

# Vaccination and situation severity of hospitalization due to severe acute respiratory syndrome due to COVID 19, Maranhão, 2021

Situação vacinal e gravidade das internações por síndrome respiratória aguda grave por COVID 19, Maranhão, 2021

Situación de vacunación gravedad de la hospitalización por síndrome respiratorio agudo severo por COVID 19, Maranhão, 2021

## RESUMO

Objetivo: caracterizar e comparar as hospitalizações por COVID-19 no Maranhão, segundo a situação vacinal contra a doença. Método: Trata-se de um estudo de coorte retrospectiva, baseado em dados secundários. Resultados: No ano de 2021 foram registrados 13.257 indivíduos hospitalizados com COVID-19, dos quais 6.425 (48,46%) evoluíram para alta após internação não grave, 1.573 (11,87%) evoluíram para alta com internação grave e 5.259 (39,67%) evoluíram para óbito. Em todos os três desfechos da evolução das internações, o número de indivíduos não vacinados é bem superior quando comparados aos vacinados. Conclusão: Nossos resultados reforçam o importante papel da vacinação na redução da gravidade das internações por COVID-19. Com a imunização da população do estado, poucos indivíduos internados e que estavam imunizados evoluíram para alta grave e óbito.

**DESCRIPTORIOS:** COVID-19; Hospitalização; Vacinas Contra COVID-19

## ABSTRACT

Objective: to characterize and compare hospitalizations due to COVID-19 in Maranhão, according to the vaccination status against the disease. Method: This is a retrospective cohort study, based on secondary data. Results: In 2021, 13,257 individuals hospitalized with COVID-19 were registered, of which 6,425 (48.46%) evolved to discharge after non-serious hospitalization, 1,573 (11.87%) evolved to discharge with severe hospitalization and 5,259 (39.67%) evolved to death. In all three outcomes of the evolution of hospitalizations, the number of unvaccinated individuals is much higher when compared to those vaccinated. Conclusion: Our results reinforce the important role of vaccination in reducing the severity of hospitalizations due to COVID-19. With the immunization of the state population, few hospitalized individuals who were immunized evolved to severe discharge and death.

**DESCRIPTORS:** COVID-19; Hospitalization; COVID-19 Vaccines

## RESUMEN

Objetivo: caracterizar y comparar las hospitalizaciones por COVID-19 en Maranhão, según el estado de vacunación contra la enfermedad. Método: Se trata de un estudio de cohorte retrospectivo, basado en datos secundarios. Resultados: En 2021 se registraron 13.257 personas hospitalizadas con COVID-19, de las cuales 6.425 (48,46%) evolucionaron a alta tras hospitalización no grave, 1.573 (11,87%) evolucionaron a alta con hospitalización grave y 5.259 (39,67%) evolucionado hasta la muerte. En los tres resultados de la evolución de las hospitalizaciones, el número de personas no vacunadas es muy superior al de las vacunadas. Conclusión: Nuestros resultados refuerzan el importante papel de la vacunación en la reducción de la gravedad de las hospitalizaciones por COVID-19. Con la inmunización de la población estatal, pocas personas hospitalizadas que fueron inmunizadas evolucionaron a un alta grave y muerte.

**DESCRIPTORIOS:** COVID-19; Hospitalización; Vacunas Contra COVID-19

RECEBIDO EM: 02/01/2023 APROVADO EM: 28/01/2023

### Rafaela Duailibe Soares

Master in Family Health-RENASF

Professional training: Nurse

Position held: Doctoral student in Collective Health

Institution to which it belongs: Federal University of Maranhão

ORCID: 0000-0001-9896-5318

**Rejane Christine de Sousa Queiroz**

PhD in Public Health

Professional training: dental surgeon.

Occupation: Associate Professor

Institution to which it belongs: Federal University of Maranhão.

ORCID: 0000-0003-4019-2011

**Bruno Feres de Souza**

Title: PhD

Professional background: PhD in Sciences, Computing area, from the University of São Paulo.

Occupation: Associate Professor

Institution to which it belongs: Federal University of Maranhão.

ORCID: 0000-0003-1997-4983

**Maria dos Remedios Freitas Carvalho Branco**

Title: Doctorate in Tropical Medicine and International Health

Professional training: Medical infectologist

Function held: Head teacher

Institution to which it belongs: Federal University of Maranhão.

