

ORIGINAL ARTICLE



Factors associated with hospitalizations and deaths of pregnant women from Paraná due to COVID-19: a cross-sectional study

Fatores associados a hospitalizações e óbitos de gestantes paranaenses por COVID-19: estudo transversal

Larissa Silva Bergantini^I , Sueli Mutsumi Tsukuda Ichisato^{II} , Maria Aparecida Salci^{III} ,
Marcela Maria Birolim^{III} , Márcia Lorena Alves dos Santos^{IV} , Carla Franciele Höring^{IV} ,
Roberta Rossa^{II} , Luiz Augusto Facchini^V

^IUniversidade Estadual de Maringá, Postgraduate Program in Physiological Sciences – Maringá (PR), Brazil.

^{II}Universidade Estadual de Maringá, Postgraduate Program in Nursing – Maringá (PR), Brazil.

^{III}Centro Universitário Guairacá, Postgraduate Program in Health Promotion – Guarapuava (PR), Brazil.

^{IV}Universidade Estadual de Maringá, Department of Statistics – Maringá (PR), Brazil.

^VUniversidade Federal de Pelotas, Department of Social Medicine – Pelotas (RS), Brazil.

ABSTRACT

Objective: To analyze the factors associated with hospitalization in the ward and intensive care unit (ICU), and with death from COVID-19 in pregnant women with confirmed cases. **Methods:** Observational, cross-sectional study, carried out with data from pregnant women with a confirmed case of COVID-19 from the Influenza Epidemiological Surveillance Information System and the Paraná's state COVID-19 notification system. The association between the independent and dependent variables (hospitalization in the ward and ICU, and death) was investigated using the Poisson regression model with robust variance. **Results:** 4,719 pregnant women comprised the study population. 9.6 and 5.1% were hospitalized in wards and ICU, respectively. 1.9% died. There was an association between advanced maternal age and hospitalization in wards (PR=1.36; 95%CI 1.10–1.62) and ICU (PR=2.25; 95%CI 1.78–2.71), and death (PR=3.22; 95%CI 2.30–4.15). An association was found between the third trimester and hospitalization in wards (PR=5.06; 95%CI 2.82–7.30) and ICU (PR=6.03; 95%CI 3.67–8.39) and death (PR=13.56; 95%CI 2.90–24.23). The second trimester was associated with ICU admission (PR=2.67; 95%CI 1.36–3.99). Pregnant women with cardiovascular disease had a higher frequency of hospitalization in wards (PR=2.24; 95%CI 1.43–3.05) and ICU (PR=2.66; 95%CI 1.46–3.87). Obesity was associated with ICU admission (PR=3.79; 95%CI 2.71–4.86) and death (PR=5.62; 95%CI 2.41–8.83). **Conclusions:** Advanced maternal age, the end of the gestational period and comorbidities were associated with severe COVID-19.

Keywords: COVID-19. Cross-sectional studies. Pregnant women. Hospitalization. Intensive care units. Maternal mortality.

CORRESPONDING AUTHOR: Larissa Silva Bergantini. Avenida Colombo, 5790, Jardim Universitário, CEP: 87020-900, Maringá (PR), Brasil. E-mail: larissasbergantini@gmail.com

CONFLICT OF INTERESTS: nothing to declare

HOW TO CITE THIS ARTICLE: Bergantini LS, Ichisato SMT, Salci MA, Birolim MM, Santos MLA, Höring CF, et al. Factors associated with hospitalizations and deaths of pregnant women from Paraná due to COVID-19: a cross-sectional study. Rev Bras Epidemiol. 2024; 27: e240005. <https://doi.org/10.1590/1980-549720240005>

This is an open article distributed under the CC-BY 4.0 license, which allows copying and redistribution of the material in any format and for any purpose as long as the original authorship and publication credits are maintained.

Received on: 08/11/2023

Reviewed on: 11/14/2023

Accepted on: 11/14/2023



INTRODUCTION

In March 2020, the World Health Organization recognized the Coronavirus disease 2019 (COVID-19) pandemic¹, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)², as a Public Health Emergency of International Concern. The disease has multisystemic manifestations³, and its spectrum varies from asymptomatic, mild and moderate, to severe and fatal stages⁴.

Pregnant and postpartum women, who were initially not considered more prone to severe conditions compared to the general population⁵, constitute a vulnerable group for severe forms of the pathology⁶. Immunological, anatomical, and physiological changes generate a state of greater susceptibility to respiratory infections in women during the gestational period^{7,8}. Furthermore, unfavorable prognoses were observed in pregnant women affected by other coronaviruses from the family of the etiological agent of COVID-19⁹.

