**COVID-19: impact of original, Gamma, Delta, and Omicron variants of SARS-CoV-2 in vaccinated and unvaccinated pregnant and postpartum women**

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**ABSTRACT**

**Objective** To compare vaccinated and unvaccinated hospitalized pregnant and postpartum women with original, Gamma, Delta, and Omicron variants of SARS-CoV-2 in terms of demographic and clinical characteristics and disease progression using Brazilian epidemiological data.

**Methods** A retrospective study using the Brazilian national database of severe acute respiratory syndrome (SARS) included hospitalized pregnant and postpartum women, from 10 to 49 years, with COVID-19 confirmed by PCR, from February 2020 to April 2022. Both groups were divided into vaccinated against COVID-19 (with at least one dose) and unvaccinated and among the variants of concern – original, Gamma, Delta and Omicron – according to the dominant variant circulating in Brazil. Comparisons regarding demographic and clinical characteristics, comorbidities, signs, symptoms, and outcomes were performed.

**Results** A total of9,681 pregnant and 2,283 postpartum women were identified. In the unvaccinated group, postpartum women were more likely to be admitted to an ICU with the original, Gamma and Omicron variants, to need invasive ventilation with the original, Gamma and Omicron variants, or to die for the original and Gamma variants. Vaccine was effective in reducing adverse outcomes such as ICU admission, invasive ventilatory and deaths in both groups.

**Conclusion** Postpartum women had higher risk of developing severe forms of COVID-19 (need for ICU, use of invasive ventilatory support, and death) among the different variants, mainly in unvaccinated groups. The end of pregnancy should not underestimate the risk of COVID-19. Vaccinated women had less percentage of severe outcomes; this should reinforce vaccination in both groups as a priority.

**KEYWORDS**

COVID-19 - SARS-CoV-2 - vaccine - variants – pregnancy – postpartum – outcomes

**INTRODUCTION**

Covid-19 is a severe acute respiratory syndrome caused by the coronavirus SARS-CoV-2, which was first reported at Wuhan, China, in December 2019. It has spread around the world and WHO declared a pandemic in March 2020.[[1]](#endnote-1) Until May 22, 2022, globally, over 520 million confirmed cases with more than 6.2 million deaths have been reported.[[2]](#endnote-2)

The infection is a multi-systemic disease with clinical spectrum ranging from asymptomatic to severe and critical disease. So, it raised a concern about morbidity and mortality in pregnant women and about perinatal outcomes. First reports didn’t find higher mortality or severity rates compared to non-obstetric population; subsequent studies, however, showed that obstetric population had higher risk not only for death but also for intensive care admission and invasive ventilation compared to nonpregnant women. [[3]](#endnote-3) [[4]](#endnote-4) [[5]](#endnote-5) [[6]](#endnote-6) [[7]](#endnote-7) [[8]](#endnote-8) [[9]](#endnote-9) [[10]](#endnote-10) [[11]](#endnote-11)

Over time SARS-CoV-2 developed mutations, and some of the new variants, defined by WHO as Variants of Concern (VOC), were observed to cause higher transmissibility, change in Covid-19 epidemiology, increased virulence, modification in clinical disease presentation, or decreased effectiveness of public health, social measures, and available therapeutics.[[12]](#endnote-12) Until April 1, 2022, three VOCs have been detected in Brazil: Gamma, Delta, and Omicron.[[13]](#endnote-13)

Since the beginning of the pandemic, a high number of maternal deaths due to Covid-19 was reported in Brazil (124 deaths until June 18, 2020).[[14]](#endnote-14)  This trend continued since then, with 295 maternal deaths at the end of the last 2020 epidemiologic week (January 2, 2021).[[15]](#endnote-15) In 2021, until vaccination campaigns start for this population in Brazil (May 1), pregnant and postpartum women continued to have higher risk of admission to ICU, intubation, and death in comparison to nonmaternal women and men.[[16]](#endnote-16) [[17]](#endnote-17)

As vaccination is one of the most effective strategies to reduce transmission and severity of infectious diseases, it is important to evaluate not only the effectiveness of the vaccines in the obstetric population, but also their protection against the new variants.[[18]](#endnote-18) [[19]](#endnote-19)

Therefore, the authors of the present study aim to compare pregnant women and postpartum women, vaccinated and unvaccinated, among the different variants of concern, according to data related to the SARS-CoV-2 infection by using population statistics from SIVEP-Gripe (System of Information about Epidemiological Surveillance of Influenza) of the Health Ministry of Brazil.

# MATERIALS AND METHODS

A retrospective assessment of the subjects from SIVEP-Gripe, a Brazilian national database containing surveillance data on severe acute respiratory syndrome (SARS) was performed.[[20]](#endnote-20) The notification of SARS is compulsory in cases of the flu syndrome (acute respiratory condition, characterized by at least two of the following signs and symptoms: fever [even if reported], chills, sore throat, headache, coryza, cough, anosmia, and ageusia), associated with dyspnea (respiratory distress), persistent chest pressure, oxygen saturation (SpO2) below 95% in room air, or cyanosis. SIVEP-Gripe is notified of all cases of hospitalization both in public and in private hospitals, as well as of all deaths caused by SARS-CoV-2, irrespective of hospitalization.

SIVEP-Gripe registers include demographic data (sex, age, skin color/ethnicity, schooling, obstetric status, city of residence); clinical data (signs and symptoms, risk factors and comorbidities); epidemiological data (previous flu vaccination, community-acquired infection, or nosocomial infection); laboratory and etiological diagnoses. There is also information about hospital admission, ICU admission, use of ventilatory support (invasive and noninvasive), and disease outcome (cure or death).