ORCID: 0000-0002-3537-0840

**INTRODUÇÃO**

The pandemic of COVID-19 in the world scenario was responsible for a considerable increase in the rates of hospital admissions in wards and intensive care unit (ICU) beds, the need for use of advanced respiratory support and health professionals trained to act against the disease<sup>1</sup>. In Brazil, since the first records of the disease until December 2021, 22,277,239 cases of COVID-19 have been confirmed, of which 618,984 have died<sup>2</sup>.

Several measures to contain the spread of the disease have been taken, highlighting the vaccination against COVID-19 that started in December 2020 in the UK. In Brazil, vaccination started in January 2021 among frontline healthcare workers, the elderly in long-stay institutions, institutionalized disabled people (aged 18 years and older), and the indigenous population living on indigenous lands<sup>3</sup>. By the end of 2021, vaccination in Brazil will have reached all age groups above 12 years old, with a booster dose for everyone aged 18 or older<sup>3</sup>.

Vaccination against COVID-19 in several countries has been shown to be associated with decreased mortality rates, decreased risk of hospitali-

zation for disease complications, and substantial reductions in symptomatic COVID-19<sup>4,5</sup>. In Brazil, studies have also demonstrated the efficacy of vaccination in the population among health care workers<sup>6</sup>, adults<sup>7</sup>, and the elderly<sup>8,9</sup>. Other studies show the relationship of vaccination with decreased mortality, among them in Londrina-PR<sup>4</sup> and in Ceará<sup>9</sup>. In Manaus-AM we observed changes in the pattern of hospitalizations and deaths from COVID-19 after substantial vaccination<sup>10</sup>.

However, there are few studies that relate vaccination status with hospitalizations for COVID-19. For residents of New York, USA, the vaccination against COVID-19 was highly effective against hospitalization in fully vaccinated individuals<sup>11</sup> and in Brazil, in the state of Mato Grosso do Sul, with the immunization of the population, few cases of immunized individuals evolved to Severe Acute Respiratory Syndrome (SARS), which demonstrated the achievement of the objective of the immunization application<sup>12</sup>.

Given this context, the severity of COVID-19 in the Northeast region of Brazil<sup>13</sup>, especially in Maranhão, a state marked by socioeconomic inequalities and unequal access to health services, the absence of studies analyzing the cha-

acteristics of hospitalizations for this disease compared to vaccination status, and in order to answer questions about the vaccination status of individuals hospitalized for COVID-19 in the state, the aim of this study is to characterize and compare hospitalizations for COVID-19 in the state of Maranhão according to vaccination status against the disease.

**METHOD**

This is a retrospective cohort study based on secondary data and statewide. The study site is the state of Maranhão, composed of 217 municipalities and located in the northeastern macro-region of the country. The estimated population in 2021 for the state was 7,153,262 inhabitants with a Human Development Index (HDI) of 0.639<sup>14</sup>.

The study population consists of all SARS records due to COVID-19, reported in the state of Maranhão, in the year 2021.

The data source for the cases of severe acute respiratory syndrome (SARS) by COVID-19 in Maranhão was the Influenza Epidemiological Surveillance Information System (SIVEP/Gripe). While the data on vaccination status were obtained from the vaccination

campaign against COVID-19, available in the Information System of the National Immunization Program (SI-PNI). The State Health Secretariat made available the linked database with the information of hospitalizations and vaccination against COVID-19, following the General Law of Data Protection, ensuring the anonymization of personal data, with the specific purpose for conducting this study.