In relation to women of reproductive age, who were not pregnant, symptomatic pregnant women were at increased risk of developing COVID-19 in its severe form¹⁰, and, consequently, of admission to an intensive care unit (ICU)¹⁰⁻¹³, of needing mechanical ventilation¹⁰⁻¹², and of death^{10,13}.

In Brazil, more than 24 thousand cases of severe acute respiratory syndrome (SARS) due to COVID-19 have been recorded in pregnant and postpartum women, according to data from the Brazilian Obstetric Observatory SARS (*Observatório Obstétrico Brasileiro SRAG – OObR SRAG*) updated on August 2nd, 2023. 23.7% of these women required intensive care, and 8.4% of them died¹⁴.

Pregnant women from low- and middle-income countries are more vulnerable to the negative outcomes of COVID-19, such as death¹⁵. Added to this, the distribution of the number of maternal deaths due to the pathology in Brazilian states appears to be asymmetric, possibly due to socioeconomic differences resulting in unequal access to health services^{16,17}. This points to the relevance of conducting research with this population in the Brazilian context.

Considering that pregnant women are more susceptible to the worsening of COVID-19, it is crucial to determine the conditions related to severe cases of the disease. In this context, the presence of comorbidities can act as a risk factor, as well as advanced maternal age¹⁸, defined by the Brazilian Ministry of Health as the pregnancy of women aged 35 years old or older¹⁹.

The influence of the gestational period on the predisposition to severe manifestations of COVID-19 is a controversial point in the literature: there are studies that observed associations between the trimester of pregnancy and the severity of the disease^{20,21}, and others that did not find this relationship^{18,22}.

Furthermore, despite advances in scientific knowledge on this topic, analyses developed in Brazil involving pregnant and postpartum women predominantly investigated the risks of morbidity and mortality in the in-hospital setting, based on data from the Influenza Epidemiological Surveillance Information System (*Sistema de Informação*

de Vigilância Epidemiológica da Gripe – SIVEP-Gripe), which monitors SARS cases^{17,23}.

This research aimed to contribute to the understanding of the relationship between COVID-19 and pregnancy by exploring the factors associated with severe conditions, considering pregnant women affected at different levels of severity, including non-hospitalized cases. Thus, the objective was to analyze the factors associated with hospitalization in the ward and ICU, and death from COVID-19 in pregnant women with a confirmed case.

METHODS

Study design

Observational, cross-sectional research, which used secondary data from two COVID-19 epidemiological surveillance databases: SIVEP-Gripe and the specific information system of the state of Paraná, called *Sistema Estadual Notifica COVID-19* (Notifica COVID-19).

The first 18 months of the pandemic were defined as the investigation period. Specifically, the study comprised pregnant women notified in SIVEP-Gripe between March 29th, 2020 (date of the first registration of a pregnant woman from Paraná in this base) and September 29th, 2021, and those registered in Notifica COVID-19, from March 30th, 2020 (date of the first notification of a pregnant woman from Paraná in the state system) to September 30th, 2021. The date of notification of the case in the aforementioned systems was considered for the inclusion of pregnant women in the study.

The research was described based on the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) initiative²⁴.

Study background

The state of Paraná, in South Brazil, is the most populous in the region, and fifth in the Brazilian rank according to data from the 2022 Demographic Census²⁵. The human development index (HDI) of Paraná is equivalent to 0.769, the seventh highest in the country²⁶. Until August 2023, the state had the fourth highest number of confirmed cases and deaths from COVID-19 in Brazil²⁷.

Participants

The study population consisted of pregnant women residing in and notified by the state of Paraná, with a confirmed case of COVID-19, aged between 10 and 49 years, and without reservations regarding the gestational trimester. Women who did not require hospitalization due to the disease were included, in addition to those who required hospitalization, in a ward or ICU, regardless of whether the condition progressed to cure or death.