Data search covered 2020 (epidemiological weeks 1 to 53 from December 29, 2019 to January 02, 2021), however, the first Brazilian records began in epidemiological week 8 (onset of symptoms of the first confirmed case was on February 17, 2020); 2021 (epidemiological weeks 1 to 52 from January 03, 2021 to January 01, 2022) and 2022 (epidemiological weeks 1 to 13 from January 02, 2022 to April 02, 2022), with the last update on April 25, 2022.[[21]](#endnote-21) Search included all records on obstetric women aged 10 to 49 years hospitalized with COVID-19 confirmed with a positive RT-PCR result for SARS-CoV-2. Cases were excluded if they were not hospitalized or confirmed with an RT-PCR for SARS-CoV-2, or if gender or pregnancy status were not registered. The result was 11,964 women who were divided into two groups: pregnant women (n=9,681) and puerperal women (n=2,283). Then, each group was separated into original, Gamma, Delta, and Omicron variants according to the dominant variant circulating in Brazil at the date of notification (Figure 1). The dominance of Gamma variant started on February 01, 2021; Delta on August 01, 2021; and Omicron on January 01, 2022.[[22]](#endnote-22)As vaccination in Brazil for the maternal population began in May 2021 (during the dominance of Gamma variant), the final groups were also divided in unvaccinated and vaccinated for the analysis of signs and symptoms and outcomes.[[23]](#endnote-23) Only valid responses of each analyzed variable are considered. The number of valid observations of each variable is identified in the tables of analysis. Variables used in the analysis were age bracket, skin color/ethnicity, schooling, comorbidities, signs and symptoms, admission to ICU, invasive respiratory support, and outcome (death). Comorbidities reported were chronic cardiovascular disease, asthma, obesity, and diabetes. Signs and symptoms considered were fever, cough, sore throat, dyspnea, respiratory discomfort, oxygen saturation in room air less than 95% (SpO2<95%), diarrhea, vomiting, abdominal pain, fatigue, anosmia, and ageusia.

SIVEP-Gripe records are publicly available anonymized data. Hence, according to Brazilian Ethics regulatory requirements, ethical approval by an Institutional Review Board is not necessary.

**Figure 1: Study profile**

**DATA ANALYSIS**

Qualitative variables were displayed as absolute frequencies (n) and category percentages (%).

Chi-square or Fisher test was used to evaluate the association between groups and qualitative variables. Odds Ratio (OR) was considered as a measure of association to compare the relative odds of the occurrence of the variable of interest between groups and 95% confidence interval was also calculated. To compare the OR among the groups of variants, the Breslow Day test was applied and Bonferroni method was used to adjust alpha for multiple comparisons.[[24]](#endnote-24) As the significance level adopted was 5% (alpha=0.05), the adjusted alpha was 0.05/6=0.008.

The analyses were performed with the statistical R software (R Foundation for Statistical Computing Platform, version 4.0.3).[[25]](#endnote-25)

# RESULTS

A total of 11,964 obstetric women, aged from 10 to 49 years, and hospitalized with a positive RT-PCR for SARS-CoV-2 result was identified. Of these, 9,681 were pregnant and 2,283 were in puerperal period. There were no significant differences in age bracket, ethnicity and schooling comparing the groups; however, when comorbidities were evaluated, postpartum had lower rates of comorbidities than pregnant women (Table 1).

