Hepatitis C Viral Infection Disease Burden in Asia

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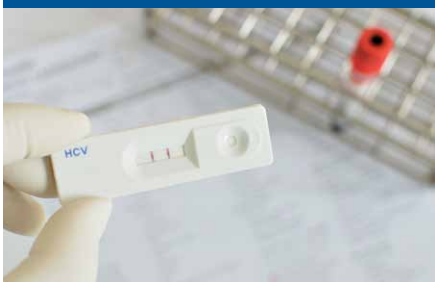
KEY POINTS . . .

Hepatitis C is a public health issue in Asia that creates significant disease burden due to long term complications (cirrhosis and hepatocellular carcinoma).

However, the awareness of hepatitis C is substantially low probably due to underreporting and lack of disease knowledge among health care providers and the public.

While national policy is urgently needed to address hepatitis C, better clinical treatments for hepatitis C are also desired immediately.



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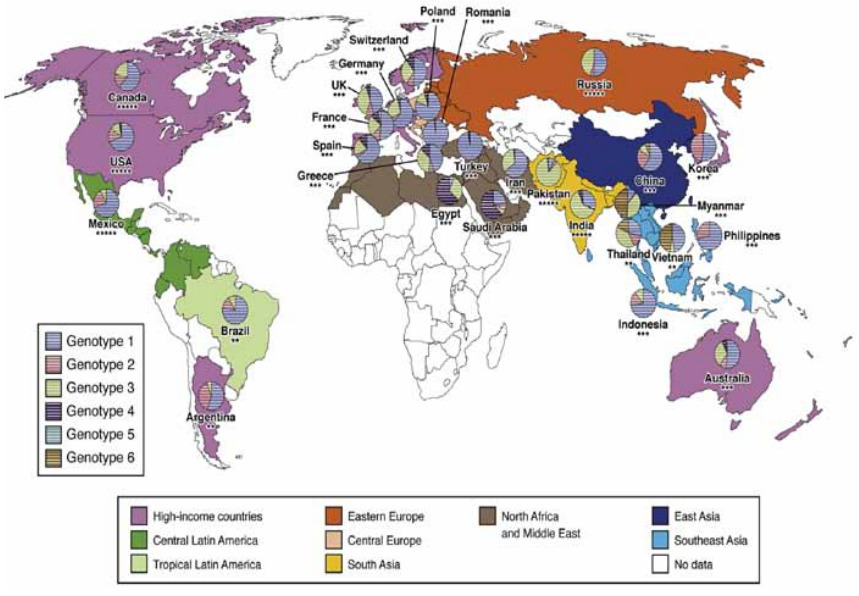
Hepatitis C viral (HCV) infection is a worldwide public health issue with 170 million chronically infected patients, among whom 32.2 million reside in Asia [1]. A few hallmarks are found in HCV infections: no obvious symptoms in early stages of the infection; development of serious complications; and low awareness of the disease among patients, health care providers, and policy makers. Since most of the Asian countries currently do not have national screening systems in place, detecting HCV in an early stage can be challenging.

HCV is relatively complicated due to unique viral genotypes found in different geographies. While there are 6 major viral genotypes of HCV in the world, genotype 1b (GT1b) constitutes the majority in Asia [2]; (Fig. 1) for example, 56.8% of cases are GT1b in China [3]. As GT1b is one of the most difficult to treat genotypes by current standard of care in treating HCV, this situation poses a significant clinical challenge in Asia. The age-adjusted incidence rates in the region range from 2.7 per 100,000 in Japan to around 22 per 100,000 in Taiwan, Thailand, and Vietnam; and 9.3 per 100,000 in mainland China [4,5]. Prevalence of HCV is positively associated with age; more patients are found among the senior population. For insistence, in Japan, the prevalence rate is reportedly 3.4% among 60 to 69 years old patients compared with 1.3% and 1.8% for patients who are 40 to 49 and 50 to 59 years old, respectively. While HCV patients in Japan tend to be more elderly, the median age of HCV patients in China is less – 46 years old [3]; this relatively young age would tend to have a substantial impact on the population productivity and economy of China.

HCV has inflicted a heavy disease burden on the public. HCV is one of the top 10 causes of mortality in the world. During the acute infection period, only 20 to 30% of patients show symptoms. About 75 to 85% of acute infections become chronic if the HCV virus is not cleared after 6 months. About 10 to 20% of chronically infected patients develop cirrhosis within 20 years

Figure 1. Global HCV Viral Genotype Distributions [2].

