

Review

Seroprevalence and Genotype Diversity of Hepatitis C Virus in the Caribbean

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Abstract: Hepatitis C (HCV) continues to present a global public health challenge with no vaccine available for prevention. Despite the availability of direct acting antivirals (DAAs) to cure HCV, it remains prevalent in many regions including the Caribbean. As efforts are made to eliminate HCV from the region, existing barriers, such as the high cost of DAAs and lack of an established database of HCV cases within the Caribbean, must be addressed. This review seeks to assess epidemiologic trends (seroprevalence and genotypic diversity) of HCV in the Caribbean and identify gaps in surveillance of the disease. Keywords: genotype distribution, and general epidemiologic characteristics. The literature for the period January 1, 2005, to October 2022, was reviewed to gather country specific data on HCV across the Caribbean. References were identified through indexed journals accessed through established databases. The usage pattern of HCV drugs was determined from information obtained from pharmacists across the Caribbean and in Jamaica. The prevalence of HCV in the Caribbean was 1.5%; the region should therefore be considered an area of moderate HCV prevalence. The prevalence of HCV among intravenous drug users (21.9-58.8%); persons living with HIV/AIDS (0.8 to 58.5%); prisoners (32.8-64%) and men who have sex with men (MSM) (0.8-6.9%) was generally higher than in the general population (0.8-2.3%). Genotype 1 (83%) was most prevalent followed by genotypes 2 (7.2%) and 3 (2.1%), respectively. Less than 50% of countries in the Caribbean have reliable or well curated surveillance data on HCV. Drugs currently being used for treatment of HCV infections across the Caribbean include Eplclusa (Sofosbuvir/velpatasvir) and Harvoni (Ledipasvir/sofosbuvir). Some of these drugs are only available in the private sector and are sourced externally whenever needed. There is a lack of reliable data on the seroprevalence of HCV in the Caribbean. While trends point to a potentially higher prevalence of HCV, it will require well-designed random surveys to obtain better estimates of the infection seroprevalence supported by strong public health laboratory systems. DAAs that are pangenotypic should translate into treatments that are affordable, accessible, and available to improve cure rates and reduce the HCV burden in the population.

Keywords: Seroprevalence; genotype diversity; Caribbean; HCV elimination; Pan genotype treatment; high-risk population

1. Introduction

According to the World Health Organization (WHO), about 1.34 million persons died from viral hepatitis in 2015 (WHO, 2017). Of this, 720,000 deaths were due to cirrhosis and 470,000 deaths were due to hepatocellular carcinoma (1). Up to 3% of the global population—equating approximately 170 million individuals—are estimated to be infected with chronic hepatitis C virus (HCV) (2, 3). A systematic review and meta-analysis by Salem et al reported a global HCV prevalence of 1.8% in the general population (2). The goal of the WHO, as stated in its HCV elimination program, is to reduce the number of new cases of HCV infection by 90% and also to achieve a decrease in worldwide deaths due to HCV from 400,000 (that occurred in 2015) to 140,000 by the year 2030 (1, 4, 5). Strategies to

prevent and control HCV infection include raising awareness through public education, ensuring the safety of blood transfusions, early diagnosis, and effective medical support (6).

HCV causes inflammation of the liver and was first described in 1989 (7, 8). It is a small (50 nm) enveloped virus that belongs to the Flaviridae family and Hepacivirus genus (9-11). HCV has eight genotypes named 1 to 8 in order of their discovery and more than 100 subtypes defined by letters (1a, 1b, 2a, 2b, 3a, etc) (4, 9,11). HCV genotypes are relevant to epidemiological surveillance, vaccine development, and clinical management of chronic HCV infection (12). Genotype 1 is the most predominant genotype circulating in the Caribbean (with subtypes 1a and 1b accounting for 70% of all cases) (4, 10-14).

Infection with HCV may be either acute or chronic; and clinically, about 60-70% of individuals infected with HCV will develop chronic disease that consists of circulating virus in the peripheral blood. HCV infects hepatocytes, which are the only known reservoir for HCV, that can result in the development of inflammation and ultimately scarring (i.e., fibrosis) of the liver. Between 20 to 30 years after initial infection, 5% to 20% of individuals will develop cirrhosis and 1% to 5% of individuals will die from the consequences of cirrhosis or hepatocellular carcinoma (HCC) according to the Centers for Disease Control and Prevention (1, 5, 15-16).

In the Caribbean, there are several existing challenges that will thwart efforts to eliminate HCV from the region. Firstly, in non-health care settings, HCV may readily be transmitted through contaminated needles used in intravenous drug use, body piercings, and tattoos and rarely from engaging in unprotected sexual intercourse. In the health care setting, the virus may be transmitted by the use of contaminated medical equipment, transfusion of unscreened blood /blood products, needle stick injuries with contaminated needles, hemodialysis, and organ transplantation (18-21). Therefore, existing gaps in infection prevention and control at hospitals and other health care facilities need to be identified and corrected in a timely manner in order to prevent nosocomial spread of the virus (1, 4-6, 9,11, 18-23). Additionally, existing barriers to harm reduction need to be identified and effectively addressed through, for example, increased access to sterile syringes and supplies. These interventions will likely reduce the risk of contracting HCV from injection drug use (19).

A review of the literature has revealed that limited data are available on the prevalence and genotype diversity of HCV in Caribbean countries. This may be attributed to lack of representative sample sizes studies; the publication of data in non-indexed sources \ or lack of publication of data generated from studies (23-25). The issues of limited data are compounded by the fact that there does not seem to be an established hepatitis virus database/registry for the region.