**Table 1. Demographic and clinical characteristics of pregnant and postpartum women, from 10 to 49 years, with severe acute respiratory syndrome (SARS) due to COVID-19 (PCR+) – Brazil, February 17, 2020 – April 04, 2021**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Variant** | **Age bracket (years)** | **Pregnant n (%)** | **Puerperal n (%)** | **p** |
| Original (n=4,735) | <20 | 260 (6.8%) | 67 (7.2%) | 0.2278C |
| 20-34 | 2,522 (66.4%) | 594 (63.5%) |
| ≥35 | 1,017 (26.8%) | 275 (29.4%) |
| Gamma (n=5,590) | <20 | 243 (5.3%) | 58 (5.7%) | 0.8146 C |
| 20-34 | 2,956 (64.6%) | 656 (64.8%) |
| ≥35 | 1,379 (30.1%) | 298 (29.4%) |
| Delta (n=681) | <20 | 38 (6.7%) | 10 (9.0%) | 0.6403 C |
| 20-34 | 388 (68.1%) | 72 (64.9%) |
| ≥35 | 144 (25.3%) | 29 (26.1%) |
| Omicron (n=958) | <20 | 66 (9.0%) | 26 (11.6%) | 0.3071 C |
| 20-34 | 519 (70.7%) | 147 (65.6%) |
| ≥35 | 149 (20.3%) | 51 (22.8%) |
| **Variant** | **Skin color/ethnicity** | **Pregnant n (%)** | **Puerperal n (%)** | **p** |
| Original (n=3,837) | White | 1,302 (42.1%) | 290 (38.8%) | 0.0884F |
| Black | 211 (6.8%) | 50 (6.7%) |
| Yellow | 38 (1.2%) | 3 (0.4%) |
| Brown | 1,526 (49.4%) | 400 (53.5%) |
| Indigenous | 13 (0.4%) | 4 (0.5%) |
| Gamma (n=4,786) | White | 1,911 (48.7%) | 400 (46.4%) | 0.5042F |
| Black | 232 (5.9%) | 56 (6.5%) |
| Yellow | 31 (0.8%) | 6 (0.7%) |
| Brown | 1,741 (44.4%) | 396 (45.9%) |
| Indigenous | 9 (0.2%) | 4 (0.5%) |
| Delta (n=587) | White | 241 (48.9%) | 48 (51.1%) | 0.8396F |
| Black | 36 (7.3%) | 4 (4.3%) |
| Yellow | 3 (0.6%) | 0 (0.0%) |
| Brown | 209 (42.4%) | 42 (44.7%) |
| Indigenous | 4 (0.8%) | 0 (0.0%) |
| Omicron (n=866) | White | 417 (62.8%) | 118 (58.4%) | 0.1714F |
| Black | 40 (6.0%) | 9 (4.5%) |
| Yellow | 7 (1.1%) | 0 (0.0%) |
| Brown | 199 (30.0%) | 74 (36.6%) |
| Indigenous | 1 (0.2%) | 1 (0.5%) |
| **Variant** | **Schooling** | **Pregnant n (%)** | **Puerperal n (%)** | **p** |
| Original (n=2,003) | No schooling | 7 (0.4%) | 3 (0.8%) | 0.5617F |
| Up to high school | 394 (24.2%) | 84 (22.5%) |
| High school | 896 (55%) | 203 (54.4%) |
| College | 333 (20.4%) | 83 (22.3%) |
| Gamma (n=2,360) | No schooling | 15 (0.8%) | 6 (1.4%) | 0.4628F |
| Up to high school | 472 (24.5%) | 109 (25.3%) |
| High school | 1,048 (54.3%) | 236 (54.9%) |
| College | 395 (20.5%) | 79 (18.4%) |
| Delta (n=281) | No schooling | 0 (0.0%) | 0 (0.0%) | 0.6307F |
| Up to high school | 72 (30.6%) | 11 (23.9%) |
| High school | 111 (47.2%) | 23 (50.0%) |
| College | 52 (22.1%) | 12 (26.1%) |
| Omicron (n=436) | No schooling | 2 (0.6%) | 1 (1.2%) | 0.6862F |
| Up to high school | 101 (28.7%) | 27 (32.1%) |
| High school | 180 (51.1%) | 41 (48.8%) |
| College | 69 (19.6%) | 15 (17.9%) |
| **Comorbidities** | **Variant** | **Pregnant n (%)** | **Puerperal n (%)** | **p** |
| Chronic cardiovascular disease | Original (n=1,887) | 240/1,305 (18.4%) | 92/582 (15.8%) | 0.1951C |
| Gamma (n=2,071) | 245/1,404 (17.5%) | 83/667 (12.4%) | 0.0044 C |
| Delta (n=253) | 29/178 (16.3%) | 8/75 (10.7%) | 0.3362 C |
| Omicron (n=323) | 32/190 (16.8%) | 7/133 (5.3%) | 0.0030 C |
| Asthma | Original (n=1,884) | 159/1,287 (12.4%) | 35/557 (6.3%) | 0.0001 C |
| Gamma (n=2,028) | 148/1,369 (10.8%) | 37/659 (5.6%) | 0.0002 C |
| Delta (n=254) | 23/182 (12.6%) | 6/72 (8.3%) | 0.4513 C |
| Omicron (n=319) | 14/188 (7.4%) | 6/131 (4.6%) | 0.4212 C |
| Diabetes | Original (n=1,885) | 275/1,318 (20.9%) | 67/567 (11.8%) | <0.0001 C |
| Gamma (n=2,120) | 335/1,442 (23.2%) | 77/678 (11.4%) | <0.0001 C |
| Delta (n=264) | 48/187 (25.7%) | 8/77 (10.4%) | 0.0095 C |
| Omicron (n=327) | 39/193 (20.2%) | 7/134 (5.2%) | 0.0002 C |
| Obesity | Original (n=1,819) | 181/1,261 (14.4%) | 62/558 (11.1%) | 0.0719 C |
| Gamma (n=2,129) | 365/1,445 (25.3%) | 110/684 (16.1%) | <0.0001 C |
| Delta (n=256) | 39/183 (21.3%) | 8/73 (11.0%) | 0.0796 C |
| Omicron (n=318) | 24/186 (12.9%) | 4/132 (3.0%) | 0.0021F |

p comparison between groups (pregnant and puerperal women); C Chi-square test, F Fisher exact test

Table 2 shows COVID-19 signs and symptoms in pregnant and postpartum women allocated by vaccination status (unvaccinated and vaccinated with at least one dose against COVID-19), and separated by the variant of concern (original, Gamma, Delta, and Omicron). Regarding the unvaccinated, puerperal in comparison to pregnant women had smaller chance of fever, cough and vomiting with original and Gamma variants, smaller chance of dyspnea, anosmia and ageusia with the Gamma variant and smaller chance of diarrhea with the original variant. Respiratory discomfort and SpO2<95% were more frequent in puerperal than in pregnant women with the original variant. In the group of vaccinated, puerperal women had less chance of fever with Gamma and Omicron variants, less respiratory discomfort with Delta variant and less vomiting and abdominal pain with Omicron variant. Dyspnea and SpO2<95% were more frequent in puerperal than in pregnant women with Omicron variant. When Gamma, Delta and Omicron variants were separately compared to the original variant, in the unvaccinated group, Gamma variant had difference regarding SpO2<95% and all the others had no significant differences. For the vaccinated group, difference was found only in Delta for respiratory discomfort.

