The Potential Influence Factors To Dengue Epidemic Changes In Different Countries During COVID-19 Pandemic

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Research Article

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Abstract

Background During the swooped coronavirus pandemic in 2020, the non-pharmaceutical interventions (NPIs) not only controlled the pandemic of coronavirus, but also had impacts on other infectious diseases. Dengue has become a disease that calls for key detection with it spreading rapidly worldwide in recent years. This study aims to discuss the impacts of the potential influence factors on dengue during the coronavirus according to the data of dengue pandemic of different countries around the world.

Methods We collected the data of 2019 and 2020 dengue cases from 57 countries around the globe. Through correlation analysis and rank sum analysis, we sought to discuss the potential effects of different factors during the outbreak of COVID-19 on dengue.

Results The results showed that dengue case subtractions had a significant correlation with the territorial area, the suffered and the deceased number of COVID-19 cases. Further rank sum analysis indicated that there is a significant difference in the number of dengue fever cases between the two years, countries with different continental locations, 2019 and 2020 GDPs per capita, the gaps between two years, territory areas, populations and coronavirus occurrences.

Conclusions The results altogether showed that the coronavirus pandemic affected dengue epidemic on a certain degree. Considering the epidemic of dengue is closely related to national economy, geography and demography, our results also further indicated that individual measures should be taken to suppress the development of dengue in different countries depending on their own circumstances, especially during major health events.

Background

SARS-CoV-2 is a newly discovered virus that can cause acute respiratory syndrome and further lead to specific inflammation, vessel damages, microangiopathy, extensive thrombosis and even death (1, 2). Its potent propagation and high mortality rate make coronavirus possible to spread furiously and become a global emergency, thus WHO declared COVID-19's pandemic in March 2020 (1–3). So far, different countries have implemented several non-pharmaceutical interventions (NPIs) to control its rapid dissemination such as quarantining the infected, tracking and isolating the close contacts, announcing the latest pandemic information, keeping social distancing (public lockdown and flux restriction) and even border restriction toward severe-pandemic regions (4–10). Those NPIs effectively inhibited the rapid coronavirus propagation (10, 11). However, to a certain extent, several other kinds of infectious diseases were also affected by the NPIs against COVID-19, for instance, it decreases the morbidity of malaria, measles and inflicts upon arbovirus diseases (7, 12, 13).

Dengue virus (DENV) belongs to the genus *Flavivirus* of *Flaviviridae* which is mainly transmitted by *Aedes aegypti* and *Aedes Albopictus* (14–18). Its different serum types, DENV1~4 (14), can all develop symptoms such as slight fever, headache, myalgia and arthralgia, which are the typical symptoms of self-limited dengue fever (DF) (16, 17, 19). A small portion of patients can further develop fatal dengue hemorrhagic fever (DHF) or dengue shock syndrome (DSS) (8, 15, 17, 20, 21). Although multiple vaccine experiments have entered to the stage of clinical trials, there are still many insurmountable obstacles in current research and development(20). Therefore, vector control may still be the major way to prevent the propagation of dengue (18).

With the development of globalization, dengue fever has been widely prevalent in tropical and subtropical regions all over the world (18). In recent years, dengue has also been reported for the first time or once again in over 100 countries of which most are developing countries (22). Approximately dengue causes at least 50 to 100 million cases annually (23, 24) and puts nearly 4 billion people at risk of dengue fever (17, 20, 25). For now, Southeast Asia, middle South America and Africa are the main epidemic areas of dengue. Additionally, more cases are reported in Asia than in other areas (8, 26, 27). WHO declared dengue as the most rapid developing infectious disease around the globe (28)and with the intensification of the epidemic, it was regarded as one of ten major health threats globally in 2019 (18, 29). Researches have proved that the recession of economy, the rise in airlines and the poor-planned urbanization etc. had increased the propagation of dengue (16, 30). Also, the development of towns and villages, road expansion and other measures can result in dengue fever spreading from high population density areas to low population density areas in both developed and developing countries (20, 24, 25). Consequently, dengue fluctuation monitoring is of pivotal importance to disease prevention.

Reports before have demonstrated the impact of NPIs induced by coronavirus on dengue in certain degrees, however, how the implementations functioned remains unclear (31). As NPIs of different countries were highly variable and difficult to qualify, therefore, this research oriented to discover the fluctuations of dengue in different countries in coronavirus era by analyzing possibly related factors towards dengue as speculated (11, 32–36). Finally, by discussing the rationality, feasibility, pros and cons of the NPIs that having implemented from the perspectives of the mentioned factors, this study advocated that countries should carry out various policies according to their own situation. Furthermore, it aimed to provide certain guidance to those who desperately combating dengue and COVID-19 pandemic at the same time.

