Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 in Latin America and the caribbean region: Symptoms and morbidities in the epidemiology of infection

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Abstract

The COVID-19 pandemic has widespread economic and social effects on Latin America (LA) and the Caribbean (CA). This region, which has a high prevalence of chronic diseases, has been one of the most affected during the pandemic. Multiple symptoms and comorbidities are related to distinct COVID-19 outcomes. However, there has been no explanation as to why different patients present with different arrays of clinical presentations. Studies report that similar to comorbidities, each country in LA and the CA has its own particular health issues. Moreover, economic and social features have yet to be studied in detail to obtain a complete perspective of the disease in the region. Herein, the impact of demographic and economic characteristics in LA and the CA on COVID-19 are presented in combination with symptoms and comorbidities related to the disease as important aspects that can influence management and treatment.

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Introduction

In May 2020, only two months after COVID-19 was declared a pandemic by the World Health Organization (WHO), Latin America (LA) and the Caribbean (CA) became COVID-19 epicenters, concentrating over 27% of the deaths caused by COVID-19 worldwide. As of April 13, 2021, South America had over 22 million confirmed COVID-19 cases, and Central America and the CA had over 3,800,000 million cases [1], with 597,000 deaths in South America and 239,000 in Central America and the CA (Worldometers; URL: https://www.worldometers.info/coronavirus/, accessed on April 13, 2021). The high rates of poverty and inequality in combination with a high prevalence of chronic diseases and constrained health systems have fueled the pandemic in the region, and the number of cases is still growing [2].

Brazil, Mexico, Colombia, Argentina, and Peru have had the highest number of deaths in the region, with Brazil and Mexico showing the highest death tolls worldwide after the United States and India (the mortality rate in Brazil is 2.6% and 9.1% in Mexico (Worldometers; URL: https://www.worldometers.info/coronavirus/, accessed on April 13, 2021). Projections of the death toll forecast estimates in the region could reach over 2,706,765 deaths by May 1, 2022 (Institute for Health Metrics and Evaluation; URL: https://covid19.healthdata.org/, accessed on January 12, 2022). Moreover, given the complex transmission dynamics associated with the emergence of new SARS-CoV-2 variants, the high rates of subclinical infection, and inconsistent and insufficient diagnostic testing from country to country, there will be an underestimation of the true number of COVID-19 cases and deaths attributable to this disease [3].

In addition to the health impact of SARS-CoV-2, the economic burden that the pandemic has imposed on LA and CA countries that were already in a fragile economic situation places the region in great danger of social consequences associated with the disease in

the following years. Therefore, to reduce the regional impact of the COVID-19 pandemic, clinicians should take into consideration the clinical manifestations of the disease in each country and carry out detailed studies of the symptoms, comorbidities, and the relationship between them to improve the clinical interventions that could successfully prevent hospitalizations and deaths.

COVID-19 vaccine in LA and the CA

With respect to continental coordination and the management of the pandemic in the region, organizations such as the Pan-American Health Organization (PAHO) have played a pivotal role in providing relief to countries by providing valuable advice regarding both public health and economic aspects of the pandemic. When the surge of the pandemic began in the region in May 2020, PAHO Director Dr. Carissa Etienne expressed concern about "the poor and other vulnerable groups at greatest risk, including those living in the Amazon Basin, particularly indigenous communities; women, who make up 70% of the health workforce in the Americas; people of African descent; migrants in temporary settlements; and prisoners in crowded jails" (PAHO; URL: https://www.paho.org/en/news/19-5-2020-paho-director-calls-protect-vulnerable-groups-effects-covid-19-pandemic). Even with highly effective vaccines against the original SARS-CoV-2 strain available in various countries, particularly in the northern hemisphere of the continent as the FDA approved the emergency use of the Pfizer vaccine in the US in December 2020 (FDA; URL: www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/pfizer-biontech-covid-19-vaccine#:~:text=On%20Deceber%2011%2C%202020,of%20age%20and%20older), the PAHO reported the surge of infections and deaths in Manaus, Brazil due to a new, more transmissible variant of the virus in January 2021 [4]. Although authorities were encouraged to double their efforts in vaccination campaigns despite the circulation of these new variants, WHO officials expressed concerns that neighboring countries could be affected unless Brazil took aggressive health measures to stop the spread of variants (Reuters; URL: https://www.reuters.com/article/us-health-coronavirus-brazil/who-warns-on-brazil-covid-19-outbreak-as-bolsonaro-blasts-senate-inquiry-idUSKBN2BW2BP).

