# Viral hepatitis in Latin America and the Caribbean: a public health challenge

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#### **ABSTRACT**

Viral hepatitis (VH) is an emergent concern in public health agendas worldwide. More than one million people die annually from hepatitis and 57% and 78% of global cirrhosis and hepatocellular carcinoma cases, respectively, are caused by VH. The burden of disease caused by hepatitis in Latin America and the Caribbean (LAC) is high. Data on hepatitis has been collected in several countries, but more accurate and comparable studies are needed. Hepatitis B vaccination and screening of donated blood are routine practices in the region. However, integrated policies covering prevention and control of disease caused by all types of hepatitis viruses are scarce. Existing preventive measures need to be reinforced. Attention must be paid to at-risk populations, awareness campaigns, and water and food safety. Affordable access to diagnosis and treatment, population screening, referral to health services and monitoring of positive cases are among the main challenges currently posed by VH in LAC. The World Health Organization framework and Pan American Health Organization regional strategy, defined in response to resolution WHA63.18 of the World Health Assembly, may help to overcome these difficulties. Successful experiences in the fight against hepatitis in some LAC countries may also provide very interesting solutions for the region.

Key words

Hepatitis, viral, human; disease prevention; population at risk; Latin America; Caribbean region.

Viral hepatitis (VH) (including types A, B, C, D and E) is a major cause of mortality and morbidity worldwide, responsible for more than one million deaths annually (1). The World Health Organization

(WHO) estimates that approximately one in three people on earth has been exposed to hepatitis B or C viruses (HBV and HCV) and an important proportion is chronically infected by these viruses (1). HBV and HCV are responsible for 57% of cirrhosis and 78% of hepatocellular carcinoma (HCC) globally (2). Hepatitis E virus (HEV) has been identified as the most common cause of acute VH (3).

Annual deaths are estimated at 340 000 for hepatitis A virus (HAV) (4), 500 000–700 000 for HBV(1), > 350 000 for HCV (1) and 68 000 for HEV (5). Globally, 240 million people are chronically infected by HBV (6) and 150 million by HCV

(1). Among chronic HBV patients, 15–20 million are co/super-infected by hepatitis D virus (HDV) (7). HAV and HEV, respectively, cause 119 million (4) and 18 million (5) annual infections worldwide. Of these, 31 million (4) and 3.2 million (5), respectively, are symptomatic.

In Latin America and the Caribbean (LAC), data on VH has been described at local, national and regional levels. However, no systematic surveillance is performed in the region and very little is known on how individual countries deal with VH. The aim of this report is to assess current knowledge and the challenges posed by VH in LAC.

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# MATERIALS AND METHODS

To obtain data on the status of VH in LAC we conducted a comprehensive literature review of published papers from global (Medline) and regional (LI-LACS) databases, combining the term "hepatitis" with each of the following: "global," "America," "Latin America," "Caribbean," "HAV," "HBV," "HCV," "HDV," "HEV," "epidemiology," "policy," "vaccine," "diagnosis," "referral," "treatment," "prevention," "blood donor," "health worker," "drug user," "HIV" and "cancer." Publications by the WHO or Pan American Health Organization (PAHO) were also included. No restriction criteria were applied for year of publication. Where available, the most recent global or regional overview (i.e. review, meta-analysis or summary report) for each topic was used. In their absence, papers from individual countries in the region were selected. Unpublished observations and knowledge on the status of VH in LAC on the part of PAHO's Viral Hepatitis Working Group members and country representatives were used to enrich the discussion.

### **RESULTS**

# **Epidemiology**

Most countries in LAC experience intermediate HAV endemicity (i.e. ≥ 50% of the population have acquired natural immunity by the age of 15) (8). Using the Global Burden of Disease Project's geographic classification (9), Andean Latin America exhibited the highest anti-HAV seroprevalence rates in the region (96%) in 2005, while the Caribbean experienced the lowest (57%) (8). Due to improvement of sanitary conditions in LAC, clinical cases of HAV are shifting from young children to older individuals, decreasing the number of adults with natural immunity and increasing the likelihood of outbreaks

HBV prevalence varies across LAC. In 2005, it was below 2% in Central and Tropical Latin America, but between 2–4% in the Caribbean, Andean and Southern Latin American regions (6). Nevertheless, HBV prevalence in LAC decreased from 1990 to 2005. This trend may be closely related to the extended use of hepatitis B immunization (6).