Methods

Data collection

To discover the relation between dengue fluctuations and potential factors, data were gathered for further analysis. We totally gathered data of 57 countries (or regions), including 42 American countries, 13 Asian countries, one Australian country and one African country. Due to the delay of data update of some websites, data for some countries remained missing.

As for data sources, please refer to **Supporting Information**.

Considering data access were limited as well as lockdowns and a country's medical health care of varying countries were too difficult to be measured by data, and the details of the NPIs reported of different countries differed greatly, this essay would apply the collected data to preliminarily reflect the factors influenced by COVID-19 pandemic. For instance, we use the COVID-19 incidence to reflect the implementation of NPIs, the death rate to health and medical conditions and the economic level to the possibilities of the clash of dengue prevention in coronavirus pandemic (11, 32–37).

Normality Test

To ascertain what indicators should be used to stratify data in rank sum analysis, we proceeded a normality test. The mean or median were chose to be used for stratification in rank sum analysis according to the result of normality test. If the data of each group showed a not-normal distribution, which was in line with the assumption of data distribution at the beginning of the study, then the median or even quartile if needed should be used for rank sum analysis. Otherwise, the average should be used for testing

Correlation Analysis

After normality test to different groups of data collected, we took dengue subtraction as dependent variable and other as independent variables, to discover the correlations between the dengue fluctuation and the factors above. Those initially speculated factors such as territory, population, GDP per capita were considered may be related to the subtractions between 2020 and 2019 dengue cases. Additionally, these factors might be related to the NPIs of COVID-19, which may further indicate the correlation between NPIs of COVID-19 and dengue epidemic.

Correlation analysis were proceeded by using **formula** through SPSS.

$$r = \frac{\sum \left(X_i - \bar{X}\right)\left(Y_j - \bar{Y}\right)}{\sqrt{\sum \left(X_i - \bar{X}\right)^2 \sum \left(Y_j - \bar{Y}\right)^2}} \quad \textbf{formula}$$

In the formula, **r** represents the correlation coefficient between the difference of dengue fever cases and the above factors, and a positive **r** represents a positive correlation, while a negative **r** represents a negative correlation; the larger the value is, the greater the correlation is. $\mathbf{X_i}$ represents the value of each influencing factor; $\bar{\mathbf{X}}$ represent the average value of influencing factors in the time was counted. $\mathbf{Y_j}$ represents the difference of dengue fever cases in different countries; $\bar{\mathbf{Y}}$ represents the average of the differences in dengue cases in each country.

Rank Sum Analysis

To further focus on the impact of different factors on the changes of dengue fever epidemic situation, we divided the data into four groups from different angles: geography, economy, population and COVID-19 related factors. In order to rank sum analyze them by corresponding stratification, we layered the possible relevant data by medium and quartiles and applied SPSS to process nonparametric tests to discuss whether there were differences in the composition of dengue epidemic changes among the different groups. The difference of the dengue cases were independent variables while other factors were independent factors. Finally, the K-W nonparametric test was carried out.

Besides the factors that ongoing normality testing, we also layered the continental and geographic differences in the K-W nonparametric test. If $p < 0.05$, it is considered that the difference of the dengue fever cases among different levels has a significant impact. On the contrary, the hypothesis does not hold.

Results

We drew a map of the distribution of dengue epidemic changes based on the data collected. The results showed that 39 countries remained still or decreased in dengue cases in 2020 compared with 2019, while other 18 countries' dengue cases in 2020 increased. These 18 countries were highly clustered, and most of them were located in the western South America. Different with that, other countries showed varying degrees of decrease in the number of dengue cases regardless of distribution location. (Figure 1)

Due to the differences among the countries, we wondered the potential related factors. Therefore, we collected the national factors, including geographical, economic, demographic factors and COVID-19 related factors in different countries, and conducted correlation analysis with dengue epidemic alteration. The results showed that the difference of dengue cases between 2019 and 2020 were highly negatively related to territory ($p = 0.020$), number of cases ($p = 0.032$) and number of deaths of COVID-19 ($p = 0.002$), but not to per capita GDP, population and other factors (Table 1). The negative correlation between dengue subtractions and the territories indicated that the larger the territory is; the number of the dengue fever cases will decrease more compared to that in 2019. In addition, results presented that while other conditions remained stable, countries with higher cases of COVID-19 and higher mortality had a smaller deduction in the number of dengue fever cases of the two years. In other words, the poorer the implementations of NPIs and the weaker the management of medical health care and treatment to coronavirus, the number of the dengue fever cases might have less chance to drop. This also implies that the worse the anti-risk ability of the medical and health system impacted by COVID-19, the greater the uncontrollability of the change of dengue epidemic.

