Articles

Infectious diseases genomic surveillance capacity in the Caribbean: a retrospective analysis of SARS-CoV-2

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Summary

Background The ongoing coronavirus diseases 2019 (COVID-19) pandemic with its numerous variants of concern has shown the need to have a robust and complete global infectious diseases genomic surveillance network worldwide. Various clinical and research institutions have stepped up to perform SARS-CoV-2 sequencing thus enhancing the understanding of this virus' global evolution. However, given that genomic sequencing capacities and capabilities are not available in every region or country, significant gaps exist, which lead to geographic blind spots. One such region is the Caribbean. This paper measures the Caribbean region's SARS-CoV-2 genomic sequencing capacity and highlights the need to improve further regional genomics surveillance capacities and capabilities, which are essential for efficient health interventions for infectious diseases.

Methods A map showing SARS-CoV-2 sequences available for each Caribbean Island was constructed using SARS-CoV-2 genomic, epidemiological and populational data obtained from GISAID, the World Health Organization, the United Nations, and the World Bank. The number of reported SARS-CoV-2 cases and the proportion of cases sequenced in each Caribbean Island was then analysed by the Gross Domestic Product per capita and political status.

Findings As of August 6, 2022, the number of SARS-CoV-2 sequences from the Caribbean are underrepresented with only 40,190 (1.07%) of the over 3.76 million documented cases sequenced, which is further exacerbated by a disparity based not only on the country's income but also on its political status (sovereign country versus dependent or integrated) and accessibility to sequencing technologies. There are a limited number of sequencing centres based in the Caribbean islands with the majority located on the American and European continents. Using mobile sequencing technologies while concomitantly investing in data analysis training could lead to greater and more sustainable coverage.

Interpretation Considering the Caribbean region's dispersed heterogeneous populations, varying political regimes, and resource-constrained healthcare systems, further development of local next-generation sequencing capacity and capabilities in the Caribbean region is needed to achieve global public health goals.

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Keywords: Genomic surveillance; Caribbean; SARS-CoV-2

Introduction

The use of next-generation sequencing (NGS) technology has proven very useful in gaining a better understanding of microbial evolution and transmission in numerous settings which is key to the One Health approach to disease prevention and control.¹ The new respiratory coronavirus disease (COVID-19) first observed in China demonstrated how important





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Research in context

Evidence before this study

A search of PubMed was conducted in order to identify SARS-CoV-2 sequencing and epidemiological studies done in the Caribbean region. Few studies assessing SARS-CoV-2 sequencing in the Caribbean were found. One early study highlighted the sparsity of genome sequencing capacity in Latin America and the Caribbean (LAC) prior to the COVID-19 pandemic and remained limited up to 2020, two studies addressed geographically limited to SARS-CoV-2 sequences from the Dominican Republic or from Puerto Rico only. A more recent publication described the implementation of a regional network for COVID-19 genomic surveillance in LAC but it initially included only four Caribbean members.

genomic sequencing is for health intervention. NGS revealed that this etiological agent, SARS-CoV-2,² was a novel coronavirus, and within a few weeks, the availability of the genome sequence of this virus permitted the design of molecular diagnostic tools to efficiently track the spread of this virus worldwide.

Further, ongoing sequencing of the SARS-CoV-2 genome helped answer numerous crucial questions throughout this pandemic as it relates to the evolution, transmission, and identification of new mutations and their potential impacts in terms of disease severity, vaccine escape, and transmissibility. The increased use and availability of genomic surveillance tools have linked each COVID-19 wave as originating in different geographical regions caused by new sequence variants.3-11 A designation of a new SARS-CoV-2 variant requires at least one mutation to differentiate it from other related viruses of the same species. New variants are classified as a variant of concern (VOC) if they are associated with demonstrated changes in transmissibility, virulence, or control measures and as a variant of interest (VOI) based on their likelihood to cause changes that can significantly negatively impact public health.11 Thus, genomic sequencing has proved to be an essential tool needed to monitor the local and global evolution and circulation of pathogens. Continuous genomic surveillance is key for timely implementation of appropriate public health measures adapted to the specific needs of each island.^{12,13} This is only possible if the generated microbial genomic data from each geographic region is shared in a timely manner. The Global Initiative on Sharing Avian Influenza Data (GISAID) is to date the most popular repository for SARS-CoV-2 genome sequence sharing.¹⁴ In addition to offering a forum where data exchange processes coupled with quality sequence displays and analytical tools can take place, GISAID also has

Added value of this study

This situational report provides an updated assessment of SARS-CoV-2 genomic surveillance capacity within 30 Caribbean islands/countries by tabulating publicly shared genome data generated from this region of the world and then analysing how factors such as socio-economic status and political structure influence the availability and accessibility of next-generation sequencing for pathogen surveillance.

