



Impact of COVID-19 pandemic on vaccination against meningococcal C infection in Brazil



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ABSTRACT

Objective: Analyzing the impact of COVID-19 pandemic on meningococcal C conjugate vaccination in Brazil.

Methods: Ecological study, based on interrupted time series, carried out with data collected through the Information System of the National Immunization Program (IS-NIP). Collected data refer to the number of meningococcal C conjugate vaccine doses administered from March 2019 to December 2020.

Results: In total, 14,832,054 meningococcal C conjugate vaccine doses were administered throughout the investigated period; 66.30% of them, from March 2019 to February 2020 and 33.70%, from March to December 2020. Statistically significant steps were observed, i.e., the COVID-19 pandemic had negative impact on the number of MenC vaccine doses administered in the North and South regions (26,98% and 41.47%, respectively) and in the eleven Brazilian States.

Conclusion: The current study has shown that the COVID-19 pandemic had negative impact on the number of MenC vaccine doses administered in the Northern and Southern Brazil, and in eleven Brazilian states. Among all challenges experienced during the COVID-19 pandemic, one finds reduced MenC vaccine coverage, which, consequently, may lead to increased meningococcal infection rates in Brazil.

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Introduction

The first records of coronavirus disease (COVID-19) resulting from severe acute respiratory infection Coronavirus 2 (SARS-COV-2) emerged in Wuhan City, China, in late 2019 [1–2]. This infection comprises different clinical manifestations. The large-scale worldwide increase in the number of COVID-19 cases has affected health services, due to need of treating individuals affected by the disease. Consequently, it compromised local resources and hindered the healthcare provided in several countries [3].

In March 2020, the World Health Organization (WHO) has classified the disease as pandemic [4] and has even considered the

likelihood of syndemic [5] due to its rapid spread [2] and new variants [6]. Prevention actions such as using masks, hygiene measures and social distancing have been adopted, by taking into consideration the COVID-19 transmission route (through droplets), to stop the virus transmission chain [7].

International and national bodies have recommended maintaining the adoption of immunization actions to avoid the emergence of vaccine-preventable diseases that were under control, up to the present time [8–9]. Although recommendations focus on instructing countries to keep on performing immunization actions, studies have shown decreased vaccination coverage among children, mainly because parents/legal guardians were afraid to take them to health services where they could get infected with COVID-19 [10–11]. It is worth emphasizing that successful immunization programs stand out among strategies accounting for reducing global under-five mortality rate [12–13].

Meningococcal C conjugate vaccine (MenC vaccine) was implemented in Brazil, in 2010. It was made available to children

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younger than 2 years due to significant increase in the number and rates of meningococcal C cases, as well as to several outbreaks that affected different regions countrywide [14]. Meningococcal disease is classified in the country as endemic, since it has sporadic outbreaks in municipal territories [15]. It has impact on Public Health due to its potential to cause outbreaks [15].

MenC vaccine is one of the meningococcal disease prevention and control measures available nowadays [15]. Besides being the most effective way to prevent MD, it plays key role in controlling outbreaks, performing vaccine blockades and reducing pockets of susceptible children [14]. The number of meningococcal disease cases among children younger than 2 years has decreased right after the MenC vaccine was introduced in the National Immunization Program (NIP) [14].

In light of the foregoing and given the relevance of maintaining or increasing vaccination coverage, even in face of the challenge experienced during the COVID-19 pandemic, the aim of the present study was to analyze the impact of the COVID-19 pandemic on meningococcal C conjugate vaccination rates in Brazil. Studies focused on assessing the impact of the COVID-19 pandemic on the rate of MenC vaccine doses applied worldwide remain scarce in the literature. To the best of our knowledge, the current study is the first to investigate this topic in Brazil.

Materials and methods

Ecological study, based on interrupted time series, carried out with data collected through the Information System of the National Immunization Program (IS-NIP) and available at <http://sipni.datasus.gov.br>. IS-NIP enables extracting information about vaccine doses applied by NIP in Brazil.

Collected data referred to the monthly number of MenC vaccine doses administered from March 2019 to December 2020. Data extraction was based on the number of doses applied to the target audience (children younger than 2 years) on a monthly basis, throughout the investigated period.