In March 2021, the PAHO also noted rising infections in Paraguay, Uruguay, and Chile and declining infections in Mexico and Central America, except in some areas of Guatemala and Panama (PAHO; URL: https://www.paho.org/en/news/23-3-2021-paho-director-warns-covid-19-surge-americas), while reporting a rise in the number of infections in other countries of the Caribbean, such as Cuba and the Bahamas (PAHO; URL: https://www.paho.org/en/news/23-3-2021-paho-director-warns-covid-19-surge-americas).

The rollout of vaccination in the region has been slow, with some exceptions, and there is increasing concern that widespread vaccine access in some countries could be delayed until late 2022. According to the New York Times vaccine tracker, Chile was the leader in the region during the initial vaccination campaigns, with 64 doses per 100 people, followed by Uruguay with 31 doses per 100 people and Dominica and Barbados with 25 and 23 doses per 100 people, respectively. At that time, the remaining countries in the region had vaccinated less than 5% of their populations (The New York Times; URL: https://www.nytimes.com/interactive/2020/us/covid-19-vaccine-doses.html).

The emergence of the Omicron variant in November 2021 highlighted the ongoing challenges of life with SARS-CoV-2 worldwide. Predicting what course the variants will take becomes difficult due to the complexity of viral evolution; pre-existing immunity related to vaccines or previous infections is only one aspect that requires analysis. Additionally, the impact of demographic and economic characteristics in combination with comorbidities highly present in specific populations and disease presentation of new variants will have to be considered to anticipate the course of the pandemic and to expand the world's capacity to manage SARS-CoV-2 outbreaks. This is particularly relevant in regions with low vaccination rates where devasting variants are likely to emerge.

Demographic and economic features in LA and the CA

The LA and CA regions include 41 countries varying greatly in size and population. Eight out of the 24 countries in the CA had fewer than 100,000 inhabitants in 2009. Brazil is the largest country, both in territory and population (Statista; URL; https://www.statista.com/statistics/990519/largest-countries-area-latin-america), with 213 million inhabitants in 2021 (Worldometers; URL; https://www.worldometers.info/world-population/brazil-population/). Mexico is the second largest country, with 130 million inhabitants (Worldometers; URL: https://www.worldometers.info/world-population/mexico-population/). The Federation of Saint Kitts and Nevis is the smallest country in territory and population, with fewer than 50 thousand inhabitants (PAHO; URL: https://www.paho.org/en/saint-kitts-and-nevis). The area is widely known as the world's most unequal region [5,6]. According to the United Nations Development Programme (UNDP) report in 2010, inequality in the region has remained virtually unchanged since the 70s; it is 65% higher than in high-income countries, 36% higher than the Far East and 18% higher than Sub-Saharan Africa (UNDP; URL: https://www.latinamerica.undp.org/cont

ent/rblac/en/home/library/human_development/human-development-report.html). The richest fifth of Latin America's population receives nearly three-fifths of total income, whereas the poorest fifth receives just 3%, which is the lowest share among all regions of the developing world; this puts the region at an outstanding risk, not only due to the socioeconomic and sociopolitical environment but also due to the fragility of its health systems that are dependent upon economic and political policies during a pandemic.

The region has experienced fast and complex epidemiological changes in recent decades [7] in its increasing rates of noncommunicable diseases, while many existing endemic and emerging infectious diseases remain uncontrolled [8]. The balance of the burden between communicable and noncommunicable diseases varies greatly by country income group, confirming the heterogeneity of the region. In low-income countries, such as Bolivia, Paraguay and Peru, communicable diseases still exerted the most influence on years of life lost from 2000 to 2004. The mortality rate from transmissible diseases was 58/100,000 people and even more in the poorer countries of the region. In Haiti, the incidence of tuberculosis is seven times that of the rest of the LA and CA regions [9,10]. In 2006, 50% of all dengue cases in LA and the CA occurred in Brazil, and malaria was endemic in 21 countries [11,12]. HIV/AIDS is also a significant and growing problem, with the CA being the second most affected area worldwide [13]. Altogether, these findings illustrate a very complex and heterogeneous picture in the region with country (and even intracountry) differences [14].

Chronic diseases and COVID-19 in LA and the CA

Regarding the prepandemic prevalence of chronic diseases in the region, examining the data reveals some concerning patterns. It is estimated that as of 2000, noncommunicable diseases mostly related to chronic disorders were responsible for the majority of disabilities in LA and the CA; from this information, one can infer the current state of health of the population and its susceptibility to negative outcomes in response to the COVID-19 pandemic (PAHO; URL: https://www.paho.org/chi/index.php?option=com_content&view=article&id=128:enfermedades-no-transmisibles&Itemid=213). Among noncommunicable deaths, cardiovascular disease has the highest toll [15]. This condition is one of the primary predictive factors for the development of severe COVID-19 [16–21]. Other important health indicators that are fundamental in patients with COVID-19 disease including obesity, diabetes, and hypertension, are also common in the region.

