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Challenges and Strategies for Access to Treatment of Hepatitis C in Latin America

David Kershenovich and Nayelli Flores

Abstract

With the advent of all oral direct-acting antiviral drugs (DAAs) with a low incidence of side effects and very high success rates, we are entering an exciting new era in the treatment of hepatitis C virus (HCV), and now the major goal is the elimination of this viral infection. However, at least in Latin America, there are multiple barriers that must be attended.

Keywords: hepatitis C, direct-acting antiviral, treatment access, virus elimination, public health

1. Introduction

We are witnessing a new era in the treatment of HCV infection due to the development of DAAs that allows to cure a chronic disease without an effective vaccine. The therapy with pegylated interferon and ribavirin is no longer the standard of care. Unfortunately, there is a gap between these advances and the real access to treatment for patients in low- and middle-income countries (LMIC). In Latin America, the main identified barrier to access to hepatitis C treatment was for long a time the high price of these DAAs. While this issue has not yet been fully resolved, it has become evident that there are other gaps that need to be attended in order to undertake a comprehensive viral hepatitis elimination effort [1]. In this chapter, we propose to portray the main challenges that have not allowed fulfilling this purpose and present new strategies that could contribute toward addressing this health challenge.

2. Challenges to effectively treat HCV infection in Latin America

Chronic HCV infection is a health problem that affects more than 71 million people worldwide. HCV is associated with several hepatic pathologies, including cirrhosis and hepatocellular carcinoma as well as many other extrahepatic manifestations that are a major cause of global health burden [2].

The real incidence of hepatitis C and cirrhosis in Latin America is unknown. It has been estimated that at least 10 million Latin Americans may be infected with HCV [3, 4]. In some Latin American countries that provided national data, cirrhosis death rates were between 5 and 17/100,000 for men and 3 and 5/100,000 for women [5].

Liver cirrhosis mortality trends vary widely among countries in Latin America. Mortality rates increased in Costa Rica, Guatemala, Honduras, and Paraguay, but fell in Chile, Mexico, and Argentina. In 1980, age-standardized cirrhosis mortality rates in Chile and Mexico were, respectively, 53.4 (43.6–67.9) per 100,000 and 45.9 (35.6–57.0) per 100,000, the highest in the region. In 2010, Mexico remained the country with the highest cirrhosis mortality rate in the region, at 38.3 (30.7–47.5) per 100,000. Liver cirrhosis was the fourth leading cause of death in Mexico in 2010, accounting for 18% of deaths in males aged 40–49 years [6]. Disability, quality of life, and social aspects should be considered when assessing the impact of the disease.

2.1 Lack of epidemiological studies

Overall updated population-based epidemiological studies of viral hepatitis in most Latin American countries are still a significant challenge. This barrier is crucial to define health policies in the region [7]. There is a paucity of epidemiological data from rural areas where a significant percentage of the population resides. Most data are focused on seroprevalence of the disease, and studies are typically cross-sectional in design. Most of the studies have been conducted in select populations and do not allow to gain the real prevalence and incidence of HCV infection.

Efforts have been made to model the disease in some countries of the region, such as Mexico, Brazil, Argentina, and Chile. All of them indicate that if the number of patients identified and treated do not increase over the years, HCV-related morbidity and mortality are expected to increase, and the impact on the development of liver cirrhosis and hepatocarcinoma may be overwhelming [8].

In Mexico, for example, with the majority of cases arising from transfusion prior to the implementation of blood screening protocol, the annual number of HCV infection was estimated to peak in the mid-1990s. The annual number of new cases was estimated at 5620 new cases in 2013 [9].

In 2013, the total number of viremic infections was estimated at 560,700 (326,900–605,200), and it was forecasted to decrease to 406,100 viremic infections in 2030. The number of HCC cases in 2013 was estimated at 2660 cases, and it was forecasted to increase by 55% by 2030. The number of liver-related deaths will increase by 55% from a base of 2370, while decompensated cirrhosis and compensated cirrhosis infections will increase 55 and 40% from a base of 6750 and 54,460 in 2013 [9].