Unlike HBV, there is no vaccine to prevent acute and/or chronic infections with HCV, primarily because HCV mutates very rapidly and it does not elicit protection against reinfection (26). Drug therapy for HCV infection includes treatment with Direct Acting Antivirals (DAAs). DAAs are almost always universally curative with a sustained virologic response (SVR) of about 99%. SVR is defined as undetectable HCV RNA three months after completing a course of therapy (26, 27). In addition, DAAs are taken orally for at most 12 weeks with minimal side effects unlike previously used HCV antivirals such as ribavirin and interferon (IFN). Pan-genotypic treatment of infections, despite its high cost, will result in decline in HCV-related morbidity and mortality in infected patients (26,27). The WHO recommends pan-genotypic treatment of all HCV-infected individuals age \geq 12 years old irrespective of disease stage (28).

Taking into consideration the above background information, the primary purpose of this review is to elucidate the seroprevalence and genotype diversity of HCV in the Caribbean and to assess the public health implications for the elimination of HCV from the region.

2. Materials and Methods

We reviewed the literature without language restrictions for the period January 1, 2005 to October 31, 2022 to gather country specific data on the prevalence and genotype distribution of HCV across the Caribbean. References were identified through indexed journals, which were found by searching PubMed and Google Scholar databases using the following terms: '[hepatitis C/HCV genotype in the Caribbean]', '[hepatitis C/ HCV in the Caribbean]'or '[hepatitis C genotype

distribution in the Caribbean]’. Overall a total of 1333 records were identified using Google Scholar and PubMed databases, nine duplicate records were removed. After screening of 1324 records, 1279 were excluded because they were not relevant to the subject of HCV in the Caribbean. Forty-five full text articles were screened for eligibility of which 25 unrelated articles were excluded based on their title or abstract. Therefore, we included a total of 20 articles in the review. Thirty-eight relevant references cited within the reviewed articles were also reviewed and then selected by the main author and a coauthor for inclusion in the review. (Figure1)

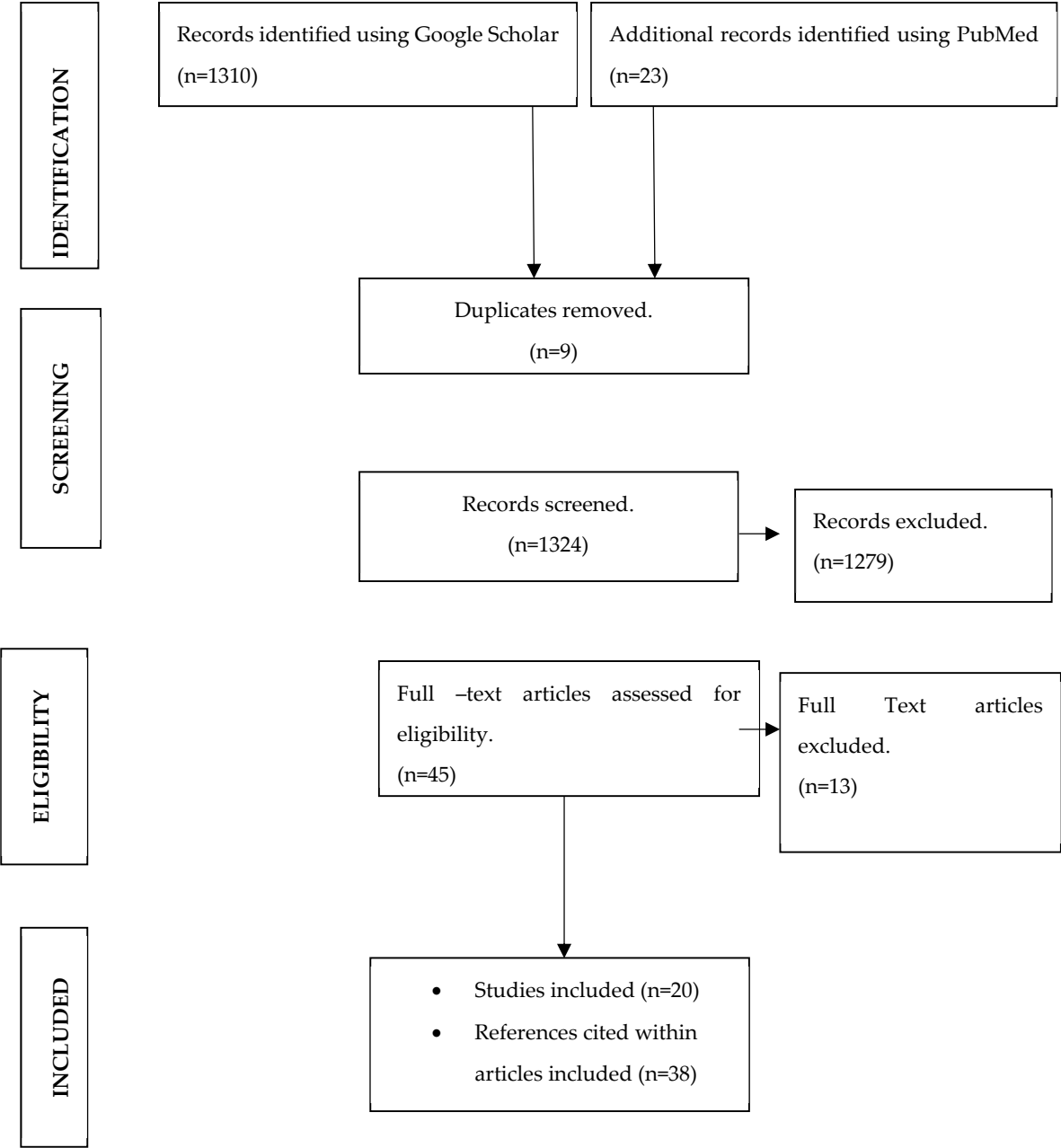


Figure 1. Flow diagram for Study Identification and Selection.

It should be noted that an extended search of the literature prior to 2005 was done specifically for Jamaica to include available data.

Information relating to the prescription of DAAs was obtained from pharmacists across the Caribbean and in Jamaica. These pharmacists communicate with each other under the umbrella of Caribbean Association of Pharmacist (CAP). A formal request was made to the organization for a mini survey to be done on HCV. The questions asked were:

1. What country do you practice in?

2. What treatments are used for HCV in your country?

This mini survey was sent to the 194 members of the CAP, however only 26 pharmacists responded via ‘WhatsApp’ or email. Of this number, information was only received for 14 countries.

