Metabolomic Signature in Youth With Perinatally Acquired HIV and Non-Alcoholic Fatty Liver Disease

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Silvia Chafino[1,2], Laura Tarancón-Diez[3,4], Jara Hurtado-Gallego[1,5], Sonia Alcolea[1,5], Antonio Olveira[6], María Luisa Navarro[1,7], Salvador Fernández-Arroyo[8], Consuelo Viladés[1,2,9,10], Maria Luis Montes[1,11], Francesc Vidal[1,2,9,10], Joaquim Peraire[1,2, 9, 10], Anna Rull[1,2,9,10] and Talía Sainz[1,5]

[1]Centro de Investigación Biomédica en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, [2]Infection and Immunity Research Group (INIM), Hospital Universitari de Tarragona Joan XXIII (HJ23), [3]Immunology Section, Laboratorio Inmuno-Biología Molecular (LIBM), Hospital General Universitario Gregorio Marañón (HGUGM), Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), [4]Centro de Investigación Biomédica en Red Bioingeniería, Biomateriales y Nanotecnología (CIBER-BBN), [5]Servicio de Pediatría, Enfermedades Infecciosas y Tropicales, Hospital Universitario La Paz y La Paz Research Institute (IdiPAZ), Hospital Universitario La Paz, [6]Gastroenterology Department, Hospital Universitario La Paz, IdiPAZ, [7]Hospital General Universitario Gregorio Marañón and Gregorio Marañón Research Institute (IiSGM) and Universidad Complutense de Madrid, [8]Eurecat, Centre Tecnològic de Catalunya, Centre for Omic Sciences, Joint Unit Eurecat-Universitat Rovira i Virgili, Unique Scientific and Technical Infrastructure (ICTS), [9]Institut Investigació Sanitària Pere Virgili (IISPV), [10]Universitat Rovira i Virgili (URV), [11]HIV and Infectious Diseases Unit. Hospital Universitario La Paz, IdiPAZ.

BACKGROUND

The prevalence of Non-alcoholic fatty liver disease (NAFLD), characterized by accumulated fat potentially leading to hepatocellular inflammation and injury, is increasing. Persistent immune activation and chronic inflammation despite ART may contribute to HIV-associated NAFLD. Currently, diagnosis and management are challenging, and few studies have addressed the unique population of people living with perinatally acquired HIV (PHIV).

METHODS

Plasma lipidomic and bile acids were analyzed by LC-QTOF and HPLC-MS/MS, respectively, in 29 PHIV on ART and virologically suppressed of whom 10 presented NAFLD and 19 did not (Control). Ultrasound and controlled attenuation parameter (CAP) ≥248 dB/m were used to establish the presence or absence of NAFLD. Statistical analyses were performed with SPSS and MetaboAnalyst 5.0 software.

RESULTS

The PHIV study cohort was composed mainly of women with a median age of 18 (14-24) years. Body mass index was higher among patients with NAFLD compared to controls (23 vs 19Kg/m2, p=0.051). A 30% of NAFLD patients were overweight and 10% obese, whereas only 5.3% was overweight in the control (p=ns). The hepatic steatosis index (HSI) was significantly increased among patients with NAFLD [33.95 (28.48-39.72) vs 27.95 (26.84-32.05), p=0.017).

Circulating concentrations of ursodeoxycholic acid (UDCA) and eight different lipid species (DG36:3 and TG53:4, TG54:4, TG54:5, TG52:4, TG52:5, TG52:3, and TG56:7) were significantly increased among patients with NAFLD (Figure 1).

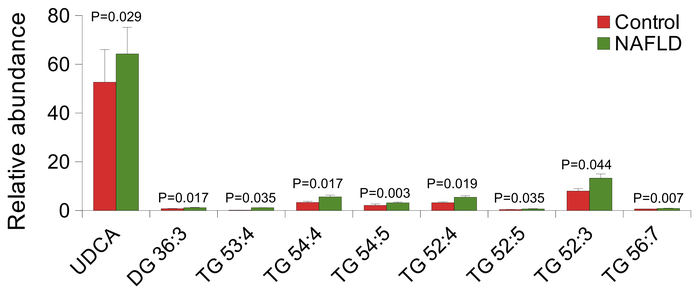


Figure 1. Relative abundance of significant metabolites. Significant differences (p<0.05) between Control and NAFLD groups were determined by the non-parametric U-Mann Whitney test. Abbreviations: DG: diglyceride and TG: triglyceride.