In Argentina, there were an estimated 342,300 (155,000–537,000) infected individuals in 2013. Prevalence is estimated to have peaked at 382,700 patients in 2002 and to decline to 237,000 by 2030. There will be 62,630 compensated cirrhotic patients in 2030 as compared to 37,110 in 2013. In addition, there will be 3510 cases of HCC, and 8470 patients will be progressing to decompensated cirrhosis by 2030. Liver-related deaths in 2030 will number 3060 as compared to 1550 deaths in 2013. In 2013, 13% of viremic cases are estimated to have compensated cirrhosis or more advanced liver disease (decompensated cirrhosis, HCC, or transplant), while this proportion will increase to 32% in 2030 [9].

This type of epidemiological pattern is most likely to occur in the different countries through Latin America unless diagnostic and treatment rates of the HCV infection are increased.

2.2 Inadequate awareness and screening

Worldwide, the number of people that are aware of the diagnosis of hepatitis C is low. One of the challenges with diagnosing HCV infection is that it is often asymptomatic and that individuals seek medical attention only when they develop symptoms or signs of liver disease. In Mexico, for example, the average age at diagnosis

of hepatitis C is 60.7 years, and 44% of them have liver cirrhosis, indicating that patients are arriving late for diagnosis and treatment [10–12].

Screening for HCV infection is central for identifying unknown cases. The early diagnosis of HCV infection can help to reduce the burden of disease and limit transmission to those at risk of infection or reinfection. Screening is critical to achieving the WHO targets by 2030 [13].

A high percentage of HCV-infected people lives in countries with limited resources to screen and treat hepatitis C. Latin America needs to overcome numerous challenges such as the lack of awareness among health professionals and the public in general. Each country in the region needs to plan its public health policy and screening strategy, but overall linkage to care remains an important hurdle.

2.3 Political disinterest

Political interest around the issue of hepatitis C treatment is uneven in the Latin American region. While affordability of DAAs has improved significantly in some countries such as Brazil, Mexico, Colombia, and Argentina, through strategies such as facilitating and speeding up the registration of the new DAAs, negotiating prices, compulsory licensing or generic competition, and exploring financial means by governments, insurance companies, or patients remain a significant task to undertake [14].

Access to treatment in different countries of Latin America is not systematic as they organize their healthcare in diverse ways so that eligibility and availability criteria vary significantly. Furthermore, specific guidance about health care entitlement is either not available, unclear, or not followed by medical professionals involved in diagnosing and treating hepatitis C.

2.4 Insufficient health care providers

Another important barrier restricting access to treatment in Latin America, particularly for the inhabitants with the lowest resources, is the limitations of providers of care. As a result, the number of patients referred for subspecialist evaluation remains low, and even when it occurs, patients may face long-distance travel, extended waiting time, and a lack of scheduling flexibility [15].

Among primary care provider's risk factors for HCV infection are not regularly sought, and deficiencies in HCV testing represent an additional barrier. Knowledge of HCV is generally inadequate.

Limited liver specialist availability through the region further contributes to the restriction of widespread opportunity of receiving treatment.

2.5 Identification of new risk factors

Risk factors for hepatitis C have changed over the years. A lack of knowledge regarding risk factors and treatment may contribute to low cure rates [16]. As blood bank screening has become almost universal, prevention and control of HCV should focus on recognizing high-risk population. In addition, rural populations, especially in areas with lower economic provision, should be under more attention. Evidence reported that intravenous or intranasal drug use and incarceration as well as the presence of hepatitis C in special populations such as patients with chronic renal failure in pre-dialysis, those in hemodialysis or co-infected individuals with HIV/hepatitis B are independent indicators of risk for past or present HCV infection [17]. The evolution of these risk factors will provide insights into understanding the future burden of hepatitis C.

