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# Simultaneous Circulation of DENV, CHIKV, ZIKV and SARS-CoV-2 in Brazil: an Inconvenient Truth

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ABSTRACT

The emergence of SARS-CoV-2 has prompted the mobilization of a network of public health laboratories to diagnose COVID-19 patients, trace contacts and identify hot-spot areas for active community transmission at the expense of arbovirus diagnosis and control practices. In this article, we discuss the unprecedented challenges faced by the Brazilian public health system in dealing with the incursion of SARS-CoV-2 in the midst of ongoing triple arboviral epidemics caused by dengue, chikungunya, and Zika virus. Finally, we highlight the importance of the introduction of one health approach as an effective inter-disciplinary response and management to mitigate the catastrophic effect caused by these pathogens.

## 1. Introduction

The triple epidemics caused by dengue virus (DENV), chikungunya virus (CHIKV) and Zika virus (ZIKV) represent a serious threat to health systems in several parts of the world, especially in tropical countries where mosquitoes from the genus *Aedes* are widespread [1]. Because *Aedes* mosquitoes are the common vector for these three viruses, their global distribution often overlaps [2]. As of September 19, 2020, according to the Brazilian Ministry of Health, the number of probable cases of dengue, chikungunya and Zika were 931,903, 71,698 and 6705, respectively (Fig. 1) [3]. Simultaneously, the country is facing the pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the etiologic agent of coronavirus disease 2019 (COVID-19). Brazil reported the first COVID-19 case in Latin America on 26 February 2020, which was diagnosed in a traveler returning to São Paulo after a work trip to northern Italy [4]. Since then, this highly pathogenic coronavirus has quickly spread to all Brazilian states, placing Brazil as the epicenter in the Americas and third most affected country in the world after the USA and India. As of December 11, Brazil has confirmed 6.7 million COVID-19 cases and 179,897 deaths, comprising over 55% of the total number of reported COVID-19 cases in Latin America [5,6].

Upon its emergence in the country, a network of public health laboratories was mobilized to diagnose COVID-19 patients, trace contacts and identify hot-spot areas for active community transmission [6]. Subsequently, due to rapid spread of the virus in Brazil, COVID-19 diagnosis had to be decentralized and many university and research laboratories became involved in SARS-CoV-2 diagnosis. Herein, we discuss the unprecedented challenges faced by the Brazilian public health system in dealing with the incursion of SARS-CoV-2 in the midst of ongoing triple arboviral epidemics.

## 2. Concomitant COVID-19 pandemic and triple arboviral epidemic

First, infection by SARS-CoV-2 or vector-borne viruses (DENV, CHIKV and ZIKV) may result in similar laboratory features and clinical symptoms during the early course of the disease, including fever, muscle ache and nausea. The similarities of clinical signs are most notable in dengue fever patients, which can also develop severe form of the disease [7–9]. Recently, some studies have reported the presence of cross-reactivity in serological tests between DENV and SARS-CoV-2, which can lead to false-positive among COVID-19 and dengue patients and vice versa [9,10]. Since the clinical management of COVID-19 and arboviral patients is quite different, differential diagnosis and the development of

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accurate tests are critical to assist clinicians during the therapeutic management of patients, especially in areas where is there a co-circulation of these pathogens.

Second, arboviruses have a seasonal pattern of incidence, which is often observed to increase at the beginning of the year due to the high temperatures and rainy season during the first half of the year with peak between March and April [11]. Interestingly, studies have been suggested that soon after 2015–2016 Zika epidemic in Brazil, the incidence of both Zika and dengue infections have declined. Following this period time, the number of dengue cases increased progressively in 2019 and the first quarter of 2020, accounting more than 2.1 million cases [12]. Paradoxically, there has been a decline in the number of dengue cases since March 2020 compared to 2019. This temporal scenario coincided with the increase in the number of COVID-19 cases in Brazil, which made health authorities and government officials direct all efforts to test and combat COVID-19 disease. Thus, this reduction can be attributed to the mobilization carried out by the state epidemiological surveillance teams and diagnostic laboratories to cope with the COVID-19 pandemic, causing a delay and underreporting for the cases of arboviruses [13].