Firstly, the number of MenC vaccine doses applied in all 26 states and in the Federal District, before and after the onset of the COVID-19 pandemic in Brazil, was calculated. Next, differences between the median number of doses applied before and during the pandemic were analyzed through Mann-Whitney *U* test, by taking into consideration the interquartile range (IQR). Rate of variation in the median number of applied doses was estimated based on the following equation:

$$\left[\frac{\text{median number of doses applied before the COVID-19 pandemic} - \text{median number of doses applied after the COVID-19 pandemic}}{\text{median number of doses applied before the COVID-19 pandemic}} \right] \times 100.$$

Interrupted time series (ITS) analysis was also performed based on Prais-Winsten [16] linear regression models. It was done to assess whether there is immediate (change in level) or progressive (change in trend) impact on ITS values when events, such as a pandemic, take place [16]. Prais-Winsten linear regression model for ITS was built based on the formula below:

$$y = \beta_0 + \beta_1 * \text{time} + \beta_2 * \text{step} + \beta_3 * \text{ramp}$$

wherein:

- y refers to the number of MenC vaccine doses at logarithmic scale;
- $\beta_1 * \text{time}$ refers to the slope of the trend curve before the COVID-19 pandemic;
- $\beta_2 * \text{step}$ refers to the change in level, by adopting 0 (zero) in points prior to the COVID-19 pandemic, and 1 in points after the onset of the pandemic;

- $\beta_3 * \text{ramp}$ refers to the slope of the trend curve after the onset of the pandemic; it measures the time after the intervention, as follows: value 0 (zero) marks points preceding the event, whereas sequential values higher than zero mark points after the beginning of the segment.

Statistically significant steps take place when the event can have immediate impact (either positive or negative) on the series. Statistically significant ramps take place, either in separate or in conjunction, when the event may have progressive impact on the series [16].

ITS was carried out for each region (Midwest, Northeast, North, Southeast and South), Brazilian State and for the Federal District.

The Mann-Whitney *U* test and time series trend analyses were performed in the Stata, version 16. All analyses adopted statistical significance level of 5%.

Since the current study used freely accessible data, it was not necessary submitting it to the Research Ethics Committee, in compliance with National Health Council Resolution n. 466/2012.

Results

In total, 14,832,054 meningococcal C conjugate vaccine doses were administered throughout the investigated period; 66.30% (9,833,073) of them were applied from March 2019 to February 2020 and 33.70% (4,998,981), from March to December 2020.

Table 1 shows the median and rate of variation in the median number of MenC vaccine doses applied in Brazil before and during the COVID-19 pandemic. All Brazilian regions, states and the Federal District recorded statistically significant reduction ($p < 0.005$) in the number of MenC vaccine doses applied during the pandemic.

The highest rate of variation in the median number of MenC vaccine doses was observed in the Southern region (−44.47%), which was followed by the Northern region (−37.11%). With respect to the analysis based on state, the highest variations in this parameter were observed in Amapá (−8.54%), Acre (−48.74%) and São Paulo (−48.06%) states, whereas the lowest rate of variation in the median number of MenC vaccine doses was observed in Mato Grosso do Sul State (−14.89%) (Table 1).

Fig. 1 and supplementary material 1 show the ITS trend analysis based on Brazilian region, state and on the Federal District. Statistically significant steps were observed, i.e., the COVID-19 pandemic had negative impact on the number of MenC vaccine doses applied in the Northern and Southern regions (Fig. 1 A and Supplementary Material 1). With respect to the states, statistically significant steps were observed in Acre, Amapá, Amazonas, Roraima, Tocantins, Ceará, Mato Grosso, Espírito Santo, Paraná, Rio Grande do Sul and Santa Catarina (Fig. 1 B and Supplementary Material 1).

Discussion

The current study has shown decrease in the number of MenC vaccine doses administered in Brazil, in all Brazilian Macroregions and States, after the onset of the COVID-19 pandemic. It also showed that the COVID-19 pandemic had negative impact on the number of MenC vaccine doses applied in the Northern and Southern regions and in the following Brazilian States: Acre, Amapá, Amazonas, Roraima, Tocantins, Ceará, Mato Grosso, Espírito Santo, Paraná, Rio Grande do Sul and Santa Catarina.

The results of this study showed that the number of MenC vaccine doses administered before the onset of the COVID-19 pandemic in Brazil (March 2019–February 2020) was considerably lower than in the period March–December 2020, which corresponded to the first nine months of the pandemic. This result does

Table 1
Median and rate of variation in the median number of MenC vaccine doses applied in Brazil, before and during the COVID-19 pandemic, per Brazilian region and state.

