P- 17 LIVER TESTS ABNORMALITIES AS PROGNOSTIC MARKERS OF DEATH IN PATIENTS HOSPITALISED BY COVID-19. A COHORT STUDY

Andrés Fernando Rodriguez-Gutierrez[1], Sergio Mauricio Moreno[2], Camilo Andrés Duarte[3]

[1] *Unidad de Medicina Interna, Hospital Universitario Nacional de Colombia, Bogotá, Colombia*
[2] *Facultad de Medicina, Universidad de los Andes, Bogotá, Colombia*
[3] *Facultad de Medicina, Universidad Nacional de Colombia, Bogotá, Colombia*

Introduction and Objectives: In COVID-19, liver alterations has multiple mechanisms. The objective of this study is to evaluate if raise in transaminases and bilirubin predicts death in COVID-19.

Materials and Methods: Retrospective cohort study of adults hospitalized with COVID-19 and hypoxemia. The primary outcome was death of any cause with a multivariate independent model for ALT, AST and total bilirubin adjusted by age, diabetes mellitus, presence of fever, lymphocyte count, D dimer and lactate dehydrogenase.

Results: Data from 702 patients was collected. The mortality rate was 38%. In admission, 64% of patients had elevated ALT, 64% elevated AST and 8.3% elevated total bilirubin. AST rise level was independently associated with death (OR=1.06, 95% CI: 1.02-1.11 by every rise of 40 U/L, p-value=0.009). Total bilirubin also was independently associated with death (OR = 1.26, 95% CI: 1.08-1.47 for every rise in 1 mg/dl, p-value=0.003). Total bilirubin was also associated with ICU admission, mechanical ventilation and length of hospital stay. Results for ALT did not allow us to conclude an independent association with death. Age, fever and lymphocyte count nadir also was associated with death.

Conclusions: In patients with COVID-19 and hypoxemia, a rise in transaminases and bilirubin is frequent. AST and bilirubin predict mortality, so it is reasonable to measure them in admission. Progress must be made in including these markers in predictive models of mortality and clinical decision rules.

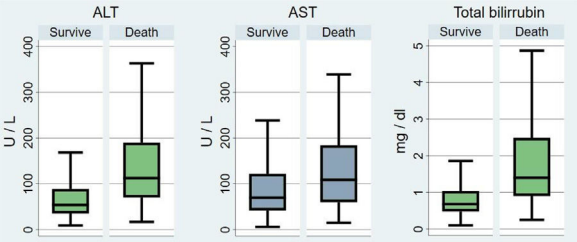

Figure. Box plot of ALT, AST and total bilirubin in patients with COVID-19 who survived or death.

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P- 18 ANASTROZOLE MAY NOT BE ASSOCIATED FATTY LIVER DISEASE AND HEPATIC FIBROSIS IN WOMEN WITH BREAST CANCER

Mateus Jorge[1], Guilherme Grossi[2], Mísia Joyner De Sousa[1], Adriana Maria Lamego[2], Carolina Martins[3], Paulo Henrique Costa[3], Fernanda Alves[4], Julia Cunha[1], Ananda Queiroz[1], Laura Melo[1], Victor Peçanha[1], Maria Clara Mendes[1], Luciana Costa[1], Claudia Alves[1]

[1] *Faculdade de Medicina da Universidade Federal de Minas Gerais, Belo Horizonte, Brasil*
[2] *Instituto Alfa de Gastroenterologia, Hospital das Clínicas da Universidade Federal, Belo Horizonte, Brasil*
[3] *Serviço de Oncologia, Hospital das Clínicas da Universidade Federal de Minas Gerais, Belo Horizonte, Brasil*
[4] *Faculdade de Ciências Médicas de Minas Gerais, Belo Horizonte, Brasil*

Introduction and Objectives: Nonalcoholic fatty liver disease (NAFLD) is highly prevalent among women undergoing androgen inhibitors therapy for breast cancer. As breast cancer survival increases, understanding the long-term impact of anastrozole therapy on NAFLD becomes crucial. This study aimed to assess the prevalence and severity of NAFLD in relation to anastrozole adjuvant therapy among breast cancer patients and to investigate the risk factors associated with the occurrence and progression of NAFLD.