**Table 2. COVID-19 signs and symptoms in pregnant and postpartum women, from 10 to 49 years, with severe acute respiratory syndrome (SARS) due to COVID-19 (PCR+) according to the SARS-CoV-2 variants – Brazil, February 17, 2020 – April 04, 2021**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **SIGNS AND SYMPTOMS** |  | **UNVACCINATED** | | | | **Vaccinated (at least one dose)** | | | |
| **Variant** | **Pregnant**  **n (%)** | **Puerperal**  **n (%)** | **Puerperal vs. Pregnant**  **OR (95% CI)** | **Comparison with original variant** | **Pregnant**  **n (%)** | **Puerperal**  **n (%)** | **Puerperal vs. Pregnant**  **OR (95% CI)** | **Comparison with original variant** |
| **Fever** | **Original (n=4,147)** | 2,285/3,343 (68.4%) | 498/804 (61.9%) | 0.75  (0.64 – 0.88) | - | - | - | - | - |
| **Gamma (n=2,788)** | 1,267/1,978 (64.1%) | 239/452 (52.9%) | 0.63  (0.51 – 0.77) | 0.1773 | 193/298 (64.8%) | 30/60 (50.0%) | 0.54  (0.31 – 0.95) | 0.2712 |
| **Delta (n=518)** | 136/210 (64.8%) | 30/47 (63.8%) | 0.96  (0.50 – 1.86) | 0.4830 | 138/226 (61.1%) | 16/35 (45.7%) | 0.54  (0.26 – 1.10) | 0.3646 |
| **Omicron (n=633)** | 96/166 (57.8%) | 26/53 (49.1%) | 0.70  (0.38 – 1.31) | 0.8289 | 159/320 (49.7%) | 27/94 (28.7%) | 0.41  (0.25 – 0.67) | 0.0206 |
| **Cough** | **Original (n=4,268)** | 2,673/3,451 (77.5%) | 574/817 (70.3%) | 0.69  (0.58 – 0.81) | - | - | - | - | - |
| **Gamma (n=2,902)** | 1,681/2,064 (81.4%) | 330/466 (70.8%) | 0.55  (0.44 – 0.69) | 0.1332 | 253/308 (82.1%) | 46/64 (71.9%) | 0.56  (0.30 – 1.03) | 0.5141 |
| **Delta (n=560)** | 179/227 (78.9%) | 40/52 (76.9%) | 0.89  (0.44 – 1.84) | 0.4858 | 185/243 (76.1%) | 25/38 (65.8%) | 0.60  (0.29 – 1.25) | 0.7319 |
| **Omicron (n=675)** | 119/174 (68.4%) | 36/56 (64.3%) | 0.83  (0.44 – 1.57) | 0.5684 | 222/339 (65.5%) | 64/106 (60.4%) | 0.80  (0.51 – 1.26) | 0.5257 |
| **Sore throat** | **Original (n=3,654)** | 822/2,959 (27.8%) | 184/695 (26.5%) | 0.94  (0.78 – 1.13) | - | - | - | - | - |
| **Gamma (n=2,528)** | 491/1,800 (27.3%) | 93/407 (22.9%) | 0.79  (0.61 – 1.02) | 0.2892 | 68/263 (25.9%) | 10/58 (17.2%) | 0.60  (0.29 – 1.25) | 0.2433 |
| **Delta (n=478)** | 48/190 (25.3%) | 8/45 (17.8%) | 0.64  (0.28 – 1.47) | 0.3791 | 67/213 (31.5%) | 8/30 (26.7%) | 0.79  (0.34 – 1.87) | 0.7100 |
| **Omicron (n=600)** | 58/159 (36.5%) | 11/46 (23.9%) | 0.55  (0.26 – 1.16) | 0.1711 | 117/301 (38.9%) | 29/94 (30.9%) | 0.70  (0.43 – 1.15) | 0.2850 |
| **Dyspnea** | **Original (n=4,082)** | 2,020/3,302 (61.2%) | 467/780 (59.9%) | 0.95  (0.81 – 1.11) | - | - | - | - | - |
| **Gamma (n=2,865)** | 1,488/2,038 (73.0%) | 308/461 (66.8%) | 0.74  (0.60 – 0.92) | 0.0792 | 218/304 (71.7%) | 39/62 (62.9%) | 0.67  (0.38 – 1.19) | 0.2505 |
| **Delta (n=536)** | 153/220 (69.5%) | 36/51 (70.6%) | 1.05  (0.54 – 2.05) | 0.7657 | 140/228 (61.4%) | 18/37 (48.6%) | 0.60  (0.30 – 1.20) | 0.2017 |
| **Omicron (n=593)** | 51/154 (33.1%) | 14/50 (28.0%) | 0.79  (0.39 – 1.59) | 0.6106 | 75/288 (26.0%) | 38/101 (37.6%) | 1.71 (1.06 – 2.77) | 0.021 |
| **Respiratory discomfort** | **Original (n=3,877)** | 1,563/3,120 (50.1%) | 413/757 (54.6%) | 1.20  (1.02 – 1.40) | - | - | - | - | - |
| **Gamma (n=2,717)** | 1,136/1,932 (58.8%) | 262/440 (59.5%) | 1.03  (0.84 -1.27) | 0.2720 | 159/282 (56.4%) | 33/63 (52.4%) | 0.85  (0.49 – 1.47) | 0.2411 |
| **Delta (n=502)** | 116/207 (56.0%) | 22/47 (46.8%) | 0.69  (0.37 – 1.30) | 0.0981 | 100/213 (46.9%) | 9/35 (25.7%) | 0.39  (0.17 – 0.87) | 0.0058 |
| **Omicron (n=584)** | 38/149 (25.5%) | 12/48 (25.0%) | 0.97  (0.46 – 2.06) | 0.5988 | 79/286 (27.6%) | 33/101 (32.7%) | 1.27  (0.78 – 2.08) | 0.8155 |
| **SpO2 <95%** | **Original (n=3,775)** | 1,015/3,039 (33.4%) | 342/736 (46.5%) | 1.73  (1.47 – 2.04) | - | - | - | - | - |
