“Genotyping of Hepatitis C virus in Patients of tertiary health care centre Kanpur”

Introduction:

Hepatitis C virus (HCV) is a globally prevalent pathogen and a leading cause of morbidity and death.\(^1\) The most recent estimates of disease burden show an increase in seroprevalence over the last 15 years to 2.8%, equating to \(>185\) million infections worldwide.\(^2\) Persistent HCV infection is associated with the development of liver cirrhosis, hepatocellular cancer, liver failure, and death,\(^3\) and HCV is now the most common cause of death in HIV-positive patients on highly active antiretroviral therapy.\(^4\) While the incidence rate of HCV infection is apparently decreasing in the developed world, deaths from liver disease secondary to HCV infection will continue to increase over the next 20 years.\(^5\)

Historically, HCV drug therapy has depended on interferon-α (administered by injection) and ribavirin over many months and is associated with severe side effects. The resources required for treating HCV patients with such drugs have been a considerable barrier for healthcare systems in many low and/or lower-middle income countries, despite treatment outcomes that are comparable to those in well-resourced settings.\(^6\) That said, the coming decade should witness a remarkable transformation in the treatment of HCV infection. While the first generation of new direct-acting antivirals (DAAs) were given in combination with interferon and ribavirin, and thus added to the burden of side effects,\(^7-10\) second-generation DAA therapies with minimal side effects and shortened courses of therapy are associated with cure rates of more than 90% in Phase II or III studies.\(^11\) Moreover, multiple DAA therapies targeting distinct HCV proteins have been developed and, when given in combination, will obviate the need for interferon treatment.\(^12\) Thus, if DAAs are made affordable, the treatment of HCV across the globe will become a realistic option for the first time.

HCV exhibits an extraordinarily high degree of genetic diversity—substantially greater than that of the HIV-1 pandemic—creating a major challenge for the development of both HCV vaccines and pan-genotypic drug therapies.\(^13\) At present, the duration of treatment, cure rates, and the need for adjuvant interferon and ribavirin with the new DAA therapies remain dependent in part on HCV genotype and subtype. Therefore, the development of rational treatment strategies using DAA therapies requires a detailed understanding of relative HCV genotype prevalence and subtypes.

HCV strains are classified into seven recognized genotypes (1-7) on the basis of phylogenetic and sequence analyses of whole viral genomes.\(^14\) HCV strains belonging to different genotypes differ at 30-35% of nucleotide sites. Within each genotype, HCV is further classified into 67 confirmed and 20 provisional subtypes. Strains that belong to the same subtype differ at \(<15\)% of nucleotide sites.\(^15\) The contemporary global geographic distribution of HCV genotypes is complex. It has already been established that a few subtypes—specifically 1a, 1b, 2a, and 3a—are widely distributed across the globe and account for a large proportion of HCV infections in high-income countries. These so-called “epidemic subtypes” are thought to have spread rapidly in the decades prior to the discovery of HCV by way of infected blood, blood products, injecting drug use, and other routes.\(^16-20\) Many other HCV subtypes are considered “endemic” strains; these are comparatively rare and have circulated for long periods of time in more restricted regions: endemic strains from genotypes 1 and 2 are primarily in West Africa, 3 in south Asia, 4 in Central Africa and the Middle East, 5 in Southern Africa, and 6 in South East Asia.\(^14,18,21,22\) To date, only one genotype 7 infection has been reported; it was isolated in Canada from a Central African immigrant.\(^23\) The global distribution of HCV genetic variation has likely been influenced by historical and contemporary trends in human migration. For example, strains from West Africa appear to have been transferred to the Americas by way of the trans-Atlantic slave trade.\(^24\)

Furthermore, the first prophylactic T-cell vaccines that aim to prevent persistent HCV infection are currently in Phase II efficacy testing, with further candidates moving into human studies.\(^25\) The first generation of vaccines in development contain a subtype-1b immunogen in viral vectors that are deployed in a heterologous prime-boost regimen.\(^26\) In countries with mixed genotype infection, crossreactive immunity will depend on the generation of an immune response that targets HCV antigens that are conserved between genotypes. An alternative strategy, however, would be to develop geographically tailored vaccine immunogens for deployment at a country or regional level where detailed information on viral subtypes is available. Overall, the rational testing of HCV vaccine candidates will require a comprehensive country-level understanding of relative subtype prevalence.

The data described above provides a platform for the rational deployment and efficacy testing of new DAA therapies and vaccines for HCV.