

Global Burden of Hepatitis C: Considerations for Healthcare Providers in the United States

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An estimated 2%–3% of the world's population is living with hepatitis C virus (HCV) infection, and each year, >350 000 die of HCV-related conditions, including cirrhosis and liver cancer. The epidemiology and burden of HCV infection varies throughout the world, with country-specific prevalence ranging from <1% to >10%. In contrast to the United States and other developed countries, HCV transmission in developing countries frequently results from exposure to infected blood in healthcare and community settings. Hepatitis C prevention, care, and treatment programs must recognize country-specific epidemiology, which varies by setting and level of economic development. Awareness of the global epidemiology of HCV infection is important for US healthcare providers treating foreign-born patients from countries where HCV infection is endemic and for counseling patients who travel to these countries. Countries with a high burden of HCV infection also would benefit from establishing comprehensive prevention, care, and treatment programs.

Globally, an estimated 130–170 million persons (2%–3% of the world's population) are living with hepatitis C virus (HCV) infection [1]. This infection, particularly in its chronic form, is associated with sizable morbidity and mortality. More than 350 000 deaths are attributed to HCV infection each year, most of which are caused by liver cirrhosis and hepatocellular carcinoma (HCC) [2]. An estimated 27% of cirrhosis and 25% of HCC can be attributed to hepatitis C worldwide, and disease rates can be even more substantial in countries with a high burden of infection. For example, in Japan, up to 90% of all reported cases of HCC are caused by HCV infection [2].

Available data indicate that infection with HCV varies considerably by country and region. However, the true burden of disease is not well known in many

countries, because capacity is limited for collecting epidemiologic data. In contrast, the mode of transmission is fairly well defined and most often involves exposure to contaminated needles or syringes, although the means by which this exposure occurs differs by country. Whereas HCV transmission in developing countries frequently results from exposure to infected blood and blood products in healthcare and community settings, HCV infections in most developed countries are associated with injection drug use (ie, personal behavior typically of an illicit nature).

The global picture directly impacts the United States; tens of millions of foreign-born persons reside in the United States, many of whom are from countries where HCV infection is endemic (eg, countries with an HCV prevalence $\geq 2\%$), and >1 million new immigrants enter the United States annually. Therefore, US healthcare providers who treat immigrants and foreign-born persons must recognize that decisions to screen these patients based on established risk factors for HCV infection in the United States [3, 4] may not be sufficient to identify at-risk individuals. Identifying persons with HCV infection has become even more critical with the recent availability of more effective therapies. Providers should maintain a high index of

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suspicion for occult or active HCV infection among their foreign-born patients. To diagnose and treat illness in their foreign-born patients and counsel patients about the potential infection risks of travel to countries where HCV infection is endemic, providers need to be informed about which countries have a high burden of HCV infection and understand its epidemiology there.

EPIDEMIOLOGY

The World Health Organization (WHO) releases global estimates on the prevalence and burden of HCV infection [1]. In developed countries, these data are obtained primarily from population serologic surveys, which are considered to be the reference standard; however, because the high cost of such surveys precludes this type of data collection in many developing countries, data from other sources that typically are not generalizable to a broader population (eg, surveys of blood donors, pregnant mothers, or high-risk populations) are often used to estimate the burden in developing countries. In addition, the WHO may rely on or augment their estimates with data from regional or neighboring countries. These limitations result in inconsistencies in data quality and, consequently, may obscure real differences among countries. Nevertheless, country-specific hepatitis C data published by the WHO reveal that rates of HCV infection vary widely throughout the world (Figure 1), even among neighboring countries and in geographic regions within the same country [1, 6–8]. The hepatitis C burden in many developed countries (eg, Australia and most countries in Western Europe) is similar to that in the United States, at <2% [1, 6–8]. HCV infection rates are higher ($\geq 3\%$) in many countries in eastern Europe and Latin America, countries of the former Soviet Union (including countries under their control), and certain countries in Africa, the Middle East, and South Asia [1, 7, 9–12]. Egypt is believed to have the highest rate of hepatitis C in the world (estimated at >10%) [6, 7], and most other African countries have prevalence rates ranging from 2% to >3% [1, 10].

