



Editorial

World Hepatitis Day 2023: Are we close to the target?

Viral hepatitis is a major global health challenge. In particular, chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections are major causes of cirrhosis and hepatocellular carcinoma¹, and these two viruses account for 96 per cent of viral hepatitis-related mortality². In 2016, the World Health Organization (WHO) called for the elimination of viral hepatitis as a public health threat by 2030, aiming for a 90 per cent reduction in incidence and 65 per cent reduction in mortality due to HBV or HCV³. Since the target for hepatitis elimination was established, extensive policy changes and campaigns have been implemented worldwide². HCV treatment success rates have dramatically risen as we entered the direct-acting antivirals (DAAs) era⁴, whereas the management of HBV has also evolved with the increasing availability of nucleos(t)ide analogues⁵ and the emergence of novel drugs⁶. As we stand at the halfway mark between 2016 and 2030, it is a good opportunity to evaluate our progress. Are we close to the target?

Hepatitis B virus

Through rigorous data collection from 200 countries and regions, the WHO estimated a global HBV prevalence of 3.84 per cent (295.9 million patients) in 2019, which increased from 3.5 per cent in 2015. The global HBV-related mortality was 0.821 million in 2019, which decreased by seven per cent since 2015². These numbers have failed to reach the 2020 Interim Goals set by the WHO⁷. The HBV vaccine was developed almost four decades ago, and it is well documented to reduce transmission and long-term complications of HBV⁸. However, HBV vaccine coverage has remained suboptimal, and the global coverage for timely administration of the birth dose of this vaccine was only 43 per cent in 2019, with 85 per cent coverage for three doses of HBV vaccine⁷. Vaccination coverage is low in the African region, a region that accounts for 64.9 per cent of

new HBV infections globally, forming a vicious cycle of new infections². Barriers to HBV vaccination are multifactorial. Interventions such as increasing accessibility, providing outreach services and public education will be required to enhance HBV vaccine coverage⁹.

Most HBV patients do not know about their diagnosis as they do not have symptoms of early-stage disease. In 2019, it was estimated that only 10.3 per cent of HBV patients knew that they were infected², a number that fell far short of the WHO 2020 interim target of 30 per cent global diagnosis⁷. Large discrepancies were noted between regions, with the European, western Pacific and American regions all achieving diagnosis rates of >18.5 per cent, while the African and southeast Asian regions had diagnosis rates of 2.2 and 2.1 per cent, respectively². HBV screening is supported by the WHO and various international societies. The latest 2023 guidelines by the US Centers for Disease Control recommend universal screening of all adults by the panel of hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs) and antibody to hepatitis B core antigen¹⁰. Modelling studies have demonstrated that universal screening can be cost-effective¹¹, yet the efficacy of screening programmes may be affected by the existing knowledge gaps and social barriers¹². Tailoring interventions for at-risk populations is warranted to enhance the uptake of screening programmes. Aside from screening for HBV carriers, linkage to care is equally important. A streamlined programme to transition newly diagnosed HBV patients to long-term care would be paramount to reduce the number of patients lost to follow up¹³.

The current first line nucleos(t)ide analogues are unable to reliably induce HBsAg seroclearance; yet, they are highly effective in suppressing viral replication and reducing HBV complications⁵. As

of 2019, 21.8 per cent of treatment eligible HBV patients received therapy globally; yet, a high regional discrepancy in treatment coverage was noted. The western Pacific region accounted for 84.2 per cent of patients receiving HBV treatment worldwide, whereas the African region only accounted for 1.6 per cent of on-treatment patients². Generic tenofovir disoproxil fumarate and entecavir are now available, and treatment costs can be as low as 30 USD per year. However, as most patients require lifelong treatment, the economic impact of multiple decades of therapy may be more prominent in low-to-middle-income countries¹⁴. In recent years, many novel HBV drugs are being developed and entering clinical trials⁶. If these novel drugs can effectively induce HBsAg seroclearance, they will obviate the costs of long-term treatment and will provide a major boost to HBV elimination.

Hepatitis C virus

In 2019, the WHO estimated that chronic HCV infection affected 57.8 million patients (0.75% prevalence) and caused 0.287 million deaths worldwide². These numbers have dropped from the 2015 figures of one per cent prevalence and 400 thousand mortalities. This large improvement is primarily driven by the successful treatment of patients with DAAs².