Implications of all the available evidence

The present underrepresentation of Caribbean SARS-CoV-2 genome sequence data in global datasets needs to be addressed. The development of endogenous genomics sequencing capacity and capability will be key to improving health emergency preparedness and future responses to pathogens of epidemic and pandemic potential.

implemented an access governance mechanism which helps recognize the contribution of data generators.¹⁴

Presently, there is limited genomic sequencing data from the Caribbean region. This region of the Americas can be characterized as being heterogeneous in nature from several standpoints. It comprises both insular and continental states with income levels that range from very low to very high; populations that have varying administrative and political governance systems. The Caribbean region's diverse population of approximately 44 million persons is spread over multiple islands that are serviced by a just as varied mix of healthcare resources and services. Additionally, besides being a major tourist destination, notable inter-regional migration between the islands takes place which is conducive to the exchange and dissemination of pathogens. Few studies assessing SARS-CoV-2 sequencing in the Caribbean were found. One early study highlighted the sparsity of genome sequencing capacity in Latin America and the Caribbean (LAC) prior to the COVID-19 pandemic and remained limited up to 2020, two studies addressed geographically limited to SARS-CoV-2 sequences from the Dominican Republic or from Puerto Rico only.^{15,16} A more recent publication described the implementation of a regional network for COVID-19 genomic surveillance in LAC but it initially included only four Caribbean members.17 The WHO recommends that at least 10% of the PCR-positive SARS-CoV-2 sentinel surveillance samples should be sequenced and depending on resources availability, they propose alternatives for sequencing a minimum number of samples per week (n = 15) to ensure that sequence data is uploaded as quickly and as regularly as possible to publicly accessible databases.18 The purpose of this study is to map out the current status of SARS-CoV-2 genomic sequencing capacity against the complex geopolitical landscape of the Caribbean.

Methods

Design and setting

This is a population-based retrospective observational study using genomic and COVID-19 surveillance data collected from the Caribbean. For the purposes of this study, the Caribbean region was defined as all the territories in the Caribbean Sea, thus excluding continental Central and South American Caribbean countries and is presented in Table 1.

Data sources

SARS-CoV-2 genome sequence and epidemiologic information for the Caribbean region were obtained from GISAID (https://www.gisaid.org/) and the World Health Organization portal and dashboard, the later only for Bonaire, Saba and Sint Eustatius (https://portal. who.int/report/eios-covid19-counts/ and https://covid19. who.int, respectively), on August 6, 2022. Vaccination data were obtained from the WHO (https://covid19. who.int/table). Each island's population, Gross Domestic Product (GDP) in US dollars and GDP per capita data for 2020 (value to current) if available were retrieved from the United Nations Statistic Division (https:// unstats.un.org/home/) on January 7, 2022. Bonaire and Sint Eustatius population and GDP data for 2019 were extracted from StatLine (https://opendata.cbs.nl/ statline/#/CBS/nl/). Saint Barthelemy and Saint Martin GDP in Euro from 2014 were retrieved from the Institut d'émission des départements d'outre-mer (IEDOM) (https://www.iedom.fr/IMG/rapport_annuel_ iedom_st-barthelemy_2020/#page=1 and https://www. iedom.fr/IMG/rapport_annuel_iedom_st-martin_2020/ #page=1). The U.S. Virgin Islands GDP data for 2020 was retrieved from the U.S. Bureau of Economic Analysis (https://www.bea.gov/data) on March 30, 2022. Guadeloupe and Martinique GDP data for 2020 in Euro were found on the Institut national de la statistique et des etudes economiques (https://www.insee.fr/fr/ statistiques/5020211). Each island's income categories were found on the World Bank data website (https:// datahelpdesk.worldbank.org/knowledgebase/articles/ 906519), and when not available such as for the dependent territories or integrated areas, the income category of the affiliated country was used. The population densities for each island were retrieved from the United Nations (https://population.un.org/wpp/Download/ Files/1_Indicators%20(Standard)/EXCEL_FILES/1_General/ WPP2022_GEN_F01_DEMOGRAPHIC_INDICATORS_ COMPACT_REV1.xlsx).19 Bonaire, Saba and Sint Eustatius population density were not available in the above database and were calculated based on the following

database and were calculated based on the following equation: total population/land area (km²). No ethical review board approval was sought given that all data used in this study are publicly available and datasets are anonymized.

