

Hepatitis C Infection

A Systematic Disease

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KEYWORDS

- Hepatitis C virus • Hepatic complications • Extrahepatic complications

KEY POINTS

- It is critical to recognize that hepatitis C virus (HCV) infection is a multifaceted systemic disease with both hepatic and extrahepatic complications.
- The comprehensive burden of HCV should not only include its clinical burden, but also its burden on the economic and patient-reported outcomes.
- It is only through this comprehensive approach to HCV infection that we can fully appreciate its true burden, and understand the full benefit of curing HCV for the patient and the society.

Currently, it is estimated that approximately 170 million individuals carry hepatitis C virus (HCV) antibody worldwide, with more than 40% of the infected individuals living in the Asian countries.^{1–8} The global distribution of HCV genotype also can vary by geography. Genotype 1 (GT1) is the predominant genotype in the United States, Europe, Australia, and Japan, whereas genotype 3 (GT3) is more common in Pakistan and genotype 4 (GT4) is the predominant HCV genotype in Egypt and North Africa.^{4,8,9}

Although approximately 25% of acute HCV infection is self-limiting, 75% of these infections become chronic. This rate of chronicity can be affected by a number of factors, including the age at time of infection, gender, ethnicity, and the development of jaundice at the onset of acute infection.^{2,3,5–7}

Of patients who are chronically infected with HCV, liver disease is the most common and important complication. In this context, the rate of progression to cirrhosis can also vary by geographic location. In the United States and Europe, the rate of progression to cirrhosis is approximately 15% (range 8%–24%) over 20 to 30 years with approximately 1% to 4% annual incidence of hepatocellular carcinoma

Disclosure: Dr. Z.M. Younossi has received research funding or consultation fees from BMS, Gilead, Intercept, GSK and Allergan.

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Clin Liver Dis ■ (2017) ■–■

<http://dx.doi.org/10.1016/j.cld.2017.03.001>

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(HCC).^{10–17} In contrast, the rate of HCV progression to cirrhosis in Japan is higher, ranging from 30% to 46% with approximately 5% to 7% annual incidence of HCC.¹⁸ It has been recognized that a number of host factors can influence the rate of liver disease progression in HCV, including older age, male gender, coinfection with human immunodeficiency virus or hepatitis B virus, and comorbid conditions, such as immunosuppression and insulin resistance as well as superimposed nonalcoholic steatohepatitis, hemochromatosis, and schistosomiasis.^{19–24} In addition to the host factors, a number of external factors can also negatively impact the progression of HCV-related liver disease. In this context, chronic alcohol use is an important factor for the progression of chronic hepatitis C to cirrhosis and hepatocellular carcinoma.²⁵

As liver disease progresses, patients with HCV can develop hepatic decompensation, leading to increased liver-related mortality.¹⁸ The cumulative probability of an episode of hepatic decompensation is 5% at year 1, increasing to 30% at 10 years from the time of diagnosis of cirrhosis. The development of gastroesophageal varices and other signs of advanced liver disease are associated with an additive increase in the risk for mortality.^{5,6,26,27} After development of decompensated cirrhosis, the 5-year survival of patients with HCV can be as low as 50%.²⁷ On the other hand, 3-year, 5-year, and 10-year survival rates of patients with HCV with compensated cirrhosis is estimated to be 96%, 91%, and 79%, respectively.^{28–30}

Although hepatic complications of HCV infection are the primary drivers of its clinical and economic burden, a number of extrahepatic manifestations (EHMs) of HCV also can influence its clinical and economic outcomes.^{31–34} The EHMs of HCV infection can be divided into those that are strongly associated with HCV and those that are possibly associated.^{31–34} Unlike the large amount of data that have been published about HCV-related liver disease, our understanding of the underlying mechanisms for the EHMs of HCV and factors that contribute to their progression or regression are more limited.

In addition to the hepatic manifestations and EHMs, chronic HCV infection impairs a number of important patient-reported outcomes (PROs). These PROs can be accurately captured through the use of validated instruments for health-related quality of life and fatigue.^{35–43}

Finally, the clinical (both hepatic and extrahepatic) and PRO manifestations of HCV can lead to substantial economic burden. Some of this burden is directly related to the clinical cost associated with caring for the liver and nonliver complications of patients with HCV infections.^{44,45} Additionally, there are a number of important indirect economic burdens of HCV, especially those related to work productivity losses and other societal costs.^{46–56}

In summary, it is critical to recognize that HCV infection is, in fact, a multifaceted systemic disease with both hepatic and extrahepatic complications. It is also important to recognize that the comprehensive burden of HCV should not only include its clinical burden but also its burden on the economic outcomes and PROs. It is only through this comprehensive approach to HCV infection that we can fully appreciate its true burden and understand the full benefit of curing HCV for the patient and the society.

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