In Brazil, the total projected number of deaths due to chronic disease by year are 928,000 (WHO Brazil; URL: https://www.who.int/chp/chronic_disease_report/media/brazil.pdf?%20ua=1). In Argentina, according to the WHO, chronic diseases accounted for more than 78% of the total deaths in 2016 (WHO Argentina; URL: https://www.who.int/nmh/countries/arg_en.pdf?ua=1), while by 2009, 27.8% of the total population was suffering from high cholesterol levels, 34.4% had high arterial pressure, 53.7% were overweight or obese and 11.9% were diagnosed with diabetes mellitus [22]. Nontransmissible and chronic diseases are the main cause of death in Uruguay, accounting for more than 40% of deaths. These diseases include hypertension and heart disease, chronic lower respiratory disease, cancer, and diabetes. The overall death rate associated with diabetes was approximately 20/100,000 people by 2018 (Ministerio de Salud Pública https://www.gub.uy/ministerio-salud-publica/comunicacion/publicaciones/mortalidad-enfermedades-transmisibles-uruguay-diciembre-2019). According to the Ministry of Health in Mexico, chronic diseases represent 7 of the 10 primary causes of death. The most relevant are diabetes and heart disease, both closely related to obesity. In Mexico, the prevalence of diabetes and hypertension is 18.4% and 10.3%, respectively, and the prevalence of overweight and obesity in adults older than 20 years is 75.2% (Instituto Nacional de Salud Pública; URL: https://ensanut.insp.mx/encuestas/ensanut2018/doctos/informes/ensanut_2018_presentacion_resultados.pdf). This is consistent with data from the last available epidemiological reports by LA countries, with Mexico scoring the highest in prevalence of hypertension at 20.9%, followed by Chile at 16% and Argentina at 13.5% of the total pool according to available reports.

With respect to metabolic disease, diabetes was primarily present in Mexico at a rate of 17.5%, followed by Brazil at 10.2% and Chile at 8.8%. Surprisingly, Venezuela had a low prevalence of diabetes mellitus in its cohort, with a rate of 0.6%. Obesity was highly prevalent in the entire population in Mexico at 16.7%, while Bolivia and Argentina had a prevalence of 5.6%. Given the impact of chronic conditions on COVID-19 outcomes once the pandemic began, these trends of chronic diseases were expected to translate into increased mortality-lethality rates. Indeed, an analysis of 728,282 patients positive for COVID-19 in eight LA countries (Brazil, Mexico, Colombia, Peru, Argentina, Venezuela, Ecuador, and Bolivia) during the first six months of the pandemic revealed that hypertension was the most frequent comorbidity related to COVID-19, with a rate of 12.1%, followed by diabetes (8.3%) and obesity (4.5%). These comorbidities were associated with poor outcome (Ministry of Health, Government of Chile; URL: https://www.minsal.cl) (Ministry of Popular Power for Health, Venezuela; URL: https://www.devex.com/organizations/ministry-of-popular-power-for-health-ministerio-del-poder-popular-para-la-salud-mpps-venezuela-143683) [23–25]. Similarly, according to a report

from the Ministry of Health in Uruguay, heart disease (48.1%) and diabetes (36.5%) were the most commonly found comorbidities related to COVID-19-associated deaths (https://www.gub.uy/ministerio-salud-publica/sites/ministerio-salud-publica/files/documentos).