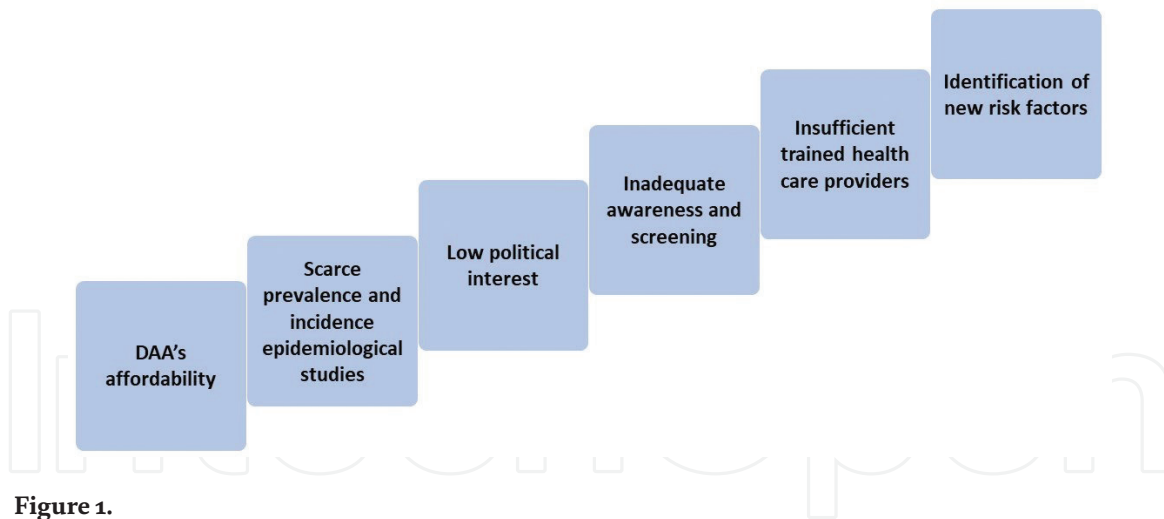


Figure 1.
Challenges to effectively treat HCV infection in Latin America.

Another important issue is the recognition that people remain at risk of reinfection with hepatitis C virus (HCV), even after clearance of the primary infection [18]. A significant issue is the recognition of cofactors that can accelerate progression of hepatic fibrosis in patients with HCV, such as obesity, diabetes mellitus, co-infection with HIV or hepatitis B, and alcohol consumption [19].

In order to achieve the continuum of care, identification of challenges in the region becomes very important. Special attention must be given at individual countries as their challenges may differ in their impact and significance (**Figure 1**).

3. Strategies for accessing HCV infection treatment

3.1 Conducting national campaigns of information and detection of hepatitis C in the general population

A social communication strategy is required to increase the perception that hepatitis C is a preventable and curable disease. It is necessary to educate the population about the risk factors and easy access to screening, utilizing massive ways of communication such as newspaper, magazine, book publishing, as well as radio, television, internet, film, and social media. It is important to make sure that messages are backed up by data in order to avoid confusion and being visionary to provide a good reason to attend the message. The inclusion of the rapid test should be recommended as part of routine test in medical examinations of high-risk individuals. This test allows point-of-care testing that can take place outside the clinical laboratory and can be administered and interpreted by nonspecialists, the results are available in 5–10 min, and its sensibility is 95–99% and specificity 99–100% [20]. In those cases with a positive test, it is necessary to determine a viral load to detect viremic cases and guarantee access to treatment.

3.2 Training programs for medical and nursing staff

It is recommendable to expand the number of health care professionals who can diagnose and administer DAAs, especially in rural areas fostering engagement in the continuum of care. Primary care physicians are in an ideal position to offer screening and diagnosis. Patients with advanced liver disease or complicated cases should be referred to the gastroenterologist, infectious disease specialist, or hepatologist. Nurses are at the forefront of providing information about the spread and diagnosis and treatment options available [21].

To pursue this goal, we propose to connect health teams from remote areas with specialists in medical centers in order to promote the continuity of patient care.