Materials and Methods: Cross-sectional study, recruiting women with breast cancer from an oncology outpatient clinic. Participants underwent abdominal ultrasound to detect liver steatosis and transient elastography for hepatic fibrosis evaluation. Two groups were formed: those not receiving hormone therapy and those exposed to anastrozole.

Results: 91 patients (mean age 58±12 years) were included (71 in the no hormone therapy group and 20 in the anastrozole-exposed group). Follow-up period ranged from 1-315 months [median 25, interquartile range (IQR) 70]. Prevalent comorbidities were diabetes mellitus (27.5%), arterial hypertension (52.7%), dyslipidemia (26.4%), and obesity (47.7%). Exposure to anastrozole ranged from 1 to 60 months (mean 23 ± 15.8). Liver steatosis was detected in 50.5% of the patients, with no significant difference between groups (p = 0.652). Median liver stiffness was also similar (5.2kPa, IQR 2.2, p = 0.102), with 6.7% of patients showing liver stiffness 8kPa (p = 0.613) and 4.5% with measurements 12kPa (p = 0.217). Variables associated with fatty liver were diabetes mellitus (p = 0.018), arterial hypertension (p = 0.047), dyslipidemia (p = 0.021), body mass index (BMI) (p = 0.001), and follow- up time (p = 0.002). Liver stiffness 8kPa was associated with BMI (p = 0.033).

Conclusions: Half of breast cancer patients present NAFLD, with approximately 7% presenting advanced fibrosis. Anastrozole therapy was not associated with NAFLD. Shared metabolic risk factors may play a role in NAFLD in women with breast cancer.

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P-19 CHARACTERIZATION, PROGNOSTIC FACTORS, AND SURVIVAL IN MODERATE ALCOHOL-ASSOCIATED HEPATITIS: A MULTICENTER STUDY

Francisco Idalsoaga[1], Luis Antonio Díaz[1], Oscar Corsi[1], Gustavo Ayares[1], Jorge Arnold[1], Winston Dunn[2], Yanming Li[2], Ashwani Singal[3], Doug Simonetto[4], María Ayala-Valverde[5], Carolina A. Ramirez[6], Dalia Morales-Arraez[7], Wei Zhang[8], Steve Qian[8], Joseph Ahn[4], Seth Buryska[4], Heer Mehta[2], Muhammad Waleed[3], Horia Stefanescu[9], Adelina Horhat[9], Andreea Bumbu[9], Bashar Attar[10], Rohit Agrawal[11], Joaquín Cabezas[12], Berta Cuyàs[13], Maria Poca[13], German Soriano Pastor[13], Shiv K Sarin[14], Rakhi Maiwall[14], Prasun K Jalal[15], María Fátima Higuera-De La Tijera[16], Anand Kulkarni[17], Nagaraja Rao[17], Patricia Guerra Salazar[18], Lubomir Skladaný[19], Natália Bystrianska[19], Veronica Prado[20], Ana Clemente-Sanchez[21], Diego Rincón[21], Tehseen Haider[22], Kristina R Chacko[22],

Gustavo A Romero[23], Florencia D Pollarsky[23], Juan Carlos Restrepo[24], Luis G Toro[25], Pamela Yaquich[26], Manuel Mendizabal[27], Maria Laura Garrido[28], Sebastian Marciano[29], Melisa Dirchwolf[30], Victor Vargas[31], Cesar Jimenez[31], Guadalupe García-Tsao[32], Guillermo Ortiz[32], Juan G Abraldes[33], Patrick Kamath[4], Vijay Shah[4], Ramon Bataller[34], Juan Pablo Arab[35]