States and Regions	Median (Interquartile range)		Variation (%)	p*
	Mar –19 to Feb – 20	Mar-20 to Dec-20		
BRAZIL	19,139 (10,424.5–37,413)	12,335.5 (7,008–24,216)	–35.55	<0.001
NORTH	7,892 (4,409–20,421.5)	4,963(2,328–12,373)	–37.11	<0.001
Acre	4,692.5 (4,149.5–5,126.5)	2,405.5 (2,328–2,518)	–48.74	<0.001
Amapá	4,524.5 (3,584.5–4,793.5)	1,423.5 (863–1,867)	–68.54	<0.001
Amazonas	24,773 (22,246–27,246)	16,208.5 (13,262–17,912)	–34.57	<0.001
Pará	36,142 (30,333–39,584.5)	20,729.5(15,566–24,423)	–42.64	<0.001
Rondônia	8,789(8,067–9,855)	6,227.5(5,695–6,583)	–29.14	<0.001
Roraima	3,287.5 (3,201.5–3,572.5)	2,364.5 (2,069–2,598)	–28.08	<0.001
Tocantins	8,433(7,520–9,117.5)	5,292 (4,843–5,591)	–37.25	<0.001
NORTHEAST	14,967.5(11,590–32,425.5)	10,929.5(8,105–21,888)	–26.98	<0.001
Alagoas	11,388 (9,628–11,891)	8,572 (7,446–10,152)	–24.73	0.035
Bahia	59,631.5(46,967.5–63,415)	33,880(28,865–36,501)	–43.18	<0.001
Ceará	41,243 (35,770–43,022.5)	22,612 (19,427–24,453)	–45.17	<0.001
Maranhão	29,344.5(24,979.5–32,293.5)	15,992.5(12,902–18,078)	–45.50	<0.001
Paraíba	13,858(12,599–15,211.5)	9,536.5(7,831–10,565)	–31.18	<0.001
Pernambuco	30,865.5(27,215.5–32,482.5)	24,043.5(21,570–25,128)	–22.10	0.007
Piauí	14,130(12,390.5–14,834)	9,119(7,966–9,894)	–35.46	<0.001
Rio Grande do Norte	12,265.5 (10,561–14,519.5)	8,545(7,107–9,088)	–30.33	0.001
Sergipe	10,547.5(8,283–11,567.5)	5,712(5,167–6,097)	–45.84	<0.001
MIDWEST	14,320(11,879.5–20,302.5)	10,534 (8,695–14,052.5)	–26.44	<0.001
Distrito Federal	13,033.5 (11,965–14,067.5)	8,420 (7,067–8,653)	–35.40	<0.001
Goiás	28,245 (23,396.5–29,467.5)	17,220.5(15,964–17,979)	–39.03	<0.001
Mato Grosso	19,069.5 (17,133–19,419)	12,214(11,442–13,390)	–35.95	<0.001
Mato Grosso do Sul	11,394 (9,678–11,879.5)	9,697(8,737–10,264)	–14.89	0.016
SOUTHEAST	48,900.5(25,087–112,321)	39,338(16,995–65,910.5)	–19.56	0.016
Espírito Santo	18,262.5 (16,587–20,209.5)	11,580(10,337–12,393)	–36.59	<0.001
Minas Gerais	91,031(73,432–97,658)	51,000.5 (47,970–54,628)	–43.97	<0.001
Rio Janeiro	38,381.5 (35,320.5–43,841)	30,910(27,580–32,691)	–19.47	0.001
São Paulo	174,258(161,532.5–183,541)	90,504.5 (79,832–97,115)	–48.06	<0.001
SOUTH	45,417(36,055–52,827.5)	26,581.5 (21,807–30,739)	–41.47	<0.001
Paraná	54,836 (46,453.5–58,201)	31,126(29,812–33,796)	–43.24	<0.001
Rio Grande do Sul	46,199 (42,082.5–50,646.5)	28,132(26,139–30,717)	–39.11	<0.001
Santa Catarina	35,659(30,871.5–37,640.5)	20,116.5(17,981–21,807)	–43.59	<0.001

Notes: p = Percentile * Mann-Whitney test (difference between medians).

