorbidities (adjusted OR 4.98; 95 % CI 1.9–13.5).

**Conclusions:** In dyspeptic adults with MASLD, Hp cagA carriage is linked to worse non-invasive liver indices. The cagA +/NOD1-GG genotype independently predicts significant fibrosis, underscoring a bacterial–host genetic synergy that may accelerate MASLD progression.

**Conflict of interest:** Yes, Fundacion HA Barcelo

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## #90

### CONCORDANCE BETWEEN EXPERT GASTROENTEROLOGISTS AND ARTIFICIAL INTELLIGENCE TOOLS IN SOLVING HEPATOLOGY CLINICAL CASES

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**Introduction and Objectives:** Evidence regarding the utility of artificial intelligences (AI) for the diagnosis of clinical cases in gastroenterology is limited, and is even scarcer in hepatology.

Determine the concordance between the responses of various AI models and those of specialist physicians in the resolution of hepatology clinical cases.

**Materials and Methods:** This was a clinical, observational, analytical, and prospective study. The assessment instrument comprised six hepatology clinical cases, each featuring five questions. A panel of eight experts from different institutions was convened; and their individual responses were subjected to calculation of the kappa coefficient ( $\kappa$ ) and Cronbach's alpha. Items that failed to meet the

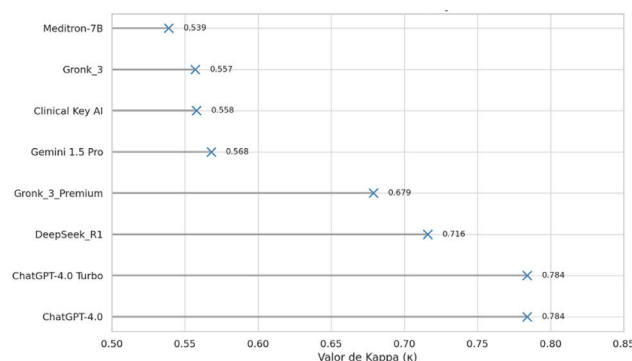
validation threshold ( $\geq 80$  % agreement and  $\kappa \geq 0.6$ ) were reviewed through iterative rounds of a modified Delphi method. Finally,  $\kappa$  was calculated to evaluate concordance between responses generated by the AI models and the expert consensus.

**Results:** The expert consensus demonstrated a high overall concordance ( $\kappa = 0.901$ ; 95 % CI [0.860, 0.943];  $z = 61.57$ ;  $p < 0.001$ ). Individual model concordance ranged from moderate to substantial, with  $\kappa$  values between 0.539 (Meditron-7B) and 0.784 (ChatGPT-4.0 and ChatGPT-4.0 Turbo), all statistically significant. In terms of the percentage of correct responses, the highest performing models were ChatGPT-4.0, ChatGPT-4.0 Turbo, and Deepseek-R1 (figure 1).

**Conclusions:** A moderate to substantial concordance was observed between diagnoses generated by different AI models and expert judgment in hepatology clinical cases, although variations were noted among the evaluated systems.

**Conflict of interest:** None

**Figure 1**



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## #91

### HIGH RATE OF EARLY ALP NORMALIZATION WITH UDCA–BEZAFIBRATE COMBINATION THERAPY IN TREATMENT-NAÏVE PRIMARY BILIARY CHOLANGITIS: PRELIMINARY RESULTS

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**Introduction and Objectives:** Six-month alkaline phosphatase (ALP) normalisation predicts one-year response and survival in primary biliary cholangitis (PBC). Bezafibrate (BZF) benefits incomplete ursodeoxycholic-acid (UDCA) responders. We therefore assessed ALP normalization at six-month with UDCA alone versus UDCA+BZF at two different doses.

**Materials and Methods:** in an open-label trial (January 2022–2025) antimitochondrial-antibody-positive, non-cirrhotic PBC patients were randomised 2:2:1 to UDCA 13–15 mg kg<sup>-1</sup> day<sup>-1</sup> (n=21), UDCA+BZF 400 mg (n=23) or UDCA+BZF 800 mg (n=8). Liver tests were obtained monthly for six months. The primary end point was ALP  $\leq 1 \times \text{ULN}$  at month 6; secondary end points were changes in other enzymes, pruritus and safety.

**Results:** Fifty-two patients (94 % female,  $57 \pm 11$  years, BMI  $25 \pm 6$  kg m<sup>-2</sup>, 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 ( $\times$  ULN) at six months was  $1.5 \pm 0.7$  (UDCA),  $0.98 \pm 0.2$  (UDCA+BZF 400 mg), and  $0.8 \pm 0.2$  (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 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  $\mu$ mol/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 transcriptomic databases from patients with hepatic steatosis.

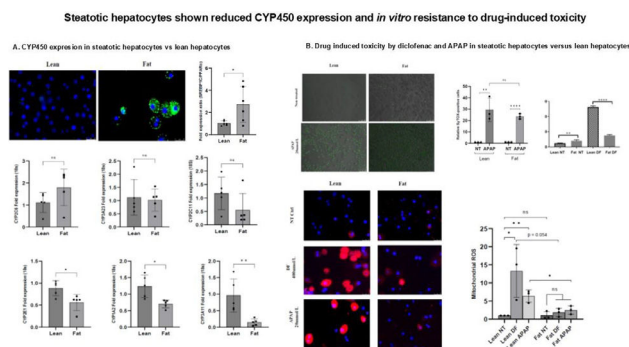
**Results:** Decreased expression of CYP2E1 and CYP3A11(CYP3A4 human homologue) was observed in steatotic Zucker rat hepatocytes. No regulation of CYP450 expression was observed in FFA-treated Wistar hepatocytes (acute lipid accumulation). Lipid droplets

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).