COVID-19-related symptoms in LA and the CA

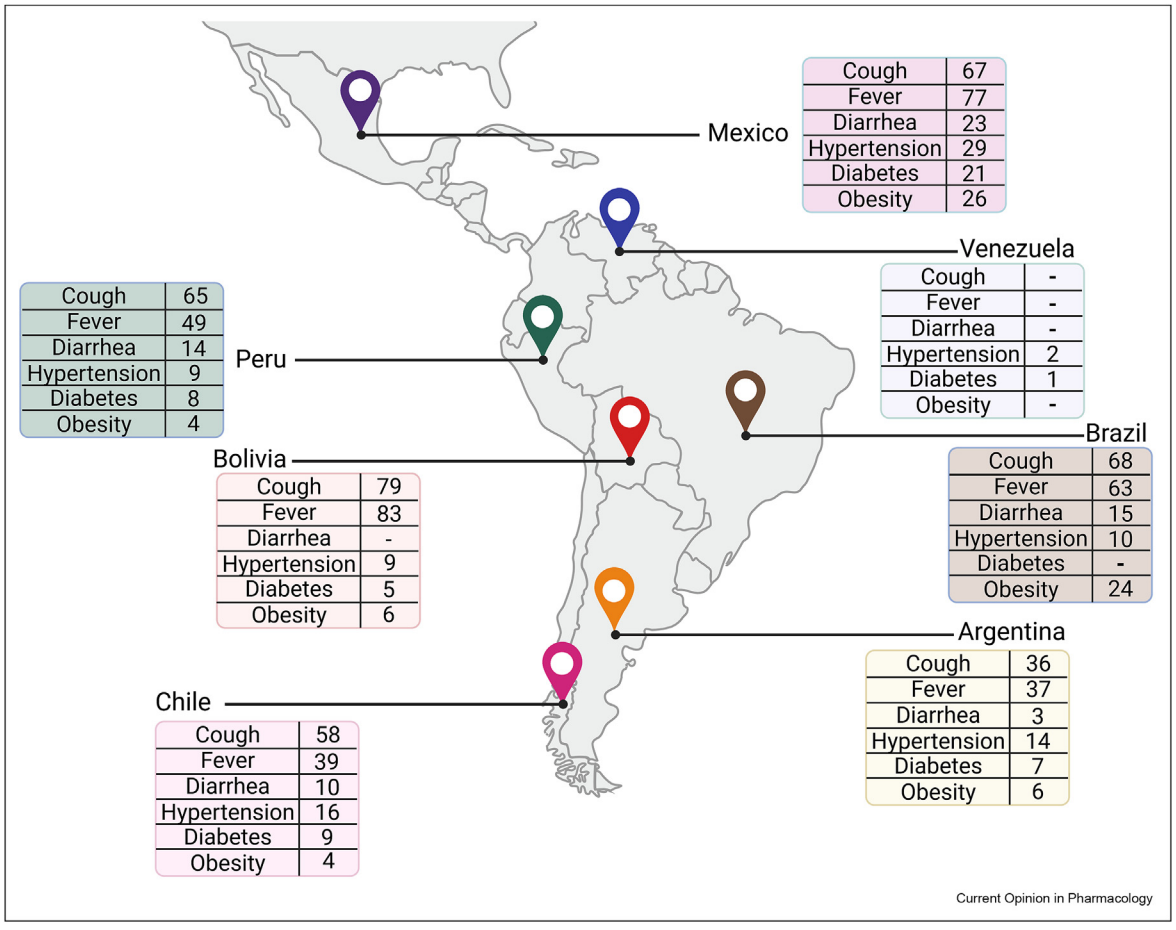
An analysis of Brazil, Mexico, Colombia, Peru, Argentina, Venezuela, and Bolivia with respect to COVID-19 shows that it manifests differentially among the countries of LA and indicates that fever is widely represented in LA, with frequencies as high as 83% in Bolivia, 77% in Mexico, 63% in Brazil and 49% in Peru. With respect to respiratory symptoms, cough is the most common symptom, including at least 67% of patients in both Mexico and Brazil and 79% in Bolivia. Dyspnea is a common symptom in Mexico at 28.7% and is as low as 4.3% in Argentina. Therefore, in contrast to first reports indicating fever and cough as the top symptoms in LA, fever is the fourth most common after cough, fatigue, and sore throat [24]. Interestingly, the same analysis emphasizes that the prevalence of diarrhea in these countries was higher than that reported in other regions worldwide. Diarrhea was present in 23% of patients in Mexico versus 3% of patients in Argentina; abdominal pain was also highly prevalent in Mexico, at 17%, and nausea and vomiting were as high as 8% in Peru [23,24,26]. The finding of gastrointestinal symptoms being common in LA may be related to the high prevalence of diarrhea in the region even before the SARS-CoV-2 outbreak. Moreover, the expression of angiotensin viral receptor 2 in the esophagus and small and large intestines, along with patients' positive stool samples and negative nasopharyngeal samples [27–30], emphasizes the need for adequate monitoring of patients with gastrointestinal symptoms, as they are likely to play a role in the dissemination of the disease.