| **Gamma (n=2,737)** | 1,119/1,954 (57.3%) | 261/444 (58.8%) | 1.06  (0.86 – 1.31) | 0.0003 | 129/277 (53.4%) | 30/62 (48.4%) | 0.82  (0.47 – 1.42) | 0.0097 |
| **Delta (n=508)** | 114/209 (54.5%) | 32/47 (68.1%) | 1.78  (0.91 – 3.48) | 0.9395 | 89/217 (41.0%) | 15/35 (42.9%) | 1.08  (0.52 – 2.22) | 0.2082 |
| **Omicron (n=566)** | 25/148 (16.9%) | 10/45 (22.2%) | 1.41  (0.62 – 3.20) | 0.6269 | 40/280 (14.3%) | 25/93 (26.9%) | 2.21  (1.25 – 3.89) | 0.4205 |
| **Diarrhea** | **Original (n=3,537)** | 402/2,878 (14.0%) | 72/659 (10.9%) | 0.76  (0.58 – 0.99) | - | - | - | - | - |
| **Gamma (n=2,462)** | 221/1,749 (12.6%) | 37/400 (9.2%) | 0.70  (0.49 – 1.02) | 0.7636 | 22/253 (8.7%) | 6/60 (10.0%) | 1.17  (0.45 – 3.02) | 0.3852 |
| **Delta (n=463)** | 18/187  (9.6%) | 5/44 (11.4%) | 1.20  (0.42 – 3.44) | 0.3962 | 21/202 (10.4%) | 1/30  (3.3%) | 0.30  (0.04 – 2.30) | 0.3589 |
| **Omicron (n=557)** | 11/146  (7.5%) | 2/44  (4.5%) | 0.58  (0.12 – 2.74) | 0.7478 | 13/280 (4.6%) | 3/87  (3.4%) | 0.73  (0.20 – 2.64) | 0.9647 |
| **Vomiting** | **Original (n=3,537)** | 398/2,883 (13.8%) | 45/654 (6.9%) | 0.46  (0.33 – 0.64) | - | - | - | - | - |
| **Gamma (n=2,469)** | 245/1,758 (13.9%) | 30/401 (7.5%) | 0.50  (0.34 – 0.74) | 0.7606 | 34/252 (13.5%) | 6/58 (10.3%) | 0.74  (0.30 – 1.85) | 0.3383 |
| **Delta (n=461)** | 22/186 (11.8%) | 1/44  (2.3%) | 0.17  (0.02 – 1.32) | 0.3332 | 23/201 (11.4%) | 2/30  (6.7%) | 0.55  (0.12 – 2.47) | 0.8169 |
| **Omicron (n=560)** | 21/148 (14.2%) | 2/43  (4.7%) | 0.30  (0.06 – 1.31) | 0.5631 | 38/283 (13.4%) | 3/86  (3.5%) | 0.23  (0.07 – 0.77) | 0.2741 |
| **Abdominal pain** | **Original (n=1,880)** | 157/1,558 (10.1%) | 25/322 (7.8%) | 0.75  (0.48 – 1.17) | - | - | - | - | - |
| **Gamma (n=2,436)** | 174/1,737 (10.0%) | 34/395 (8.6%) | 0.85  (0.58 – 1.24) | 0.6900 | 27/245 (11.0%) | 2/59  (3.4%) | 0.28  (0.07 – 1.23) | 0.1975 |
| **Delta (n=457)** | 24/185 (13.0%) | 2/44  (4.5%) | 0.32  (0.07 – 1.41) | 0.2671 | 20/198 (10.1%) | 4/30 (13.3%) | 1.37  (0.43 – 4.32) | 0.3340 |
| **Omicron (n=556)** | 16/146 (11.0%) | 2/43  (4.7%) | 0.40  (0.09 – 1.80) | 0.4200 | 39/280 (13.9%) | 5/87  (5.7%) | 0.38  (0.14 – 0.99) | 0.1968 |
| **Fatigue** | **Original (n=1,926)** | 390/1,590 (24.5%) | 73/336 (21.7%) | 0.85  (0.64 – 1.13) | - | - | - | - | - |
| **Gamma (n=2,531)** | 635/1,807 (35.1%) | 125/404 (30.9%) | 0.83  (0.66 – 1.04) | 0.8627 | 101/258 (39.1%) | 19/62 (30.6%) | 0.69  (0.38 – 1.25) | 0.5167 |
| **Delta (n=469)** | 52/191 (27.2%) | 17/45 (37.8%) | 1.62  (0.82 – 3.21) | 0.0861 | 58/203 (28.6%) | 6/30 (20.0%) | 0.62  (0.24 – 1.61) | 0.5339 |
| **Omicron (n=560)** | 30/145 (20.7%) | 7/46 (15.2%) | 0.69  (0.28 – 1.69) | 0.6528 | 46/280 (16.4%) | 14/89 (15.7%) | 0.95  (0.49 – 1.82) | 0.7701 |
| **Anosmia** | **Original (n=1,978)** | 439/1,632 (26.9%) | 78/346 (22.5%) | 0.79  (0.60 – 1.04) | - | - | - | - | - |
| **Gamma (n=2,476)** | 372/1,764 (21.1%) | 54/395 (13.7%) | 0.59  (0.44 – 0.81) | 0.1705 | 56/257 (21.8%) | 9/60 (15.0%) | 0.63  (0.29 – 1.37) | 0.5931 |
| **Delta (n=460)** | 40/184 (21.7%) | 4/44  (9.1%) | 0.36  (0.12 – 1.07) | 0.1605 | 39/201 (19.4%) | 6/31 (19.4%) | 1.00  (0.38 – 2.60) | 0.6482 |
| **Omicron (n=546)** | 7/143  (4.9%) | 2/42  (4.8%) | 0.97  (0.19 – 4.86) | 0.8049 | 9/273 (3.3%) | 2/88  (2.3%) | 0.68  (0.14 – 3.22) | 0.8538 |
| **Ageusia** | **Original (n=1,953)** | 397/1,612 (24.6%) | 67/341 (19.6%) | 0.75  (0.56 – 1.00) | - | - | - | - | - |
| **Gamma (n=2,476)** | 333/1,764 (18.9%) | 54/397 (13.6%) | 0.68  (0.50 – 0.92) | 0.6417 | 59/257 (23.0%) | 7/58 (12.1%) | 0.46  (0.20 – 1.07) | 0.2823 |
| **Delta (n=460)** | 40/182 (22.0%) | 5/44 (11.4%) | 0.46  (0.17 – 1.23) | 0.3435 | 38/202 (18.8%) | 7/32 (21.9%) | 1.21  (0.49 – 3.00) | 0.3222 |
| **Omicron (n=545)** | 7/143  (4.9%) | 1/42  (2.4%) | 0.47 (  0.06 – 3.96) | 0.6736 | 13/272 (4.8%) | 2/88  (2.3%) | 0.46  (0.10 – 2.09) | 0.5372 |

