











# Mortality rates and epidemiological changes in critically ill Coronavirus Disease 2019 patients after a vaccination program in Brazil

Donato da Silva Braz Junior<sup>1</sup>, Guilherme Jorge Costa<sup>2</sup>,  
Nathália Alves de Barros e Lyra<sup>3</sup>, Mirela Muniz Arantes Viana<sup>3</sup>,  
Vinícius Santos Borba<sup>3</sup>, Luiz Claudio Santos Thuler<sup>4,5</sup>,  
Eduardo Jorge da Fonseca Lima<sup>6</sup>, Maria Júlia Gonçalves de Mello<sup>6</sup>

## TO THE EDITOR,

The Coronavirus Disease 2019 (COVID-19) emerged as a serious public health problem worldwide.<sup>(1)</sup> To date, more than 31 million cases and almost 669,000 deaths due to COVID-19 have been confirmed in Brazil. The highest costs and mortality rates have been attributed to critically ill elderly patients with comorbidities who underwent invasive mechanical ventilation (IMV).<sup>(2)</sup> Multiple treatments and preventive measures, such as the use of face masks, social distancing, rigorous hand hygiene, medicines, and vaccines against severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), have been used, but which of them was the best at reducing the number of cases and mortality rates?

After vaccination programs were implemented in December in Israel<sup>(3)</sup> and England,<sup>(4)</sup> there was a significant reduction in the number of symptomatic and asymptomatic cases, hospitalizations, severe disease, and deaths due to COVID-19. In Brazil, the SARS-CoV-2 vaccination program was initiated on January 17th, 2021, prioritizing health professionals and the elderly population with comorbidities. Until June 26th, 2021, 11.92% of the Brazilian population was completely vaccinated, and 33.21% received only one dose; this period was the worst in terms of the number of cases and lethality in 2021, mainly in younger age groups.<sup>(5)</sup> Thus, in the present letter, we aimed to compare the changes in the mortality rates and epidemiology of critically ill COVID-19 patients before and after the first 6 months following the vaccination program against SARS-CoV-2 in Brazil.

This retrospective study analyzed the data of adult patients with COVID-19 admitted to intensive care units (ICUs) in Brazil. Patients were included when SARS-CoV-2 infection was confirmed by real-time polymerase chain reaction (RT-PCR) testing. Ethics committee approval was not required since the data were obtained from a national registry of the Influenza Epidemiological Surveillance Information System (SIVEP-Gripe), which is available online at <https://covid.saude.gov.br>.

The critically ill COVID-19 patients were divided into two groups according to hospitalization date. Those admitted

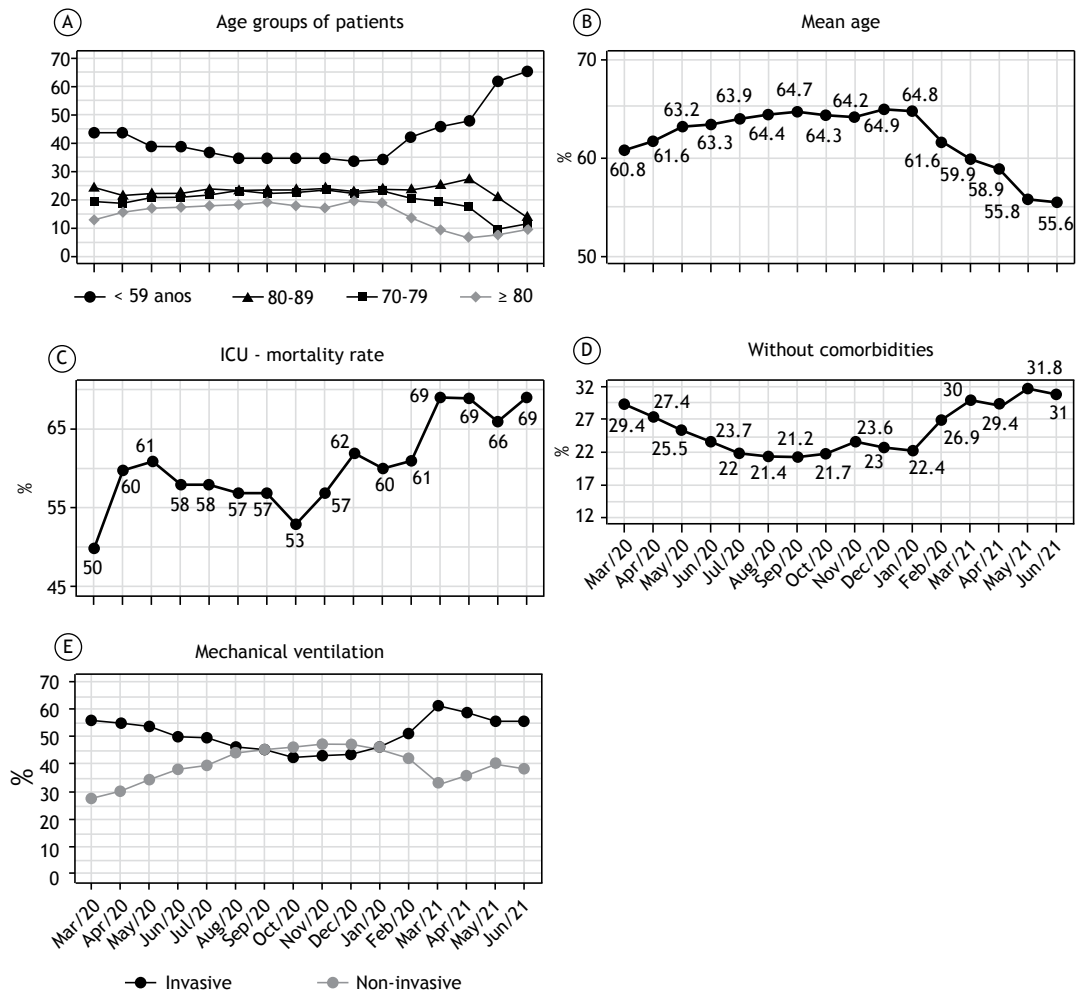
between March 1–December 31, 2020, were included in the pre-vaccination period group, while those hospitalized between January 1–June 26, 2021, were included in the post-vaccination period group. The monthly evaluated variables were mean age, the frequency of patients without comorbidities, and mortality rate.