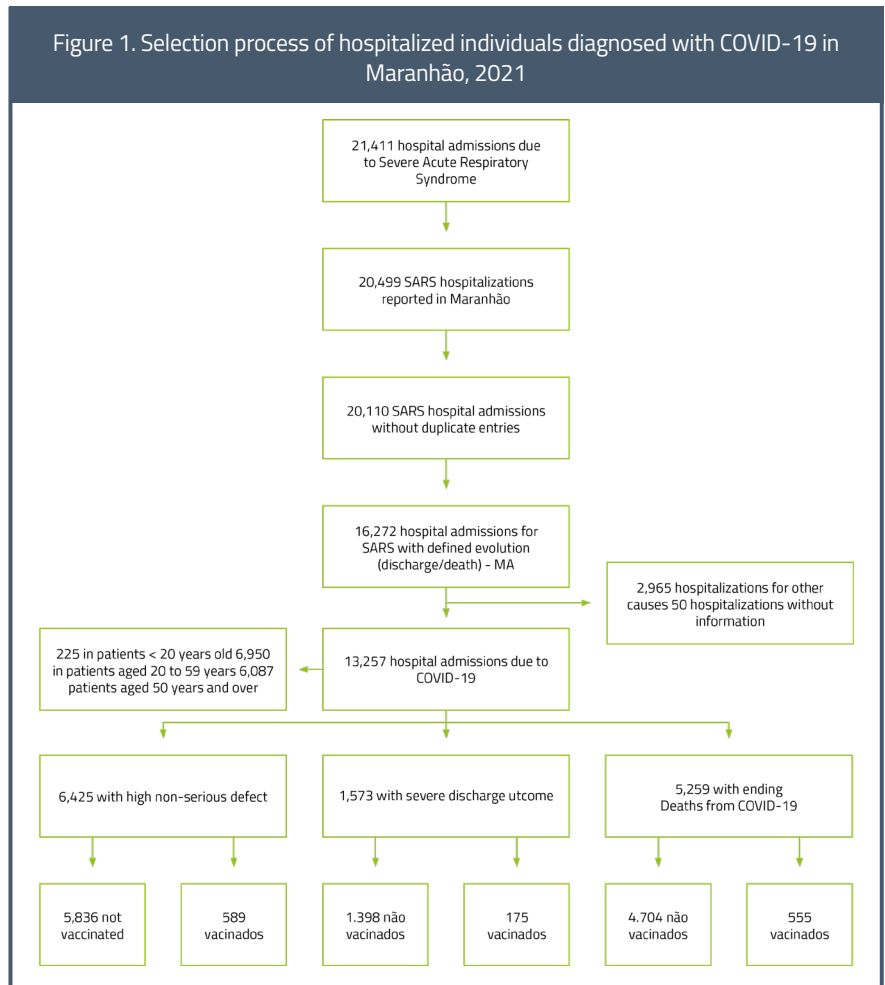
We considered for the study all cases recorded in the SIVEP/Gripe in the period January to December 2021, totaling 21,411 hospitalizations. Of these, only individuals with confirmed diagnosis of COVID-19 and who were discharged or died during the study period remained for analysis, totaling 13,257 hospitalizations. We excluded from the database all cases with notification performed in a state other than Maranhão and also the cases considered duplicates (Figure 01).

For the purpose of classification and analysis of vaccination status, individuals who received the full basic schedule (two doses of Coronavac immunizer, Pfizer and Astrazeneca) or a single dose (Janssen immunizer) within 14 days of the end of the schedule were considered vaccinated. Individuals who received only the first dose of the basic scheme or with a vaccination date after hospitalization were considered unvaccinated at the time of hospitalization.

For severity of the outcome of hospitalization for COVID-19, we considered: death, severe discharge, when hospitalizations required the use of ventilatory support and/or ICU admission, and non-severe discharge, when hospitalized individuals did not require the use of ventilatory support and/or ICU.

The characteristics of the hospitalized individuals were grouped according to the following characteristics/conditions:

- Sociodemographic characteristics: sex (male; female; ignored); age group (<20 years; 20 to 39 years; 40 to 49 years; 50 to 59 years; 60 to 69 years;



Source: The authors, 2023.

- 70 to 79 years; >80 years); race/skin color (white; black; yellow; brown; indigenous; ignored); education (no education; elementary 1; elementary 2; high school; higher education);

- Geographic characteristics: place of hospitalization (big island; inland);

- Risk conditions: have (0; 1 to 2; 3 or more);

- Protection conditions: vaccination status (unvaccinated; vaccinated);

- Characteristics of the hospitalization: outcome (death; non-severe hospital discharge; severe hospital discharge); ICU admission (yes; no; ignored); ventilatory support (no; yes/non-

-invasive; yes/invasive; ignored); length of hospital stay (in days).

For descriptive data analysis, means and standard deviation (SD) were calculated for quantitative variables and relative frequencies for categorical variables. The analyses were performed using R software, version 4.2.1.

The study was approved by the Research Ethics Committee of the University Hospital of the Federal University of Maranhão and by the National Research Ethics Commission (CONEP) under Opinion number: 4.098.427 and CAAE 32206620.0.0000.5086, dated June 19, 2020, in accordance with Resolution No. 466/2012 of the National

Health Council.

## RESULTS

In the year 2021, 21,411 cases of individuals with SARS were reported in the state of Maranhão, according to SIVEP-Gripe data. Of these, 912 (4.25%) were excluded for having been reported outside the state of Maranhão, 398 (1.86%) for being duplicate entries in the system, 3,832 (17.90%) for not presenting a determined evolution (high or death), and 3,015 (14.11%) for not having SARS by COVID-19.