OR, Odds Ratio; 95% CI, 95% confidence interval; SpO2, oxygen saturation in room air.

Until the date, Brazil had 1242 deaths by COVID-19 confirmed by RT-PCR in the obstetric population: 856 pregnant and 386 postpartum women. The rate of lethality was 9.5% in pregnant and 18.1% in postpartum. Most of them (n=846, 68.1%) were not vaccinated, 350 (28.2%) had no information about vaccination status (excluded from our analysis) and 46 (3.7%) were vaccinated. In unvaccinated group, compared to pregnant, puerperal women had a higher risk of needing admission to the ICU in original (OR: 1.81), Gamma (OR: 1.58) and Omicron (OR: 2.60), requiring invasive respiratory support in original (OR: 2.66), Gamma (OR: 2.17) and Omicron (OR: 3.55) and dying in original (OR: 2.49) and Gamma (OR: 1.97) variants groups. When vaccinated with at least one dose, compared to pregnant, postpartum women had higher chance of being admitted to ICU (OR: 1.85) and dying (OR:4.66) in Omicron variant group (Table 3). The comparison of Gamma, Delta, and Omicron separately with the original variant did not show any difference.

**Table 3. Comparison of outcomes in pregnant and postpartum women, from 10 to 49 years, with severe acute respiratory syndrome (SARS) due to COVID-19 (PCR+) according to the SARS-CoV-2 variants – Brazil, February 17, 2020 – April 04, 2021**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** |  | **Unvaccinated** | | | | **Vaccinated (with at least one dose)** | | | |
| **Variant** | **Pregnant**  **n (%)** | **Puerperal**  **n (%)** | **Puerperal vs. Pregnant**  **OR (95% CI)** | **Comparison with original variant** | **Pregnant**  **n (%)** | **Puerperal**  **n (%)** | **Puerperal vs. Pregnant**  **OR (95% CI)** | **Comparison with original variant** |
| **ICU admission**  **(n=8,823)** | **Original (n=4,432)** | 833/3,561 (23.4%) | 310/871 (35.6%) | 1.81  (1.54 – 2.12) | - | - | - | - | - |
| **Gamma (n=2,995)** | 789/2,140 (36.9%) | 231/482 (47.9%) | 1.58  (1.29 – 1.92) | 0.2871 | 88/307 (28.7%) | 27/66 (40.9%) | 1.72  (0.99 – 2.98) | 0.8663 |
| **Delta (n=569)** | 90/229 (39.3%) | 26/51 (51.0%) | 1.61  (0.87 – 2.96) | 0.7105 | 74/246 (30.1%) | 16/43 (37.2%) | 1.38  (0.70 – 2.71) | 0.4401 |
| **Omicron (n=827)** | 21/220 (9.5%) | 17/79 (21.5%) | 2.60  (1.29 – 5.23) | 0.3219 | 39/406 (9.6%) | 20/122 (16.4%) | 1.85  (1.03 – 3.30) | 0.9496 |
| **Invasive respiratory support (n=8,525)** | **Original (n=4,232)** | 299/3,384 (8.8%) | 174/848 (20.5%) | 2.66  (2.17 – 3.27) | - | - | - | - | - |
| **Gamma (n=2,911)** | 408/2,087 (19.5%) | 161/466 (34.5%) | 2.17  (1.74 – 2.71) | 0.1826 | 36/295 (12.2%) | 12/63 (19.0%) | 1.69  (0.82 – 3.47) | 0.2325 |
| **Delta (n=567)** | 35/229 (15.3%) | 11/51 (21.6%) | 1.52  (0.71 – 3.25) | 0.1608 | 19/244 (7.8%) | 4/43 (9.3%) | 1.21  (0.39 – 3.76) | 0.1723 |
| **Omicron (n=815)** | 7/218 (3.2%) | 8/76 (10.5%) | 3.55  (1.24 – 10.14) | 0.5993 | 12/399 (3.0%) | 6/122 (4.9%) | 1.67  (0.61 – 4.54) | 0.3662 |
| **Death**  **(n=8,776)** | **Original (n=4,433)** | 230/3,549 (6.5%) | 130/884 (14.7%) | 2.49  (1.98 – 3.13) | - | **-** | **-** | **-** | - |
| **Gamma (n=2,939)** | 323/2,093 (15.4%) | 125/472 (26.5%) | 1.97  (1.56 – 2.50) | 0.1680 | 22/313 (7.0%) | 9/61 (14.8%) | 2.29  (1.00 – 5.25) | 0.8496 |
| **Delta (n=531)** | 22/215 (10.2%) | 8/48 (16.7%) | 1.75  (0.73 – 4.22) | 0.4492 | 7/227 (3.1%) | 1/41 (2.4%) | 0.79  (0.09 – 6.56) | 0.2662 |
| **Omicron (n=873)** | 6/228 (2.6%) | 2/81 (2.5%) | 0.94  (0.19 – 4.74) | 0.2261 | 3/436 (0.7%) | 4/128 (3.1%) | 4.66  (1.03 – 21.08) | 0.4146 |