[1] *Departamento de Gastroenterología, Pontificia Universidad Católica de Chile, Santiago, Chile*
[2] *University of Kansas Medical Center, KS, USA, Kansas, Estados Unidos (EEUU)*
[3] *Division of Gastroenterology and Hepatology, Department of Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, SD, USA, Sioux Falls, Estados Unidos (EEUU)*
[4] *Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA, Rochester, Estados Unidos (EEUU)*
[5] *Hospital El Pino, Santiago, Chile*
[6] *Department of Anesthesia, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada*
[7] *Center for Liver Diseases, Division of Gastroenterology, Hepatology and Nutrition, University of Pittsburgh Medical Center, PA, USA, Pittsburgh, Estados Unidos (EEUU)*
[8] *Division of Gastroenterology and Hepatology, University of Florida, Gainesville, FL, USA, Gainesville, Estados Unidos (EEUU)*
[9] *Regional Institute of Gastroenterology and Hepatology, Cluj-Napoca, Romania, Cluj-Napoca, Rumania*
[10] *Division of Gastroenterology & Hepatology, Cook County Health and Hospital Systems, Chicago, Illinois, USA, Estados Unidos (EEUU)*
[11] *Division of Gastroenterology and Hepatology, University of Illinois, Chicago, Illinois, Estados Unidos (EEUU)*
[12] *Gastroenterology and Hepatology Department. Research Institute Valdecilla (IDIVAL). University Hospital Marques de Valdecilla. Santander. Spain*
[13] *Department of Gastroenterology, Hospital de la Santa Creu i Sant Pau, CIBERehd, Barcelona, Spain*
[14] *Institute of Liver and Biliary Sciences, New Delhi, India*
[15] *Department of Gastroenterology and Hepatology, Baylor College of Medicine, Houston, TX, USA, Houston, Estados Unidos (EEUU)*
[16] *Servicio de Gastroenterología, Hospital General de México, Universidad Nacional Autónoma de México, México DF, México*
[17] *Asian Institute of Gastroenterology, Hyderabad, India*
[18] *Instituto de Gastroenterología Boliviano-Japonés, La Paz, Bolivia*
[19] *Division of Hepatology, Gastroenterology and Liver Transplantation, Department of Internal Medicine II, Slovak Medical University, F. D. Roosevelt University Hospital, Banska Bystrica, Slovak Republic*
[20] *Centre Hospitalier de Luxembourg, Luxembourg*
[21] *Liver Unit, Department of Digestive Diseases Hospital General Universitario Gregorio Marañón Madrid, Spain*
[22] *Division of Gastroenterology and Hepatology, Montefiore Medical Center, Bronx, NY, USA, Estados Unidos (EEUU)*
[23] *Sección Hepatología, Hospital de Gastroenterología Dr. Carlos Bonorino Udaondo, Buenos Aires, Argentina*
[24] *Hospital Pablo Tobon Uribe, Universidad de Antioquia, Medellín, Colombia*
[25] *Hospitales de San Vicente Fundación, Medellín-Rionegro, Antioquia, Colombia*
[26] *Departamento de Gastroenterología, Hospital San Juan de Dios, Santiago, Chile*
[27] *Hepatology and Liver Transplant Unit, Hospital Universitario Austral, Buenos Aires, Argentina*
[28] *Hospital Central San Luis, San Luis, Argentina*
[29] *Liver Unit, Hospital Italiano De Buenos Aires, Buenos Aires, Argentina*
[30] *Unidad de Hígado, Hospital Privado de Rosario, Rosario, Argentina*
[31] *Liver Unit, Hospital Vall d'Hebron, Universitat Autonoma Barcelona, CIBEREHD, Barcelona, Spain*
[32] *Section of Digestive Diseases, Yale University School of Medicine/VA-CT Healthcare System, New Haven/West Haven, USA, New Haven/West Haven, Estados Unidos (EEUU)*
[33] *Division of Gastroenterology, Liver Unit, University of Alberta, Edmonton, Canada*
[34] *Liver Unit, Hospital Clinic, Barcelona, Spain*
[35] *Division of Gastroenterology, Department of Medicine, Schulich School of Medicine, Western University & London Health Sciences Centre, London, Ontario, Canada*

Introduction and Objectives: Alcohol-associated hepatitis (AH) corresponds to a severe entity with high short-term mortality; however, few studies have been published in patients with moderate AH. This study aimed to characterize patients with moderate AH in a global study, identifying prognostic factors and survival at 30, 90, and 180 days.

Materials and Methods: Multi-center retrospective cohort study, which included patients with moderate AH (2009-2019). Moderate AH was defined as MELD 20 at presentation. We used competing-risk models with liver transplantation as a competing risk to assess variables associated with mortality.