3. Results

Regional Prevalence of HCV

A search of the literature revealed that across the Caribbean, published data on HCV were available from Cuba, Jamaica, Haiti, Dominican Republic, Puerto Rico (Greater Antilles), Guadeloupe, and Martinique (From Lesser Antilles). The overall prevalence of 1.5% (with a viraemic rate of 70%) in the general population has been reported for HCV in the Caribbean with a range between 0.55% and 6.3% (29-31). Overall, genotype 1 was found to be the most predominant genotype (83%) in circulation in the Caribbean, followed by genotypes 2 (7.2%), 3 (2.1%), 4 (0.6%), 6 (0.1%), 5 (nil) respectively (4, 10-14, 24, 32, 33) (Table1).

Table 1. Genotype distribution of HCV in 3 Caribbean Countries based on Published Studies.

Country	Study Population	Predominant Genotype(s) (%)	Sample Size	Reference
Cuba	--	G1 (98.0)	--	Petruzziello et al 2016
Puerto Rico	--	G1 (82.1)	--	Petruzziello et al 2016
Dominica Republic	--	G1 (62.6)	--	Petruzziello et al 2016
French Island Guadeloupe	General clinic-based	G1 (80.0) G2 (20)	2,200	Gelu-Simeon et al, 2014

Genotype 1 was most prevalent in studies cites; -----indicate that information was not seen in the literature.

Prevalence of HCV

Greater Antilles

Seroprevalence among Latino veterans in Puerto Rico was 2.3% (32-34). A second study reported a prevalence of 6.3% (29) among 964 household representatives aged 21-64 years in San Juan. In 2016, the prevalence of HCV in Puerto Rico was reported as 2.3% (32).

In Cuba, HCV prevalence rates of 0.8% and 1.8 % were reported based on data from country reports and population prevalence from population-based studies in 2010 and 2016, respectively (32-34). While in Haiti and Jamaica, HCV prevalence was reported to be 4.4% and 0.75%, respectively, in the general population, (30). In Jamaica, for example, 20,250 HCV cases were reported, and with an estimated population of 2.7 million inhabitants, HCV prevalence was estimated at 0.75%. Similarly, based on the population of 10,500 HCV-infected individuals in the Dominican Republic in 2014, the prevalence of HCV was estimated at 1.0% (0.8%-2.4%) (35) (Table 2 & Figure 2).

Lesser Antilles

The reported prevalence of anti-HCV antibodies was highest in Grenada (5.0%), followed by Trinidad and Tobago (3.9%), St Kitts and Nevis (2.2%), St Vincent and the Grenadines (1.0%). Barbados, Bahamas, Dominica, and Guyana had a reported HCV prevalence of 0.75% (30) (Table 2).

Table 2. Prevalence of Hepatitis C virus in the Caribbean- by country 2010*.

Country	Location	Anti-HCV antibodies (%)	Absolute No. Infected**
Grenada	Lesser Antilles	5.0	5,150
Haiti	Lesser Antilles	4.4	448,272
Trinidad & Tobago	Lesser Antilles	3.9	50,583
St Kitts &Nevis	Lesser Antilles	2.2	1,232
Cuba	Greater Antilles	1.8	202,842
St Vincent & the Grenadines	Lesser Antilles	1.0	1,180
Bahamas	Lesser Antilles	0.75	2,250
Barbados	Lesser Antilles	0.75	2,100
Dominica	Lesser Antilles	0.75	593
Dominican Republic	Greater Antilles	0.75	66,713
Guyana	Lesser Antilles	0.75	5,633
Jamaica	Greater Antilles	0.75	20,250
St Lucia	Lesser Antilles	0.75	1,232

*Based on published data adapted from Lavenchy 2011. The seroprevalence of HCV antibodies across the region varied from 0.75% to 5.0%.