Third, similar to other developing countries, Brazil has been facing several challenges for COVID-19 diagnosis, especially with regarding the lack of supplies and equipments required for SARS-CoV-2 detection [14]. Moreover, many laboratories redirected all their efforts to diagnose SARS-CoV-2, including the reference arbovirus laboratories, which had a direct impact on arbovirus detection. In this context, the Brazilian government has increased the number of tests for COVID-19 as the pandemic advance, but the rate of testing is still much lower compared to other countries. For instance, as of December 07, 2020 Brazil is doing 120,536 tests per million of its inhabitants, whereas the USA is doing 625,164 tests per million people, which represents 5-fold less testing (https://www.worldometers.info/coronavirus/). While current laboratory-based centralized RT-qPCR continues used as a gold standard method for the diagnosis of COVID-19 patients, the implementation of diverse and de-centralized diagnostic approaches will be of paramount importance [15].

Fourth, the COVID-19 crisis led to a reduction of population mobility as a result of social distancing measures imposed. Recently, Lorenz and co-workers hypothesized that social distancing practices to contain SARS-CoV-2-may have helped to reduce the true incidence of dengue and the other urban arbovirus in Brazil, since the introduction of viruses into areas is mediated by travel or circulation of infected individuals to other areas given the short flight capacity of mosquito vectors [16,17]. However, other factors should be taken into account to understand the officially reported arbovirus cases during the COVID-19 pandemic: i) *Aedes aegypti* mosquitoes are known to bite during daylight, [18] and with distribution in or around the houses and areas with high human density [19], this behavior may have facilitated the increase contact between the vector and susceptible humans during the social isolation; ii) the activities of community health workers responsible for surveillance programs was interrupted during the pandemic, which made it