Table 1
Correlation of dengue subtractions and related factors

Factors	Cases	Pearson correlation	Significance
GDP per capita in 2019 (thousand dollars)	48	0.160	0.277
GDP per capita in 2020(thousand dollars)	47	0.170	0.252
GDP subtraction (thousand dollars)	47	-0.043	0.774
Territory (km^2)	56	-0.311	0.020*
2019 population (million)	56	-0.138	0.312
Population density(/km^2)	56	0.056	0.683
COVID-19 cases in 2020	57	-0.284	0.032*
COVID-19 deaths in 2020	57	-0.404	0.002**
COVID-19 incidence (%)	56	-0.060	0.660
COVID-19 mortality (%)	56	-0.133	0.330
COVID-19 fatality (%)	57	-0.086	0.525

Significant and greatly significant p-values ($p < 0.05$ and $p < 0.01$) are indicated by *, **. Gross domestic product (GDP).

To further explore their potential influences on the changes of dengue epidemic, we clustered the collected data into layers to analyze their contribution. We first explored the geographical related factors. Tropical and subtropical countries distributed in Asia and the Americas were mainly collected as they were the high dengue incidence and prevalence areas. According to its located continents and climate zones, they were divided into the Americas, Asia, Africa and Oceania; the tropical, the temperate and the frigid zone, respectively. Rank sum analysis showed that there were differences in the dengue subtractions in different continents ($p = 0.014$) and no differences in different climatic zone ($p = 0.825$) (Table 2). The results proved that the number of epidemic changes was significantly affected by geographical location and less by climatic conditions. The territories area were further divided into four layers by the median and quartile for rank sum analysis. The results showed that there were significant differences in the number of dengue cases in two years under different territory areas ($p = 0.008$), which suggested that the number of epidemic changes was affected by regional scope (Table 2). In terms of geographical factors, the epidemic changes of countries with different plate distribution and territorial area were significantly different.

Table 2
Rank sum analysis of dengue cases subtractions and related factors

Factors	n	Medium/Quartile	Layers	Case numbers of each layer	H(K)	P
Located continents	57	Americas/Asia/Africa/Oceania	4	42/13/1/1	10.684	0.014*
Climate zone	56	tropical/temperate/frigid zone	3	46/9/1	0.385	0.825
GDP per capita in 2019 ($10^3$$)	48	17.28/8.75/4.2	4	12/12/12/12	9.438	0.024*
GDP per capita in 2020 ($10^3$$)	47	15.33/7.44/3.82	4	12/12/12/11	8.772	0.032*
GDP subtraction ($10^3$$)	47	-0.28/-0.9/-2.06	4	12/12/12/11	9.764	0.021*
Territory (km^2)	56	756102(513120)/109884(108889)/2512(1702)	4	14/14/14/14	11.733	0.008**
2019 population (million)	56	37.89/9.75/0.4	4	14/14/14/14	11.028	0.012*
Population density (/km^2)	56	319.767/139.900/35.031	4	14/14/14/14	4.853	0.183
COVID-19 cases in 2020	57	42702	2	29/28	1.692	0.193
COVID-19 deaths in 2020	57	471	2	28/29	1.996	0.158
COVID-19 incidence (%)	56	2.012	2	28/28	4.894	0.027*
COVID-19 mortality (%)	56	0.009	2	28/28	3.309	0.069
COVID-19 fatality (%)	57	1.8	2	28/29	0.954	0.812

Significant and greatly significant p-values ($p < 0.05$ and $p < 0.01$) are indicated by * and **. Gross domestic product (GDP).