Participants

The study population used in this analysis included all SARS-CoV-2 epidemiologic and genomic surveillance data in the Caribbean region available during the study period of December 2019 to August 6, 2022.

Measures and variables

In this study, we analyzed the total numbers of SARS-CoV-2 genome sequences, VOC and VOI sequences, total number of COVID-19 cases and COVID-19 deaths and the vaccination coverage for each Caribbean Island studied (Table 1). The VOC and VOI included in this study were Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Lambda (C.37), Mu (B.1.621), Delta (B.1.617) and Omicron (B.1.1.529) assigned Pangolin lineages on GISAID. Sequence submitter information was retrieved from GISAID and used as a surrogate geographic locator to where the sequencing was performed. The GDP per capita was calculated by dividing GDP per population if it was not available on the United Nation Statistic Division's website. GDP data given in Euro currency was converted to U.S. dollars using the year's average (USD 1.142 for 2020) on Exchange Rates (https://www.exchangerates. org.uk). The study period which covered more than 2 years starting from December 1, 2019, to August 6, 2022, was chosen to include all cumulative COVID-19 data from the emergence of the SARS-CoV-2 virus until the date the data were retrieved.

Analysis and statistical methods

The case-fatality ratio based on the retrieved data of documented COVID-19 deaths and confirmed COVID-19 cases was analyzed. COVID-19 prevalence was calculated based on COVID-19 confirmed cases over the population for each island. A Caribbean geographical map was then constructed using the geographic information system QGIS (v3.20.3, https://qgis.org) (Fig. 1). Spearman's rank correlation for the GDP per capita analysis, Mann–Whitney–Wilcoxin Test for the political status analysis and interquartile range (IQR) analysis were performed using R (v4.2.0) in Rstudio (v2022.07.1).

Role of the funding source

No funding source was required to complete this study.

Results

Table 1 provides details of the SARS-CoV-2 sequences obtained and the epidemiologic characteristics for this virus in the Caribbean region. In the Caribbean, island population sizes vary greatly from a low of 1911 in Saba to 11,402,528 in Haiti. As of August 6, 2022, 3,759,226 confirmed COVID-19 cases were recorded in the 30