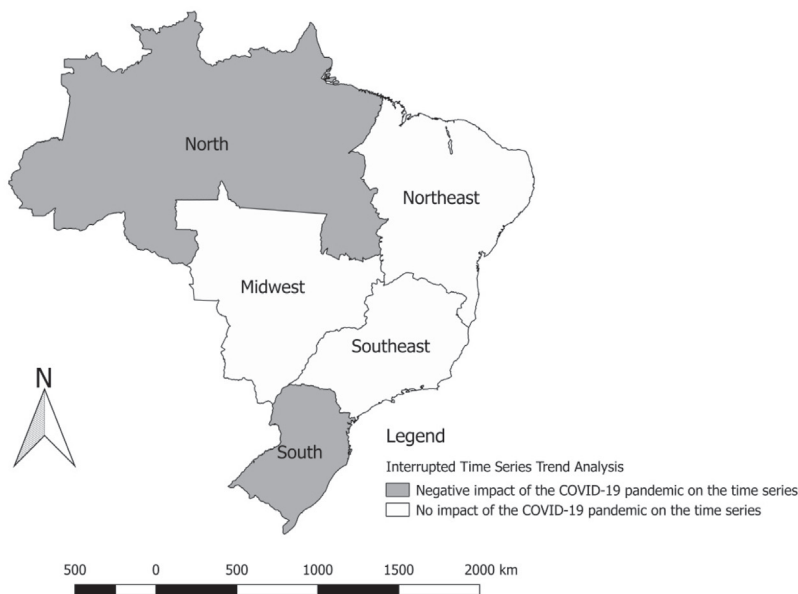
not dismiss the evidence presented by the literature that: 1. Contextual influences - historical, socio-cultural, environmental, health system/institutional, economic, or political factors; 2. Individual and group influences - arising from the personal perception of the vaccine or influences of the social environment; and 3. Specific issues of vaccines and directly related to their characteristics or the vaccination process [13]; can act synergistically, favoring the decline in the number of doses applied of all vaccines recommended for childhood during the last two decades, but lead to the reflection that the social isolation measures instituted in response to the COVID-19 pandemic, contributed to the reduction in the number of doses applied of the MenC vaccine [17–20]. This fact can also be proven by the statistically significant reduction in the number of MenC vaccine doses applied during the pandemic in all Brazilian regions, states and the Federal District. It is believed, therefore, that the results of this research can contribute to the identification of locations in Brazil that showed a decrease in the number of doses of MenC vaccine and, consequently, a greater chance of concentration of individuals susceptible to meningococcal C, directing, for these locations, health strategies that aim to reduce regional inequalities of pre-existing vaccine coverage in Brazil, and that were aggravated by the pandemic COVID-19[19].

There is little evidence to date showing such a scenario, however, previous studies conducted in Brazil had already shown heterogenous health conditions among Brazilian macro-regions [21–22]. Such a heterogeneity is often explained by socioeconomic conditions of these macro-regions and is a key point for the elaboration of health promotion actions [21]. Brazil is a middle-income

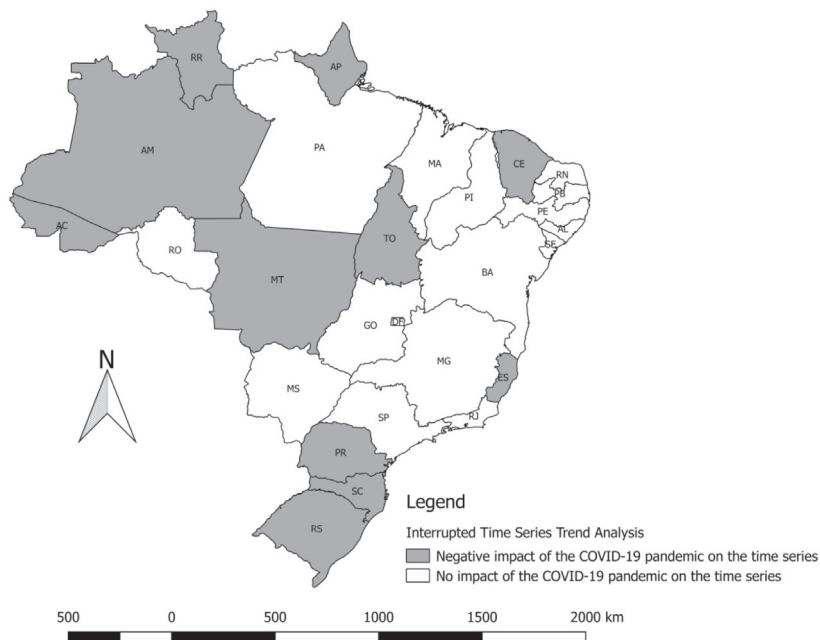
country, whose socioeconomic inequalities [23] influence the health status of its population and constitute a determining factor in citizens' access to health services [24].