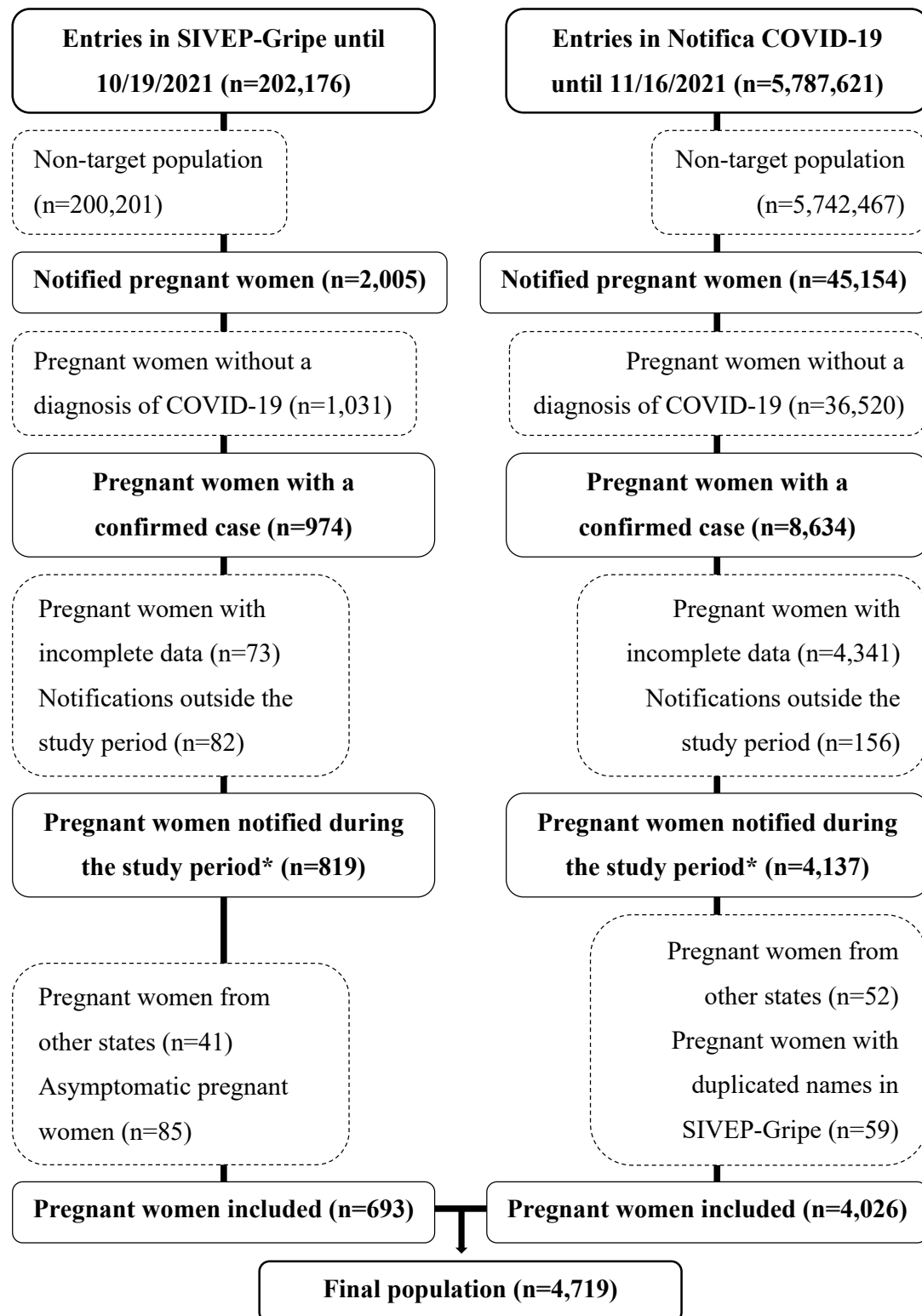
Women with incomplete information on the following were excluded from the analysis: gestational age, date of first

symptoms, outcome (cure or death), and place of hospitalization (ward or ICU). Asymptomatic hospitalized pregnant women were not included, with the aim of avoiding hospitalizations caused by obstetric reasons, such as childbirth.

The processes for defining the study population are illustrated in Figure 1.

Data Sources

Information was extracted from SIVEP-Gripe and Notifica COVID-19 databases combined. SIVEP-Gripe is a nationwide information system that monitors SARS cases, whose notification is mandatory in the country. In 2020, COVID-19 surveillance was incorporated into SIVEP-Gripe²⁸.



*The study period corresponded to the first 18 months of the pandemic, that is, the period from March 2020 to September 2021.

Figure 1. Flowcharts for sample selection of pregnant women from the SIVEP-Gripe (left) and Notifica COVID-19 (right) databases.

Records of mild and asymptomatic cases of COVID-19 in Brazilian territory were sent to the e-SUS Notifica²⁸ system. In the state of Paraná, however, the State Health Secretariat (*Secretaria de Estado da Saúde – SESA/PR*) implemented Notifica COVID-19, its own system for monitoring mild occurrences. Subsequently, data from Notifica COVID-19 is passed on to e-SUS Notifica.

For this research, data were collected from non-hospitalized pregnant women, treated only on an outpatient basis, through the Notifica COVID-19 database. Occurrences of hospitalization in the ward and ICU were identified using the SIVEP-Gripe database. In order to avoid duplicates, the pregnant women's names were checked in both databases and, in case of duplicity, only the SIVEP-Gripe data were kept.

Versions of databases that are not available to the general public and that contain sensitive data were analyzed. The SIVEP-Gripe database provided to the authors by SESA/PR covered notifications made until October 19th, 2021, and the Notifica COVID-19 database until November 16th, 2021. The information was collected in December 2021.