	2020							No. of SARS-CoV-2 sequences per year											Cumulative No. of SARS-CoV-2 sequences										Proportion of cases sequenced (%)		
	2020 Variants								202	2021 /ariants					2022 Variants				Variants									Per year			
· ·		varia	ants						varia	ints							-	_													
Caribbean Islands	Alpha	Gamma	Delta	Others / Unknown	lotal	Alpha	Beta	Gamma	Delta	Lambda	Mu	Omicron	Others / Unknown	Total	Delta	Omicron	Others / Unknowr	Total	Omicron	Delta	Alpha	Beta	Gamma	Lambda	Mu	Others / Unknown	Fotal	2020	2021	2022 Cumulative	
Anguilla	0	0	0	0	0	2	0	0	40	1	0	7	8	58	2	33	2	37	40	42	2	0	0	1	0	10	95	0	3.49	1.9 2.62	
Antigua and Barbuda	0	0	0	2	2	20	2	3	115	0	0	18	7	165	0	47	5	52	65	115	20	2	3	0	0	14	219	1.27	3.99	1.16 2.50	
Aruba Barbados	0 4	0	0	11 2	11 6	551 45	4	123 5	1863 44	2 0	94 1	17 6	457 7	3111 108	1	333 45	0	334 45	350 51	1864 44	551 49	4	123 5	2	94 1	468 9	3456 159	0.2	22.79 0.39	1.44 8.17 0.07 0.17	
Bonaire	0	0	0	0	0	183	0	1	746	0	10	66	21	1027	7	628	0	635	694	753	183	0	1	0	10	21	1662	0	32.49	10.98 18.25	
British Virgin Islands	0	0	0	0	0	2	0	2	56	0	62	27	29	178	0	17	0	17	44	56	2	0	2	0	62	29	195	0	5.63	0.44 2.73	
Cayman Islands Cuba	4 0	0	0	9 40	13 40	34 0	1	1	37 2	0	2 0	0 96	13 1063	88 1162	0	0 303	0 16	0 319	0 399	37 2	38 0	1	1	0	2 0	22 1119	101 1521	3.99 0.34	1.04 0.12	0 0.34	
Curacao	0	0	0	40	40	318	0	14	2 591	0	22	90 49	60	1054	18	809	0	827	858	609	318	0	14	0	22	100	1921	0.96	6.58	3.33 4.26	
Dominica	0	0	0	1	1	4	0	0	13	0	0	0	10	27	1	10	0	11	10	14	4	0	0	0	0	11	39	1.04	0.4	0.14 0.26	
Dominican Republic	1	1	0	52 0	54	19 3	0	60 0	582 48	6 0	120 0	57	248 7	1092 58	0	313 0	2	315 0	370	582 48	20 3	0	61 0	6 0	120 0	302 7	1461 58	0.03	0.44	0.15 0.23	
Grenada Guadeloupe	0	0	0	26	0 26	3 136	4	1	48 1548	0	0	0 48	132	58 1869	0	409	0	411	457	48 1550	3 136	4	1	0	0	158	2306	0	3.96	0 0.31 0.31 1.24	
Haiti	0	0	0	159	159	2	0	93	15	0	6	5	29	150	1	71	0	72	76	16	2	0	93	0	6	188	381	1.59	0.93	1.18 1.18	
Jamaica	5	0	0	9	14	216	0	0	464	0	43	139	27	889	1	1132	0	1133	1271	465	221	0	0	0	43	36	2036	0.11	1.1	2.13 1.39	
Martinique Montserrat	0	0	0	0	0	264 2	2	5	1507 12	0	0	74 0	425 0	2277 15	5	1045 12	246 0	1296 13	1119 12	1512 13	264 2	2	5	0	0	671 0	3573 28	0	5.26 46.88	0.8 1.69	
Puerto Rico	0	0	0	295	295	980	1	67	3562	6	64	1251	685	6616	1	4776	2	4779	6027	3563	980	1	67	6	64	982	11690	0.39	3.64	0.79 1.36	
Saba	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 0.00	
Saint Barthelemy Saint Kitts and Nevis	0	0	0	2	2 3	0	0	0	12 2	0 42	0	0 3	0	12 48	0	0 11	0 12	0 23	0 14	12 2	0	0	0	0 42	0	2 16	14 74	1.06 9.38	0.78 1.66	0 0.27 0.65 1.14	
Saint Kitts and Nevis Saint Lucia	3	0	0	3	6	54	0	0	2 56	42 0	0	3	20	48	0	43	3	46	45	2 56	57	0	0	42	0	26	74 184	9.38	1.66	0.65 1.14 0.32 0.66	
Saint Martin	0	0	0	10	10	0	0	0	28	0	0	169	2	199	0	116	0	116	285	28	0	0	0	0	0	12	325	1.01	6.35	1.54 2.79	
Saint Vincent and the Grenadines	0	0	0	1	1	0	0	48	50	0	22	26	22	168	11	39	3	53	65	61	0	0	48	0	22	26	222	0.87	2.88	1.54 2.36	
Sint Eustatius	0	0	0	4	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	4	21.1	0	0 0.36	
Sint Maarten The Bahamas	0	0	0	0 25	0 25	436 75	1 0	1 2	1328 149	2 0	3 0	213 1	75 11	2059 238	1	526 0	0	527 0	739 1	1329 149	436 75	1 0	1 2	2 0	3 0	75 36	2586 263	0 0.32	56.71 1.43	9.23 24.02 0 0.72	
Trinidad and Tobago	0	1	0	64	65	9	0	1118	691	0	0	17	241	2076	124	1088	1	1213	1105	815	9	0	1119	0	0	306	3354	0.91	2.48	1.5 1.95	
Turks and Caicos Islands	0	0	0	0	0	11	0	2	29	0	2	0	11	55	0	17	0	17	17	29	11	0	2	0	2	11	72	0	2.27	0.56 1.14	
United States Virgin Islands	0	0	2	21 779	23	133	0	2	677	0	6	385	19	1222 26153	1	944	1	946	1329 15443	680 14446	133 3516	0	2	0	6	41	2191	1.14	17.35	7.35 9.99	
Total Average	17 2.13	2 0.25	2 0.25	779 97.38	800 100.00	3499 13.38	16 0.06	1549 5.92			457 1.75	2676 10.23	3630 13.88	26153 100.00	177	12767 96.45	293 2.21	13237	15443 514.77	14446 481.53	3516 117.20		1551 51.70			4702 156.73	40190 1339.67	0.25 1.64	1.45 7.77	0.81 1.07 1.63 3.16	
Standard Deviation		0.25		59.96	59.84				793.38					1378.72		903.00				795.30						288.76		4.08	14.03	2.72 5.42	
	D-19 cases Epidemiology												Demographics Political status																		
Confirmed COVI							cases	5				Ep	oidemi	ology							Demo	ograp	hics					Pol	litical	status	
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Legend. D: Dependant territory, HI: High income for the island, HI^a: High income for the affiliated country as data for the island was not available, I: Integrated area, LMI: Lower middle income, NA: not applicable, S: Sovereign, UMI: Upper middle income. GDP values are for the year 2020, unless annotated with * or **, which are for the years 2019 and 2014, respectively.

