Leveraging genomic surveillance to enhance elimination strategies for hepatitis C virus

Lancet Microbe 2022
Published Online
August 16, 2022
https://doi.org/10.1016/S2666-5247(22)00204-X

The COVID-19 pandemic has accelerated genomic surveillance of viruses, which has been lauded for its use in improving pandemic preparedness and informing public health strategy. WHO estimates that 68% of countries globally now have the capacity for viral genomic surveillance and the ability to rapidly share genetic information with the global community.[1] The scaling up of genomic surveillance during the past 2 years offers an unparalleled opportunity for initial investment and mobilisation of capacity towards other pathogens, such as hepatitis C virus.

Hepatitis C virus is an ideal candidate for genomic surveillance as it has a high mutation rate, resulting in high genetic diversity at the population and intra-host levels. This molecular plasticity has given rise to eight diverse genotypes, each differing by 30%, and over 90 subtypes with 15% variation at the nucleotide level. This breadth of diversity is a huge obstacle to vaccine development. Despite the absence of a prophylactic hepatitis C virus vaccine, the success of direct-acting antivirals has led to effectively curing patients with chronic hepatitis C virus. Nevertheless, the WHO target of eliminating viral hepatitis by 2030 includes the goal of reducing the number of new hepatitis C virus infections by 80%. These targets are going to be challenging to meet by treatment alone, in particular when there are many high-risk groups who are difficult to engage in care and represent important sources for new infections.

Marginalised populations, including people who use injection drugs, people who have been incarcerated, people who are transgender, men who have sex with men, and people who are homeless or vulnerably housed, are all susceptible to health inequities (eg, access to testing and treatment).[2] As access to hepatitis C treatment and care becomes more affordable, there will be a need for an improved understanding of which populations new infections are occurring and how best to target new interventions to prevent onwards transmissions. Even in well-described hepatitis C virus-serodiscordant injection partners, pinpointing the source of infection is challenging.[3] Thus, the goals of achieving hepatitis C virus elimination will emphasise the need for a more concerted public health response that must focus on tackling transmission within well-defined populations (known as microelimination).

It seems evident that there is a need to augment public health surveillance to facilitate earlier effective strategies to mitigate and contain outbreaks among blood-borne infections. For example, in 2014, a cluster of 215 HIV infections was detected among people in Scott County, Indiana, which was linked to injection-drug use of oxymorphone.[4] A retrospective analysis of this population revealed a pre-existing dense and dynamic network of hepatitis C virus transmission among people who inject drugs. 92% of individuals with HIV who use injection drugs are coinfected with hepatitis C virus, and it has been shown that hepatitis C virus was circulating without detection within the same networks before the emergence and dissemination of HIV in this community.[5] Given the incidence of hepatitis C virus within this community, it is probable that genomic surveillance could have detected these transmission networks that perpetuated for years and prevented this HIV outbreak. Similar transmission networks have been found across other parts of the USA and globally, in which injection drug use has led to a high prevalence of hepatitis C virus infections that has been considered by public health experts as a potential harbinger for HIV transmission networks.[6,7] One concern from the COVID-19 pandemic is that, globally, there are so-called blind spots to genomic surveillance, which increase the opportunity for a novel variant to circulate and upend public health measures. In comparison, for hepatitis C virus surveillance, there has been a dearth of genetic sequence data with less than 5000 genomes publicly released, compared with the extraordinary 11 million genomes shared for SARS-CoV-2. For years, molecular hepatitis C virus surveillance has been marred by insufficient data and geographical inequities. This scarcity of data could prolong the hepatitis C virus epidemic, especially in some regions such as sub-Saharan Africa where it could increase resistance to current direct-acting antiviral regimens.[8] There are formidable challenges, but substantial opportunities also exist to harness the tools, infrastructure, and networks for large scale molecular hepatitis C virus surveillance that is not

only informative but is sustainable and cost-effective. As recognised by public health bodies during the COVID-19 pandemic, the deployment of genomic surveillance is a powerful tool that can augment traditional surveillance approaches and track nascent transmission networks to provide actionable information to public health officials and policy makers. The integration of such data could be key to facilitating the WHO's 2030 elimination strategy, particularly when considering tailored microelimination strategies.

I declare no competing interests.

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