To research into economic related factors, we stratified data of per capita GDPs of 2019 and 2020 as Table 2 presented and rank sum analyzed them with dengue case differences. The results showed that dengue fever had significant impact in different countries before and after lockdown, which was according to the per capita GDPs of 2019 ($p = 0.024$) and 2020 ($p = 0.032$) respectively (Table 2). Under the impact of COVID-19 pandemic, GDPs of most countries decreased significantly and only a few countries' GDP rose in COVID-19 pandemic. Thus, we further analyzed the subtraction of per capita GDPs of 2019 and 2020, which showed there were differences in the dengue epidemic changes in countries with different economic shocks ($p = 0.021$) (Table 2). In total, there were differences in dengue cases subtractions with different per capita GDPs in 2019 and 2020, as well as with different economic shocks.

Total population and average population density were stratified to explore the influences of population factors The rank test analysis showed there were differences in the dengue cases subtractions with different population sizes ($p = 0.012$). For further study, the average population density was obtained by the ratio of population to territorial area, results showed that there is no difference in the two-year change in the number of dengue cases in countries with different average population densities ($p = 0.183$).

COVID-19 related factors were included in the analysis as they might represent different levels of NPIs against COVID-19. COVID-19 incidence rate was calculated by using the newly collected COVID-19 cases and population data collected. Also, COVID-19 mortality was regarded as the proportion of COVID-19 deaths in the infected population. After quartile stratified, dengue subtractions were rank sum analyzed. There were differences in the number of dengue fever cases in two countries with different incidence rate of COVID-19, which indicated that the incidence rate of COVID-19 was an indicator of health precaution in a country. It is considered that there was a significant difference between the preventive measures taken by different countries and the subtractions of dengue. However, other COVID-19 related factors made no difference in epidemic changes apart from incidence rate, including number of cases ($p = 0.193$), number of deaths ($p = 0.158$) and mortality ($p = 0.069$) of COVID-19 (Table 2).

Discussion

At present, COVID-19 was wreaking havoc on the world and has brought enormous burden to the people's economy and health. To curb the rapid spread of COVID-19, different levels of non-pharmaceutical interventions (NPIs) have been implemented. These measures have effectively suppressed COVID-19's rapid propagation. However, it has affected the prevalence of other infectious diseases to varying degrees. Among them, dengue fever, as the fastest spreading recurrent arbovirus disease, has had a great impact on people all over the world (15). At present, the reports on the impact of COVID-19 are various in different countries. Therefore, in this study, we intended to explore the possible influence factors on dengue epidemic by analyzing the characteristics of dengue epidemic in different countries under COVID-19.

The results of correlation analysis on the potential relevant factors showed that the dengue cases subtractions were significantly negatively related to the territory area, the total number of COVID-19 cases and the number of COVID-19 deaths. In many countries, the implementation of various NPIs and the medical health care could not be fully collected and precisely measured. Therefore, we used the total number of COVID-19 cases to indicate the implementation of NPIs, that is, to a certain extent, the higher the cases, the worse the implementation of prevention and control (32–36). Also, the medical treatment of the current year was indicated by the total deaths, mortality and fatality of COVID-19, that was, the higher the occupation of medical resources for the prevention and control of COVID-19, the worse the medical intervention for dengue, and the higher the total number of deaths. The correlation above indicated the impact of COVID-19 epidemic on dengue fever. Finally, the negative correlation between dengue subtractions and territory areas indicated that when facing global pandemic, countries with larger territories can exert advantage in dengue prevention. As for rank sum analysis, results showed that there were significant differences in dengue fluctuations of countries with different continental locations, 2019 and 2020 GDPs per capita, gaps between two years, territory areas, populations and coronavirus occurrences.

Differences in territories may due to the strong correlation between dengue vector distribution and the location. As the host of dengue virus, *Aedes aegypti* is widely distributed in South America and Southeast Asia. On the other hand, dengue is also mainly affected by local weather, and there may be different weather conditions in the same region, therefore, the number of epidemic changes measured here is consequently less affected by the climate zone. Therefore, it is still suggested that countries in those regions should be vigilant against the outbreak of dengue fever in the face of large-scale lockdown.

Furthermore, this study proved that different countries' economies of two years were affected during the COVID-19 pandemic, which were speculated that it had an impact on dengue surveillance and treatment. In other words, implementation of dengue prevention were highly various due to the countries' own and COVID-19-affected economy. Consequently, as a country's economy was a determined factor of whether it can effectively combat dengue, in face of large-scale infectious diseases pandemic, countries of different developed degrees should formulate economic distribution measures in line with national conditions to deal with the economic recession in the pandemic.