Between 7 and 9 million adults in LAC are estimated to be anti-HCV positive (11). Grenada, Bolivia, Haiti, Trinidad and Tobago and El Salvador have the highest prevalence (≥ 2.5%) in the region (12). Combined, HBV and HCV are estimated to be responsible for 31% of cirrhosis and 64% of HCC cases in LAC (data extracted from studies in Brazil, Mexico and Peru) (2).

HDV infection among HBV cases has been observed in Amazonia (13). A study in Colombia showed that 5.2% of HBV-positive cases were also positive for HDV. All but one of these cases were from Amazonia (14). HDV genotype III, with origins in the Amerindian population, is exclusive to this region and may interact differently with HBV than do other HDV genotypes (15).

Although both low and high HEV prevalences and outbreaks of HEV have been reported in LAC, little is known about HEV in the region (16). Studies in Brazil showed prevalence rates of around 3% in adults, while in Bolivia rates ranged from 1.7 to 16.2% (16).

# **Policy**

The World Hepatitis Alliance conducted an analysis of global policy and practice related to viral hepatitis; countries in the Region of the Americas submitting data for some or all questions of interest included: Argentina, Bahamas, Barbados, Belize, Brazil, Canada, Colombia, Costa Rica, Cuba, Ecuador, Guatemala, Honduras, Jamaica, Panama, Paraguay, Peru, Suriname, Trinidad and Tobago, United States of America and Venezuela (17). Sixteen of 20 (80%) countries report having a national strategy for HBV and/or HCV prevention and control. In 12 (75%), a leader for the strategy has been designated, but only 5 of these (43%) work exclusively on hepatitis (17). National goals with respect to prevention and control of hepatitis have been established in 14 of 19 (74%) countries, mostly focusing on hepatitis B immunization (17). In some countries in the Americas, work with civil society organizations, international organizations and groups of patients has been essential for the planning and implementation of national VH programs (17).

In 2010, the World Health Assembly (in resolution WHA63.18) directed the WHO to take immediate action to prevent and control VH (18). In response, the WHO defined a framework for global action (19) that PAHO is using to define a regional strategy for the Americas. Both tools aim to guide countries in the establishment of integrated national VH strategies, programs and plans, including the prevention and control of disease caused by all types of hepatitis viruses.

#### Prevention

As of 2012, all countries in LAC had officially incorporated HBV vaccine in their vaccination schedules, corresponding, in several, to a > 70% decrease in the prevalence of infection and carriers among vaccinated individuals (20-22). A neonatal dose of HBV vaccine, recommended by PAHO/WHO, is used in thirteen countries and territories of LAC (23). HAV vaccination has been incorporated in the immunization programs of three countries (Argentina, Panama and Uruguay) (23). In Argentina, the introduction of a single dose of HAV vaccine reduced HAV cases by > 80% in a two year period (24).

In 2009, > 99% of donated blood units in LAC were screened for HBV and HCV, with > 78 000 units found to be positive for at least one of the viruses (25). The same year, 500 000 potential blood donors were deferred from donating due to the presence of risk factors for HBV, HCV or human immunodeficiency virus (HIV) (25). Promotion of regular voluntary donations and control measures in polytransfused patients has contributed to preventing regional transmission of HBV and HCV.

In 2002, 65% to 80% of hepatitis B and 55% of hepatitis C cases in health workers in LAC were due to accidental needlestick injuries (26). Prevention of work-related accidents in health systems has been promoted in the region, including through the definition of policies and guidelines for the reduction of unnecessary injections, promotion of safe injection practices, and immunization campaigns among health workers. However, a recent study indicated that VH prevention associated with patient health care has not been completely achieved in some LAC countries, increasing the risk of VH transmission in the hospital environment (27).

Prevalence of hepatitis B and C among injecting drug users (IDUs) is high. For

instance, the prevalence of hepatitis B core and hepatitis C antibodies in IDUs was 63.9% and 55.8%, respectively, for Brazil, and 97.4% and 85% for Mexico (28). In WHO's framework for global action and PAHO's regional strategy, IDUs have been included as one of the main target populations for the prevention of VH transmission (19).

Risk of contracting VH in people infected with HIV/AIDS is high. For instance, in Brazil prevalences of almost 70% for HBV and 55% for HCV were detected among HIV patients (29). Some countries in LAC have included VH within existing structures or programs for HIV/AIDS and sexually transmitted infections (STIs); others are considering individual approaches for VH (30, 31).

Prevention of hepatitis among LAC indigenous populations is very important, as high prevalence of the disease has been reported among these populations, especially in Amazonia (15, 32–35). Although the factors that explain VH hyperendemicity in these communities have not been confirmed, horizontal transmission, living conditions, close contact with body fluids or skin lesions, and social practices (such as puncturing the skin or sharing masticated food) have been suggested as possible explanations (15, 32–35).