 Table 1: Epidemiological characteristics of COVID-19 in the Caribbean region.

Articles

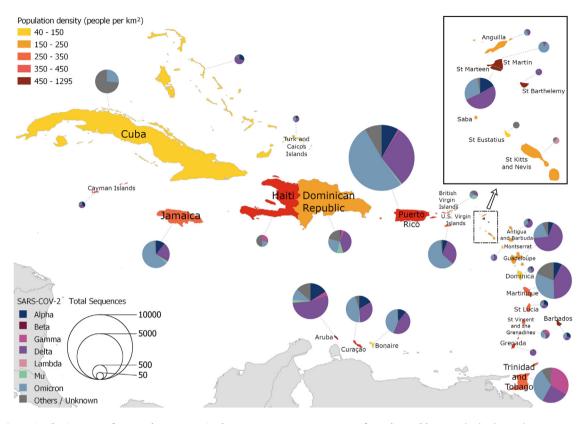


Fig. 1: Distribution map of VOC and VOI categorized SARS-CoV-2 genome sequences from the Caribbean. Each island's pie chart represents the cumulative number of sequences from each island available on GISAID, as of August 6, 2022. VOC and VOI are color-coded to identify their proportion, with non-categorized sequences being included in Other/Unknown. The map was built with the geographic information system QGIS.

Caribbean islands studied (total population of 43,532,696) since the beginning of the pandemic causing 31,019 documented deaths. Thus, 8.64% of this population has documented exposure to COVID-19 with an estimated case-fatality ratio of 0.83%. The prevalence ranged from 0.28% in Haiti to 56.38% in Martinique. The case-fatality ratio also varied from a low of 0.10% in Cayman Island and Saint Barthelemy to a high of 2.59% in Haiti. For those islands where vaccination data were available, coverage ranged from 1.43% in Haiti to 93.63% in Puerto-Rico.

Of the over 3.7 million COVID-19 cases documented in the 30 Caribbean islands reviewed in this study, only 40,190 (1.07%) sequences were uploaded onto GISAID as of August 6, 2022 (Table 1 and Fig. 1). Most of the 40,190 sequences from the Caribbean were from Puerto-Rico (11,690; 29.08%). However, these sequences from Puerto Rico represented only 1.36% (11,690/859,663) of their documented COVID-19 cases. At the other end, Saba did not have sequences available for the 674 documented cases and Sint Eustatius had only few sequences available (4/40,190; 0.009%) and sequenced 0.36% (4/1114) of their documented COVID-19 cases. The percent sequenced of confirmed cases showed that Sint Maarten had the highest proportion of sequenced samples (2586/10,765; 24.02%) whereas Cuba had the lowest proportion of sequenced samples (1521/1,108,492; 0.14%), when we exclude Saba that did not have sequences available.

Based on the sequence data available, the proportion of different variants varies between the countries (Table 1 and Fig. 1). Omicron was the most frequent variant with (15,443/40,190; 38.42%) and the most sequences originated from Puerto Rico (6027/15,443; 39.02%). Jamaica, Puerto Rico, U.S. Virgin Islands and Saint Martin had more than 50% of the sequences identified as Omicron lineage. The Delta variant was the second most common lineage with the available sequences (14,446/40,190; 35.90%). The Delta variant was found in 28/30 islands, except in Saba and Sint Eustatius. Of note, there was no sequence available for Saba, and only four for Sint Eustatius. The Alpha lineage was not found in seven islands, and present in others at varying rates. Based on the data analyzed, the most affected country was Cayman Island where it presented 37.62% (38/101) of the sequences submitted. The Beta

lineage, in the countries where it was present, represented less than 0.04% (16/40,190) of the sequences. Gamma is generally present in less than 10% of the sequences per island with the notable exceptions of Haiti, Saint Vincent and the Grenadines, and Trinidad and Tobago where it represented 24.41% (93/381), 21.62% (48/222), and 33.36% (1119/3354), respectively. Lambda was detected on a few islands and in general at less than 0.5% with the exception of Saint Kitts and Nevis where it represented 56.75% (42/74) of the sequences submitted by this country. Mu was not found in 16 countries. When present, Mu variant was generally below 5% with the exception of the British Virgin Islands, Dominican Republic and Saint Vincent and the Grenadines where it represented 31.79% (62/195), 8.21% (120/11,461), 9.90% (22/222) of the sequences, respectively. Moreover, the others/unknown category represented a significant proportion of the sequences in two countries: Cuba 73.57% (1119/1521) and Haiti 49.34% (188/381).