Results: We included 564 patients (24 centers, 12 countries). Median age was 48±11.6 years, 29.2% female, and 46.2.5% Caucasian. 51.7% had cirrhosis, and 1.4% underwent liver transplantation. The MELD score on admission was 17 [6-20]. In the entire cohort, 37.7% used corticosteroids. Survival rates at 30, 90, and 180 days were 93.7% (0.911−0.955), 89.1% (0.860−0.916), and 87% (0.836−0.898), respectively. The most frequent causes of death were multiple organ failure (30.4%) and infections (11.5%). In the univariate analysis, variables associated with mortality were age (sHR 1.035, 95%CI:1.020−1.049; p <0.001), Maddrey's discriminant function (sHR 1.013, 95%CI:1.007 −1.020; p<0.001), albumin at admission (sHR 0.837, 95%CI:0.682 −1.026; p 0.087), INR (sHR 1.534; 95%CI: 1.070−2.198, p=0.020), renal replacement therapy (RRT) (sHR 7.066; 95%CI:4.381−11.392; p<0.001) and infections during hospitalization (sHR 2.079; 95%CI:1.308−3.306; p=0.002)(Table). However, in the multivariate-adjusted model, only age (sHR 1.042; 95%CI:1.019−1.0656, p<0.001), RRT (sHR 7.796; 95%CI:3.993−15.218, p<0.001) and infections during hospitalization (sHR 1.666; 95%CI:0.999−2.779; p=0.050) were associated with mortality. Of note, corticosteroids did not demonstrate benefit.

Conclusions: Patients with moderate AH have a significant mortality at short-term. Infections are associated with higher mortality

and are the most important cause of death in these patients. Better models are necessary to predict mortality in moderate AH adequately.

Table.- Univariate and multivariate competing risk analyses. Mortality is the primary event, and liver transplant is the competing risk.

	Univariate analysis			Multivariate analysis		
Variables	sHR	95% CI	p-value	sHR	95% CI	p-value
Age (years)	1.035	1.020–1.049	< 0.001	1.042	1.019–1.0656	< 0.001
Sex (Female)	0.918	0.658–1.280	0.616	1.237	0.734–2.084	0.423
MELD	1.00	0.955–1.054	0.885	-	-	-
MELD-Na	1.00	0.997–1.006	0.316	-	-	-
MELD 3.0	1.025	0.988–1.064	0.177	-	-	-
mDF	1.013	1.007–1.020	< 0.001	1.013	0.993–1.033	0.179
Cirrhosis	1.037	0.682–1.577	0.863	-	-	-
Corticosteroids use	1.036	0.730–1.469	0.842	-	-	-
Albumin at admission	0.837	0.682–1.026	0.087	-	-	-
Bilirubin at admission	1.013	0.989–1.038	0.267	-	-	-
Serum creatinine	0.992	0.488–2.015	0.983	-	-	-
INR	1.534	1.070–2.198	0.020	-	-	-
Renal replacement therapy	7.066	4.381–11.392	< 0.001	7.796	3.993–15.218	< 0.001
Infections during hospitalization	2.079	1.308–3.306	0.002	1.666	0.999–2.779	0.050

sHR: Subdistribution Hazard ratio; mDF: Maddrey's discriminant function; INR: International Normalized Ratio.

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P-20 OXIDATIVE STRESS MARKERS IN ALCOHOLIC LIVER DISEASE

GABRIELA GUTIÉRREZ[1], Abigail Hernandez[1], Zaira Medina[1], Marisela Hernandez[1], Moisés Martínez[1], José Luis Pérez[2], Fátima Higuera[2], Jacqueline Córdova[3]

[1] *Lab HIPAM, UIME, Facultad de Medicina, UNAM. Hospital General, Ciudad de México, México*
[2] *Gastroenterología, Hospital General de México Dr. Eduardo Liceaga, Ciudad de México, México*
[3] *Gastroenterología, Hospital General Manuel Gea Glz, Ciudad de México, México*

Introduction and Objectives: Several mechanisms participate in the physiopathology of Alcoholic Liver Disease (ALD), such as deregulation in the immune system and oxidative stress. Aim: To analyze markers of lipoperoxidation and oxidative proteins in patients with ALD: Alcohol hepatitis (AH) and liver cirrhosis (CiR).