Of the total of 13,257 individuals with SARS due to COVID-19, 6,425 (48.46%) were discharged from the hospital after a non-severe hospitalization, 1,573 (11.87%) were discharged with a severe hospitalization, and 5,259 (39.67%) died. Among individuals who were discharged from the hospital after a non-severe hospitalization, to a severe hospitalization, and died, the number of non-vaccinated individuals is much higher: 5,836, 1,398, and 4,704, respectively.

Most individuals were between 60 and 69 years old, totaling 2,603

(19.64%), of which 2,325 (89.32%) were not vaccinated and 278 (10.68%) were vaccinated. It is also noteworthy that among vaccinated individuals younger than 20 years of age, there were no hospitalizations. Males had the highest proportion of hospitalizations (57.72%), and the highest proportion among those not vaccinated (90.42%). The prevalent color/race was brown (77.29%), of which 90.39% were not vaccinated.

Most of the records occurred in the interior of the state, representing 52.73%, and mostly in unvaccinated in-

Table 1. Sociodemographic characteristics, place of hospitalization, health and hospitalization conditions, and vaccination status of individuals hospitalized with COVID-19 (n=13,257), Maranhão, 2021

Variable	Not Vaccinated		Vaccinated		Total	
	N	%	N	%	N	%
Age Group						
<20	225	100	0	0,00	225	1,7
20a29	578	98,30	10	1,70	588	4,44
30a39	1578	98,20	29	1,80	1607	12,12
40a49	2127	97,97	44	2,03	2171	16,38
50a59	2507	97,02	77	2,98	2584	19,49
60a69	2325	89,32	278	10,68	2603	19,64
70a79	1526	76,26	475	23,74	2001	15,09
>=80	1072	72,53	406	27,47	1478	11,14
Gender						
Female	5017	89,56	585	10,44	5602	42,26
Male	6919	90,42	733	9,58	7652	57,72
Ignored	2	66,67	1	33,33	3	0,02
Color/Race						
White	1398	88,43	183	11,57	1581	11,93
Black	677	89,20	82	10,80	759	5,73
Yellow	349	90,18	38	9,82	387	2,92
Brown	9261	90,39	985	9,61	10246	77,29
Indigenous	20	80,00	5	20,00	25	0,19
Ignored	233	89,96	26	10,04	259	1,95
Education						
No	635	86,04	103	13,96	738	5,57

Fundamental 1	1029	89,48	121	10,52	1150	8,67
Fundamental 2	665	91,64	61	8,40	726	5,48
Medium	1268	94,42	75	5,58	1343	10,13
Superior	573	93,02	43	6,98	616	4,65
Not applicable	53	100,00	0	0,00	53	0,40
Ignored	7715	89,39	916	10,61	8631	65,11
Region						
Big Island	5672	90,51	595	9,42	6267	47,27
Interior	6266	89,64	724	10,36	6990	52,73
No risk conditions						
No	7097	92,23	598	7,77	7695	58,04
1 or 2	4584	87,30	667	12,70	5251	39,61
3 or more	257	82,64	54	17,36	311	2,35
Outcome						
High/not severe	5836	90,83	589	9,17	6425	48,46
High/High	1398	88,87	175	11,13	1573	11,87
Death	4704	89,45	555	10,55	5259	39,67
ICU						
Yes	4429	89,31	530	10,69	4959	37,41
No	3841	91,30	366	8,70	4207	31,73
Ignored	3668	89,66	423	10,34	4091	30,86
Respirator						
Yes/Invasive	2228	89,91	250	10,09	2478	18,69
Yes/Non invasive	4550	89,94	509	10,06	5059	38,16
No	1225	90,88	123	9,12	1348	10,17
Ignored	3935	90,00	437	10,00	4372	32,98

Source: SIVEP-GRIPE and SIPNI database, adapted by the authors, 2023.

dividuals (90.51%). Regarding risk conditions, most individuals (58.04%) had none, followed by those who had 1 or 2 (39.61%), while 2.35% had 3 or more.

Most individuals were discharged non-severe (48.46%), with 37.41% not requiring ICU admission and 38.16% using non-invasive ventilatory support (Table 1).