OR, Odds Ratio; %CI, 95% confidence interval; ICU, Intensive care unit

# DISCUSSION

The analysis of our results shows that postpartum women had lower percentages of comorbidities, and, at hospital admission, they also presented lower rates of symptoms compared to pregnant women, except for respiratory discomfort and SpO2<95%, which puerperal women had higher rates in unvaccinated original variant group and dyspnea and SpO2<95% in vaccinated Omicron variant group. In the unvaccinated group, postpartum women had also a higher likelihood of ICU admission and invasive ventilatory support with original, Gamma and Omicron, and death with the original and Gamma variants. There was no difference between the two groups with the Delta variant. Postpartum women also showed a higher chance to be admitted to ICU and to die in vaccinated Omicron variant group. It is important to emphasize that those two significant results in vaccinated group have confidence interval beginning in almost 1.00. Hence, our study data suggest that puerperal women are at a higher risk of severe outcomes than pregnant women, mainly if they are not vaccinated.

When COVID-19 pandemic started, yet with few cases related, the impression was that pregnant and puerperal women were not at a higher risk for adverse outcomes, including death, than the non-obstetric population. 3 4 [[26]](#endnote-26) [[27]](#endnote-27) [[28]](#endnote-28) [[29]](#endnote-29) Later on, new studies reported higher rate of invasive ventilation and admission to ICU and an increased number of deaths in the obstetric population.6 7 8 10 [[30]](#endnote-30) [[31]](#endnote-31)

The United States Centers for Disease Control and Prevention published data from January 22 to October 3, 2020, comprising 1,300,938 women with COVID-19. In that study, pregnant women, as opposed to nonpregnant, showed a higher risk of ICU admission, invasive ventilation, extracorporeal membrane oxygenation (ECMO), and death.8 Another study performed in Mexico, cohort of 5,183 pregnant and 175,905 nonpregnant women with COVID-19, compared the two groups regarding death, pneumonia, invasive respiratory support, and ICU admission. The data were analyzed with and without adjustment for propensity score matching. After pairing, pregnant women showed a higher likelihood of death (OR 1.84), pneumonia (OR 1.86), and ICU admission (OR 1.86) than nonpregnant, but both groups ran a similar risk of invasive respiratory support (OR 0.93).10 Those and other studies from that time, however, did not evaluate differences between pregnant and postpartum women; were performed including non-hospitalized population and with different diagnosis tests rather than PCR.8 9 10 11

In a study from Brazil, which included 2,475 pregnant and postpartum women with SARS, 72% of whom had COVID-19 confirmed by RT-PCR, 590 had unfavorable outcomes. The risk increased 2.4 times when the SARS notification occurred in the postpartum period rather than during pregnancy.[[32]](#endnote-32)

In another study published by our group with the same Brazilian national database containing surveillance data on SARS, we compared three groups – pregnant, puerperal, and non-pregnant nor puerperal women – from 10 to 49 years, from the beginning of the pandemics until January 02, 2021. The variables of demographic and clinical characteristics, signs and symptoms and the outcomes were analyzed. Propensity score matching (PSM) was used for estimating and assessing balancing weights for the observations to make the three balanced groups in relation to the confounding variables. After pairing with PSM, puerperal women were more likely than pregnant women to be admitted to ICU (OR 1.97), to receive invasive respiratory support (OR 2.71), and to die (OR 2.51).15

In the current research, we compared pregnant and postpartum women with SARS-CoV-2, with all VOCs identified (original, Gamma, Delta, and Omicron), and considering the vaccination status. We found similar results to our previous study: in the unvaccinated group, postpartum women were more likely to be admitted to an ICU for the original (OR: 1.81), Gamma (OR: 1.58) and Omicron (OR: 2.60) variants, to need invasive ventilation for the original (OR: 2.66), Gamma (OR: 2.17) and Omicron (OR: 3.55) variants, or to die for the original (OR: 2.49) and Gamma (OR: 1.97) variants. In the vaccinated group, postpartum had more risk than pregnant women only with Omicron variant in admission to ICU (OR: 1.85) and to die (OR: 4.66).