Materials and methods: This transversal study included 220 individuals divided into three groups: the control group (n=100), individuals with alcohol consumption 10 g/day and AUDIT score 7, the group of AH patients (n=45) and CiR patients (n=75). We measured the serum levels of MDA (thiobarbituric acid method) and carbonylated proteins (DNPH reaction). The statistical analysis was performed by the SPSS v25 software. Data expressed as mean values ± SEM, p-value <0.05 was considered statistically significant.

Results: The control group (CT), with 30.47±0.52 years old, alcohol consumption of 2.32±0.21 gOH/day and AUDIT 2.24±0.10. The ALD patients, had 41.68±6.3 years old, consumption of 354.25± 139.54 gOH/day and AUDIT 30±5.45. The AST, ALT, GGT, total and indirect bilirubin serum were higher in AH and CiR compared to CT (p<0.001), ratio of AST/ALT 2. The albumin levels were lower (p<0.001) in AH vs. CT. The carbonylated proteins serum concentrations were higher in patients with AH compared to CT and CiR (p<0.001). Differences in MDA serum levels were found between CiR versus HA and CT groups (p< 0.005).

Conclusions: Our results suggest that carbonylated proteins and MDA are markers of oxidative damage in the alcohol hepatitis and liver cirrhosis Mexican patients. This damage may increase the risk of malnutrition, susceptibility to infections and sepsis, deficient coagulation factors production, gastrointestinal bleeding, among other complications that increase mortality. According these results is necessary to counteract oxidative damage for improving and complementing the actual treatment of alcoholic liver disease.

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P-21 FIBROSIS DEVELOPMENT AND MALIGNANCIES ARE DELAYED BY PIRFENIDONE WHILE INCREASING SIRT1 NUCLEAR TRANSLOCATION AND HISTONE 3 DEACETYLATIONS IN A HEPATOCARCINOMA MODEL

Hugo Christian Monroy, Scarlet Arceo, Araceli Guadalupe Cabral, Marina Galicia, Juan Armendariz

Departamento de Biología Molecular y Genómica, Universidad de Guadalajara, Guadalajara, México

Introduction and Objectives: Hepatocellular carcinoma (HCC) is the most common liver neoplasm worldwide. Pro-inflammatory and pro-fibrogenic processes are fundamental in tumor development. On the other hand, Pirfenidone (PFD) has anti-inflammatory and antifibrogenic properties useful to counteract hepatocarcinogenesis; however, effects of this drug on SIRT1, and epigenetic regulations in this type of damage are unknown. The aimed of this study is to evaluate PDF effects on SIRT1 translocation, and deacetylation of histone H3 lysines 9 and 14 (H3K9 and H3K14) in a HCC model.

Materials and Methods: Male Fischer-344 rats (n=18) were divided into three groups: CTL: control group, HCC: damage group, rats weekly administrated with diethylnitrosamine (DEN,50mg/kg/i.p.) and 2-aminofluorene (2AAF, 25mg/kg/p.o.) for 16 weeks. HCC/PFD group of rats administrated with DEN and 2AAF plus PFD (300mg/kg/day/p.o.). Tumor development and fibrosis markers were analyzed histologically. In addition, expression of SIRT1 deacetylase, p300 acetylase, H3 and H3K9 and H3K14 acetylated were analyzed by western blot.

Results: Normal liver architecture is disturbed by dysplastic nodules formation surrounded by extracellular matrix and fibrosis, also an increase in cells with anaplasia and steatotic foci was observed in liver tissues of HCC group. PFD was effective in preventing these changes. Immunohistochemistry revealed an overexpression of GPC3 and -SMA in damage group, which correlates with malignant degeneration; these responses were also prevented by PFD. Finally, western blots evidenced an overexpression of SIRT1 in nuclear fraction of PFD group, triggering H3K9 and H3K14 deacetylation, in addition, a decrease in p300 acetylase expression in nuclear fractions was noted. Noteworthy, c-Myc was decreased.

Conclusions: PFD reduces fibrotic and malignant patterns development. Likewise, PFD induces SIRT1 expression and nuclear translocation along with H3K9 and H3K14 deacetylation, compacting chromatin and possibly down expression of oncogenes. These results demonstrate the capability of PFD to regulate epigenetic hallmarks on histones.

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