The COVID-19 pandemic has worsened social inequalities experienced in the country [25–26]. In addition, social inequalities (along with the pandemic) have also affected population's vaccination [8,27–28]. The Northern region, for example, experienced collapse in its health services due to lack of oxygen and medication. This Brazilian region experiences historical precariousness when it comes to investments in health services [21,29–31]. Thus, it is clear that the epidemiological condition triggered by the pandemic has brought to light health inequity issues. Study carried out in the United States has evidenced issues similar to those experienced in Brazil, namely: infrastructure limitations, limited distribution and access to COVID-19 screening tests, insufficient resources such as personal protective equipment for health workers, inconsistent factual information, overburden health professionals, among others. Therefore, the aforementioned study has evidenced some pandemic-associated issues capable of significantly affecting public and social health. In fact, the major adverse effect generated by the pandemic lies on the wide inequality in the approach to healthcare [32].

With respect to the Southern region, which is one of the most favored macro-regions in the country, there was different perception about the reduction in the number of administered vaccine doses. This region recorded the best social distancing rates during the early months of the COVID-19 pandemic, as well as early implementation of social distancing measures [33–34]. Although



A – Analysis based on region.



B – Analysis based on state and on the Distrito Federal.

Fig. 1. Interrupted time series trend analysis based on Brazilian region and states, and on the Federal District. **Note:** Acre – AC; Alagoas – AL; Amapá – AP; Amazonas – AM; Bahia – BA; Ceará – CE; Distrito Federal - DF; Espírito Santo – ES; Goiás – GO; Maranhão – MA; Mato Grosso – MT; Mato Grosso do Sul – MS; Minas Gerais – MG; Pará – PA; Paraíba – PB; Paraná – PR; Pernambuco – PE; Piauí – PI; Rio de Janeiro – RJ; Rio Grande do Norte – RN; Rio Grande do Sul – RS; Rondônia – RO; Roraima – RR; Santa Catarina – SC; São Paulo – SP; Sergipe – SE; Tocantins – TO.

the adoption of social distancing measures to help mitigating the pandemic is a highly effective measure, one cannot ignore the fact that the adoption of such a measure is not a barrier to other asso-

ciated impacts, such as economic issues and social damage [35]. In addition, it is worth emphasizing that the pandemic had direct effects on public health, such as on vaccination coverage in the

overall Brazilian population; these effects were justified by lack of inputs and human resources to carry out basic activities linked to campaigns [36].

Although there was a reduction in the total incidence coefficient after the introduction of the MenC vaccine, from an average coefficient of 1.5 cases in the period prior to vaccination (2007–2010) to 0.4 cases/100 thousand inhab., in the last four years (2017–2020) [37]. However, it is known that the incidence tends to increase considering that the MenC vaccine application rate in Brazil has decreased in recent years: vaccination coverage in 2013 reached 99.7%; however, it decreased to 83% in 2018. If one takes into consideration the overall meningococcal disease incidence in Central and South America, there is evidence of wide variation depending on the geographic region. Although meningococcal infection is a notifiable disease, surveillance and notification systems - associated with the quality of published data about it - do not operate in a uniform manner, in all regions [38]. Furthermore, it is noted that as a result of the pandemic, there was also a drop in measles vaccination in children and adults [39].

Moreover, international studies and also in Brazil, showed that due to the pandemic COVID-19, there was a reduction in the search for health services by the population, which can also impact the decline in vaccination coverage not only for MenC vaccine, but for other vaccines [8,27–28,40–41].

Furthermore, limited access to healthcare services, as well as lack of laboratory infrastructure to incorporate routine tests in some countries, can contribute to minimize the true impact of the disease on the region [42]. There is evidence that Brazil, Chile and Argentina account for the highest meningococcal disease incidence; serogroups B, C and W account for most meningococcal disease cases reported in the region [43]. Therefore, it is evident that the impact on immunization coverage results from structural problems and inequalities that got worse due to issues caused by the COVID-19 pandemic. In addition, it is known that the number of meningococcal disease cases can only decrease after successful immunization process, a fact that does not meet the current findings and those reported in other studies [38,43].

Finally, the current study presented some limitations, such as the use of secondary data and standardized filling of IS-NIP records, which cannot always happen in a homogeneous manner.

Conclusion

The current study has shown that the COVID-19 pandemic had negative impact on the number of MenC vaccine doses applied in Northern and Southern Brazil, as well as in the following Brazilian states: Acre, Amapá, Amazonas, Roraima, Tocantins, Ceará, Mato Grosso, Espírito Santo, Paraná, Rio Grande do Sul and Santa Catarina.

It is worth highlighting the methodological rigor applied to all research stages, which enabled concluding that, among all challenges experienced during the COVID-19 pandemic, decreased MenC vaccine coverage can lead to increased meningococcal disease rates in Brazil.

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jvacx.2022.100156>.

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