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.

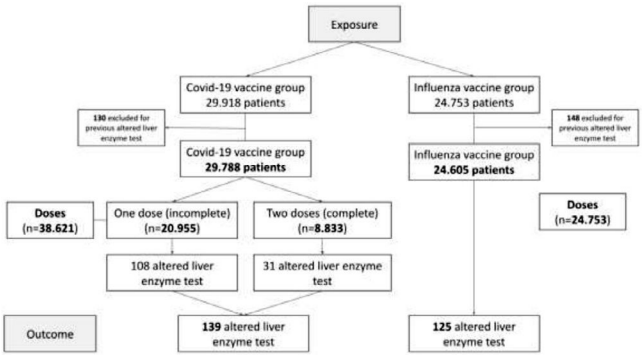

Figure 1. Flowchart diagram for study participants

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

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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 miRDeep2. 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 (log_2FC=-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 (log_2FC=-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.

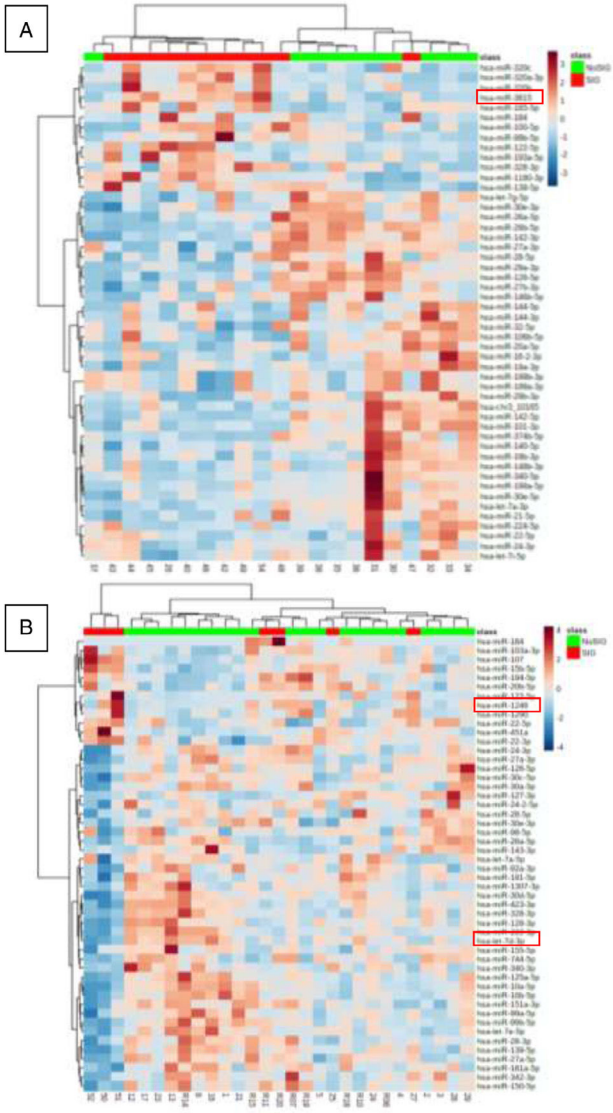

Figure 1. Heatmap showing the top 50 miRNAs between patients with F<2 and F≥2 in A) HCV and B) HCV/HIV cases.

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