A **lipidomic panel** containing ursodeoxycholic acid and 2 lipid species increases the predictive performance of **HSI** to identify PHIV with **NAFLD** or at risk of progression

Random forest analyses identified UDCA, TG56:7, and TG54:5 as the metabolites that better differentiate both groups (Figure 2). Overall, TG56:7 obtained the best discriminatory power to identify NAFLD with an AUC of 0.898 (Figure 3A).

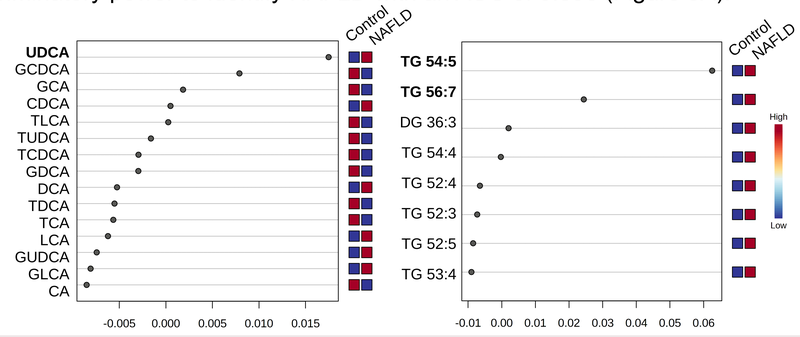


Figure 2. Selection of candidates for distinguishing NAFLD from control. Random forest of significant bile acids and lipids between Control and NAFLD by MetaboAnalyst 5.0. The intensity of colors indicates the significance of the compound in differentiating groups (high:red and low:blue).

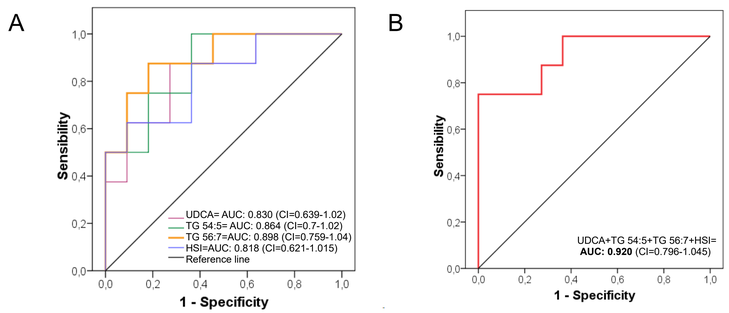


Figure 3. Biomarkers analysis for distinguishing NAFLD from control. A) Receiver operating characteristic (ROC) curves of the most significant bile acid (UDCA), two first lipids (TG54:5 and TG 56:7) in random forest analysis and the clinical parameter HSI to discriminate Control from the NAFLD group and B) binary logistic regression combining different parameters using IBM SPSS Statistics 21.0.

Additionally, regression model combining UDCA, TG56:7, and TG54:5 with the clinical HSI parameter increased the discriminatory power of the model up to an AUC of 0.920 (Figure 3B). Of interest, principal compound analysis based on bile acid levels identified two possible subpopulations within the control group. One subpopulation was differentiated from the NAFLD group (n=6) and the other one (n=13) showed an intermediate profile, suggesting that the biomarker panel could identify patients at risk for progression to NAFLD (Figure 4).

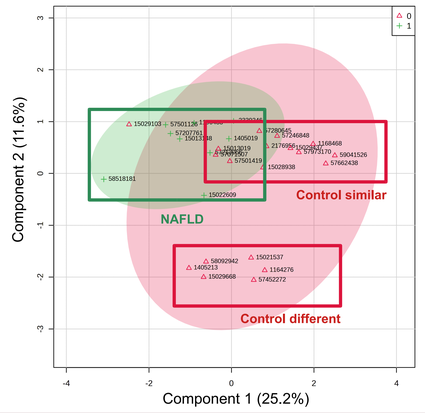


Figure 4. Different Control sub-population. The principal compound graph represented the distribution of the sample based on levels of bile acids.

CONCLUSION

A distinct metabolomic signature, including UDCA, TG56:7 and TG54:5 identify youth living with perinatally acquired HIV with NAFLD.

ADDITIONAL KEY INFORMATION

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Author Contact Information: silvia.chafino@ciberinfec.es