** Indicate absolute number of persons that were found to be seropositive for HCV antibodies.

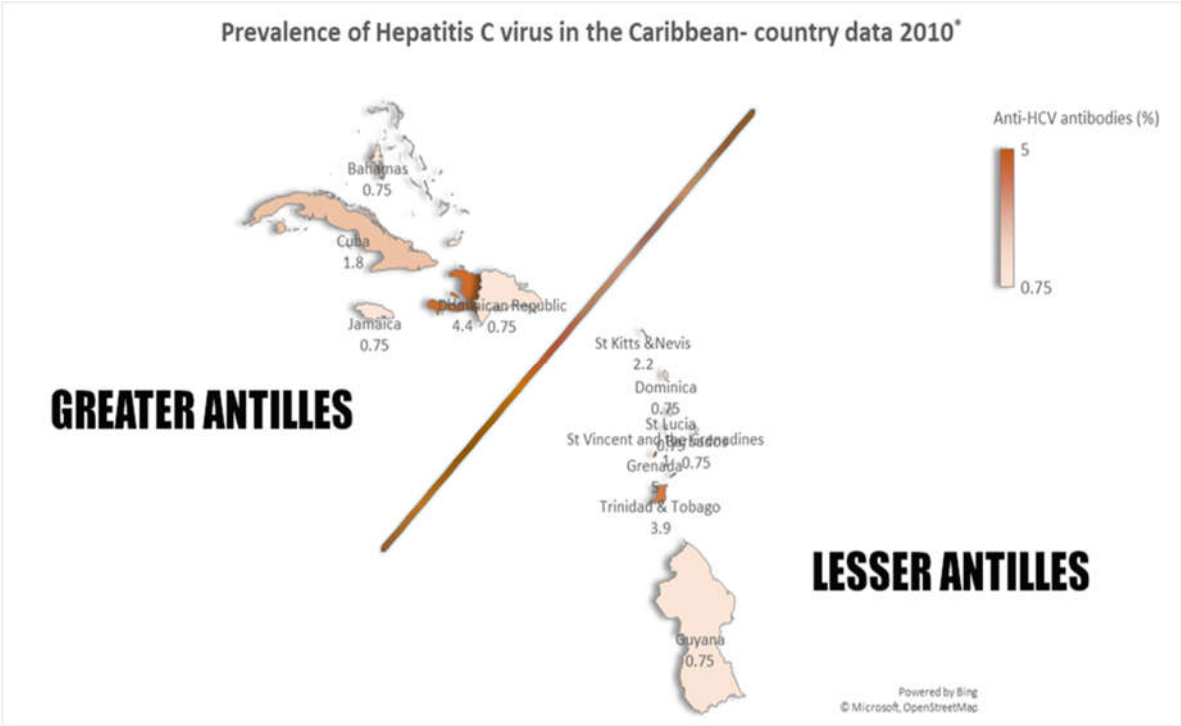


Figure 2. Prevalence of HCV in the Caribbean by country -2010.

Prevalence of hepatitis C virus in the Greater and lesser Antilles respectively. Overall prevalence varied from 0.75% to 5.0%. In the Greater Antilles, the highest prevalence was found in Cuba (1.8%) while both in Jamaica and the Dominican Republic, the prevalence was <1.0%. Similarly, in the Lesser Antilles, the highest prevalence was found in Grenada (5.0), while for the other countries prevalence varied from 0.75% to 3.9%.

Treatment of HCV

DAAAs currently being used for treatment of HCV infections across the Caribbean include Epclusa (Sofosbuvir/velpatasvir) and Harvoni (Ledipasvir/sofosbuvir). Some of these medications are only available in the private sector and are sourced externally whenever needed (Table 2). Lack of epidemiological studies has impeded elimination efforts. The Caribbean Public Health Agency (CARPHA), in an effort to eliminate HCV from the region, has recommended: enhancement or development of national hepatitis strategic plans; increased diagnostic testing; bridging the gap in infection control and control capacity in health care facilities, and a focus on barriers to harm reduction (19). In the Dominica Republic, efforts to eliminate HCV have included an enhancement of the screening activities, such that it is done for employment applications, prior to medical procedures, marriages and for pregnant females, and not only for blood banking (36). While in Puerto Rico, discriminatory restriction on access to HCV treatment that was affecting more than 1 million Puerto Ricans covered by Medicaid program, has been lifted (37).

Another limitation to HCV elimination in the Caribbean is the lack of a registry of the drug distribution or prescription of HCV medications in the region. However, we collected information directly from the pharmaceutical supplier that market the relevant drugs. Unfortunately, however, the data are not standardized.

Table 2. Information relating to use of HCV drugs across Caribbean Islands.

List of Caribbean Countries	Comments
Antigua and Barbuda	-----
Aruba	Routine use of Epclusa (Sofosbuvir/velpatasvir 400/100)
Bahamas	- In the private sector patients are treated with Epclusa (Sofosbuvir/velpatasvir 400/100), and Harvoni (Ledipasvir/sofosbuvir 90/400)
Barbados	- Epclusa (Sofosbuvir/velpatasvir 400/100) will be supplied if needed for treatment of HCV infected patient (s)
Bermuda	Harvoni (Ledipasvir/sofosbuvir 90/400)
Curacao	Routine use of Epclusa (Sofosbuvir/velpatasvir 400/100)
Virgin Islands	Currently no cases of hepatitis C.
Guyana	Discontinued use of Epclusa (Sofosbuvir/velpatasvir 400/100) and currently uses cheaper combo-Daclatasvir/Velpatasvir
Jamaica	- Using Epclusa (Sofosbuvir/velpatasvir 400/100 & Harvoni (Ledipasvir/sofosbuvir 90/400) for those with age more than 6 years- order from USA /through local distributor
Saint Lucia	Currently no cases of hepatitis C on the island.
Saint Maarten	Routine use of Epclusa (Sofosbuvir/velpatasvir 400/100)
The protocol members of the Organisation of Eastern Caribbean States (OECS) are:	
<ul style="list-style-type: none"> Antigua and Barbuda Commonwealth of Dominica <ul style="list-style-type: none"> Grenada Montserrat St. Kitts and Nevis Saint Lucia St. Vincent and The Grenadines 	
The associate members of the OECS are:	
<ul style="list-style-type: none"> The British Virgin Islands <ul style="list-style-type: none"> Anguilla Martinique Guadeloupe 	
	One patient for the period 2020-2022 received Epclusa (Sofosbuvir/velpatasvir 400/100)

There is limited availability of data on treatment for HCV in the Caribbean. A dashed line indicates that no information are available for that country. Data was collected via a mini survey from members of the Caribbean Association of Pharmacists (CAP). Members responded via email or 'whatsapp'. Abbreviations: HCV, hepatitis C

Greater Antilles

No information relating to DAAs for HCV was obtained for Cuba and Puerto Rico, Haiti, and the Dominican Republic. In Jamaica, older therapies included Pegasys (Peginterferon alpha-2a) and ribavirin, these have been replaced by newer therapies- Epclusa (Sofosbuvir/velpatasvir 400/100) and Harvoni (Ledipasvir/sofosbuvir 90/400).

Lesser Antilles

For the protocol members of the Organization of Eastern Caribbean States (OECS)- (Antigua and Barbuda, Dominica, Grenada, St Kitts & Nevis, St Lucia and St Vincent & the Grenadines) DAAs are ordered from the USA as needed. Similarly, for associate members of the OECS (Anguilla, Guadeloupe, Martinique, and the British Virgin Islands), DAAs are ordered from the USA whenever needed. For the years 2020 to 2022, only one case of HCV infection was identified and treated with Epclusa (Sofosbuvir/velpatasvir (400/100) in any full or associate OECS country.