The training course includes:

- Epidemiology of HCV infection.
- Transmission of HCV infection.
- Detection of HCV infection in risk groups.
- Treatment of HCV infection.
- Strategies for the prevention of hepatitis C.

The Extension for Community Healthcare Outcomes (ECHO) model by the University of New Mexico Health Sciences Center (UNMHSC) has developed a platform to deliver complex specialty medical care to underserved populations through an innovative educational model of team-based interdisciplinary development. Using state-of-the-art telehealth technology, best practice protocols, and case-based learning, ECHO trains and supports primary care providers to develop knowledge and self-efficacy in hepatitis. ECHO has signed agreements in some Latin American countries which will contribute to advance the continuum of care for hepatitis C [22].

These types of programs will increase the familiarization of hepatitis C among general practitioners and nurses. They can be implemented taking advantage of the structure of the available health subsystems in every Latin American country.

3.3 Implementation of central laboratories to perform diagnostic tests

Rural communities face barriers when accessing health services, including facilities to perform laboratory studies. Latin America is confirmed by a diverse group of countries with great urban and rural disparities. Their health systems are usually structured in three levels: national, state, and local or their equivalents for every nation. Since 1990 every country in the region has gone through a series of health sector reforms with the aim of increasing equity, effectiveness, and coverage of health systems; unfortunately, despite their positive results, they have not achieved the proposed goals.

An important strategy would be the implementation of point-of-care testing in rural areas and instrument the structure to send blood samples to central laboratories when necessary. One of the primary goals of central laboratories is to achieve a 48-hour or less turnaround on the shipment of laboratory specimens from laboratory sites to the central lab location. These laboratories must have minimum levels of infrastructure, human resources, and quality standards to guarantee technical competence in the analytical framework. At the local level, this reference network could be established at health centers, hospitals, or other places defined by the state, with operational scope within a geographical area.

3.4 Regional programs to integrate medical specialists and health care providers from the prisons and addiction centers

Among these populations prevalence of hepatitis C is markedly increased and has been documented between 4 and 96% in several studies [23]. They are by far undiagnosed and unlinked to care. Very seldom do they seek medical attention unless they present overt clinical liver disease. As a preventive

strategy, these patients should be screened actively, diagnosed, and be treated with DAAs. Treatment programs should include opiate substitution treatment and various harm reduction programs, including needle exchange programs. Ideally, these services should be delivered in the same place with an integrated approach [24, 25].

In the annual budgets of the prisons, it is necessary to foresee human and material resources to ensure they have medical facilities that improve HCV screening by point-of-care testing, outreach methods with mobile teams, rapid tests, and FibroScan to allow them to offer access to DAAs. We must strengthen the system of general prevention of hepatitis among all inmates as well.

3.5 Providing care in hospitals with focus on high-risk populations

A micro-elimination strategy should be implemented at individual hospitals, screening, diagnosing, and treating high-risk population attending for medical care. These populations include patients with liver diseases, patients with chronic renal failure, patients in pre-dialysis, patients with solid organ transplants, hemophiliacs, diabetics, and immunosuppressed patients from different etiologies as well as those pursuing emergency care. The micro-elimination strategy at these places should include the medical and paramedical personnel.

At the level of hospitals and health centers, an anonymous record of information on patients with hepatitis C should be implemented. This registry will provide epidemiological information on the route of acquisition of the disease, comorbidities and barriers to treatment access and document the response to DAAs and serve as an instrument that permits recording follow-up.

3.6 Simplification of bureaucratic procedures

Often in Latin American countries, access to DAAs is mired in bureaucracy implying excessive requirements difficult to meet for both patient and doctors. It is necessary to speed up the process in order to reduce the long queue of medication assignment, awaiting approval response, and shorten the long queue of medications awaiting review. At the institutional level, the form of payment (refund) of the medication can take months or years, so this is another important issue to overcome in order to make DAAs easily accessible.