In developed countries, where donated blood is routinely screened for HCV and measures are in place to facilitate infection control and safe-injection practices, HCV is now transmitted primarily through injection drug use [6, 13]. In developing countries, injection drug use also can be an important risk factor for HCV transmission [14, 15]. China has the highest estimated number of HCV-infected injection drug users (IDUs) in the world [15], and in Mexico, Pakistan, and Thailand, >80% of IDUs are anti-HCV positive [15]. Still, in developing countries, the most common modes of transmission are healthcare associated [6, 16, 17]. Unsafe injections in healthcare settings are a leading cause of HCV transmission worldwide, resulting in 2 million new HCV infections each

year [16]. Recipients of blood and blood products also are at risk of HCV infection; a 2007 blood safety survey revealed that, of responding countries, 20% fail to conduct HCV screening on all blood and blood products [18]. Countries in which donors are paid or coerced to donate blood or blood products may experience greater risk of HCV transmission and other blood-borne pathogens [18].

In some countries, high HCV infection prevalence rates have been attributed to specific practices and events. For example, in Egypt, with the highest rate of HCV infection in the world, the reuse of syringes during a schistosomiasis eradication program in the 1960s and 1970s is the purported cause of the widespread introduction and spread of HCV in that country [19]. However, Egypt is experiencing continued HCV transmission associated with unsafe injection practices, poor infection control in hospitals, and widespread use of unscreened blood for transfusions; up to 500 000 new infections are estimated to occur annually [20]. Ongoing transmission in Pakistan, where HCV infection is highly endemic, also is associated with unsafe injections. At a mean of 13 injections per person annually [12, 21], Pakistan has the highest documented rate of injections in the world. A recent surveillance report revealed an association between the number of injections received in the 6 months preceding diagnosis of viral hepatitis and cases of acute infection [22], confirming the ongoing risk of transmission posed by frequent and unsafe injection practices. Other modes of transmission have been implicated in some countries; community exposures, such as those associated with traditional healers, unqualified medical providers, tattoo parlors, and barber shops, have been reported from countries where HCV infection is highly endemic, such as Pakistan [9, 12].

The epidemiology of HCV infection in many developed countries mirrors that occurring in the United States. For instance, similar to the United States, in Western Europe, persons born during 1945–1965 account for three-fourths of all HCV infections [6]. In countries such as Japan and Taiwan, remarkably high rates of HCV infection occur among older persons, with a very sharp decrease in prevalence among subsequent, younger age cohorts [23, 24]. This epidemiologic pattern, along with a disproportionate burden of HCC and liver cirrhosis relative to overall prevalence, suggests a high prevalence of HCV infection among persons infected in the distant past [2, 6].

COINFECTION WITH HIV

Worldwide, up to 30% of the 33 million persons infected with HIV also are infected with HCV [25]. The prevalence of HIV-HCV coinfection varies by region, with countries in sub-Saharan Africa having particularly high rates. In developed