In the Bahamas, private sector patients are treated with Epclusa (Sofosbuvir/velpatasvir 400/100), and Harvoni (Ledipasvir/sofosbuvir 90/400). If treatment for HCV infection is required in Barbados, Epclusa (Sofosbuvir/velpatasvir 400/100) is supplied.

Prevalence of HCV in Special Populations

Persons considered to be 'at risk' for infection with HCV including intravenous drug users, prisoners, and men who have sex with men. All these groups may feel stigmatized and hesitant to seek medical treatment and diagnostic testing (19). Also, the majority of seropositive persons may be unaware of their infection status and may not seek medical attention until they become seriously ill, oftentimes resulting from liver decompensation, resulting in increased morbidity and mortality from the infection. Therefore, public/national education on the risk factors, modes of transmission, clinical presentation and methods of control and prevention of infection with HCV is needed (20-23).

A review of the literature by Grebely in 2019 found that in the Bahamas, Bermuda, Dominican Republic, Haiti, and Jamaica, there was evidence of injection drug use but no estimate of the prevalence of HCV infection in this high-risk group, so it is not known how common injection drug use is. However, there were no reports of injection drug use in several countries including Antigua & Barbuda, Barbados, Cuba, Dominica, Grenada, Saint Kitts & Nevis, Saint Lucia, St Vincent and the Grenadines, and Trinidad & Tobago (38).

Greater Antilles

In Puerto Rico, HCV prevalence was significantly higher than in the general population among study participants with a history of heroin use (39.2%), cocaine use (39.6%) and imprisonment (32.8 %) (29). In Metropolitan San Juan, varying prevalence (78.4%-89.0%) of HCV antibodies was reported among injection drug users; while in the rural areas, the prevalence is slightly lower in the rural population (78.4%) (39,40-42). This prevalence was more than two times higher than that reported in Southern Puerto Rico by Colon-Ruiz et al in a cross-sectional data analysis of medical records of HCV infected adults for the period January 2005- March 2013 (43).

Overall, in the Caribbean, except for Puerto Rico, intravenous drug abuse, (IVDA) is not a major problem. In Puerto Rico, HCV prevalence is 89% of IVDA. In addition, 17% of IVDA are positive for Human Immunodeficiency syndrome (HIV) with 95% co-infected with HCV. This may be attributed to increased injection and needle sharing and decreased sterile syringe programs (20,)

In Jamaica, a prevalence of HCV antibodies in (Non injection drug use) NIDU of 1.7% was reported among residents at detoxification unit by Smikle et al (44).

Further, the prevalence of HCV among hemophiliacs in Jamaica was reported to be 41% and associated risk factors included increasing age, disease severity, and frequency of blood transfusions (45).

HCV infection was identified as a public health problem in Cuba in the 1990s. Despite universal blood donor screening, which was achieved in 1995, the infection is still found in multi-transfused patients (46). In 2005, the prevalence of HCV antibodies among 318 Cuban patients who were transfused with ≥ 10 units of allogenic blood/blood products on ≥ 2 occasions was reported to be 51.6% (46). A systematic review of the literature (2000-2013) by Alonso et al cited only four studies from the Dominican Republic where the prevalence of HCV among gay, transsexual and men who have sex with men ranged from 0.8% to 6.8% and 2 studies on injection drug use in Puerto Rico reported an HCV prevalence of 39% and 89%, respectively (23, 47,48).

For the period 2005-2013, in the Southern area of Puerto Rico, the prevalence of anti-HCV among adults that received blood transfusion was found to be 33% (43).

Lesser Antilles

In Guadeloupe, among a general clinic-based population, a low prevalence of HCV of 0.55% was found, this is in comparison to a prevalence of 0.8% found previously among blood donors; risk factors for HCV acquisition included gynecological surgery, endoscopy, tattoo, shaving, intravenous drug use (IVDU) and familial exposure (31).

4. Discussion

Overall, limited data currently exist on the prevalence and genotype distribution of HCV in the Caribbean. This limitation has been highlighted by several systematic reviews (25, 32, 39, 40, 49). The epidemiological burden of HCV in the region needs to be fully assessed as only a few estimates are available (50). The data deficiency may be attributed to lack of representative study sample sizes, the publication of data in non-indexed sources, or lack of publication of data generated from studies (23, 24, 32). Updated data are needed to reflect the true prevalence and assessment of the burden of HCV infection in the general and 'high risk' populations in the region.

The estimated prevalence of HCV in the Caribbean was 1.5% with genotype 1 being the most dominant genotype (83%). Similar prevalence (1.5%-3.5%) has been seen in other regions considered to have moderate prevalence of HCV, including East, South and Southeast Asia, West and East Africa, North Africa, the Middle East, Southern and Tropical Latin America, Australasia, and Eastern Europe (4, 29-32). In consideration of these data, the Caribbean region should therefore be considered an area of moderate HCV prevalence. The persistence of HCV may be attributed to the practices of 'at risk' or vulnerable populations including illicit drug users (injection and non-injection), men who have sex with men, sex workers, and prison inmates. A relatively high disease burden of HCV has been reported in these key populations (23, 47,48).

Despite the fact that no data were found on drug use in several Caribbean countries except for Puerto Rico, there is reported evidence of injection drug use, but no estimate of the prevalence of HCV infection in this high-risk group, in the Bahamas, Bermuda, Dominican Republic, Haiti, and Jamaica, (38). Additionally, injection drug use is uncommon in most Caribbean countries (49,50). Based on the high prevalence of HCV in injection drug users in Puerto Rico, needle exchange and drug treatment programs are a necessity.

Blood transfusions that occurred prior to the introduction of widespread screening of blood/blood products in mid-1990s may be considered a risk factor in persons already infected. This may lead to persistence of the infection in multiple transfused persons, such as hemophiliacs.