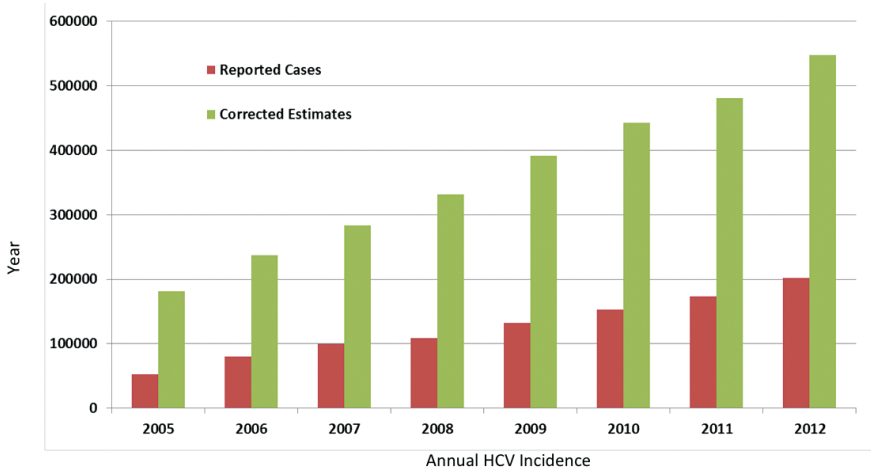


of infection; furthermore, decompensated cirrhosis and hepatocellular carcinoma (HCC) may develop after the cirrhotic stage [6]. Reports from South Korea show that both cirrhosis and HCC is prevalent among HCV patients. A prospective multi-center cohort study in South Korea found 27% of HCV patients had cirrhosis and HCC [7]. Patients with HCV account for 79% of HCC cases in Japan, 20% in South Korea, and 12% in mainland China [8,9]. Among all the diagnosed HCV treatment naïve patients with cirrhosis in China, half of them have already had decompensated cirrhosis which is strongly associated with developing HCC [3].

Development of HCC from HCV is multi-factorial; GT1b is identified as one of the key independent factors that are positively associated with a higher cumulative risk of developing HCC. The Risk Evaluation of Viral Load Elevation and Associated Liver (REVEAL) study [10], a prospective cohort of hepatology research in Taiwan, examines the relationship among key factors via data from 1,095 subjects of positive anti-HCV anti-body in the study. Among the factors that have a positive association with subsequent risk to develop HCC HCV genotype 1 (GT-1), RNA, and ALT [11]. For example, GT1b has 17.3% cumulative risk of developing HCC over a period of 20 years; in comparison, the percentage of other viral genotypes (1a, 2a, and 2b) is 10.7%. Based on this study, a model has been built to estimate the risk of HCC and cirrhosis development [12]. With an excellent predictive accuracy and discriminatory ability, this model integrates host and virus characteristics, such as age, gender, ALT, HCV genotype, and HCV RNA levels. Using this model, not only can a risk score be generated for an individual patient based on his/her clinical characteristics to inform clinical decisions in treating HCV, but predictions of complication development at a macro level can be made to inform policy making on HCV public health issues.

In spite of a high impact from the disease, HCV awareness in the region is still low. In South Korea, for example, 55% of the population has been screened for HBV; but only 10% of the population has been screened for HCV [13]. Among all patients with HCV who were enrolled in the CCgenos study in mainland China, 64.4% of them did not know they were infected with HCV prior to the study [3].

Figure 2. Significant Differences between Reported [15] and Corrected Estimated [16] New Cases.



The relatively low awareness of HCV may have been attributable to the disease being under-reported. Since 2004, mainland China has set up a web-based, real-time reporting system covering 39 infectious diseases from hospitals across the country and hepatitis C is under "Viral Hepatitis" of Group B in the system [14]. This system shows an increasing incidence of HCV since 2005 but even this may be underreported as the system only covers patients who are seen and diagnosed with HCV from reporting health facilities [15]. To improve the accuracy of disease burden evaluation in China, a corrected estimate of HCV new infections between 2005 and 2013 using the back calculation method was made (Fig. 2) [16]. This study suggests that the number of reported annual new cases of HCV via the national reporting system in mainland China between 2005 and 2013 represents probably 30% of the total estimates.

National public health policy is urgently needed to address HCV related issues.

Another key factor that would also contribute to the low awareness of HCV is the poor understanding of the disease among health care providers. A survey of HCV disease knowledge was conducted to 1,362 none specialists in mainland China in 2009 [17]. The results suggest these surveyed physicians did not have a correct comprehension of HCV regarding its etiology, epidemiology routes, prevention, diagnosis, and current treatment options. For example, about 44% of the physicians in this survey thought that anti-HCV antibody test was not a routine procedure in hospitals; 71% of these physicians did not even recognize that HCV is a curable disease.

HCV can also impose a heavy economic burden. A national survey of HCV treatment costs was conducted in mainland China in 2012 [18]. The study found that while most of the inpatient cases had health insurance coverage, 49.6% of the outpatient cases were paid out of pocket. Median cost for an HCV related hospital admission was US$1,369; of which medications, both western and traditional, accounted for 61.1%. This study also found that the more advanced the disease had progressed, the higher the costs: for chronic HCV, cirrhosis, and hepatocellular carcinoma, the median costs were US$1,351, US$1,399, and US$2,404, respectively.

A macro level estimate of disease burden was estimated for mainland China. Based on the revised estimates of newly reported HCV between 2005 and 2013 [16], if all reported cases did not have proper treatments, cirrhosis cases reported via health care institutes in 5, 10, and 15 years are projected to be 102,527, 259,196, and 421,093, respectively, in mainland China. The estimated incidence of HCC in 5, 10, and 15 years would be 38,680, 121,301, and 254,375,

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respectively. The associated direct medical costs of these cases of cirrhosis and HCC would be US$236.5 million US$654.5 million, and US$1,101 million, for the country in 5, 10, and 15 years, respectively.

In summary, HCV is a silent disease that would bring significant disease burden, clinically and financially, to the public due to its long term complications. National public health policy is urgently needed to address HCV related issues. In the meantime, better clinical regimens for HCV treatments are also desired to help patients fight the disease.

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