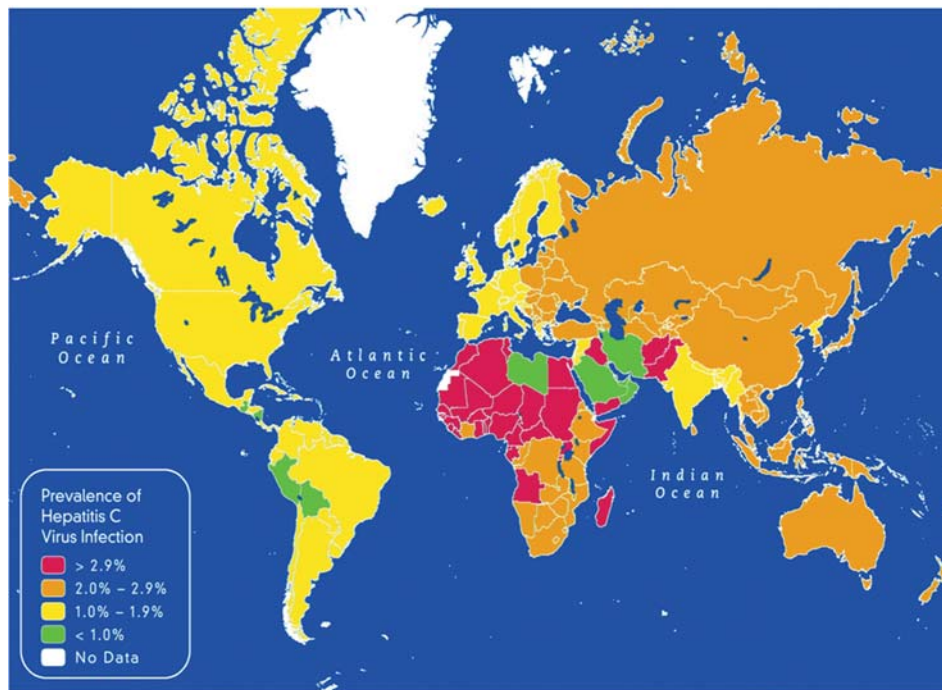


Figure 1. Global prevalence of chronic hepatitis C virus infection (reprinted from Holmberg S [5]).

countries, HCV infection is becoming an increasing problem among HIV-infected men who have sex with men [26]; in a study of HIV-infected men who have sex with men in western Europe, incidence of HCV infection increased annually during 2002–2007 [27]. Coinfection with HIV is associated with accelerated progression of liver disease and increased mortality among HCV-infected persons [28, 29], and some studies suggest that it may increase the risk of mother-to-child HCV transmission [30]. Early initiation of antiretroviral therapy among HIV-HCV-coinfected individuals is critical to health outcomes, because it may slow the progression of liver disease. However, HCV treatment is expensive and can be cost prohibitive in developing countries with large burdens of HIV-HCV coinfection, such as those in sub-Saharan Africa.

TESTING, CARE, AND TREATMENT

In many countries, including those that are developed (eg, the United States), most persons living with HCV infection are unaware that they are infected and, consequently, do not receive the timely care and treatment needed to prevent HCV-associated complications, such as cirrhosis and liver cancer [31]. Furthermore, they can serve inadvertently as a reservoir for continued HCV transmission. In developed countries, barriers to screening include inadequate knowledge and awareness of hepatitis C among healthcare providers and their patients,

cost-related factors (eg, lack of health insurance), and lack of HCV screening policies. Most developed countries have faced challenges in screening persons at highest risk for HCV infection.

Developing countries face these and other substantial barriers to screening, including low political, provider, and community awareness of hepatitis C as a significant health threat, leading to deprioritization of testing and other preventive health services. In addition, public health officials in many developing countries do not understand the true burden of disease in their borders because their surveillance infrastructure may be inadequate; one-third of the WHO Member Countries do not collect prevalence data for viral hepatitis. Robust surveillance for HCV infection, particularly serosurveillance, is critical for assessing this burden, because many newly infected persons are asymptomatic and do not seek care for their infection until years, even decades, after they are infected. Despite these challenges, some countries have taken proactive steps to address prevention, screening, and treatment [32, 33]; these programs have had mixed results, and significant challenges remain.

FOREIGN-BORN POPULATIONS IN THE UNITED STATES

Current recommendations for HCV screening in the United States are for persons with recognized high-risk behaviors,

those with conditions associated with high prevalence of HCV infection, recipients of transfusions or organ transplants before July 1992, children born to HCV-infected mothers, and persons who may have experienced an occupational exposure (eg, a needle-stick injury or mucosal exposure to HCV-positive blood) [3, 4]. Because this approach to screening, coupled with the asymptomatic nature of the infection, has not been highly successful in identifying persons with HCV infection and because serologic studies have shown that, in the United States, persons born during 1945–1964 have an approximately 4-fold greater risk of being HCV infected [34], a birth cohort approach to screening is being considered. Such an approach is expected to help identify persons who may have had exposures in the distant past and do not recognize themselves as being at risk for HCV infection; birth cohort-based screening also has been shown to be cost-effective and lead to fewer cases of advanced liver disease, liver cancer, and death [35].