Data were analyzed using the SPSS software, version 27.0. A descriptive analysis of the study population was performed using mean and standard deviation measures as continuous variables and absolute and relative frequency distribution as categorical variables. The t-test was used to compare continuous variables, while the chi-square test was performed to compare categorical variables. Differences were considered significant when the *p*-value was < 0.05.

This study evaluated a total of 116,640 patients admitted to the ICU in the pre-vaccination period and 124,153 patients hospitalized in the post-vaccination period, of whom 68,052 (58.3%) and 82,402 (66.4%) died, respectively. After the vaccination program against SARS-CoV-2, the critically ill COVID-19 patients were compared with those from the pre-vaccination period. The frequency of infection among patients < 60 years of age increased, and the mean age of the patients decreased, especially after the vaccination period when compared to the pre-vaccination period group (Figures 1A and 1B). However, there were temporal trends of increase in the ICU mortality rate, the frequency of patients without comorbidities, and the need for IMV (Figures 2A, 2B, and 2C).

The present study identified consistent changes in the age group profiles in confirmed, critically ill COVID-19 patients after the vaccination program against SARS-CoV-2 in Brazil. Patients younger than 60 years of age became the group that was more frequently admitted to the ICU, with increased ICU mortality rates and the need for IMV. This outcome strongly suggests that the SARS-CoV-2 vaccines protect the Brazilian population and should be widely offered to all age groups, including children and adolescents.

1. Departamento de Terapia Intensiva, Hospital de Câncer de Pernambuco, Recife (PE), Brasil.  
2. Departamento de Ensino e Pesquisa, Hospital de Câncer de Pernambuco, Recife (PE), Brasil.  
3. Programa Institucional de Iniciação Científica, Faculdade Pernambucana de Saúde, Recife (PE), Brasil.  
4. Instituto Nacional de Câncer, Rio de Janeiro (RJ), Brasil.  
5. Universidade Federal do Estado do Rio de Janeiro, Rio de Janeiro (RJ), Brasil.  
6. Departamento de Pesquisa Clínica, Instituto de Medicina Integral Professor Fernando Figueira, Recife (PE), Brasil.



**Figure 1.** Temporal distribution of COVID-19 patients admitted to the ICU: (A) Frequency of patients by age group; (B) Mean age of the COVID-19 patients. (C) ICU mortality rate; (D) Frequency of patients without comorbidities; (E) Frequency of patients under different kinds of mechanical ventilation.

Some drugs have shown beneficial effects in the treatment of critically ill COVID-19 patients. Dexamethasone presented a rate ratio of 0.83 (95% CI, 0.75–0.93) for all hospitalized patients and 0.64 (0.51–0.81), especially for patients undergoing invasive ventilation.<sup>(6)</sup> Interleukin-6 receptor blockers (tocilizumab, sarilumab) also promoted decreased mortality,<sup>(7)</sup> although their high costs hampered the availability for treating patients mainly in the public health system. Furthermore, more knowledge on COVID-19, particularly the use of non-invasive and invasive ventilation, could improve the quality of health assistance.<sup>(8)</sup>

The World Health Organization (WHO) and all the medical societies have suggested that everyone be vaccinated as soon as possible. Different vaccines against SARS-CoV-2 have been considered efficacious and safe.<sup>(3,4,9)</sup> The most important endpoints related to the effectiveness of a vaccine are the ability to reduce hospital or critical care admission and/or death.<sup>(10)</sup> Our study identified changes in the frequency of the age groups of critically ill COVID-19 patients after the

vaccination program, specifically in older vaccinated adults, who exhibited a reduction in ICU admission frequency. Thus, it can be inferred that the vaccination program against SARS-CoV-2 was the most important measure to control the COVID-19 pandemic.

The COVID-19 frequency and mortality rates were much more uncontrolled until the 1st semester of 2021 in Brazil. The SARS-CoV-2 Gamma variant was predominant in this period and related to higher severity and mortality, mainly in younger age groups when compared to variants B.1.1.28 and B.1.1.33, which were the most prevalent in 2020 in Brazil.<sup>(5)</sup> Our study showed that patients below 60 years of age increased ICU mortality rates, due to the fact that elderly people were a priority for vaccination. This finding is of concern since the younger population is economically active and probably responsible for the financial obligations of their families and labor companies. Therefore, we can infer that the Gamma variant had a higher capacity to spread than the other variants. However, it occurred especially among younger people since they had not yet been vaccinated.

In conclusion, this study identified an important change in the age group frequency of critically ill COVID-19 patients, decreasing in the older population after the vaccination program against SARS-CoV-2 in Brazil. Although these findings suggest that vaccine distribution prevented new critical care admissions, especially in priority groups that underwent vaccination, there was a concern regarding increased ICU mortality rates and/or the need for IMV, which affected mainly younger patients because they had not yet been vaccinated. Investing in vaccines against SARS-CoV-2 was the quickest and most appropriate way to control this terrible COVID-19 pandemic, which, unfortunately, is still underway.

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