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*WJH* covers topics concerning liver biology/pathology, cirrhosis and its complications, liver fibrosis, liver failure, portal hypertension, hepatitis B and C and inflammatory disorders, steatohepatitis and metabolic liver disease, hepatocellular carcinoma, biliary tract disease, autoimmune disease, cholestatic and biliary disease, transplantation, genetics, epidemiology, microbiology, molecular and cell biology, nutrition, geriatric and pediatric hepatology, diagnosis and screening, endoscopy, imaging, and advanced technology. Priority publication will be given to articles concerning diagnosis and treatment of hepatology diseases. The following aspects are covered: Clinical diagnosis, laboratory diagnosis, differential diagnosis, imaging tests, pathological diagnosis, molecular biological diagnosis, immunological diagnosis, genetic diagnosis, functional diagnostics, and physical diagnosis; and comprehensive therapy, drug therapy, surgical therapy, interventional treatment, minimally invasive therapy, and robot-assisted therapy.

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## Lurking epidemic of hepatitis C virus infection in Iran: A call to action

Reza Taherkhani, Fatemeh Farshadpour

Reza Taherkhani, the Persian Gulf Biomedical Research Center, Bushehr University of Medical Sciences, Bushehr 7514633341, Iran

Fatemeh Farshadpour, the Persian Gulf Tropical Medicine Research Center, Bushehr University of Medical Sciences, Bushehr 7514633341, Iran

ORCID number: Reza Taherkhani (0000-0001-6499-0531); Fatemeh Farshadpour (0000-0002-8317-9573).

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Correspondence to: Fatemeh Farshadpour, PhD, the Persian Gulf Tropical Medicine Research Center, Bushehr University of Medical Sciences, Moallem Street, Bushehr 7514633341, Iran. [f.farshadpour@yahoo.com](mailto:f.farshadpour@yahoo.com)  
Telephone: +98-91-71712653  
Fax: +98-77-14550235

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### Abstract

Despite having a relatively low prevalence in the Iranian general population, the burden of hepatitis C virus (HCV) infection is on the rise, and hepatitis C is predicted to be the most important leading cause of viral hepatitis-related mortality in the near future in Iran. The recent population-based epidemiological studies have revealed the predominant role of injecting drug use in increasing prevalence of HCV infection. Undoubtedly, new management paradigm is required to drive down the rising wave of hepatitis C in Iran. Priority should be given to young injecting drug users as the cornerstone of the lurking epidemic of HCV infection in Iran.

**Key words:** General population; Injecting drug user; Epidemiology; Hepatitis C virus; Iran

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**Core tip:** Iran is known as a low-endemic country for hepatitis C virus (HCV) infection, while the recent population-based epidemiological studies have revealed the increasing burden of HCV infection in the Iranian population. The asymptomatic nature of HCV infection and the undiagnosed HCV-infected injecting drug users have fueled this increase. Obviously, the current management paradigm is inadequate if control of HCV infection is aimed to be achieved.

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## TO THE EDITOR

Less than 0.5% of the population, as many as 186500 patients are infected with hepatitis C virus (HCV) in Iran<sup>[1]</sup>. The majority of HCV-positive patients have been infected by injecting drug use, equivalent to 75% of the HCV-infected population<sup>[2]</sup>. The burden of HCV infection shows a rising trend, and HCV infection is projected to be the most important leading cause of viral hepatitis-related mortality in the near future in Iran<sup>[1,3]</sup>. Obviously, the current management paradigm is inadequate if control of HCV infection is aimed to be achieved.

Mandatory screening of all blood donors for hepatitis C resulted in a remarkable decrease in the prevalence of HCV infection<sup>[1,2,4,5]</sup>. In view of the success in the Iranian Blood Transfusion Organisation, the talk of HCV elimination has been intensified. However, all hopes came to knot due to rising wave of HCV infection among injecting drug users (IDUs), those whom the control of HCV transmission among is the most difficult. The shared use of drug paraphernalia and lack of awareness among young IDUs regarding the risk of acquiring HCV infection *via* needle-sharing are the root cause of the increasing prevalence of HCV infection among IDUs community<sup>[1]</sup>. At the same time, the asymptomatic nature of HCV infection and the undiagnosed HCV-infected IDUs would accelerate this increase<sup>[1]</sup>.

The recent changes in the genotype distribution of HCV have also fueled this epidemic<sup>[6]</sup>. High rates of mutation in HCV genome have resulted in the emergence of seven major genotypes and at least 67 subtypes<sup>[7]</sup>. Each geographic region has a distinct genotypic pattern, which depends on the predominant mode of transmission, risk factors, life style, the source of infection, disease transmission patterns and age distribution in that particular region<sup>[8,9]</sup>. These genotypic patterns are not constant, change overtime and influence the epidemiology of HCV infection in that region<sup>[10,11]</sup>. The most prevalent subtype in Iran is 1a, followed by 3a and 1b. Over the last decade, however, a gradual decrease in the frequency of subtypes 1a and 1b and an increase in subtype 3a have been reported due to changes in the routes of transmission of HCV from blood transfusion to injecting drug use<sup>[6,9-12]</sup>. These changes should be taken in to consideration to establish better strategies for managing the silent epidemic of hepatitis C in Iran.

Another challenge is treatment of HCV-infected population. Despite having poor tolerability, prolonged treatment course and frequent side effects, interferon (IFN)-based therapy is still recommended as the first-line therapy in Iran due to affordability and local

availability<sup>[3,9]</sup>. Annually, 2.4% of the Iranian HCV-infected population is treated by pegylated IFN plus ribavirin, with approximately 58%-78% of patients showing a sustained virological response (SVR) depending on the HCV genotype<sup>[2]</sup>. Introduction of IFN-free direct-acting antivirals (DAAs) has revolutionized the treatment course of HCV infection due to superior rates of SVR, favorable tolerability, fewer side effects and shorter treatment period<sup>[13-15]</sup>. However, in reality, the restricted accessibility and high price of DAAs outweigh these benefits. Recently, the production of a domestic DAA, the combination of daclatasvir and sofosbuvir, with health insurance coverage has been announced in Iran, paving the way for low-cost access to DAAs and subsequently widespread use of these drugs in the near future<sup>[1,3]</sup>. This domestically produced DAA, Sovodak, has shown favorable SVR rates in Iranian patients infected with genotypes 1 or 3 HCV, the most predominant genotypes in Iran, providing an opportunity to improve the treatment rate and subsequently eliminate HCV infection in the future<sup>[1]</sup>.

These challenges in the management of hepatitis C epidemic cannot be neglected any longer. Resent changes in the epidemiology of HCV would demand changes in health policies, prevention and management strategies. In view of the success of the transfusion-safety measures implemented in the Iranian Blood Transfusion Organization<sup>[4,9]</sup>, screening of high-risk populations for hepatitis C, new therapeutic strategies with an emphasis on timely diagnosis and treatment, expansion of harm-reduction interventions, public education regarding the risk of HCV infection, as well as comprehensive cooperation and mobilization of health care providers are required to drive down the rising wave of HCV infection in Iran once again. Priority should be given to young IDUs as the cornerstone of this silent epidemic. Furthermore, national health policies should be prioritized in a way to curb the lurking epidemic of HCV infection once and for all.

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