Annually, >1 million persons become permanent legal residents in the United States, and many more undocumented persons enter the country [36]. Large numbers of these persons are from countries where HCV infection is endemic. Of the 40 million foreign-born persons living in the United States, nearly 20 million are from Latin America, where rates of HCV infection approach 3% in some countries [11]. Most of the remainder of immigrants come from Asia, Europe, and Africa [37]; Egypt and Pakistan, both of which are countries of very high HCV endemicity, serve as countries of origin for 130 000 and 280 000 persons living in the United States, respectively [38]. Whether HCV infection rates in the US immigrant population are reflective of the background rates of the birth country is unknown and warrants further research. However, a study of foreign-born persons living in England found that some persons of South Asian descent had high rates of both hepatitis B virus and HCV infection [39].

Healthcare providers who care for foreign-born patients should be aware of the risk of HCV infection from different countries and regions and should consider screening patients from certain countries where HCV infection is highly endemic, such as Egypt and Pakistan. In many countries of endemicity, HCV infection is not associated with the established risk factors that have been defined in the United States [16, 20, 22]. As such, healthcare providers need to be aware that their patients may be at risk of HCV infection simply by having immigrated from one of these countries. Healthcare providers who care for travelers should advise their patients of the risk of blood-borne pathogens that may be elevated when receiving routine healthcare (including receipt of injections, blood, or blood products) in countries where infection is highly endemic. Furthermore, travelers to these countries should be informed of the potentially elevated risk of HCV infection

following receipt of certain community and unconventional medical services, such as public shaving or acupuncture.

GLOBAL PREVENTION AND CONTROL

Many countries have yet to address primary prevention of HCV infection, particularly in the healthcare setting. However, even when control of HCV transmission is realized in these countries, HCV-associated morbidity and mortality from cirrhosis and HCC will continue to increase for years, even decades, in the absence of effective care and treatment programs. Linking prevention and control to testing, care, and treatment of HCV infection requires a comprehensive, cohesive approach tailored to meet the needs of individual countries. Public health officials must be familiar with the epidemiology of HCV infection within their borders and know whether widespread transmission is ongoing and in what settings it is occurring. Addressing transmission should be the first priority for any country.

Unlike global efforts to prevent and control HIV infection and other infectious diseases, those for HCV infection are limited and largely unaccompanied by community advocacy and awareness. This lack of grassroots support complicates efforts to ensure that populations most affected by hepatitis C, which typically are hard to reach and disenfranchised, receive needed services.

Also challenging is the absence of viral hepatitis control programs at the Ministry of Health level in many lower-to-middle income countries. This absence leads to fragmented and indirect efforts to prevent and control not only hepatitis C but all forms of viral hepatitis. As an example, efforts to address HCV transmission in healthcare settings may be performed by infection control programs, whereas efforts to test IDUs may be coordinated by a different Ministry of Health entity, such as the HIV program. This lack of coordination was first recognized in 2009, when the World Hepatitis Alliance surveyed its 193 member countries to determine the state of global viral hepatitis prevention and control [40]. This WHO-funded survey revealed that although most countries have hepatitis C policies and goals in place, most existing programs are disconnected; 60% of these countries requested assistance from the WHO in establishing a more coordinated approach to prevention and control of HCV infection. In response, in 2010 the WHO passed World Health Assembly Resolution 63.18, calling for increased viral hepatitis education and improved testing and provision of care and treatment to the 500 million persons infected with hepatitis B virus and HCV worldwide [41]. The WHO has since formed a Global Hepatitis Program to assist member countries in achieving control of these diseases.

CONCLUSION

Hepatitis C continues to cause substantial morbidity and mortality worldwide, and transmission continues unabated in many countries. Control of HCV infection requires a comprehensive approach that incorporates primary prevention of transmission through enhanced infection control and injection safety in healthcare settings and in the community, universal screening of blood and blood products, harm reduction programs, and increased public awareness about risk factors for HCV infection. For the 130–170 million persons already infected, newer, more effective therapies are available. However, lack of access to screening, care, and treatment limit the use of these therapies for most persons living with HCV infection globally, and deaths from preventable cirrhosis and liver cancer continue to increase. Governments need to address viral hepatitis comprehensively by improving surveillance, prevention, care, and treatment. In the United States, healthcare providers must be cognizant of the global burden and epidemiology of HCV infection and follow current screening care and treatment recommendations. In addition, they should consider screening foreign-born patients as appropriate, particularly those from countries where HCV infection is highly endemic, who may not have recognized risk factors for HCV infection.

Notes

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