Across the Caribbean, drugs currently being used for treatment of HCV infections include Epcusa (Sofosbuvir/velpatasvir 400/100) and Harvoni (Ledipasvir/sofosbuvir 90/400). In some islands, such as St Lucia and the Virgin Islands, there are no active cases of HCV. The COVID-19 pandemic has adversely impacted routine national health services in individual countries resulting in limited routine laboratory testing and treatment for HCV. A high mortality rate has been found in patients co-infected with HCV and COVID-19 and with cirrhosis as they all contribute to a decline in liver function (6). As such, treatment of HCV infection is important to remove an additional insult from COVID-19 patients.

There exists a need for the establishment of an effective epidemiological surveillance system to provide information needed for planning, implementation, and intervention strategies for HCV

infection. Furthermore, in some populations within the Caribbean, such as drug users, access to medical and other existing therapy is limited (20-23). Therefore, there is a need to enhance or develop HCV prevention plans that clearly outline actions necessary to control and ultimately eliminate the virus.

Data on the epidemiology of HCV across the region can provide crucial information to policymakers and public health agencies, such as CARPHA, on the need for targeted interventions for prevention and treatment. To assess the scope of chronic hepatitis, the burden of disease and seroprevalence, in both the general and most at-risk populations, are necessary. Countries in the English-speaking Caribbean are all members of the Caribbean Community (CARICOM), and they often implement common healthcare policies. Continuous surveillance and intensive prospective epidemiologic research studies should be performed to aid in the elimination of this growing hepatitis epidemic.

The establishment of a viral hepatitis C data base/registry in the region is highly recommended. Based on the 2021 WHO Technical Report, for the elimination of HCV (and other types of viral hepatitis) as a public health problem, goals that should be realized for country validation include the following: annual incidence of ≤ 5 cases/100,000 inhabitants; ≤ 2 cases/100 persons who inject drugs (PWID). Also, with respect to testing and treatment, the goal is the diagnosis of $\geq 90\%$ of persons and the treatment of $\geq 80\%$ of those diagnosed with HCV. Prevention strategies include 0% unsafe injections, 100% blood safety, and 300 needles/syringes/PWID/year (51).

An excellent mechanism to eliminate hepatitis C is through CARICOM where CARPHA establishes health interventions and research policies for all 15 full member and 5 associate member countries. However, the first step is the elucidation of the epidemiology of the infection in individual countries based on rigorous prospective studies to include high-risk populations.

In low-and middle-income countries, such as India, Cambodia, and Indonesia with limited infrastructure, recent efforts to eliminate HCV infection included political support and decentralized programs. These approaches have enabled intensive low-cost screening and a reduction in the cost of medication and have resulted in a cure rate exceeding 90% in 120 individuals (52).

In European countries, such as France, plans to eliminate HCV infection include the availability of oral antivirals to members of various 'high-risk' populations, such as HIV-infected patients and men who have sex with men for the years 2015 and 2016 respectively. Universal HCV treatment, with full coverage by French National Health Care, was introduced in 2017. This intervention has resulted in the treatment of about 60,000 patients during the period of 2017 to 2022 (53).

Two limitations of the study are, firstly there is a lack of published papers on the prevalence or genetic diversity of HCV in the pediatric population in the Caribbean. Unlike hepatitis B virus, there are currently no vaccines available for the prevention of HCV infection; therefore, there is risk of vertical transmission during pregnancy (54-56). According to Schmelzer et al, the disease burden of HCV in children is poorly understood (57). This lack of data further highlights the need for studies on HCV in the pediatric population in the Caribbean, which will help to guide national policies to eliminate the virus. Secondly, in the Caribbean, the percentage of the general detained population with HCV antibody prevalence was unknown since no sources of data were identified for the region. Individuals incarcerated in prisons usually have a known history of drug use (injecting or non-injecting), promiscuity, homosexuality, and tattooing, all of which increase the risk of HCV transmission. Current, well-designed studies are needed to ascertain the true prevalence of HCV in these population in the region in an effort to completely eliminate HCV from the region.

Future Directions

Increased diagnostic capacity, including the introduction of molecular tests to diagnose and confirm HCV infection, is necessary. For example, screening for HCV in Jamaica is done by serology, and samples that test positive for HCV antibodies are shipped to diagnostic laboratories overseas for confirmatory testing at a cost to the patient. The cost is prohibitive to most patients that results in delays in definitive diagnosis and treatment. In addition, there is a need for the widespread use of

rapid, low cost diagnostic tests; these should be introduced as screening tools in hospitals, health centers and point-of-care sites.

The introduction of DAAs for HCV, coupled with pan genotypic treatment of HCV infection, has resulted in effective management of patients (58). Therefore, in the Caribbean, the therapeutic focus for HCV can now be on complete elimination of the virus from the region. Conducting seroprevalence and molecular studies specifically targeting the Caribbean would have great benefit in identifying and improving public health management of hepatitis infections in the region.