We hypothesized that the overall low proportion of cases sequenced, 1.07% (40,190/3,759,266), in the Caribbean could be explained by not only a disparity based on island income, but also by NGS sequencing capacity and state policies. For example, only 58 sequences from Grenada (Upper-middle income) are available to the global scientific community while 18,786 cases have been documented (0.31%) and only 381 sequences from Haiti (Lower middle-income) with 32,296 cases documented (1.18%) as of August 6, 2022.

We investigated the possibility of a correlation between the proportion of cases sequenced and the GDP per capita and found a Spearman's rank correlation coefficient of 0.168 (p-value 0.3708) indicating no relationship between these variables (Fig. 2A). We then explored whether the proportion of cases sequenced was influenced by the island's political status (dependent territory or integrated area versus independent sovereign state) given that this can materially impact the level of access and resources allocated to genomic sequencing (Fig. 2B). For all islands combined, the proportion of cases sequenced was 1.07%, with the average proportion of cases sequenced by island being 3.16% with a standard deviation of 5.42%. When dependent territories and integrated areas were combined, the proportion of cases sequenced were 2.08% with an average of 4.82% and a standard deviation of 6.79%. When analysing the independent sovereign islands only, the proportion of cases sequenced was 0.43% with an average of 1.00% and a standard deviation of 0.84%. Thus, this analysis revealed a five-fold difference between the proportion of cases sequenced as well as the average proportion of cases sequenced per island between the combined dependent territories and integrated areas group compared to the sovereign group. These group differences were statistically significant (p-value 0.01967). However, the standard deviations for the dependent territories and integrated areas group was high (6.79%). In our initial IQR analysis, three islands with the highest proportion of cases sequenced were pointed as potential outliers: Bonaire, Sint Maarten, and the U.S. Virgin Islands. When we remove from that group these three islands as potential outliers, we come with a proportion of cases sequenced for each island of 1.69%, average 2.11% and standard deviation 2.13%. After removal of these three outliers, there is a about threefold difference in the proportion of cases and two-fold difference in the averages between the dependent and integrated areas compared to the sovereign. However, these group differences were not statistically significant (p-value 0.08499).

We analyzed how the number of sequences and the proportion of cases sequenced varied throughout the years of COVID-19 pandemic (Table 1). There were 800,

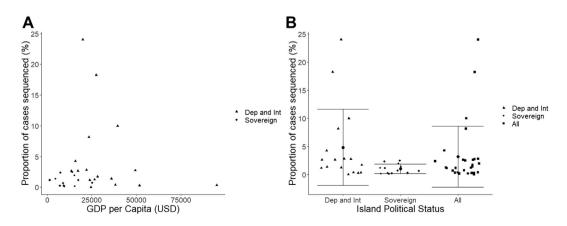


Fig. 2: Proportion of cases sequenced (%) in each Caribbean Island plotted against (A) economic (GDP per capita) and (B) political status. Islands were grouped based on their political status: Dependent and Integrated territories (Dep and Int), Sovereign (Sov), or All the islands (All). Triangles, diamonds and squares represent the proportion of cases sequenced for each island. Round dots and the bars, represent the averages and standard deviations, respectively, for each group.

26,153, and 13,237 sequences generated in 2020, 2021, and 2022 (up to August 6), respectively. For the years 2020, 2021 and 2022 (up to August 6, 2022), 0.25%, 1.45%, and 0.81% of COVID-19 cases were respectively sequenced. We assessed how many islands met the WHO alternative recommendation for genetic characterisation of at least a minimum of 15 PCR-positive sentinel specimens per week when available resources are limited. The average number of sequences per week per island was estimated for the first half of 2022. We took into consideration a possible one-month delay between specimen collection and genome data submission on GISAID and therefore calculated based on 26 weeks. Only 9 of 30 islands meet the alternative minimum of 15 sequences per week: Bonaire, Curacao, Guadeloupe, Jamaica, Martinique, Puerto Rico, Sint Maarten, Trinidad and Tobago, U.S. Virgin Islands.

