

## Editorial

## Hepatitis C elimination by 2030: Are we on the road to miss the target

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Hepatitis C virus infection represents a major global health concern, with Pakistan estimated to have the highest prevalence worldwide, affecting over 12 million individuals.<sup>1</sup> The historical spread of HCV in Pakistan started with mass vaccination of the population for smallpox but later on is attributed to various factors, including unsafe medical practices, contaminated injections, and blood transfusions.<sup>2</sup> Initially recognized as non-B chronic hepatitis, HCV was identified as a leading cause of chronic liver disease, often leading to cirrhosis, liver failure, and hepatocellular carcinoma. We recognize more than 6 genotypes of hepatitis C virus, and in Pakistan, genotype 3 has been the most prevalent one.<sup>3</sup> In the 90s and first decade of the 2000s, people were presenting with blood vomiting, ascites, and subsequent liver failure, and the number of people requiring liver transplants out-matched the available facilities. Lots of people died in their late 30s and mid-40s, the most productive age of humans, because of liver failure. From 2010 onwards, we saw a rapid increase of hepatocellular carcinoma arising out of chronic hepatitis C patients suffering from advanced liver fibrosis.<sup>4</sup>

The treatment of hepatitis C underwent a significant transformation from the 1990s until 2015. During this period, the cornerstone of therapy consisted of interferons combined with ribavirin. However, this approach was characterized by limited efficacy and a

substantial burden of adverse effects.<sup>5</sup> Treatment regimens typically spanned 6 to 12 months, contributing to the considerable cost associated with these therapies. While public health departments implemented hepatitis control programs, access to these medications remained restricted, often necessitating patients to secure treatment through private resources. It is estimated that between 1995 and 2015, approximately 500,000 patients received interferon-based treatment, with a reported sustained virological response (SVR) rate of approximately 30%. National hepatitis control programs primarily concentrated on hepatitis B vaccination as a preventative measure and on raising public awareness regarding hepatitis B and C infection.

The landscape of hepatitis C treatment shifted dramatically with the initial publication in 2014 of research highlighting the safety and efficacy of directly acting agents (DAAs).<sup>6</sup> These compounds, belonging to diverse categories, demonstrated significant promise. Combination therapies involving DAAs proved highly effective and required substantially shorter treatment durations. Furthermore, these regimens exhibited pangenotypic activity, rendering them effective against all hepatitis C genotypes, and could be administered at all stages of disease progression.<sup>7</sup> Initially recommended for individuals aged 18 and above, DAAs are now considered safe and effective across

all age groups, including during pregnancy.<sup>8</sup> Although DAA-based therapy initially posed a significant financial burden in many countries,<sup>9</sup> collaborative initiatives involving the World Health Organization (WHO)<sup>10</sup> and pharmaceutical companies, such as Gilead, have facilitated the provision of more affordable treatment options in high-prevalence regions, such as Egypt and Pakistan.

Pakistan's endeavors to combat Hepatitis C demonstrate a complex interplay of progress and persistent challenges. The nation's commitment is evident in the development and subsequent revision of its National Hepatitis Strategic Framework (NHSF), culminating in the ambitious goal of eliminating Hepatitis C infection by 2030. Following the devolution of healthcare services in 2010, provincial authorities were tasked with formulating localized strategies, allocating resources, and integrating treatment protocols within existing healthcare systems. This decentralized approach, while empowering provinces, necessitates consistent and equitable implementation across the nation.

Initial progress under the 2017-2022 NHSF was notable, particularly in Punjab, where the enactment of the Punjab Hepatitis Control Act and the Safe Blood Transfusion Act, coupled with policies promoting safe waste disposal and the use of auto-destructible syringes, established a robust regulatory framework. Furthermore, substantial investments in infrastructure, including the establishment of over 200 hepatitis treatment centers, specialized gastroenterology units, and a dedicated liver transplant hospital, significantly enhanced treatment capacity. The creation of a national dashboard and interlinked clinics facilitated data management and streamlined patient care. Complementing these efforts, the

College of Physicians and Surgeons, Pakistan, implemented specialized training programs to augment the pool of qualified healthcare professionals. The domestic pharmaceutical industry played a crucial role by providing directly acting agents (DAAs) at competitive prices, a key factor in expanding treatment access. However, the lack of comparable engagement from diagnostic firms, resulting in persistently high prices for PCR diagnostics, presents a significant obstacle. Technical advisory groups at both national and provincial levels formulated treatment guidelines for HCV and HBV infections, further contributing to standardized care.<sup>11</sup>

While Punjab's early adoption of these measures provided a valuable model for other provinces, the observed disparities in implementation timelines underscore the critical need for more uniform and equitable progress across the nation.<sup>12</sup> The political transition of 2018, compounded by the unforeseen challenges of the 2019 COVID-19 pandemic, significantly disrupted program momentum, resulting in the diversion of crucial resources and a shift in public health priorities. Despite initial successes in providing treatment to approximately 1.6 million individuals between 2017 and 2019, subsequent treatment rates experienced a decline, primarily attributable to shortages in both diagnostic resources and essential medications. During this period, a substantial proportion of patients independently sought and financed their own treatment regimens. It is estimated that by 2022, more than 2.2 million of people got the treatment, either through public health programs or from their own resources. The current viremic rate stands at 54%, highlighting a substantial reduction in the actual patient pool. Consequently, the program's strategic focus has shifted towards the more complex and resource-intensive endeavor

of identifying and treating the undiagnosed population, a task that necessitates the development and implementation of innovative and targeted strategies. It is hypothesized that a significant proportion of individuals aware of their infection status have already received treatment, leaving a substantial reservoir of undiagnosed cases within the community, thereby posing a continued public health challenge.<sup>13</sup>

Pakistan's response to Hepatitis C has yielded commendable achievements, particularly in infrastructure development and treatment provision. However, the enduring challenge of high diagnostic costs, coupled with the disruptive impact of external factors and the imperative to reach undiagnosed individuals, necessitates a renewed and intensified effort. Addressing the affordability of diagnostics and implementing targeted interventions to identify and treat the "missing millions" are critical for the realization of the 2030 elimination target.

Following the COVID-19 pandemic, a renewed emphasis on hepatitis control activities was expected. However, ongoing political and economic instability within the nation has thus far precluded this anticipated resurgence, remaining an unrealized objective. Various modeling studies have consistently demonstrated that a failure to address the current hepatitis C situation will have significant repercussions for both the health economy and the broader macroeconomic context.

The second iteration of Pakistan's National Hepatitis Strategic Framework (2024-2030) has been initiated with a budget allocation of PKR 68.25 billion, sourced from the Public Sector Development Program.<sup>14</sup> Provincial governments are tasked with actively mobilizing resources to support the diverse components of the national hepatitis control strategy. Strategic

discussions have revealed differing perspectives, with public health departments advocating for macro-elimination strategies, while non-governmental organizations (NGOs) are prioritizing micro-elimination approaches, frequently leveraging media and social media platforms to enhance public visibility. While the micro-elimination approach may possess an inherent appeal, its implementation at the national level presents significant cost constraints. Consequently, a nationwide macro-elimination strategy is deemed essential, requiring a multi-faceted communication approach encompassing mobile phone messaging campaigns, print and electronic media outreach, public advocacy initiatives, robust contact tracing mechanisms, and effective linkage to care through established public and private healthcare infrastructure. Although the elimination of HCV by 2030 remains a theoretically attainable objective, a substantial augmentation of current efforts is imperative to successfully meet this ambitious target.

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