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References

1. World Health Organization. Global hepatitis report, 2017. Available at <http://www.who.int/hepatitis/publications/global-hepatitis-report2017/en/website>
2. World Health Organization. Hepatitis C: Fact Sheet No. 164. World Health Organization 2011; Available from: <http://www.who.int/mediacentre/factsheets/fs164/en/index.html>
3. Salari N, Kazeminia M, Hemati N, Ammari-Allahyari M, Mohammadi M, Shohaimi S. Global prevalence of hepatitis C in general population: a systemic review and meta-analysis. *Travel Med Infect Dis*. 2022; 46:102255. doi:10.1016/j.tmaid.2022.102255
4. The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol*. 2017; 2:161-176
5. Centers for Disease Control and Prevention. Hepatitis C questions and answers for health professionals. 2020. Available at: <http://www.cdc.gov/hepatitis/hcv/hcvfaq.htm>. Accessed 29 July 2021
6. Stasi C, Silvestri C, Voller F, Update on Hepatitis C Epidemiology: Unaware and Untreated Infected Population Could be the Key to Elimination. *SN Comprehensive Medicine* 2020; Available at <https://di.org/10.1007/s42399-020-00588-3>
7. Houghton M. Hepatitis C Virus: 30 years after its Discovery. *Cold Spring Harb Perspect Med* 019:9: a030769
8. Simmonds P. The origin of hepatitis C virus. *Hepatitis C virus from Molecular Virology to Antiviral therapy* 2013; 369: 1-15
9. Dennis BB, Naji L, Jajarmi Y, Ahmed A, Kim D. New hope for hepatitis C virus: Summary of global epidemiologic changes and novel innovations over 20 years *World J Gastroenterol* 2021; 27: 4818-4830
10. Martinez MA, Franco S. Therapy Implications of hepatitis C Virus Genetic Diversity. *Viruses* 2021; 13,41. Available at <http://doi.org/10.3390/v13010041>. Accessed 05 June 2021
11. Daniel Castaneda, Adalberto Jose Gonzalez, Mohammad Alomari, Kanwarpreet Tandon, Xaralambos Bobby Zervos. From hepatitis A to E: A critical review of viral hepatitis. *World J Gastroenterol* 2021 April 28; 27(16): 1691-1715
12. González-Horta, EE; Marante, J; Amador-Cañizares, Y; ÁLVAREZLAJONCHERE, L; Guerra, I; Martínez-Donato, G; Dueñas-Carrera, S. Analysis of hepatitis C virus core encoding sequences in chronically infected patients reveals mutability, predominance, genetic history and potential impact on therapy of Cuban genotype 1b isolates. *Eur Rev Med Pharmacol Sci* 2011; 15: 1320-7
13. Kato N. Genome of human hepatitis C virus (HCV): gene organization, sequence diversity, 7 variation. *Microb Comp Genomics* 2005; 5:129-51
14. Messina JP, Humphreys I, Flaxman A, Brown A, Cooke GS, Pybus OG, Barnes E. Global distribution and prevalence of hepatitis C virus genotypes. *Hepatology* 2015, 61:77-87
15. Irshad M, Mankotia DS, Irshad K. An insight into the diagnosis and pathogenesis of hepatitis C virus infection. *World J Gastroenterol* 2013; 19: 7896-7909
16. Grebely, J, Dore, G.J, Kim, A.Y, Lloyd, A, Shoukry, N.H, Prins, M, Page, K. Genetics of spontaneous clearance of hepatitis C virus infection: A complex topic with much to learn. *Hepatology* 2014, 60, 2127–2128
17. Foreman KJ, Marquez N, Dolgart A et al. Forecasting life expectancy, years of life lost and all cause-specific mortality for 250 cause of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet* 201

18. Thomas DL. Global Elimination of Chronic Hepatitis. *N Engl J Med* 2019; 380:2041-50
19. <https://www.who.int/campaigns/world-hepatitis-day>. CARPHA calls on the Caribbean to enhance surveillance for viral hepatitis on World Hepatitis Day 2021. Available: <https://carpha.org/More/Media/Articles/ArticleID/505/CARPHA>
20. Perez CM, Albizu-Garcia C, Torres EA. Tackling the health challenge posed by hepatitis C in Puerto Rico: A call for immediate Public Health Actions. *PR Health Sci J* 2015; 34:53-9
21. Soto-Salgado M, Perez CM, Burgos-Calderon R, Torres EA, Suarez E. Factors associated to the prevalence of antibodies to hepatitis C virus among patients receiving hemodialysis at selected dialysis centers in Puerto Rico, 2005. *PR Health Sci J* 2009; 28:18-23
22. Vickers IE, Brathwaite AR, Levy M, Figueroa JP. Seroprevalence of sexually transmitted infections among accepted and deferred blood donors in Jamaica. *West Indian Med J*. 2006 Mar; 55(2):89-94.
23. Alonso M, Gutzman A, Mazin C, Reveiz L, Ghidinelli M. Hepatitis C in key populations in Latin America and the Caribbean: systematic review and meta-analysis. *Int J Pulic Health* 2015; 60: 789-798
24. Dehesa-Violante M, Nunez-Nateras R. Epidemiology of hepatitis B and C, *Arch Med Resv* 2007; 38:606-11
25. Diez-Padriza N, Castellanos LG. PAHO Working Group. Viral hepatitis in Latin America and the Caribbean: a public health challenge. *Rev Panam Salud Publica* 2013; 34: 275-281
26. European Association for the Study of the Liver. EASL Recommendations on Treatment of Hepatitis C. *J Hepatol* 2018; 69: 461-511
27. Andreone, P, Colombo, M, Enejosa, J, Koksai, I, Ferenci, P, Maieron, A, Bernstein, B. ABT-450, Ritonavir, Ombitasvir, and Dasabuvir Achieves 97% and 100% Sustained Virologic Response With or Without Ribavirin in Treatment-Experienced Patients With HCV Genotype 1b Infection. *Gastroenterology* 2014; 359-365
28. Guidelines for the care and treatment of persons diagnosed with hepatitis C infection, updated July 2017. Geneva: WHO; 2018 Available at: <https://www.who.int/publications/i/item/9789241550345>, accessed 09/04/2023
29. Perez CM, Suarez E, Torres EA, Roman K, Colon V. Seroprevalence of hepatitis C virus and associated risk behavior: a population-based study in San Juan, Puerto Rico. *Int J Epidemiol* 2005; 34:593-9
30. Lavanchy D. Evolving epidemiology of hepatitis C virus. *Clin Microbiol Infect* 2011; 17:107-15
31. Gelu-Simeon M, Pillas V, Deloumeaux J, Delacroix-Millard H, Saint-George G et al. Seroepidemiology of chronic hepatitis B and C in the French Island of Guadeloupe. *BMC Research Notes* 2014; 7:55
32. Petruzzello A, Marigliano S, Loquercio G, Cozzolino A, Cacciapuoti C. Global epidemiology of hepatitis C virus virus genotypes. *World Journal of Gastroenterology* 2016; 22:7824-40
33. Tengan FM, Ibrahim KY, Dantas BP, Manchiero C, Magri MC, Bernardo WM. Seroprevalence of Hepatitis C virus among people living with HIV/ AIDS in Latin America and the Caribbean: a systematic review. *BMC Infect Dis* 2016 (1) 663
34. Santiago-Rolon A, Purcell D, Grigg N, Toro DH. Chronic hepatitis C: treatment, complications, and long-term outcomes in a population of Latino veterans. *P R Health Sci J*. 2016; 35: 30-34.
35. Maaroufi, A; Vince, A; Himatt, SM; Mohamed, R; Fung, J; Opare-Sem, O; Workneh, A; Njouom, R; Al Ghazzawi, I; Abdulla, M et al. Historical epidemiology of hepatitis C virus in selected countries- volume 4 *J viral Hep* 2017;24 (Suppl2): 8-24
36. Contreras F. Viral hepatitis in Central America and the Caribbean 2014: Available at: https://www.vhpb.org/files/html/Meetings_and_publications/Presentations/BRAS52.pdf (accessed 11/04/2023)
37. Puerto Rico lifts barriers to hepatitis C treatment access for Managed Care. Available at :<https://abarcahealth.com/puerto-rico-lifts-barriers-to-hepatitis-c-treatment-access-for-managed-care/> (accessed 11/04/2023)
38. Grebely J, Larney S, Peacock A, Colledge S, Leung J et al. Global, Regional and Country-level estimates of hepatitis C among people who have recently injected drugs. *Addiction* 2019; 114: 150-166
39. Hanafiah MK, Groeger A, Flaxman A, Wiersma ST. Global Prevalence of hepatitis C infection: new estimates of age-specific antibody to HCV seroprevalence. *Hepatology* 2013; 57:1333-42
40. Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection, *J Hepatol* 2014; 61(1 Suppl): S45-57
41. Reyes JC, Colon HM, Robles RR et al. Prevalence and correlates of hepatitis C virus infection among street-recruited injection drug users in San Juan, Puerto Rico. *J Urban Health* 2006 83(6):1105-1113
42. Reyes JC, Welch-Lazoritz M, Zayas-Martinez L, Khan B, Dombrowski K. Prevalence and Risk factors associated with homelessness among drug users in Puerto Rico. *PR Health Sci J* 2019; 38: 54-59
43. Colón-Ruiz D, Rosado Carrión B, Bredy R. The epidemiologic profile of HCV infected Hispanic patients from the southern area of Puerto Rico since 2005. *Bol Asoc Med P R*. 2012 Apr-Jun;104(2):42-7. PMID: 23882973.
44. Smikle MF, Dowe G, Williams EM, Thesiger C. Antibodies to hepatitis B and hepatitis C in residential detoxification client in Jamaica. *Human antibodies* 2000; 9: 231-3