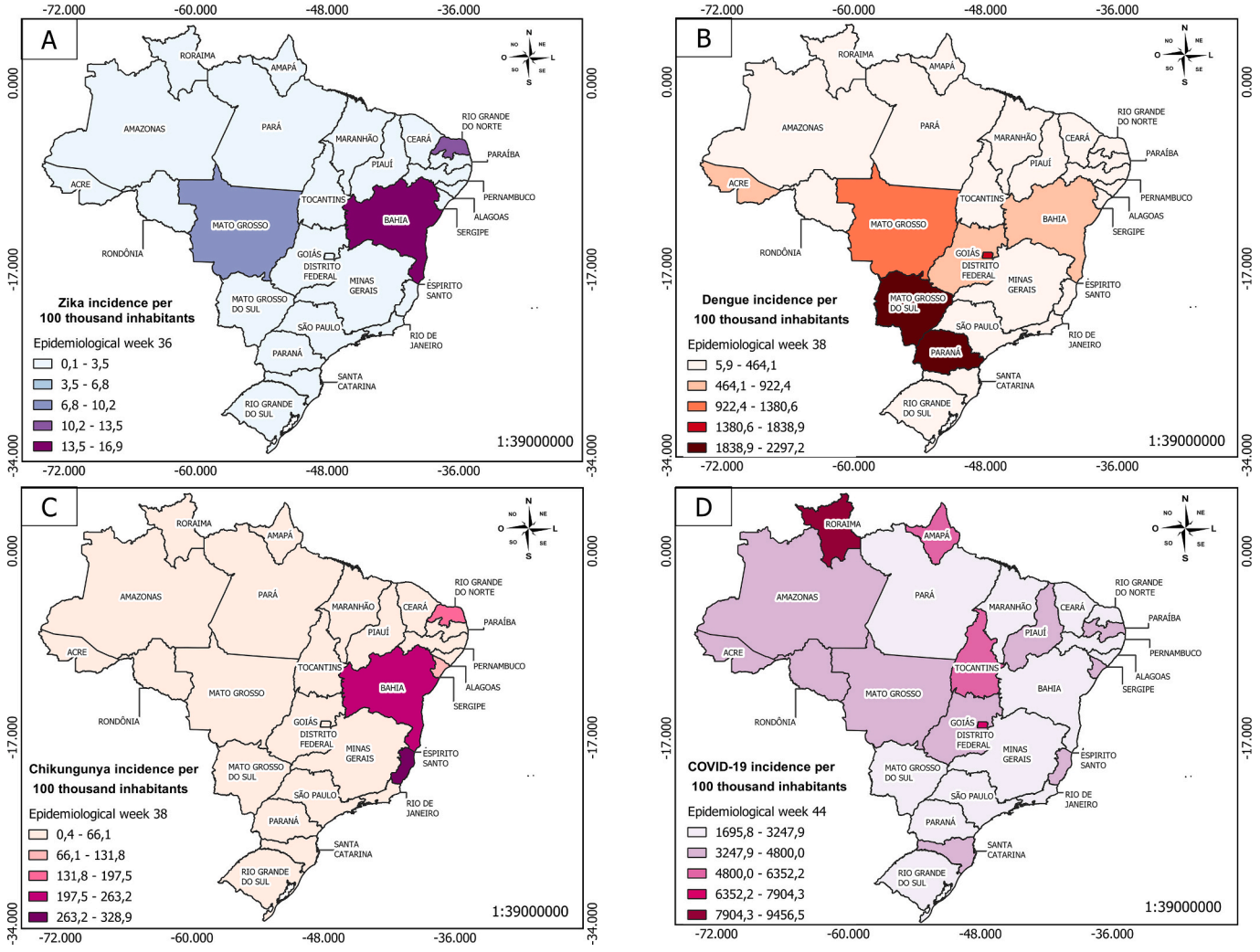


**Fig. 1.** Incidence of Zika, dengue, chikungunya and COVID-19 in all Brazilian states. A) Zika incidence rates per 100 thousand inhabitants. B) Dengue incidence rates per 100 thousand inhabitants. C) Chikungunya incidence rates per 100 thousand inhabitants. D) COVID-19 incidence rates per 100 thousand inhabitants.

difficult the application of larvicides inside households to eliminate larval mosquitoes, which have been commonly used to control vector-borne viral diseases and to reduce the contact between mosquito vectors and people [20]; iii) arbovirus testing was abruptly reduced since diagnostic resources were redirected for SARS-CoV-2.

## 3. Conclusion

The simultaneous circulation of SARS-CoV-2 and arboviruses in Brazil requires the integration of disease control measures and effective surveillance programs for these pathogens based on one health approaches. Early detection of arbovirus activity in new areas or increased viral activities in vector populations coupled with prompt medical attention to patients are key to successfully control the associated diseases and reduce their case fatality rate. The control of these urban epidemic arboviruses are based on actions focused on the *Aedes aegypti* mosquito, the main vector for these diseases in the Americas. Overall, these actions rely on two main pillars: (i) the control of various stages of *Aedes aegypti*, preventing the mosquito from developing from egg to adult or reducing its longevity or abundance and (ii) reducing the possibility of contact between the vector and humans, such as by application of repellents, wearing protective clothing to minimize mosquito bites and screening of doors and windows to prevent *Aedes aegypti* entering the home. These measures should be undertaken while observing the social distancing and hygiene practices currently being used by health authorities to control the COVID-19 pandemic, including the use of adequate personal protective equipment for COVID-19 prevention, not entering houses with suspected or confirmed cases of COVID-19 and maintaining a minimum two-meters distance from the residents of the homes.

Even though there is an approved vaccine for dengue in the country and there are currently four SARS-CoV-2 vaccines being tested in phase III clinical trials in Brazil, there is a pressing need for ZIKV and CHIKV vaccines. For this, government investment and public-private partnerships are essential to accelerate the development and approval of safe and effective vaccines against these devastating pathogens. But vaccines are not definitive approach to keep these viruses under control. Vaccine development must be coupled with the search for effective antivirals to treat infected patients since no vaccine is 100% effective and these viruses will likely continue to circulate in this tropical region of the world.

## Author statement

All authors contributed equally to this paper with the design of the manuscript, literature review and analysis, critical revision, edition, and approval of the final version.

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## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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