ORIGIN, DIVERSITY AND TRANSMISSION DYNAMICS OF HEPATITIS C VIRUS GENOTYPES IN PORTUGAL

Authors:
Marinho RT[1,*], Palladino C[2,*], Ezeonwumelu IJ[2], Marcelino R[3], Briz V[4], Moranguinho I[2], Serejo F[1], Velosa JF[1], Borrego P[2,5#], Taveira N[2,6 #]

*The first two authors (R.T.M. and C.P.) contributed equally to this work.
#The last two authors (P.B. and N.T.) contributed equally to this work.
[1]Department of Gastroenterology and Hepatology, Santa Maria Hospital, Universidade de Lisboa, Lisbon, Portugal, [2] Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Lisbon, Portugal, [3] Global Health and Tropical Medicine (GHTM), Unit of Medical Microbiology, Instituto de Higiene e Medicina Tropical (IHMT), Universidade Nova de Lisboa, Lisbon, Portugal, [4] Laboratory of Viral Hepatitis, National Center for Microbiology, Institute of Health Carlos III, Majadahonda, Madrid, Spain, [5] Centro de Administração e Políticas Públicas (CAPP), Instituto Superior de Ciências Sociais e Políticas, Universidade de Lisboa, Lisbon, Portugal, [6]Centro de Investigação Interdisciplinar Egas Moniz (CiiEM), Instituto Universitário Egas Moniz, Caparica, Portugal.

Background:
Any successful strategy to prevent and control HCV infection requires an understanding of the epidemic behaviour among the different subtypes. Here, we performed the first characterization of the epidemic history and transmission dynamics of HCV subtypes in Portugal.

Methods:
Direct sequencing of HCV NS5B was performed on plasma samples collected from a cross-section of 230 DAAs-naïve patients attending the Hospital Santa Maria in Lisbon, Portugal. Phylogenetic analysis was used for subtyping and transmission cluster identification. Bayesian methods were used to reconstruct the epidemic history of HCV subtypes. Sequences were analysed for resistance associated substitutions (RASs).

Results:
The majority of strains were HCV-GT1 (62.6%), GT3 (18.3%) and GT4 (16.1%). Among GT1, the most frequent subtype was 1a (75.5%) and 1b (24.5%). All GT3 were subtype 3a. Among GT4, the most frequent subtypes were 4a (10.4%) and 4d (4.3%). Except for 12 HCV lineages segregating into six transmission clusters, polyphyletic patterns were found suggesting multiple and old introductions of the different HCV subtypes in this population. Four distinct epidemics were identified. The first was caused exclusively by GT1b, occurred during 1930s and 1960s and was likely associated with contaminated blood transfusions. The second and third epidemics were likely associated with widespread use of intravenous drug use and were caused by GT3a in the 1960s and GT1a in the 1980s. The most recent HCV epidemic in Portugal was caused by GT4a and seems to be associated with the resurgence of opioid use. There were no RASs to sofosbuvir in our patients but C316N that confers low-level resistance to dasabuvir was found in > 31% of 1b-infected patients.

Conclusion:

Distinct epidemics caused by different HCV subtypes were identified over time in Portugal. Close surveillance of patients bearing this mutation and undergoing dasabuvir-based regimens will be important to
determine its impact in treatment outcome.

Disclosure of Interest Statement:
The authors declare no competing interests.