45. Wharfe G, Smikle M, Dowe G, Buchner L, Choo-Kang E, Graham S, King D. Seroprevalence of hepatitis C virus in hemophiliacs in Jamaica. *Hum Antibodies*. 2002;11(3):61-4.
46. Ballester JM, Rivero RA, Villaescusa R, Merlin JC, Arce AA et al. Hepatitis C virus antibodies and other markers of blood-transfusion-transmitted infection in multiple transfused Cuban patients. *J Clin Virol* 2005;34: S39-46
47. Alfonso AP, Corcho AR, Monzón VH, Jam Morales BC, Jiménez YB, Cabanes P, et al. Coinfección VIH-hepatitis B y C en la provincia de Cienfuegos/HIV/ hepatitis B and C co-infection in Cienfuegos province. *Rev Cuba Med Trop*. 2008; 60:141-7.
48. Johnston LG, Vaillant TC, Dolores Y et al (2013) HIV, hepatitis B/C and syphilis prevalence and risk behaviors among gay, transsexuals and men who have sex with men, Dominican Republic. *Int J STD AIDS* 24(4):313-321
49. Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of Viral hepatitis and preventive strategies. *World J Clin Cases* 2018; 6:589-599
50. Soto-Ramirez LE. World Hepatitis day. Fighting hepatitis C in Latin America and the Caribbean; an urgent call. *Journal of the International AIDS Society* 2017; 120:22183
51. WHO releases first-ever global guidance for country validation of viral hepatitis B and C elimination: available at: <https://www.who.int/news/item/25-06-2021-who-releases-first-ever-global-guidance-for-country-validation-of-viral-hepatitis-b-and-c-elimination> accessed 09/04/2023
52. Mangia A, Cotugno R, Cocomazzi G, Squillante M, Piazzolia V. Hepatitis C virus Micro-elimination: Where do we stand? *World J Gastroenterol* 2021; 27: 1728-1737
53. Pol S, Lair-Mehiri L, Vallet-Pichard A. Is elimination of HCV realistic by 2030: France.DOI101111/liv.14862
54. Yeung CY, Lee HC, Chan WT, et al. Vertical transmission of hepatitis C virus: current knowledge and perspectives. *World J Hepatol*. 2014; 6: 643-651
55. Prasad MR, Honegger JR. Hepatitis C virus in pregnancy. *Am J Perinatol* 2013; 30: 149-159
56. Indolfi G, Guido M, Azzari C et al. Histopathology of hepatitis C virus in children, a systematic review: implications for treatment. *Expert Rev Anti Infect Ther*. 2015;13: 1225-1235
57. Schmelzer J, Dugan E, Blach S, Coleman S, Cai Z, De Paola M et al. Global prevalence of hepatitis C virus in children in 2018: a modelling study. *The Lancet Gastroenterology & Hepatology* 2020;5: 374-392
58. Burstow, Nicholas J; Mohamed, Zameer; Gomaa, Asmaa I; Sonderup, Mark W; Cook, Nicola A; Waked, Imam; Spearman, C Wendy; Taylor-Robinson, Simon D. Hepatitis C treatment: where are we now? *Int J Gen Med* 2017; 10: 39-52.