

¹ Buenos Aires Italian Hospital, Liver Unit, Buenos Aires, Argentina

² Buenos Aires Italian Hospital, Department of Research, Buenos Aires, Argentina

³ 4 de Junio Hospital, P. R. Sáenz Peña, Argentina

⁴ Churrucá Visca Hospital, Buenos Aires, Argentina

⁵ Güemes Sanatorium, Buenos Aires, Argentina

⁶ Germany Hospital, Buenos Aires, Argentina

⁷ A.C. Padilla Hospital, San Miguel de Tucumán, Argentina

⁸ T J Schestakow Hospital, San Rafael, Argentina

⁹ Centenary Provincial Hospital, Rosario Argentina

¹⁰ Bi-Institutional Liver Transplant Unit, Clinics Hospital – Military Hospital, Montevideo, Uruguay

¹¹ Rossi Hospital, La Plata, Argentina

¹² San Martín Hospital, Paraná, Argentina

¹³ Parque Sanatorium, Rosario, Argentina

¹⁴ Sagrado Corazón Sanatorium, Buenos Aires, Argentina

¹⁵ Muñiz Hospital, Buenos Aires, Argentina

¹⁶ Regional Hospital of Rio Gallegos, Rio Gallegos, Argentina

¹⁷ Boratti Sanatorium, Posadas, Argentina

¹⁸ Argerich Hospital, Buenos Aires, Argentina

¹⁹ Rosario Private Hospital, Rosario, Argentina

²⁰ Buenos Aires Italian Hospital, Infectious Diseases Section, Buenos Aires, Argentina

²¹ Austral University Hospital, Pilar, Argentina

²² Fernández Hospital, Buenos Aires, Argentina

²³ Center for Farmacoepidemiology, Karolinska Institutet, Stockholm, Sweden

Introduction and Objectives: Selecting an empiric antibiotic treatment in patients with cirrhosis and spontaneous bacterial infections is challenging. It is of paramount importance to have local epidemiological data to maximize pathogen coverage while minimizing the unnecessary use of broad-spectrum antibiotics. This study aimed to describe the patterns of antibiotic resistance of spontaneous bacterial infections according to the site of acquisition.

Materials and Methods: Analysis of the multicenter prospective cohort study of cirrhotic patients with bacterial infections in Argentina and Uruguay (NCT03919032). Only culture-positive spontaneous infections were included in this study: spontaneous bacterial peritonitis (SBP), spontaneous bacterial empyema (SBE), and spontaneous bacteremia (SB). We estimated the proportion of infections that were sensitive to various antibiotics according to where the infection was acquired: community-acquired (CA), healthcare-associated (HCA), or nosocomial (NOS). Approximately 80% coverage is advisable for empiric treatments in stable patients and 90% for critically-ill patients.

Results: The main cohort included 472 patients, of whom 97 presented culture-positive spontaneous infections and were included: with 57 (59%) SBP, 34 (35%) SB, and 4 (6%) SBE. Regarding the site of acquisition, 43% were CA, 36% NOS, and 21% HCA. Gram-positive and negative bacteria were found in 53% and 47% of the infections. The most frequent isolations were *Streptococcus* spp (26%), *E. coli* (20%), *K. pneumoniae* (15%), *S. Aureus* (10%), *E. faecium* (6%) and *E. faecalis* (4%). Multidrug-resistant organisms (MDROs) were isolated in 35% of the patients. As shown in the table, cefepime and ceftriaxone offer the most rational coverage for CA and HCA infections, and imipenem or meropenem for NOS infections. However, in critically-ill patients, broader-spectrum antibiotics are needed to achieve a coverage closer to 90% (table).

Conclusions: We present, for the first time in our region, evidence-based recommendations for the empirical treatment of spontaneous bacterial infections. Prior colonization and/or infections by MDROs might refine even more the antibiotic selection and should be explored.

Table: Proportion of isolations that were susceptible to selected antibiotics, according to the site of acquisition of the infection (n=97)

| | Community Acquired (n=42) | HCA (n=20) | Nosocomial (n=35) |
|------------------------------------|------------------------------|---------------|----------------------|
| Ceftriaxone | 71% | 75% | 58% |
| Cefepime | 74% | 80% | 58% |
| Ceftazidime | 40% | 35% | 33% |
| Piperacillin-tazobactam | 79% | 80% | 60% |
| Carbapenems | 81% | 85% | 76% |
| Imipenem or meropenem | 73% | 70% | 65% |
| Imipenem or meropenem + Vancomycin | - | - | 97% |
| Ertapenem | 73% | 70% | 65% |

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P-7 LIVER INJURY AFTER COVID-19 VACCINATION COMPARED TO POST-INFLUENZA VACCINES: RETROSPECTIVE COHORT STUDY