Higher rates of DAA treatment must be accompanied by efficient screening, increased awareness, and more prescribers. It is necessary to innovate in the screening process, uncovering previously unidentified cases and those in the greatest need of treatment or at a high risk of transmitting the infection.

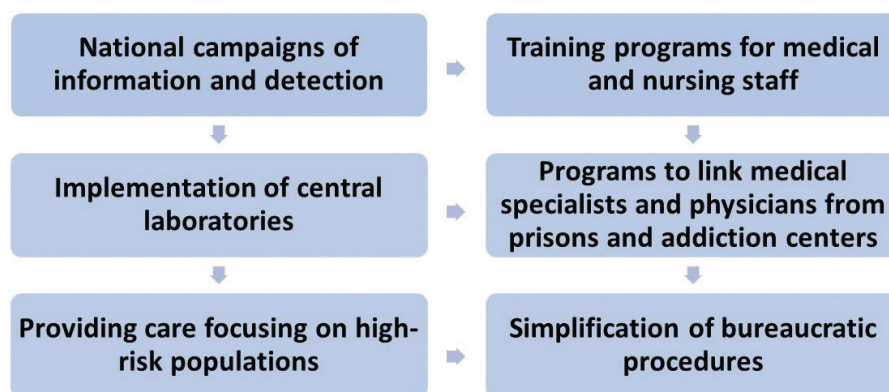


Figure 2.
Strategies for accessing HCV infection treatment.

Understanding the care cascade is vital for eliminating the virus. Reducing the HCV burden requires educational effort and scale-up of DAA therapies. The simplicity of oral regimens that are effective across HCV genotypes expands the number of physicians that can prescribe DAAs with scalable treatment models. Novel prescription systems are being developed, whereby internists and general practitioners may be eligible to prescribe DAAs in consultation with specialists (**Figure 2**).

4. Conclusions

Hepatitis C in Latin America has now become an important health issue. Strategies to identify patients have changed over time, shifting from blood bank to occult patients in high-risk populations (**Figure 3**). Implementation of treatment access is the main objective in order to achieve the WHO strategy of elimination by 2030. The pathway toward this goal is flagged by several barriers, including simplified detection, drug costs, public and professional education, awareness, and government concern, so the majority of HCV-infected individuals can benefit from the new generation of HCV antivirals.

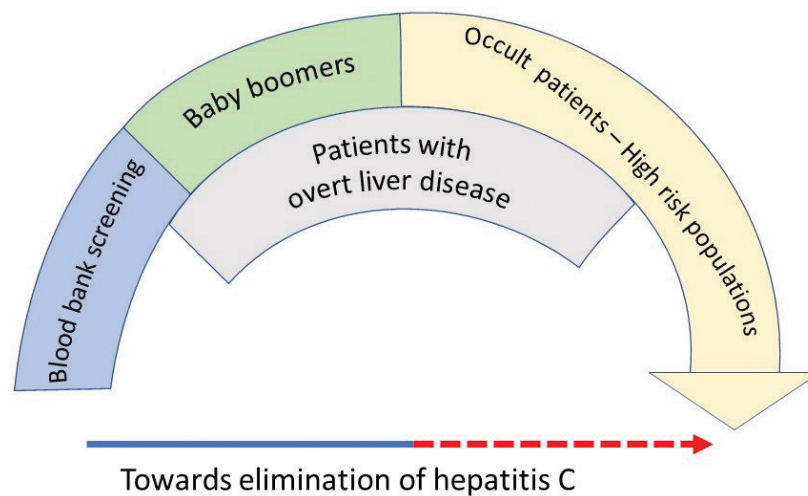


Figure 3.
Hepatitis C a Global Health issue.

Strategies to eliminate HCV infection must emphasize that this is a curable and preventable disease. As therapeutic regimens have become simpler and almost without side effects, the number of health care professionals who can diagnose and administer hepatitis C treatment is expanding the number of patients accessing treatment.

Conflict of interest

The authors declare no conflict of interest.

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