When comparing the vaccination status for each outcome of cases by age group, it was observed that the predominant age group among individuals

who were not severely discharged was 30 to 69 years old. Of the individuals with severe discharge there were fewer discrepancies, being higher in the 40 to 69 age groups. Among individuals who died, we observed a tendency to increase as the age range increased, being higher in the 60 to 69 age group (Figure 2).

The first semester of the year 2021 registered more cases, with May having the most cases among individuals with COVID-19 with non-severe discharge (1,323 cases), of which 90.60% were

not vaccinated. Among individuals with severe discharge, the month of June was the one with the highest number of cases (270), of which 85.25% were not vaccinated. Among the cases that died, March was the peak month (1,161 deaths), of which 98.5% were unvaccinated (Figure 3).

The mean number of days of hospitalization among vaccinated individuals was slightly lower in those who progressed to discharge/serious. No difference was observed between the mean days

of hospitalization between vaccinated and non-vaccinated individuals who progressed to non-severe discharge and death (Figure 4).

**DISCUSSION**

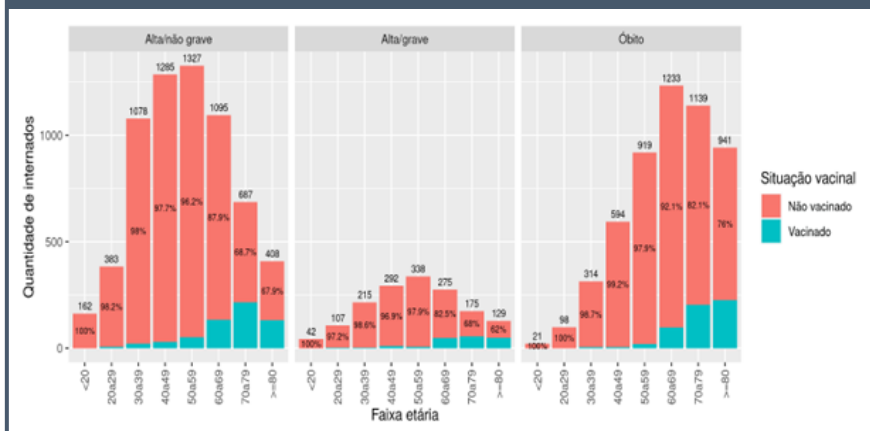
In Maranhão, on January 18, 2021 vaccination against COVID-19 started, and it was possible to compare hospital admissions by the disease according to the vaccination situation since the beginning of the year. Among the records in SIVEP Influenza by COVID-19 that were discharged from hospital, most were considered as not severe, i.e., with no need for ICU admission and/or without use of ventilatory support, corroborating the study conducted in Manaus-AM11, which found substantial change in the patterns of hospitalizations and deaths by COVID-19 after the beginning of vaccination.

Regardless of the outcome (non-severe discharge, severe discharge, and death) there was a lower proportion of vaccinated individuals. These findings suggest that immunization against COVID-19 may mitigate disease severity among patients who develop the disease<sup>15</sup>.

The age group under 20 years had the lowest percentage of hospitalization and of these all were unvaccinated, since the inclusion of this group for vaccination against COVID-19 only occurred in late 2021 and early 2022. Previous studies show that children and adolescents have been shown to be less susceptible to the severe forms of COVID-19<sup>16,17</sup>. When comparing the vaccination status by age group in each of the three outcomes of hospitalization, it was observed that those with non-severe discharge and severe discharge were higher in the 30 to 69 age group, considered to be an economically active age group with a lower rate of social isolation.

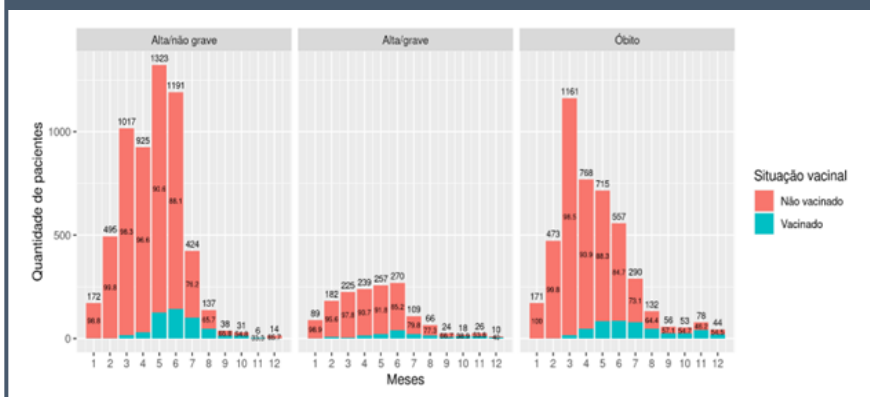
The number of hospitalized individuals who died increased with age, with a peak of deaths in the 60 to 69 age group. These results are similar to those

Figure 2. Outcomes of hospitalizations for COVID-19 according to vaccination status by age group, Maranhão, 2021.