Marlene Padilla Lopez¹, Natalia Sobenko¹, Valeria Ines Aliperti², Vanina Cecilia Stanek³, Maria Florencia Grande Ratti^{4,5}, Fernando Ezequiel Jabif⁶, Marcelo Gabriel Vallone⁶, Alejandra Villamil¹

¹ Hepatology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina

² Epidemiology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina

³ Infectology Section, Buenos Aires Italian Hospital, Buenos Aires, Argentina

⁴ Internal Medicine Research Area, Buenos Aires Italian Hospital, Buenos Aires, Argentina

⁵ Conicet, Assistant Researcher, Buenos Aires, Argentina

⁶ Medical Clinic Service, Buenos Aires Italian Hospital, Buenos Aires, Argentina

Introduction and Objectives: Cases suggestive of immune-mediated acute hepatitis following SARS-CoV-2 vaccination have been reported. The risk of liver injury after Covid-19 vaccination is unknown. This study aimed to estimate the cumulative incidence of liver injury within 90 days after the Covid-19 vaccine, defined as the occurrence of AST and/or ALT increases at least two times the limit of normal or ALP increases at least x 2. To compare with an active comparator group (influenza vaccine).

Materials and Methods: Retrospective cohort study. We analyze a consecutive sample of adult patients vaccinated with Covid-19 vaccines (Sputnik, AstraZeneca/Oxford, Covishield, or Sinopharm) between January 1 and May 30, 2021, and a historical control group vaccinated with influenza between March 1 and July 30, 2019. Qualifying labs were collected as part of routine clinical care or the development of symptoms.

Results: From a total of 29,918 subjects who received the Covid-19 vaccine in 2021 and 24,753 who received the Influenza vaccine in 2019, 130 and 148 patients, respectively, were excluded because of previously altered liver function tests or known hepatic disease. Both groups were comparable in age (73 years old (IQR 65-80), p=0.125) and gender (67% were females). In the Influenza group were more dysmetabolic and immunosuppressed patients.

A total of 269 and 273 patients, respectively, presented altered liver function tests within 90 days post-vaccination. The cumulative incidence of liver injury was 4.6 per 1,000 (95% CI 3.9-5.5) for Covid-19 and 5.1 per 1,000 (95%CI 4.3-6.1) for Influenza (p=0.453). Although, two patients from the COVID group had a more severe injury, with hyperbilirubinemia, development of autoantibodies and requirement of steroids for disease control.

Conclusions: The occurrence of events was similar in subjects vaccinated with Covid-19 compared to the control group. Acute hepatitis characteristics arising after the COVID-19 vaccine needs to be further clarified.

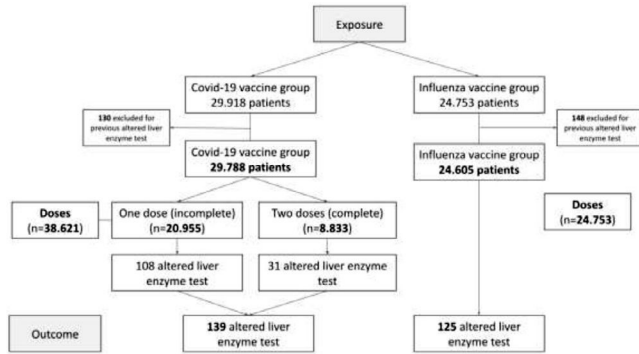


Figure 1. Flowchart diagram for study participants

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P-8 EXTRACELLULAR VESICLE-DERIVED MICRORNA SIGNATURE IN HCV AND HCV/HIV PATIENTS WITH DIFFERENT STAGES OF LIVER FIBROSIS

Victoria Cairolí¹, Daniel Valle Millares², Pablo Ryan³, Lourdes Dominguez⁴, Luz Martín-Carbonero⁵, Beatriz Ameigeiras⁶, Verónica Briz², Amanda Fernandez Rodriguez^{2,7}, Ma Victoria Preciado¹, Pamela Valva¹

¹ Multidisciplinary Institute for Pediatric Pathology Research (Imipp-Conicet-Gcba), Buenos Aires, Argentina

² National Microbiology Center, Instituto de Salud Carlos III, Madrid, España

³ Infectious Diseases Department, Hospital Universitario Infanta Leonor, Madrid, España

⁴ HIV Unit. Internal Medicine Service. Instituto de Investigación Hospital 12 de Octubre (I+12), Madrid, España

⁵ La Paz Hospital Research Institute (Idipaz), Madrid, España

⁶ Hepatic Unit, Hospital Ramos Mejía, Buenos Aires, Argentina

⁷ Alfonso X El Sabio University, Villanueva de la Cañada, Madrid, España

Introduction and Objectives: Extracellular vesicles (EVs) are essential players in cell communication, and their cargo modulates the receptor cell response. MicroRNAs (miRNAs) proved to modulate the immune response both in physiological and pathological conditions. Hepatitis C (HCV) and Human Immunodeficiency (HIV) virus infection could modify EVs miRNA content and, therefore, the immune response. This study aimed to analyze the significant differentially expressed (SDE) EVs-derived miRNAs between HCV and HCV/HIV-infected patients, analyze differences according to liver fibrosis stages and explore the associated molecular pathways.