We finally reviewed where the sequencing was performed for the SARS-CoV-2 samples from the Caribbean. We analysed the submitting laboratories entered in GISAID (Supplemental Table S1). Thirty-six laboratories submitted sequences to GISAID in the studied period. Of those, 53.8% (19/36) were on continental lands (Brazil, France, Netherlands, Panama and United States) while 47.2% (17/36) were on islands (Cayman Islands, Cuba, Dominican Republic, Guadeloupe, Jamaica, Martinique, Puerto Rico, Trinidad and Tobago).

Discussion

The ability of individual Caribbean islands to participate in genomic surveillance efforts varies since the capability to perform NGS varies among the islands. Some Caribbean islands benefit from a network set up by the Pan American Health Organization (PAHO) for the LAC region and have access to PAHO'S Regional Reference Laboratory which is based in Trinidad and Tobago.^{17,20} The Caribbean islands currently participating in this network comprise Anguilla, Antigua and Barbuda, Bahamas, Barbados, Dominica, Dominican Republic, Haiti, Jamaica, Trinidad and Tobago, and Turks and Caicos. The Caribbean country that had the greatest number of SARS-CoV-2 sequences was Puerto-Rico which is an unincorporated territory of the United States. Some of the sequencing was performed in laboratories located on Puerto Rico with the rest sequenced in laboratories located on the continental United States. In general, most of the Caribbean islands ship their specimens to the PAHO regional laboratory in Trinidad and Tobago or to laboratories located on the American and European continents.

Different SARS-CoV-2 variants circulated throughout the Caribbean islands (Fig. 1). This variability in the variants seen in the Caribbean may be linked to the multiple international exchanges many Caribbean islands have with other countries, thus facilitating the introduction and then spread of more

transmissible strains. For example, the Omicron variant was first identified in several countries in November 2021.¹¹ Omicron is largely represented in this dataset, which is most likely a reflection that at this stage of the pandemic the importance of genomic surveillance and sequencing was becoming more and more evident, and a lot of effort was put into increasing the number of sequences done to detect this VOC, as well as improve the region's ability to detect other VOCs that might emerge in the future. Over the data capture time window that was analyzed, there was an increase in the proportion of cases sequenced from 2020 to 2021, however, not from 2021 to 2022. This decrease could be due to the fact that there are usually delays in submitting sequence data to GISAID, whereas data on COVID-19 confirmed cases are submitted and counted in a much shorter timeframe by WHO.

No clear correlation between the proportion of cases sequenced and GDP per capita was found (Fig. 2A). It is possible that the Caribbean Island political status is only one of several factors that can influence the island's ability to generate sequencing data (Fig. 2B). Sovereign island states had limited sequencing capabilities. Among the thirteen sovereign islands, only four locally generated genome sequences: Cuba, the Dominican Republic, Jamaica, and Trinidad and Tobago. However, since the original submission of this manuscript, Grenada has acquired NGS technology to perform SARS-CoV-2 sequencing. Presently, Grenada does not submit their sequence data to GISAID. Hence it is important to encourage countries that do commence genomic surveillance to submit these sequences to global dataset repositories such as GISAID for the benefit of those engaged in global surveillance research studies.

The WHO and the European commission for Europe recommend that at least 10% of the SARS-CoV-2positive specimens originating from sentinel sources be sequenced.¹⁸ While meeting this recommended number of sequences will depend on available resources and samples, surveillance systems should aim for a minimum of 15 SARS-CoV-2 PCR-positive sentinel specimens per week.¹⁸ It is of interest to note that while a few developed countries eventually achieved a rate of sequencing at least 10% of reported cases, there were no more than 4.5% of weekly global confirmed cases sequenced between September 2020 and October 2021.²¹ For the time period covered by this study, the Caribbean islands sequence data covers only 1.07% of the reported COVID-19 cases and less than a third met the minimum of 15 sequences per week. One possible solution to this low sequencing rate would be to set up a structured network of national pathogen genomics laboratories supported by regional and specialized centres, similar to what has been proposed for Africa by Inzaule et al.22 This requires capacity building within each Caribbean Island's national public health laboratories

and other non-governmental organizations, such as academic research centers and private laboratories, where epidemiological surveillance systems are already in place. NGS, and portable nanopore systems, in particular, offer a cost-efficient solution to develop a critical mass of expertise for operating sequencing facilities. Regional hubs should be set up to first train regional neighbours and then progressively transfer NGS skills and expertise throughout the region. Mobile sequencing units could also be deployed to respond to evolving situations. This would thus require that investments be made to train and develop a cadre of professionals who are specialized in bioinformatics, molecular epidemiology, infectious disease epidemiology, and public health in each island.^{22,23}