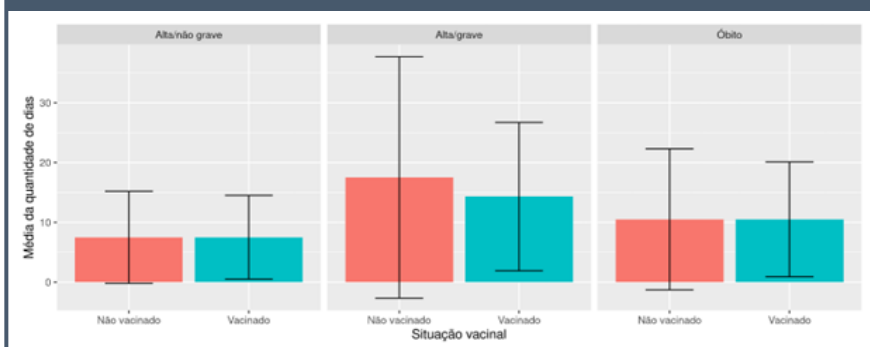
Source: SIVEP-GRIPE and SIPNI databases, adapted by the authors, 2023.

Figure 3. Outcomes of hospitalizations for COVID-19, according to vaccination status by months of the year, Maranhão, 2021.



Source: SIVEP-GRIPE and SIPNI databases, adapted by the authors, 2023.

Figure 04. Average days of hospitalization among those hospitalized for COVID-19, according to hospitalization outcome and vaccination status, Maranhão, 2021.



Source: SIVEP-GRIPE and SIPNI databases, adapted by the authors, 2023.

of studies on the effect of vaccination in the Israeli population, where the elderly, having been prioritized for vaccination, came to represent a lower number among hospitalizations and deaths<sup>18,19</sup>.

The number of vaccinees among those who were discharged (non-severe and severe) or died was also progressive according to increasing age, since, even in the face of various measures to contain the disease, such as vaccination, studies have reported that the elderly population is more vulnerable to severe forms, hospitalization, and death from COVID-19, when compared to younger individuals<sup>20</sup>. This occurs due to the natural physiological changes of the aging process that compromise the immune system and due to the greater number of complications resulting from chronic diseases.<sup>21</sup>

The months of the first semester of the year 2021 were those that registered more cases of hospitalization for COVID-19, justified by the circulation of the variants of concern and of public health interest in Brazil, which present as characteristics greater transmission,

increased resistance to neutralizing antibodies, increased virulence, and increased risk of reinfection. In Brazil, four variants classified as Variants of Concern by the WHO (Alpha - B.1.1.7, Beta - B.1.351, Gamma - B.1.1.28.1 and Delta - B.1.617.2) and two of the seven variants classified as Variants of Interest (Zeta - B.1.1.28.2 and Lambda - C.37) were identified in this period<sup>22</sup>. In Maranhão, the most circulating variant in this period was Gama, followed by Delta, being the first state to notify it.<sup>23</sup>

With the advance of vaccination in Brazil and in the state of Maranhão, a drop in the number of cases of COVID-19 is observed in the second half of the year in all hospitalization outcomes from July 2021 onwards, following the patterns of behavior of the disease in the country<sup>2</sup>.

Regarding the limitations of the study, it is noteworthy that, since the data were collected from secondary sources, their accuracy may decrease due to the quality of information filling. Despite this, it was considered that the methodology used proved to be sufficient to

meet the objective of the study, providing relevant information about the severity of the disease according to the vaccination status.

## CONCLUSION

This study allowed characterizing and comparing hospitalizations for COVID-19 in the State of Maranhão according to the vaccination status against the disease. We found positive implications of vaccination as a public health measure to reduce the severity of COVID-19 in individuals hospitalized for the disease. With immunization of the population, few immunized hospitalized individuals progressed to severe hospitalization, i.e., use of ventilatory support and/or ICU admission, and death, compared to unvaccinated individuals, which showed that vaccination had an impact on reducing the occurrence of severe cases. Most immunized individuals who developed the disease and died were of advanced age, which worsens the disease prognosis.