Materials and Methods: Plasma from 21 chronic HCV and 29 HCV/HIV patients were analyzed. EVs were isolated and total EV-containing RNA enriched with small RNAs was high-throughput sequenced (1 × 50). Raw reads were analyzed with Fastqc and trimmed with Cutadapt. Human-miRNA identification was performed with miDeep2. R

package edgeR was used to detect SDE miRNAs between groups and *in silico* miRNA target prediction was performed with DIANA-mirPath.

Results: HCV patients [54 years (46.5; 62.5), 52.4% F_{≥2}] showed 38 SDE miRNAs compared with the HCV/HIV group [50 years (45; 53), 22.58% F_{≥2}] that modulate pathways related to fatty acids biosynthesis, extracellular matrix interaction and viral carcinogenesis. Regarding fibrosis, HCV patients with F<2 showed downregulation of hsa-miR-3615 (log₂FC=-0.92, p=0.039), which modulates genes involved in the cell cycle and the mRNA surveillance pathway. On the other hand, HCV/HIV patients with F<2 had 13 SDE miRNAs compared with F_{≥2}. Among them, hsa-miR-122-5p (downregulated) and hsa-miR-328-3p (upregulated) showed the most significant differences (log₂FC=-1.22, p=0.034, log₂FC=1.33, p=0.042, respectively). Together, they regulate genes involved in cancer-related pathways and fatty acid metabolism.

Conclusions: Differentially expressed EVs-derived miRNAs in HCV and HCV/HIV chronic infection and in different stages of liver fibrosis were observed. The specific miRNA signature of each liver fibrosis stage may elucidate potential mechanisms involved in the clinical evolution of these patients and the identification of biomarkers of unfavorable progression.

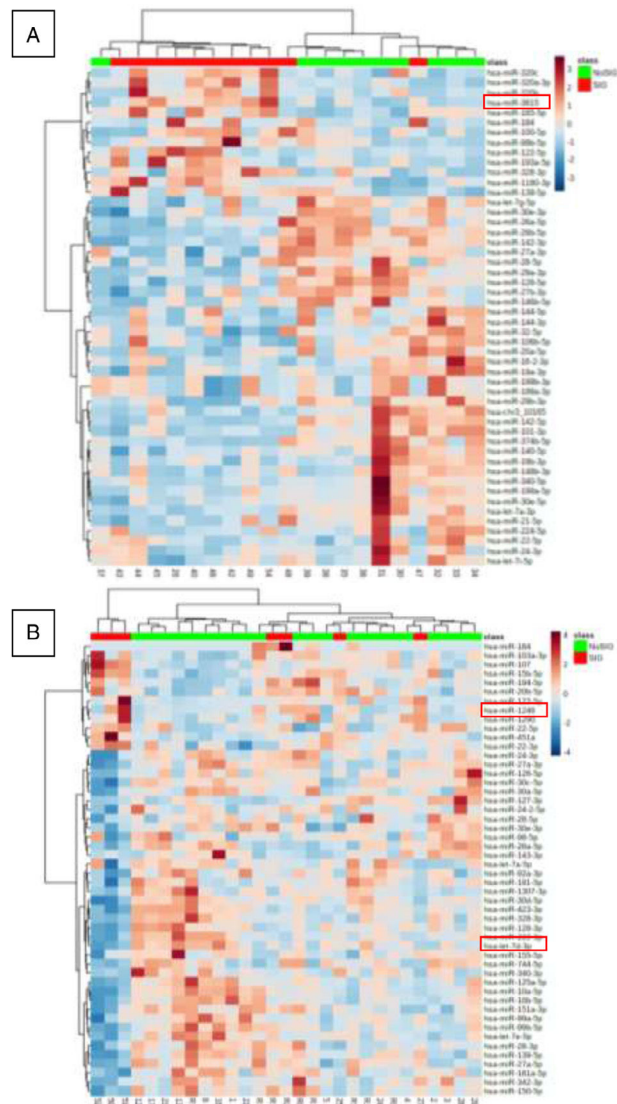


Figure 1. Heatmap showing the top 50 miRNAs between patients with F<2 and F_{≥2} in A) HCV and B) HCV/HIV cases.

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