In another Brazilian study, which analyzed same database with data retrieved up to August 17, 2020, and included women from 15-49 years, the postpartum period was associated with worse outcomes in the obstetric population. When stratified by pregnancy status, postpartum women had increased rates of admission to the ICU (34.0%), invasive ventilation (20.9%), and death (19.0%) when compared to pregnant women (18.7%, 7.4% and 6.7%, respectively).[[33]](#endnote-33) In this study, considering unvaccinated women, we could see same behavior (postpartum women with worse prognosis), not only in original variant, but also in Gamma, Delta, and Omicron variants. Respectively to the original, Gamma, Delta, and Omicron variants, admission to ICU was 35.6%, 47.9%, 51.0% and 21.5%; invasive ventilation was 20.5%, 34.5%, 21.6% and 10.5%; and death was 14.7%, 26.5%, 16.5% and 2.5%. Only Omicron variant had a similar percentage for death compared to pregnant women (2.6%).

Until the updated research of published studies, some observational studies and surveillance data concerning vaccination during pregnancy have been reassuring. Most of the subjects received the Pfizer/BioNTech or Moderna vaccines and the available data do not demonstrate adverse outcomes nor side effects of vaccination during pregnancy.[[34]](#endnote-34) [[35]](#endnote-35) [[36]](#endnote-36) [[37]](#endnote-37) In Brazil, pregnant women are immunized with Sinovac/Butantan and Pfizer/Wyeth vaccines.[[38]](#endnote-38) We could find only one observational study using the same Brazilian database which evaluated the association between COVID-19 vaccines and maternal mortality by SARS-CoV-2 in women with SARS. In hospitalized pregnant and postpartum women with severe COVID-19, those who had received two doses of a COVID-19 vaccine had a 46% reduction in the odds of ICU admission, an 81% reduction in the odds of invasive ventilatory support, and an 80% reduction in the odds of death compared to those who did not receive any COVID-19 vaccination.19 Our findings support those findings and suggest vaccines have been effective in reducing adverse outcomes such as ICU admission, invasive ventilatory and deaths in both groups (pregnant and postpartum women). Therefore, vaccines an important public health strategy across the globe, and pregnant and postpartum women should be included in randomized clinical trials (RCTs), in agreement with the ethical principles of research, the characteristics of vaccines, and the context in which the RCT is conducted.19 [[39]](#endnote-39)

The worst prognosis for postpartum women can be supported by some theories. We believe that the most important of them is the three-delays model.[[40]](#endnote-40) During the postpartum, women generally delay seeking medical assistance as they are focused on taking care of the newborn, ignoring their own health care.[[41]](#endnote-41) [[42]](#endnote-42) Also, it could be partially explained by the high risk of thromboembolism in postpartum women, such as COVID-19, which may have an increment on these occurrences.[[43]](#endnote-43) [[44]](#endnote-44) [[45]](#endnote-45) [[46]](#endnote-46) Besides, as SIVEP-Gripe does not provide information regarding date of birth or week of pregnancy at diagnosis neither detail of the onset of symptoms, postpartum women may also comprise women infected with SARS-Cov-2 while pregnant who progressed to SARS after delivery. Additionally, pregnant women with SARS may undergo a termination of pregnancy as a therapeutic measure, and possible death in the postpartum period. Furthermore, C-sections are the most common delivery mode in Brazil (more than 57%), with higher rates in severe cases of COVID-19, which could strengthen the risk of maternal mortality.[[47]](#endnote-47) [[48]](#endnote-48) [[49]](#endnote-49) [[50]](#endnote-50)

The strong points of our study are: 1) the use of a large dataset with nationwide coverage, with no duplicates. The same surveillance database was used as source for another research published with 250 000 hospital admissions due to COVID-19 in Brazil, supporting the quality of the data analyzed herein.[[51]](#endnote-51) 2) the inclusion of hospitalized obstetric women due to severe acute respiratory syndrome, confirmed by RT-PCR laboratory test; 3) separation of obstetric population in pregnant and postpartum women for more accurate evaluation; 4) analysis of the impact of the different SARS-CoV-2 variants to obstetric population; this was not found in any other research published until the date; 5) subdivision of pregnant and postpartum women according to the vaccination status (unvaccinated and vaccinated with at least one dose) with comparison of the groups.

The main limitations of our study rely on its retrospective nature based on secondary database analysis. Although the notification of COVID-19 hospital admissions is compulsory in Brazil, we cannot guarantee that all patients with COVID-19 who were hospitalized were included and that bias due to missingness or inaccurately filled fields could be eliminated. It is important to emphasize that asymptomatic or mildly symptomatic women are not notified through SIVEP-Gripe, so the analysis of non-hospitalized population is not possible. Another limitation is that the database used does not provide information about other obstetric variables such as gestational age, delivery mode, date of birth, comorbidities, week of pregnancy at diagnosis and perinatal data. Additionally, as it is an anonymous database, we cannot link it with the public database of birth registers and mode of delivery.

As postpartum women have higher risk of developing severe forms of COVID-19 (need for ICU, use of invasive ventilatory support, and death) among the different variants, mainly in unvaccinated groups, it is essential to create health care strategies to the obstetric population, which include vaccination. It is recommended not to underestimate the severity risks for the postpartum women and health care workers should closely monitor all postpartum women infected by COVID-19, especially those who were not vaccinated. As the group of vaccinated women had, in general, less percentage of severe outcomes, this should influence public health decisions to reinforce vaccination in both groups as a priority. For those cases in which SARS-CoV-2 infection is acquired during pregnancy, unless fetal maternal severity indicates resolution, the delivery should be considered only after overcoming the disease.

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🡪 Passar as notas de fim para esta parte

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