Title: Integrated Clinical and Immune Profiling of Treatment-Naive Chronic Hepatitis C Patients from a Real-World Western Indian Cohort

Authors:
Kumar V[1,4], Athalye S[1], Khargekar N[1], Chandnani S[2], Taklikar S[3], Banerjee A[1,4]

[1] Department of Transfusion Transmitted Diseases, Indian Council of Medical Research (ICMR) – National Institute for Research on Blood and Immune Disorders (NIRBID) formerly National Institute of Immunoheamatology (NIIH), Mumbai, India

[2] Department of Gastroenterology, Lokmanya Tilak Municipal Medical College and General Hospital (LTMGH), Mumbai, India

[3] Department of Microbiology, Lokmanya Tilak Municipal Medical College and General Hospital (LTMGH), Mumbai, India

[4] Academy of Scientific and Innovative Research (AcSIR), Ghaziabad- 201002, India

Background: Beyond liver fibrosis, chronic HCV infection is increasingly recognized as a complex inflammatory and metabolic disease associated with persistent immune dysregulation even after direct-acting antivirals (DAAs) have transformed the management of chronic hepatitis C virus (HCV) infection. However, integrated baseline profiling of treatment-naive patients remains limited in real-world Indian cohorts. As part of an ongoing cohort study, we performed an exploratory integrated analysis of clinical, metabolic, and immune profiles in chronic HCV patients prior to antiviral therapy.

Methods: A cross-sectional exploratory baseline analysis was performed in 21 treatment-naive chronic HCV patients enrolled at tertiary referral centre in India. Clinical evaluation included liver stiffness measurement (LSM), APRI score, ultrasound attenuation parameter (UAP), liver biochemistry, platelet counts, and lipid profile assessment. Immune phenotyping was performed using flow cytometry to assess immune activation and exhaustion markers. Spearman correlation analysis, hierarchical clustering, and integrated correlation matrix analysis were used to examine.

Results: Exploratory analysis demonstrated substantial baseline biological heterogeneity across the cohort. Moderate positive association between LSM and UAP values (ρ=0.432, p=0.051) suggested concurrent fibrotic and steatotic liver alterations. CD3+PD1+ expression showed a significant negative correlation with HDL cholesterol levels (ρ=-0.597, p=0.004) and a significant positive correlation with mono_HLADR_PD1+ populations (ρ=0.588, p=0.005), suggesting immune–metabolic dysregulation and coordinated innate–adaptive immune perturbation. CD3+PD1+ expression also demonstrated positive trends with APRI (ρ=0.402, p=0.071), AST (ρ=0.420, p=0.058), and ALT (ρ=0.394, p=0.077), suggestive of ongoing inflammatory liver injury and fibrosis-associated disease burden.

Conclusion: This exploratory analysis highlights substantial clinical, immune, inflammatory, and metabolic heterogeneity in treatment-naive chronic HCV patients, suggesting broader underlying biological burden beyond fibrosis assessment alone. Patients from the ongoing cohort will be longitudinally followed to evaluate post-treatment immune–metabolic and clinical changes following antiviral therapy.

Disclosure of Interest Statement: This work was conducted as part of an ongoing academic research project at National Institute for Research on Blood and Immune

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