While population size of a country can affect the fluctuation of dengue, we believed that as the average density was obtained by the ratio of population to territorial area, it has not been investigated at the urban level. The impacts on dengue fluctuation induced by the uneven demographic distribution can strongly surpassed the average model. Therefore, the population density in this analysis would be different from reality in dengue epidemic areas, so more data were needed to fully explain this conclusion.

Among many measures, lockdowns and border restrictions were considered capable of inhibiting the imported cases overseas and the spreading of dengue. In the case of COVID-19's outbreak and dissemination, many countries have adopted NPIs, such as Spain, China, Malaysia and other places (6, 7, 31). Furthermore, international tourists were often regarded as the cause of cross-border transmission of dengue (38–40), so the restrictions could slow down the dengue fever propagation from high incidence areas to other regions (41, 42). Studies have shown that COVID-19's travel restrictions had a positive effect on dengue fever epidemics in many European countries (42). Also during COVID-19 pandemic, it was the isolation of the close contacts, the monitoring methods and the epidemic information release on large datasets that effectively suppressed coronavirus pandemic. Furthermore, strict NPIs have also greatly reduced the dengue epidemic in China. However, travel restrictions had little effect on areas with high incidence of dengue fever. In addition, closing crowd-gathering places such as schools and lockdowns centered on families and communities were also important restrictive measures for the prevention and control of COVID-19 (5). This reduction in mobility between families can inhibit the spread of dengue fever. Reports showed that the daily activities of infected individuals and their contacts were often similar. Therefore, daily human activities played a key role in the spread of vector borne pathogens. Consequently, when the lockdown was limited to small families, the possibility of transmission from one household to another was reduced (43). All these help to explain the reduction of dengue epidemic in most countries under COVID-19.

It is acceptable that the impact of NPIs against COVID-19 on dengue epidemic existed globally, but this impact was not absolute. No matter how worse the COVID-19 pandemic, countries should pay attention to the prevention and control of dengue, especially in low-income countries where dengue fever is prevalent. Considering that COVID-19 and dengue might share the similar clinical manifestations that affect the medical control and diagnosis (31, 44–46) and the overlap outbreak will lead to competition for medical resources (47–50), countries should formulate strategies for their own situation and strictly control the dengue epidemic. The data collection of this study is limited. With the inclusion of more types of data in the future, the impact of COVID-19 on the dengue epidemic will be more comprehensively displayed. This can also provide data support and theoretical basis for timely adjustment of dengue epidemic prediction, prevention and control when dealing with the impact of major new and recurrent infectious diseases in the future.

Conclusion

In summary, this study collected data on dengue epidemics and possible factors of 57 countries around the world, and explored the possible influence factors on dengue fever through correlation analysis and rank sum analysis. The results showed that the two-year dengue cases subtractions were related to the territory, total COVID-19 cases and deaths, which confirmed that coronavirus and its NPIs had an impact on dengue. Further analysis showed that there were significant differences in the two-year changes of dengue among countries with different per capita GDP and different populations. These suggested that when facing the impact of major infectious diseases, countries should pay more attention to the occurrence and development of the dengue epidemic and adjust the epidemic prevention and control strategy timely according to their own situation.

Declarations

Ethics approval and consent to participate

This is an anonymous secondary data-based study. All methods were carried out in accordance with relevant guidelines and regulations. Consent to participate not applicable.

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Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are publically available from:

Pan American Health Organization repository, https://www.paho.org/data/index.php/en/mnu-topics/indicadores-dengue-en/dengue-nacional-en/252-dengue-pais-ano-en.html?start=2; Agence de santé du territoire des îles Wallis et Futuna repository, http://www.adswf.fr/pdf/bulletins_de_surveillance/bulletin_de_surveillance_04-2021.pdf; Agence Régionale de Sante La Réunion repository https://www.lareunion.ars.sante.fr/liste-de-contenus/Dengue; Epidemiology Unit, Ministry of Health (EPID) repository, http://www.epid.gov.lk/web/index.php?option=com_casesanddeaths&Itemid=448&lang=en; European Centre for Disease Prevention and Control repository, https://www.ecdc.europa.eu/en; National Institutes of Health (NIH) repository, https://www.nih.gov/ ; Surveillance Atlas of Infectious Diseases repository http://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=16; International Monetary Fund repository, https://www.imf.org/external/datamapper/NGDPDPC@WEO/OEMDC/ADVEC/WEOWORLD/COL/BRA/KHM; Onegreen repository, http://www.onegreen.net/maps/HTML/23472.html; National Health Commission of People's Republic of China repository http://www.nhc.gov.cn/; World Health Organization repository, https://worldhealthorg.shinyapps.io/covid/; Population mondiale repository, http://www.chamiji.com/countryrank; Access Gideon repository, https://app.gideononline.com/search?q=dengue&type=graph; John Hopkins University Coronavirus Resource Center repository, https://coronavirus.jhu.edu/map.html; National Environment Agency repository, https://www.nea.gov.sg/, therefore, no permissions were required.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Ziyang Sheng conceived the study, while Jing An, Peigang Wang and Ziyang Sheng secured funding. Bo Fan and Tianhui Kang collected data, conducted analyses and drafted manuscript with oversight from Ziyang Sheng. Bo Fan and Tianhui Kang contributed equally to this paper. All authors contributed and approved the final manuscript.

