describe the characteristics of the Mexican population with overlap syndrome treated at the liver clinic of the General Hospital of Mexico.

Materials and Patients: This is a retrospective, observational and analytical study in which records of patients with ADHD who met overlapping criteria (two or more hepatic autoimmune diseases) between 2020 and 2024 were reviewed to evaluate demographic variables and their presentation. Descriptive statistics with measures of central tendency and dispersion were used using SPSS 25.0. Liver enzymes AST, ALT, GGT, in addition to BT and FA of EHAI, CBP and CEP compared to CEP+EHAI were compared with Student's t-test for independent groups. Values are expressed as means and standard deviations. The Z test for contingency tables for difference of proportions with Bonferroni correction was used to compare the percentages of the degree of fibrosis among the four groups (EHAI, CBP, CEP and CEP+EHAI). A significance level of less than 5% was considered in all tests.

Results: A total of 256 patients with AHD were evaluated, of whom 55 (21.4%) were found to be compliant for overlap syndrome. Of these, 93.6% were female and 7.3% male, with a mean age of 51.89 ± 12.72 years (range: 50.34-53.44). The most common phenotype was CBP/HAI (73.2%). The most frequent autoimmune comorbidities were hypothyroidism, rheumatoid arthritis, Sjögren's syndrome and systemic sclerosis. 32.1% had grade F3 fibrosis and 16.3% cirrhosis, Child A 12.5%, Child B 62.5% and Child C 25%. A higher proportion of fibrosis was observed in F2 and F3 for overlap syndrome compared to EHAI. Regarding enzymatic tests, significant differences were found in GGT (183.5±254.5 vs. 318.5±232.8) and AF between EHAI and overlap syndrome. The most frequent decompensation was variceal gastrointestinal bleeding in 62.5%, and three patients were transplanted.

Conclusions: Overlap syndrome is an uncommon entity, frequent in women, which is usually associated with other autoimmune pathologies. It is associated with more severe results in liver biochemical tests, especially in GGT and AF levels, as well as with a higher degree of fibrosis.

Ethical statement: the research was carried out in accordance with the Helsinki Declaration of the World Assembly 2013.

Declaration of interests: None.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

https://doi.org/10.1016/j.aohep.2025.101874

High Prevalence of the *FTO* T allele (rs9939609 T>A) and its association with a high risk of Type 2 diabetes or metabolic-associated steatotic liver disease (MASLD) in the Mexican population

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Introduction and Objectives: The *FTO* rs9939609 (T>A) polymorphism has been associated with obesity and metabolic disorders, including type 2 diabetes and MASLD. This study examined the distribution of the *FTO* (T>A) polymorphism in Native and admixed populations and its impact on an admixed Mexican cohort's anthropometric and metabolic profiles.

Materials and Patients: In this cross-sectional study, we evaluated 684 unrelated adults from various regions of West Mexico, categorizing them into Native, Mestizo (admixed), and Mestizo-Caucasian groups based on ancestry. Genotyping for the *FTO* rs9939609 polymorphism was performed using an allele discrimination assay via Real-Time PCR. Given the low prevalence of the A allele among the Mestizo subjects (n=333), the biochemical and anthropometric measurements were adjusted by genotypes AA+AT vs. TT. Anthropometric measurements were assessed using body circumferences and electrical bioimpedance. Metabolic profiles were evaluated by measuring glucose, insulin, triglycerides (TG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), aspartate aminotransferase (AST), and alanine aminotransferase (ALT). Metabolic abnormalities were defined as follows: hypercholesterolemia (HCL) with TC ≥200 mg/dL, high LDL-c (H-LDL) with LDL-c ≥130 mg/dL, hypoalphalipoproteinemia (HALP) with HDL-c <40 mg/dL, hypertriglyceridemia (HTG) with TG ≥150 mg/dL, hyperglycemia (HGL) with fasting glucose ≥100 mg/dL, hyperinsulinemia (HINS) with insulin >9 μUI/dL, and insulin resistance (IR) with HOMA-IR ≥2.5. Principal Component Analysis (PCA) was used to visualize genetic divergence focusing on the TT genotype. Univariate and multivariate logistic regression analyses were conducted to assess the risk association between the TT genotype and metabolic abnormalities. Statistical analyses were performed using R Studio and SPSS software.

Results: The Huicholes Native population exhibited the highest T allele frequency and TT genotype frequency (94% and 89%), followed by Mestizos from Guadalajara (74% and 56%). In contrast, Mestizo-Caucasians from Cuquio had the lowest T allele frequency (28.1%) and the highest A allele frequency (32.4%) within the Mestizo-Caucasian population of Villa Purificación. Genetic distance analysis using PCA based on *FTO* TT genotype prevalence revealed that the Mestizo-Caucasian population formed a distinct cluster, while Native populations displayed the highest genetic divergence among groups. When analyzing the Mestizos by genotype (AA+AT vs. TT), no significant differences were found in BMI or body fat percentage. However, metabolic profiles of TT genotype carriers showed higher waist-to-height ratios (0.49±0.08 vs. 0.52±0.07, p<0.001), insulin levels (8.8±5.2 vs. 10.8±7.3 μUI/dL, p<0.041), TG (125.8±65.3 vs. 141.8±66.5 mg/dL, p<0.017), and VLDL-c (25.6±14.2 vs. 29.1±14.8 mg/dL, p<0.015). Univariate analysis indicated that the TT genotype was associated with a higher risk of HTG (OR=1.7, 95%CI:1.07-2.73, p<0.027), IR (OR=1.79, 95%CI:1.06-3.07, p<0.031), and HGL (OR=2.77, 95%CI:1.5-5.36, p<0.002) compared to AA+AT genotypes. Multivariate logistic regression further confirmed that TT genotype carriers had a higher risk of HGL compared to AA+AT genotype carriers (OR=2.50, 95%CI:1.213-5.152, p<0.013).

Conclusions: The T allele of the *FTO* (rs9939609 T>A) is more prevalent in Native and Mestizo populations and is associated with higher risks of IR, HTG, and HGL, all of which are linked to type 2 diabetes and MASLD. These results highlight a genetic predisposition to metabolic diseases in populations with significant Amerindian ancestry, particularly in hepatopathogenic environments.

Ethical statement: The Institutional Review Board approved this study, and participants signed a written informed consent form prior to entry.

Declaration of interests: None.

Funding: Supported by the University of Guadalajara, Guadalajara, Mexico – Programa de Fortalecimiento de Institutos, Centros y Laboratorios.

https://doi.org/10.1016/j.aohep.2025.101875

Utility of the CLIF-C AD score to assess readmission in patients with acute decompensation of non-ACLF cirrhosis.

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