Sanitation with respect to food and water has been substantially improved in LAC in recent years. However, no specific and integrated actions (including education of the population) have been taken to prevent and control transmission of HAV and HEV through these sources. WHO and PAHO have both defined water sanitation and food safety as essential elements in the fight against hepatitis (19).

Just a few governments in the region have funded and promoted VH awareness campaigns. In particular, 7 of 20 (35%) countries report having undertaken public awareness campaigns, in most cases integrated in wider vaccination, HIV/AIDS and sexual education efforts (17). Awareness campaigns usually involve collaboration with nongovernmental organizations using mass media (17). Commemoration of World Hepatitis Day (as called for in 2010 in resolution WHA63.18) is helping to raise awareness and mobilize governments and resources in the fight against VH. Since 2010, World Hepatitis Day campaigns launched by PAHO/WHO have focused on increasing knowledge about hepatitis, reducing stigma and promoting diagnosis.

# Screening, diagnosis and referral

Nine (47%) of 19 countries in the Americas report offering free HBV and HCV testing to all citizens, while 5 (26%) offer it only to particular risk groups (17); HBV and HCV diagnosis is mandatory for particular risk groups in 15% of countries (17). Corresponding data are not available for HAV, HDV and HEV. Repeated efforts to strengthen HBV and HCV detection often limit efforts to promote HAV, HDV and HEV diagnosis in the region. Blood services have played a major role in hepatitis screening in LAC. Outside blood services, lack or delay of diagnosis is common. This can be attributed to the silent course of the disease, the lack of information among the general public and health workers and the limited availability and high cost of diagnostic tests (36).

Selection of diagnostic tests from among the wide range of assays available in the market is difficult. Local needs and the characteristics of each test (e.g. operational factors, cost, availability, sensitivity and specificity) may influence the selection process. In 2001, WHO evaluated various hepatitis B and C assays (all with sensitivity and specificity > 90%) to help match appropriate tests to local needs (37-40). Although different scenarios for conducting VH diagnosis have been analyzed at local or country level, no guidelines for diagnostic practices with tests currently commercialized in LAC is available.

In the case of a positive test, patients should be referred to health services for counseling and assistance. However, only 12 of 19 (63%) countries in the Americas report having an integrated patient pathway covering diagnosis, referral, treatment and monitoring (17). In blood banks, for instance, where screening is routine, referral of positive cases or at-risk populations to health services is uncommon.

### Treatment and monitoring

Although 18 of 19 (95%) countries in the Americas report that hepatitis treatment is totally or partially funded by the government (17), it is clear that treatment has not been successfully implemented in all LAC. This is likely related to the rapid evolution of recommendations for clinical management of hepatitis and the high expense of treatment (36). Additionally, the need for treatment and monitoring in the case of a diagnosis of hepatitis may be underestimated by the general public and health workers (36). However, some countries have made enormous efforts to overcome these barriers. In the last decade, for instance, Brazil has incorporated universal access to hepatitis treatment in its public health agenda and clinical guidelines for HBV and HCV have been updated (30).

In 2010, a systematic review suggested that hepatitis B treatment is cost-effective in countries with economic profiles similar to Peru (41). Also, a recent meta-analysis showed that hepatitis C treatment success rates are similar in resource-limited settings to those in developed countries, given that cost of treatment represents the major current barrier in low and middle income countries (42).

### DISCUSSION

VH has been only partially addressed in LAC. Data has been collected in several countries and certain actions to reduce the burden of disease are in place. However, some gaps remain in terms of obtaining more accurate data and effectively preventing and controlling disease caused by all types of hepatitis viruses (Table 1). WHO's framework for global action (19) and PAHO's regional strategy may help to address these challenges.

Although regional estimates for HAV, HBV and HCV exist, they are limited in scope; no similar data has been published for HDV or HEV. Most available data is local and national, rather than regional. In some cases, data has not been published or is published in non-indexed sources. The heterogeneity of the region and studies also hinders comparisons among data. The development of a universally compatible and validated system for data collection and surveillance in all LAC could help to overcome these limitations.