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Figures

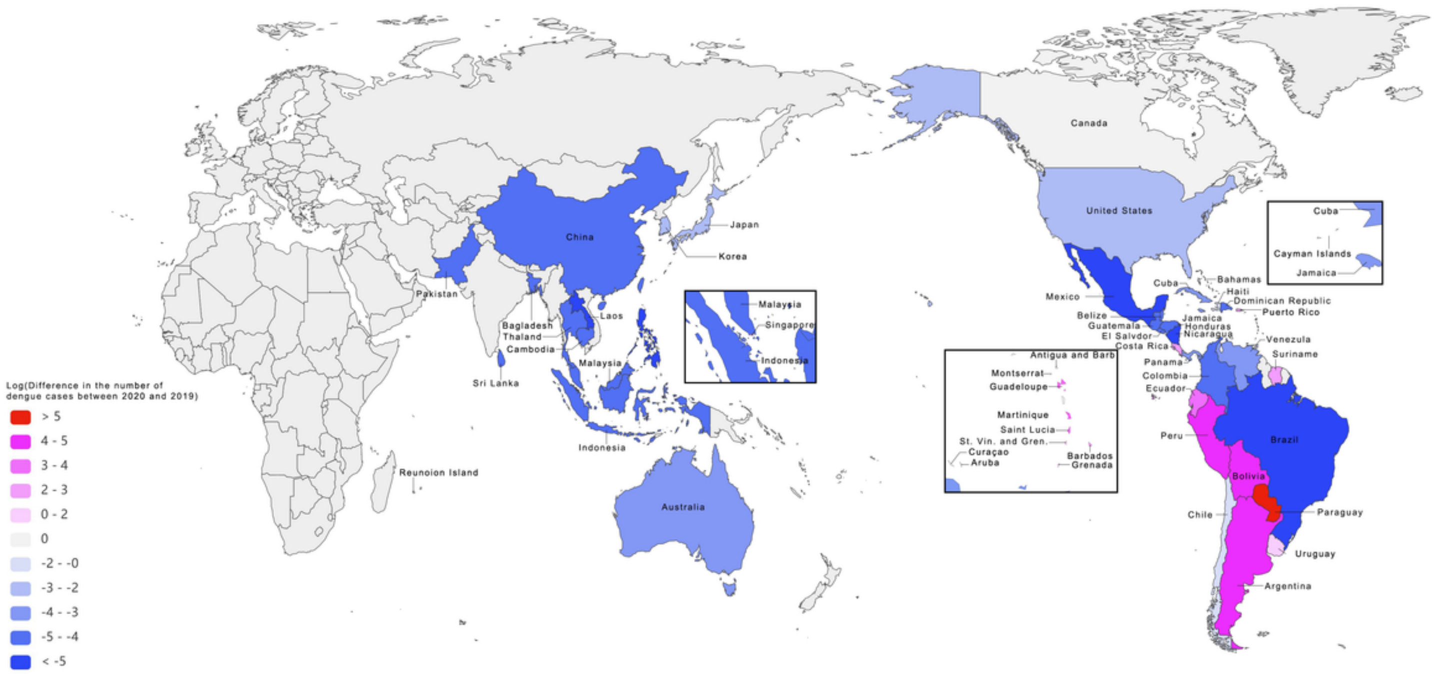

Figure 1

The dengue epidemic alteration in studied countries between 2019 and 2020 The alteration between cases of dengue fever in 2019 and 2020 were displayed based on the data collected of different countries. There were 18 countries' dengue cases in 2020 increased compared with 2019 (shown in red), while other 39 countries remained still or decreased in case number (shown in blue). The dengue difference was calculated by logarithm based on 10.

Supplementary Files

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