One year after the pandemic began, examining behavior with a focus on Brazil was important because it was the country with the most cases and deaths in the region and was in the top five in the world; an investigation from Sao Paulo included 444 positive patients [31]; 55% of affected patients were female and 44.4% were between 20 and 39 years old. The most frequent comorbidities in this study were cardiovascular disease in 20.4% of the cohort and diabetes mellitus in 11.1%. The most common symptoms were headache (82%), myalgia (80%), anosmia (56%) and ageusia (56%), likely because most of the cases in this study were young adults. Another study from Bahia with 3896 patients revealed that diabetes and cardiovascular disease were significantly correlated with negative outcomes, as well as sore throat and shortness of breath [32].

With respect to Colombia, another severely affected country in the region, one study with a cohort of 44 patients [33] revealed that 65.9% of affected patients were male, with the majority belonging to the 70–79 years old age group (29.5%). The most common comorbidities were hypertension (40.9%), dyslipidemia (34.1%) and diabetes (18.2%). The most common symptoms were cough (93.2%) and fever (70.5%), and the least common was anosmia (only 9.1%). Regarding Argentina, in a study including more than 200,000 cases, the most frequent age at diagnosis was 18.8 years, with 50% of the cohort being male. The mortality rate was 5.3%. With respect to clinical characteristics, the most common symptoms were fever (58.5%), cough (58%) and sore throat (42.1%), and diarrhea (9.9%) was the most common gastrointestinal symptom. The most frequent comorbidities were hypertension (19.2%), diabetes (9.7%) and obesity (5.2%). Interestingly, most of the cases described in this cohort were in patients between 15 and 39 years old [34].

Mexico is the country in LA with one of the highest mortality rates in the world associated with COVID-19. The lethality of the virus in this country has been over 3 times higher than that reported in the Americas (WHO; URL: https://www.who.int/news/item/30-01-2020-statement-on-the-second-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-outbreak-of-novel-coronavirus-(2019-ncov)), which might be due in part to the epidemiological surveillance for COVID-19 which is carried out in Mexico through the Sentinel Surveillance System in which SARS-CoV-2 testing is performed only in 10% of the total cases, thereby overestimating the deaths associated with the infection (https://coronavirus.gob.mx/wp-content/uploads/2020/04/Lineamiento_de_vigilancia_epidemiologica_de_enfermedad_respiratoria-_viral.pdf). Additionally, the high lethality associated with COVID-19 in Mexico might be related to the high prevalence of chronic degenerative diseases in the country. In a study with a cohort of 38,000 COVID-19 positive individuals [35], most patients were between 41 and 60 years old, and males were most affected at over 58.3% of the patient population; the overall mortality rate was 10.2% with the most common comorbidities being hypertension, diabetes mellitus and obesity. In countries such as China, obesity is not considered a risk factor for poor prognosis due to COVID-19. There, the prevalence of obesity is 6.6% (more than 4 times lower than that in Mexico) [36–39]. In this sense, overweight and obesity in the Mexican population have been reported to increase mortality and the need for intensive care in people with COVID-19, especially in patients who also suffer from diabetes [40,41]. Therefore, obesity apparently plays a more important role in Mexicans than in other nationalities in the risk of poor prognosis associated with COVID-19.

Figure 1



Comparison of the most common symptoms and morbidities associated with COVID-19 in select studies from different Latin American countries. Data were retrieved and adapted from systematic reviews [24,42] that analyzed published articles and sources from official health organizations in Latin American countries. The frequencies of the total cases of symptoms and morbidities associated with COVID-19 are shown. Symbol – denotes not retrieved information.

Furthermore, COVID-19-associated lethality was distinct across different regions in Mexico, and these differences might be related to differences in the frequencies of comorbidities [25]. Thus, the development of COVID-19-associated symptoms and comorbidities might vary among geographical regions as illustrated in the analysis from Latin American countries when the pandemic began (Figure 1). Evidence shows that human genetics contribute to the onset of several chronic diseases, including those of an infectious nature [43,44]. The LA and CA regions consist of populations with heterogenic heritage [45–47]. Therefore, the complex intra- and intercountry heterogeneity in the region in combination with fragile economic and health systems and a high prevalence of chronic diseases emphasizes the need to study possible differences in the distribution of COVID-19-related symptoms and comorbidities and their effect on disease outcomes in distinct populations.

Remarks

Studies report that similar to comorbidities and symptoms, each country in LA and the CA region has its own particularities when it comes to COVID-19. Prevention strategies require continuous and detailed study of regional features to obtain a complete perspective of the disease, with the goal of designing guidelines for the management and treatment of each specific population.

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Authors' contributions

AP and NAF conceived and designed the study. JYA-C, SM, JT-F, GD and EL carried out the study. JYA, AP

and NAF wrote the manuscript. All authors have read and approved the manuscript for publication.

Conflict of interest statement

Nothing declared.

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