

Future of therapy for Hepatitis C in India: A Matter of Accessibility and Affordability?



An estimated 170–185 million people (about 3% of the world's population) are chronically infected with hepatitis C virus (HCV). Untreated chronic hepatitis C increases the risk of cirrhosis of liver, liver failure and hepatocellular carcinoma. Chronic hepatitis C is also the most common cause for liver transplantation and liver related death in USA, which has recently eclipsed human immunodeficiency virus (HIV) infection as a cause of death.¹ Globally, HCV is implicated in 28% of cases of liver cirrhosis and 26% of cases of hepatocellular carcinoma, which accounts for almost 500,000 deaths per year.² The burden of HCV is enormous in low- and middle-income countries from South Asia including India, East Asia, North Africa, the Middle East, and Southeast Asia, which accounts for more than 80% of the global HCV burden.^{3,4} Despite a low to moderate (1–1.5%) prevalence of HCV, India accounts for a significant share of global HCV infections due to the large population; approximately 12–18 million population is infected with HCV. A previously validated HCV disease burden model with historical inputs from India projected that under the current standard of care, advanced liver disease and liver-related mortality will increase despite decreasing prevalence.⁵ In the absence of therapies with higher sustained virologic response (SVR), prevention of HCV will decrease overall prevalence, but will not impact short-term liver related mortality or development of hepatocellular carcinoma. Hence, in India a dual approach reducing incidence and increasing treatment is appropriate in showing short-term improvements in advanced stage outcomes with reductions in prevalence.⁵

The treatment of chronic hepatitis C, which started with the use of interferon- α in 1990s, has been revolutionized with the arrival of directly acting antivirals (DAAs) in 2014. SVR, which was in single digit with interferon α monotherapy, has improved to over 90% with DAAs. Last 2 decades witnessed gradual improvement in SVR in these patients. With the advent of combination therapy with pegylated interferon- α and ribavirin, the overall SVR remained between 40% and 50% in chronic hepatitis C patients with HCV genotype 1, and a rate of approximately 80% in patients with HCV genotype 2 or 3.^{6,7} Telaprevir and boceprevir, NS 3A-4A protease inhibitors and the first DAAs and each designed for the treatment of HCV genotype 1, were approved by FDA in 2011. SVR with triple therapy (pegylated interferon- α , ribavirin and

telaprevir or boceprevir) improved from 40 to 50% to 65 to 75%.^{8,9} Telaprevir and boceprevir were effective both in patients who did not receive prior treatment and in those who did.^{10,11} However these agents have a low genetic barrier to the development of viral resistance and drug interactions especially with antiretrovirals. Both telaprevir and boceprevir had an obituary before they could enter in the Indian market. Current anti-HCV drug development and therapy is undergoing an insurrection. Two drugs (sofosbuvir and simeprevir) against the HCV have been approved by the FDA and many more DAAs and host-targeted agents are in the pipeline for the approval.^{12,13} The day is not far from the reality when an interferon free single-pill containing potent fixed-dose combinations will provide the high cure rates in majority of chronic hepatitis C patients including those with advanced fibrosis and cirrhosis, co-infection with HIV, end-stage renal disease, after solid organ transplantation, etc.

With the pricing of sofosbuvir at \$1,000 (~INR 60,000) a pill – \$84,000 (~INR 4.98 million) for a 12-week course, the most challenging question to answer is whether the majority of chronic hepatitis C patients from all areas of the world particularly from low- or middle-income countries will get the benefit from newer highly potent DAAs? The question is relevant since majority of patients with HCV infection reside in low- or middle-income countries and cannot afford the exorbitant price of the treatment. In India, since health insurance coverage is poor and public healthcare does not provide such expensive therapy to the majority, the patients have to bear the cost of drug, which is considered to be the single biggest barrier to treatment of chronic hepatitis C. It is with this background that one must look at the consensus statement of HCV task force of the Indian National Association for Study of the Liver on HCV infection in India, which have been published in this issue of the *Journal*.^{14,15}

Indian practice guidelines have come at a time when there is dramatic shift in the management of hepatitis C, especially with the advent of DAAs. These guidelines recommend standard of care therapy for chronic hepatitis C patients with presently available drugs while awaiting the entry of newer DAAs in the Indian market.¹⁴ Considering financial burden to be enormous and the predominant HCV genotype in India is 3, the current Indian guidelines even consider conventional interferon- α in the management of chronic hepatitis C and is relevant in the Indian context. The members of the INASL task force, however, are very well aware that this consensus statement

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is likely to get time-barred very soon. They are prepared to update these recommendations in the near future, as soon as the newer DAAs appear in the Indian market.

The issue is not just about availability but more so about accessibility and affordability. Even after the FDA approved DAAs reach the Indian shores, their widespread use can only be a reality, if they are accessible and affordable to the patients because the drug costs are traditionally borne out of their pocket.

The 12-week course of sofosbuvir, marketed by Gilead Sciences is sold in the west at a cost of \$84,000, which would make it inaccessible to the majority of the patients if it was to be sold at the same rates in India. However, considering that the manufacturing cost of the 12-week treatment is estimated to be between \$100 and \$270,¹⁶ it is possible that the price will fall to a level that low- and middle-income countries can afford. Lessons from previous experience of anti-retroviral therapy against HIV give hope that these drugs may become affordable and accessible. In 1990s, annual costs for first-line ART was more than \$10,000, which came down to less than \$100 per person in the mid-2000s. One hopes for a similar success with regards to anti-HCV treatment with newer DAAs.¹⁷ In March 2014, Gilead Sciences, which manufactures sofosbuvir, announced a deal with Egypt to provide sofosbuvir at \$900 for a 12-week course, which gives reassurance to Indian healthcare providers. Sofosbuvir is effective against all HCV genotypes and is a high genetic barrier drug to the development of viral resistance and has no or minimal drug interactions. Gilead is in negotiations with several Indian manufacturers to produce a generic version of sofosbuvir.¹⁷ In the recent past, India's Supreme Court also allowed the manufacture of generics such as sorafenib for hepatocellular carcinoma and imatinib for chronic myelogenous leukemia resulting in the affordable access to Indian patients. With much expected lower cost of newer DAAs in near future and the shorter duration (12 weeks) with minimal side effects and the ease of administration of all-oral regimens, it is hoped that treatment of hepatitis C will be accessible and affordable for Indian patients who need them.⁵

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Radha K. Dhiman

Department of Hepatology, Postgraduate Institute
of Medical Education and Research,
Chandigarh 160012, India
E-mail: rkpsdیمان@hotmail.com

Address for correspondence: Department of Hepatology,
Postgraduate Institute of Medical Education and Research,
Chandigarh 160012, India.