## REFERÊNCIAS

- Ranzani, O. T., Bastos, L. S. L., Gelli, J. G. M., Marchesi, J. F., Baião, F., Hamacher, S., & Bozza, F. A. Characterisation of the first 250,000 hospital admissions for COVID-19 in Brazil: a retrospective analysis of nationwide data. *The Lancet. Respiratory medicine*, 9(4), 407–418, 2021. [https://doi.org/10.1016/S2213-2600\(20\)30560-9](https://doi.org/10.1016/S2213-2600(20)30560-9)
- PAINEL CONASS | COVID-19 [Internet]. [www.conass.org.br](http://www.conass.org.br). Available from: <https://www.conass.org.br/painelconasscovid19/>
- BRASIL. Ministério da Saúde. Secretaria de Vigilância em Saúde. Secretaria Extraordinária de Enfrentamento à COVID-19. Plano Nacional de Operacionalização da Vacinação Contra a COVID-19. 2022.
- Passarelli-Araujo, H., Pott-Junior, H., Susuki, A. M., Olak, A. S., Pescim, R. R., Tomimatsu, M. F. A. I., Volce, C. J., Neves, M. A. Z., Silva, F. F., Narciso, S. G., Aschner, M., Paoliello, M. M. B., & Urbano, M. R. The impact of COVID-19 vaccination on case fatality rates in a city in Southern Brazil. *American journal of infection control*, 50(5), 491–496, 2022. <https://doi.org/10.1016/j.ajic.2022.02.015>
- Vasileiou, E.; Simpson, C.R.; Shi, T.; Kerr, S.; Agrawal, U.; Akbari, A.; Bedston, S.; Beggs, J.; Bradley, D.; Chuter, A.; et al. Interim findings from first-dose mass COVID-19 vaccination roll-out and COVID-19 hospital admissions in Scotland: A national prospective cohort study. *Lancet* 2021, 397, 1646–1657. DOI:10.2139/ssrn.3789264.
- Hitchings, M. D. T., Ranzani, O. T., Torres, M. S. S., de Oliveira, S. B., Almiron, M., Said, R., Borg, R., Schulz, W. L., de Oliveira, R. D., da Silva, P. V., de Castro, D. B., Sampaio, V. S., de Albuquerque, B. C., Ramos, T. C. A., Fraxe, S. H. H., da Costa, C. F., Naveca, F. G., Siqueira, A. M., de Araújo, W. N., Andrews, J. R., ... Croda, J. Effectiveness of CoronaVac among healthcare workers in the setting of high SARS-CoV-2 Gamma variant transmission in Manaus, Brazil: A test-negative case-control study. *Lancet regional health. Americas*, 1, 100025, 2021. <https://doi.org/10.1016/j.lana.2021.100025>
- Oliveira LN de, Santos AKF de S, Carvalho RMC de, Cosme FH de S, Querino CAC, Nascimento RF do, Macedo CL. Avaliação da eficácia e segurança das principais vacinas utilizadas contra COVID-19 no Brasil / Evaluation of the efficacy and safety of the main vaccines used against COVID-19 in Brazil. *Braz. J. Develop.* [Internet]. 2022 Apr. 28 [cited 2023 Jan. 4];8(4):31753-67. Available from: <https://ojs.brazilianjournals.com.br/ojs/index.php/BRJD/article/view/47202>