Since the approval of sofosbuvir in 2013, HCV treatment has officially entered the all-oral DAA era. The current DAAs are well tolerated, have pangenotypic coverage and can induce cure in over 95 per cent of patients⁴. DAAs for HCV are more costly than nucleos(t)ide analogues for HBV. However, HCV therapy encompasses a single course of treatment, and universal treatment has been established to be cost-effective¹⁵. Allocating a lump sum for universal HCV treatment may be challenging, yet this can be a worthwhile investment. For example, Egypt had the highest HCV prevalence in the world before 2015. Through implementing HCV treatment campaigns with assistance from the World Bank, the national HCV prevalence in Egypt dropped from 2.3 per cent in 2015 to 1.6 per cent in 2019². Among 66 countries with the high viral hepatitis burden, Egypt is one of only eight countries that are on track to eliminate HCV by 2030¹⁶.

With effective treatment, the challenge in HCV elimination lies in case finding and treatment coverage. As of 2019, only 21 per cent of the 57.8 million HCV patients worldwide knew of their infection status. Among these patients, only 9.4 million received treatment between 2015 and 2019². Globally, only

the Eastern Mediterranean region reached the WHO 2020 interim targets for HCV diagnosis and treatment coverage, and this was primarily driven by the HCV elimination efforts in Egypt². HCV is predominantly spread through intravenous injections in the modern era, resulting in disproportionately high HCV prevalence in marginalized populations such as people who inject drugs (PWID)¹⁷. Screening programmes targeting the general population may, hence, be ineffective for HCV. Even if HCV is diagnosed, patients may default clinic appointments, and poor adherence to follow up is the main reason for low treatment coverage⁴. Dedicated micro-elimination programmes are thus required to improve HCV control¹⁷. Micro-elimination programmes are influenced by economic, geographical and cultural factors. There is no one-size-fits-all HCV elimination programme, and each nation must tailor their own programmes to enhance effectiveness.

Unlike HBV, the anti-HCV antibody does not offer seroprotection. Reinfection is, hence, a unique challenge among patients who have been treated for HCV. Education and behavioural interventions are critical to reduce the risks of HCV reinfection. Multidisciplinary care involving addiction specialists, mental health services and sexual health education also have a role in reducing HCV reinfection¹⁸.

Are we close to the target of hepatitis elimination?

Modelling studies have shown that we are not on track to reach the 2030 hepatitis elimination target^{2,16}. A major hurdle in hepatitis elimination lies in healthcare inequity. While some countries have made major strides towards hepatitis elimination, some countries have not been able to implement basic policies¹⁶. While at the global level, collaborative efforts are necessary to tackle healthcare inequities, at national levels, further acceleration and scaling up of effective programmes are necessary.

A recent study¹⁶ showed that the number of national hepatitis policies did not correlate with progress in hepatitis elimination. As we move closer to 2030, simply pushing out new policies would not be sufficient. It is, perhaps, more important to consider the granular details such as quality of implementation, clinician and patient adherence as well as successful outreach to high-risk groups. Outcome assessment is also necessary, and interventions should aim to achieve tangible outcomes that are sustainable and can benefit patients¹⁶.

The COVID-19 pandemic was an unforeseen challenge with a major impact on hepatitis elimination. All facets of hepatitis elimination, including screening, referral and treatment, have been delayed by at least 20 per cent in multiple countries¹⁹. It is estimated that a one year delay in hepatitis elimination can result in over 44000 hepatocellular carcinoma cases and 72000 liver related mortalities²⁰. While COVID-19 would undoubtedly have a short-term impact on viral hepatitis care, the lessons learnt from the pandemic may be applicable to hepatitis care in the long run. The development of COVID-19 therapeutics highlighted the potential of global collaborations to expedite drug provision. Other concepts such as self-testing and telehealth have also been popularized, and these interventions can be applied to boost hepatitis elimination efforts.

As we stand at the halfway mark to 2030, we are not on pace to achieve hepatitis elimination. Nonetheless, massive progress has been made, and we must remain optimistic. July 28th is World Hepatitis Day, an annual event that has been observed since 2010. World Hepatitis Day is a perfect opportunity for us to reflect on our progress, raise awareness and further concentrate our efforts towards hepatitis elimination. The 2030 target for hepatitis elimination is not out of reach and now is the time to push towards it.

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