Policies for VH prevention and control exist in LAC but are usually partial, covering only a particular type of virus or aspect of hepatitis (e.g. hepatitis B

Table 1. Current situation and challenges of viral hepatitis (VH) in Latin America and the Caribbean (LAC)

	Current Situation	Challenge
Epidemiology	Regional estimates available for HAV, HBV and HCV	Access regional estimates for HDV and HEV
	Heterogeneous data, studies and sources of information	Develop a regional data collection and surveillance system
		Publish data in indexed sources
Policy	Policies in place for specific hepatitis viruses and/or measures (e.g. hepatitis B immunization)	Establish integrated national programs and plans covering all types of hepatitis viruses and measures
		Use WHO global framework and PAHO regional strategy as reference
Awareness	Limited knowledge and awareness among general public, health policy makers and health workers	Increase knowledge and awareness through awareness campaigns, focusing on general population and health workers
	World Hepatitis Day established in 2010	Increase number of countries observing World Hepatitis Day
Prevention	Hepatitis B immunization established throughout LAC	Expand hepatitis B vaccine coverage levels to population at risk
	Neonatal Hepatitis B vaccination established in 13 LAC countries/territories	Introduce neonatal hepatitis B vaccine in countries not using it
	Hepatitis A immunization established in three LAC countries	Introduce HAV vaccine in countries changing from high to intermediate endemicity
	Successful blood screening and voluntary donation programs	Maintain and strengthen the quality of existing interventions
	Control programs for polytransfused patients	Consider HDV and HEV screening when transferring blood to susceptible patients
		Establish referral systems for positive/at-risk patients attending blood services
	Safety practices promoted among health workers and health care services	Maintain and strengthen these practices and measures
	Isolated VH prevention actions among IDUs, HIV patients, indigenous populations and those exposed to contaminated water and food	Increase the number of VH prevention actions, reaching all at-risk populations (IDUs, HIV patients, indigenous populations, those exposed to contaminated water and food)
		Use WHO and PAHO strategies, guidelines and recommendations
		Include VH in existing programs/services, such as HIV/AIDS or STIs
Diagnosis and Treatment	Limited use of diagnosis/screening for only some types of viruses, mostly HBV and HCV in blood banks	Assess best practices for screening outside blood banks
		Improve laboratory capability to detect all types of hepatitis viruses
	Limited use of referral systems for positive/at risk cases	Establish and strengthen systems for referral to health services
	Elevated cost and limited access to diagnosis and treatment	Perform cost-effectiveness and market studies
		Establish agreements and mechanisms to reduce diagnosis and treatment costs
	Treatment recommendations evolve very rapidly	Adapt guidelines and recommendations to LAC

immunization). An integrated approach to the problem is one of the main challenges facing LAC. The VH framework established by WHO (19) and PAHO's regional strategy may help LAC countries to define or improve VH national strategies, goals, plans and programs. Both WHO and PAHO strategic axes for action include prevention, screening, diagnosis, treatment and monitoring of VH.

VH prevention is complex due to the wide range of transmission sources and populations at risk. The most consistently implemented activities for VH prevention in LAC have been immunization and blood screening. However, improvement is still needed. Current challenges for hepatitis B vaccination include expansion of coverage to highrisk groups as well as the introduc-

tion of a neonatal dose in those countries not already using it (23). In countries that have experienced a reduction from high to medium HAV endemicity, large-scale vaccination is likely to be cost-effective (43). Therefore, as per WHO recommendations (43), the use of HAV vaccination in children  $\geq 1$  year old is encouraged in most LAC countries.

Blood screening for HBV and HCV, voluntary donations and control programs for polytransfused patients have enjoyed meaningful successes. Maintenance of the quality of these interventions is essential. Recent studies indicate that HEV can be transmitted via blood and is of significant risk to immunosuppressed patients, those with chronic liver disease and pregnant women (3). HDV, also transmitted by blood, can only affect individuals with HBV (13). Although cost-effectiveness studies have not yet been established for HEV and HDV blood screening, special attention should be paid when transferring blood to patients susceptible to these viruses. To date, the main challenge facing blood services in LAC is the establishment of referral systems that guarantee the transfer of positive or at-risk cases to health services. Referral systems in a few countries, such as Cuba, could serve as models for the region.

Safety practices among health workers and health care services have been promoted in LAC. Maintenance and strengthening of these measures should continue. Isolated actions for VH prevention among other at-risk populations have taken place in some LAC municipalities and countries; expansion of such measures to all areas with at-risk populations is needed. IDUs, HIV patients, indigenous people and those living under poor sanitary conditions are among the most vulnerable.

In the case of IDUs, recent WHO publications can provide a useful reference (19, 44). Inclusion of VH in HIV/AIDS programs or services might improve both HIV and VH patients' living conditions. Scaling up such existing programs to entire populations—with an expanded focus including VH—could help to optimize resources and avoid duplication of efforts. LAC countries in which VH, HIV/AIDS and STIs are integrated in the same program—such as Argentina and Brazil—may serve as models (30, 31).