In order to effectively fight the virus that triggered the COVID-19 pandemic, the capacity to do genomic sequencing must be globally disseminated which implies that all Caribbean countries procure the technological capacity to identify and follow any emerging variants of concern or interest and then correlate them with their severity in order to take appropriate public health intervention measures. The path of many epidemics is typically unpredictable with the risk of new, more virulent or transmissible variants still unknown.24,25 The WHO recommends the use of genomic surveillance to help monitor and track pathogens that have epidemic or pandemic potential and thus help identify appropriate public health measures.13 Any insights gleaned from genomic surveillance of pathogens must then be made accessible and understandable for the general public, private institutions, and governments.26 This is an essential step in order to streamline local to global public health-decision making and action.13

The implementation of genomic capacity has proved to be extremely useful in the fight against epidemics such as Ebola in some sub-Saharan countries since it has made it possible to obtain real-time information to refine public health intervention measures.1 Uganda was able to successfully implement a genomic surveillance program in its fight against COVID-19 thus showing that it is possible for other developing countries like those situated in the Caribbean to do the same.27 Major investments in genomics capacities and capabilities during the COVID-19 pandemic has increased the number of countries able to conduct sequenced-based public health surveillance.28 The establishment of COVID-19 genomic sequencing platforms can also be leveraged against other infectious diseases such as HIV, malaria and an ever-increasing number of antimicrobial resistance pathogens which present a clear and present danger to those living in the Caribbean region.²⁹ Carlson and Phelan (2022)³⁰ discuss cases of other zoonotic coronaviruses in humans in the 2010s in Haiti that did not lead to a pandemic, and the need for international notification law reform to respond to One Health.

Limitations

We used the data available on GISAID as of August 6, 2022. There can be delays in submitting data to this platform and there are other public repositories to which sequences may be submitted to. Another limitation is that many countries worldwide shared only a fraction of the SARS-CoV-2 genome data from their territory.²¹ Hence, the data used in this situational report might not have captured all of the sequences that might have been conducted during this study's time period. Further, genomic sequencing is not being done on a regular basis in most Caribbean islands and so it is not possible to accurately estimate the real burden of each COVID-19 variant in these islands. It is also not possible to know what the contribution was, if any, of each COVID-19 variant wave that affected these countries, their risk of transmission in the Caribbean environment or the severity of these variants on clinical manifestations. We also used the submitting laboratories as a surrogate to represent the laboratories generating the sequence data, however, this may not provide a true picture in certain cases. The COVID-19 confirmed cases data were obtained from WHO and used to calculate the proportion of cases sequenced. These confirmed cases, however, most likely represent an underestimate of the true number of COVID-19 cases in a population since it is based only on those diagnosed and reported by the country's health surveillance system.

Conclusion

This situational report described the capacity and capabilities of the countries in the Caribbean region to perform pathogen genomic sequencing and surveillance. The region showed notable successes, exemplified by the significant numerical increase in the number of sequences generated from 2020 to 2021 and the PAHO COVID-19 genomic surveillance regional network development. Our study has revealed that pathogen genomic sequencing and surveillance capacity is still limited and unevenly distributed throughout the islands. The SARS-CoV-2 pandemic has opened a window of opportunity for many Caribbean islands to develop the capacity and attendant cadre of expertise to implement and employ the use of genomics in their present public health surveillance systems. The development of a Caribbean based genomic sequencing network wherein all members have local accessibility to NGS technology is a critical step needed in order to improve surveillance in this region of the world. Such an improvement in genomic surveillance capacity could not only help healthcare providers in the Caribbean develop and implement better intra-country public health responses, but this would also greatly enhance global surveillance efforts to combat this pandemic and help in the identification of appropriate intervention strategies to deal with any new emergent SARS-CoV-2

strains. It would also help this region to be better able to counter current and future infectious diseases and hence contribute to the emergence of a healthier world for all. As genomics technologies and know-how are essential for global health, we concur with WHO science council that genomics potential will not be fully achieved unless globally deployed and sustainably supported in all countries.²⁸

Contributors

M.A.B.L: Conceptualisation, data validation and analysis, methodology and original draft writing. M.S.F.: Conceptualisation, data analysis, methodology, writing. M.R.I.: Data collection, data validation and analysis, data visualisation. M.B.: Conceptualisation, data analysis, methodology, writing. S.I.: Conceptualisation, coordination, data collection, data validation and analysis, methodology, writing.

Editor's note

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Declaration of interests

The authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi. org/10.1016/j.lana.2022.100411.

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