8. Victora, P. C., Castro, P. M. C., Gurzenda, S., Medeiros, A. C., França, G. V. A., & Barros, P. A. J. D. Estimating the early impact of vaccination against COVID-19 on deaths among elderly people in Brazil: Analyses of routinely-collected data on vaccine coverage and mortality. *EClinicalMedicine*, 38, 101036, 2021. <https://doi.org/10.1016/j.eclinm.2021.101036>
9. Alencar, C. H., Cavalcanti, L. P. G., Almeida, M. M., Barbosa, P. P. L., Cavalcante, K. K. S., Melo, D. N., de Brito Alves, B. C. F., & Heukelbach, J. (2021). High Effectiveness of SARS-CoV-2 Vaccines in Reducing COVID-19-Related Deaths in over 75-Year-Olds, Ceará State, Brazil. *Tropical medicine and infectious disease*, 6(3), 129. <https://doi.org/10.3390/tropicalmed6030129>
10. Orellana, J. D.Y., Cunha, G.M, Marrero, L., Leite, I.C, Domingues, C.M.A.S., Horta, B.L.. Mudanças no padrão de internações e óbitos por COVID-19 após substancial vacinação de idosos em Manaus, Amazonas, Brasil. *Cadernos de Saúde Pública* [online]. 2022, v. 38, n. 5 [Acessado 4 Janeiro 2023], PT192321. Disponível em: <<https://doi.org/10.1590/0102-311XPT192321>>. Epub 16 Maio 2022. ISSN 1678-4464. <https://doi.org/10.1590/0102-311XPT192321>.
11. Rosenberg, E. S., Dorabawila, V., Easton, D., Bauer, U. E., Kumar, J., Hoen, R., Hoefer, D., Wu, M., Lutterloh, E., Conroy, M. B., Greene, D., & Zucker, H. A. (2022). Covid-19 Vaccine Effectiveness in New York State. *The New England Journal of medicine*, 386(2), 116–127. <https://doi.org/10.1056/NEJMoa2116063>
12. Frias DFR, Romera GR de R, Maziero L de MA, Tebet DGM, Barbosa KF. Efeitos da vacinação contra COVID-19 com relação a evolução dos casos no estado de Mato Grosso do Sul. *Rev. Cereus*, 13(4):149-57, 2021. Disponível em: <http://ojs.unirg.edu.br/index.php/1/article/view/3583>
13. Kerr L, Kendall C, Silva AAM da, Aquino EML, Pescarini JM, Almeida RLF de, et al. COVID-19 no Nordeste brasileiro: sucessos e limitações nas respostas dos governos dos estados. *Ciência & Saúde Coletiva*. 2020. Disponível em: <https://scielosp.org/pdf/csc/2020.v25suppl2/4099-4120/pt>
14. INSTITUTO BRASILEIRO DE GEOGRAFIA E ESTATÍSTICA-IBGE. Censo Demográfico. Maranhão, 2022
15. Kerr L, Kendall C, Silva AAM da, Aquino EML, Pescarini JM, Almeida RLF de, et al. COVID-19 no Nordeste brasileiro: sucessos e limitações nas respostas dos governos dos estados. *Cien Saude Colet*, 2020. Disponível em: <https://www.scielo.br/j/csc/a/kYBX-8WJpFGSzmWdtV5Cct/>
16. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, Transmission, Diagnosis, and Treatment of Coronavirus Disease 2019 (COVID-19): A Review. *JAMA*. 2020;324(8):782–793. doi:10.1001/jama.2020.12839
17. Miranda, J. DE O. F., & Morais, A. C. A COVID-19 na vida de crianças e adolescentes brasileiros: poucos sintomas e muitos impactos. *Revista Enfermagem Contemporânea*, 10(1), 6–7. <https://doi.org/10.17267/2317-3378rec.v10i1.3708>
18. Rossman H, Shilo S, Meir T, Gorfine M, Shalit U, Segal E. COVID-19 dynamics after a national immunization program in Israel. *Nat Med*. 2021;27(6):1055-1061. doi:10.1038/s41591-021-01337-2 Wise, J. Covid-19: infections in England fall by two thirds since January. *BMJ*, v. 18, n. 372, p. 491, 2021.
19. D'Adamo H, Yoshikawa T, Ouslander JG. Coronavirus Disease 2019 in Geriatrics and Long-term Care: the ABCDs of COVID-19. *J Am Geriatr Soc*. 2020;68(5):1-6. <https://doi.org/10.1111/jgs.16445>
20. Tavares DMDS, Oliveira NGN, Diniz-Rezende MA, Bitencourt GR, Silva MBD, Bolina AF. Scientific knowledge about infections by the new coronavirus in older adults: a scoping review. *Rev Bras Enferm*. 2021;74Suppl 1(Suppl 1):e20200938. Published 2021 Apr 14. doi:10.1590/0034-7167-2020-0938
21. Michelon, C.M. Principais variantes do SARS-CoV-2 notificadas no Brasil. *RBAC*. 2021;53(2):109-116. <https://doi.org/10.21877/2448-3877.202100961>
22. MARANHÃO. Secretaria Estadual de Saúde. Boletim Epidemiológico 02/2022: Monitoramento da circulação das variantes de COVID 19 no Maranhão. 2022. Disponível em: <https://www.saude.ma.gov.br/wp-content/uploads/2022/02/BOLETIM-02-MONITORAMENTO-CIRCULACAO-NOVAS-VARIANTES-MA.pdf>