Prevention needs to be improved in areas of high VH endemicity where indig-

enous populations live (mostly in Amazonia). Cooperation between countries could accelerate the success of interventions, as many such populations live in border areas and often cross borders. Although water and food sanitation conditions have improved in LAC, there is still a need to strengthen measures to prevent transmission of VH through these sources. This was recently highlighted by WHO and PAHO, which advocated for the inclusion of water sanitation and food safety in VH programs (19).

In addition to helping to prevent hepatitis transmission in the general population, VH awareness campaigns could help raise interest in hepatitis among health policy makers and increase the effort and resources invested in preventive measures, diagnosis, treatment and monitoring of the disease. Commemoration of World Hepatitis Day may represent a key starting point for facing the challenges posed by VH in several countries of the Americas.

In LAC, routine VH screening and/or diagnosis outside blood banks is not common and, when available, does not necessarily include all types of viruses (17) or referral to health services. These two aspects of VH management should be considered when choosing interventions. Promoting screening outside blood banks is a primary challenge and different strategies are currently being explored in the Americas. For example, a recent study in the USA used an economic model to compare HCV screening of individuals born during certain years with risk-based screening (45).

One of the main barriers to access for VH diagnosis in LAC is cost, and this is still more relevant in the case of VH treatment (36). Treatment is extremely expensive and clinical management recommendations change very rapidly, presenting a challenge to any public health system (36). Cost-effectiveness and market studies could help in the selection of diagnostic methods and treatments. Establishment of agreements between governments, fund-

ing institutions and international organizations could help to reduce costs. Experiences with, for example, HIV/AIDS have shown that both investment and reduction of costs in treatment and diagnosis are possible in resource-limited settings. When considering the cost of treatment, benefits arising from preventing complications, such as cirrhosis and HCC, should be taken into consideration. Over time, treatment and monitoring not only improve patients' living conditions and reduce costs associated with complications, but prevent increasing burden of disease and limit virus transmission. Guaranteeing universal access to treatment and adapting guidelines for VH treatment in LAC is also necessary.

#### **Conclusions**

VH is a growing problem and an emergent concern in public health agendas worldwide. LAC has already addressed some aspects of VH. Partial data has been collected in several countries and certain preventive measures, such as hepatitis B vaccination and screening of donated blood, are in place. However, various gaps still constrain an integrated approach to preventing and controlling disease caused by all types of hepatitis viruses. To date, the main challenges faced by LAC include: increasing awareness among the general population and health workers, strengthening preventive measures among at-risk populations (including screening), enhancing referral systems for positive cases, and reducing prices and increasing access to diagnosis, treatment and monitoring. The WHO framework for global action and PAHO's regional strategy may help to address these challenges and guide construction of national policies, plans and programs. Successful experiences in the fight against hepatitis in some LAC countries may also highlight very interesting solutions for the region.

Conflicts of interest. None.

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#### **RESUMEN**

# Las hepatitis víricas en América Latina y el Caribe: un reto para la salud pública

Las hepatitis víricas (HV) constituyen una preocupación emergente en los programas de salud pública a escala mundial. Más de un millón de personas mueren anualmente por hepatitis. Las HV causan el 57% de los casos de cirrosis y el 78% de los casos de carcinoma hepatocelular en el mundo. La carga de morbilidad causada por las hepatitis en América Latina y el Caribe (ALC) es alta. Se han recopilado datos sobre las hepatitis en varios países, pero se requieren estudios más minuciosos y comparables. La vacunación contra la hepatitis B y el tamizaje de la sangre donada son prácticas corrientes en la región. Sin embargo, son escasas las políticas integradas que abarquen la prevención y el control de las enfermedades ocasionadas por todos los tipos de virus causantes de hepatitis. Es preciso reforzar las medidas preventivas existentes y prestar atención a las poblaciones en situación de riesgo, a las campañas de sensibilización y a la inocuidad del agua y los alimentos. El acceso asequible al diagnóstico y el tratamiento, el tamizaje de la población, la derivación a los servicios de salud y la vigilancia de los casos positivos constituyen algunos de los principales retos planteados actualmente por las HV en ALC. El marco de la Organización Mundial de la Salud y la estrategia regional de la Organización Panamericana de la Salud, definidos en respuesta a la resolución WHA63.18 de la Asamblea Mundial de la Salud, pueden ayudar a superar estas dificultades. Las experiencias exitosas en la lucha contra las hepatitis en algunos países de ALC también pueden proporcionar soluciones muy interesantes para la región.

#### Palabras clave

Hepatitis viral humana; prevención de enfermedades; población en riesgo; América Latina; región del Caribe.