Characteristics

Three outcomes were determined for the analysis: hospitalization in the ward, hospitalization in the ICU, and death due to COVID-19. In the present research, response variables are counts and, therefore, have a discrete quantitative nature. They can be expressed as: Y =number of pregnant women hospitalized in the ward, Z =number of pregnant women hospitalized in the ICU, and W =number of pregnant women who died.

The objective was to model the Y/t =rate of pregnant women hospitalized in the ward; Z/t =rate of pregnant women admitted to the ICU; and W/t =rate of pregnant women who died, where t corresponds to the total number of pregnant women in Paraná diagnosed with COVID-19 in the first 18 months of the pandemic.

To construct the analysis, only the explanatory variables common to both databases were selected, namely: age range, subdivided into younger than 35 years (reference category) and 35 years or more; gestational period, categorized as first (reference category), second, and third trimesters; and the following comorbidities: heart disease, diabetes, obesity and others, all dichotomized as yes or no (reference category). Uncompleted (ignored) records for comorbidities were included in the “no” group.

The age range variable was categorized based on the advanced maternal age stratification proposed by the Ministry of Health¹⁹. The race/color factor was excluded from the inferential analysis due to the high number of incomplete cases.

Statistical methods

Data were subjected to descriptive analysis in the Excel[®] software to calculate median, mean, standard deviation

(SD) and absolute and relative frequencies. Inferential statistical analysis was performed using R[®] software, version 4.1.1.

The Poisson regression model with robust variance was used to investigate possible associations between explanatory variables and responses based on the estimation of crude and adjusted prevalence ratios (PR) and the respective 95% confidence intervals (95%CI).

The variables that presented p -value <0.20 in the crude analysis were maintained in the multiple model. Backward selection was used to determine which variables would remain in the final model, with non-significant variables (p -value $>5\%$) being removed one by one from the final model. The association between variables was considered significant when the 95% confidence interval did not include the value 1.00.

The Wald test was applied to verify the significance of the estimated coefficients. The quality of fit of the models was evaluated according to deviance and the likelihood ratio test (significance level of 5%).

Ethical aspects

The research was approved with Certificate of Presentation of Ethical Appreciation (*Certificado de Apresentação de Apreciação Ética – CAAE*) number 34787020.0.0000.0104/2020, by protocol number 4.165.272/2020.

RESULTS

A total of 4,719 pregnant women with COVID-19 made up the study population. Women's mean age was 27.8 years (SD=6.4; median=27); 25.4% were in the first, 38.1% in the second, and 36.5% in the third trimester of pregnancy; 40.5% were white, but 45.5% were missing this information.

Furthermore, 586 (12.4%) women were asymptomatic at the time of notification, and 4,133 (87.6%) had some symptoms. Most common signs and symptoms included coughing (61.9%), sore throat (41.8%), fever (32.2%), dyspnea (23.1%), symptoms related to the gastrointestinal tract (diarrhea, nausea or vomiting) (11.9%), and oxygen saturation below 95% (7.2%).

Of the total number of infected pregnant women, 4,026 (85.3%) did not require hospitalization and received outpatient care; 693 (14.7%) were hospitalized. Considering all those notified, 453 (9.6%) women were treated in the ward and 240 (5.1%) in the ICU.

The majority of patients (98.1%) recovered from the disease. 92 (1.9%) deaths from COVID-19 were recorded, 87 among those hospitalized (94.6%), 12 in the ward and 75 in the ICU, and five (5.4%) among pregnant women who were not hospitalized, registered in Notifica COVID-19.

Furthermore, 32.5% of those hospitalized for COVID-19 had more than eight years of education, however, there was a predominance (56.1%) of incomplete records for

this variable. Almost all (90.9%) of hospitalized pregnant women lived in the urban area, and 41.1% were part of the Eastern health macro-region, which encompasses Curitiba (Paraná's capital) and its metropolitan region.

The average length of stay was approximately nine days (SD=11.5; median=5), with 42.6% of those hospitalized not needing to use ventilatory support. Among those assisted in the ward, 58.3% did not receive ventilatory therapy, while the majority (85%) of patients in the ICU used the treatment. Considering the 87 hospitalized women who died, eight (9.2%) did not use ventilatory support. These eight patients were hospitalized for an average of nine days, and most were admitted to the hospital in the first half of 2021.

Of the total number of patients who required hospitalization, 108 (15.6%) received invasive ventilation. Among those hospitalized who used invasive ventilatory support, 49 (45.4%) survived and 59 (54.6%) died.

In Table 1, the prevalence of hospitalization in the ward and ICU and the proportions of deaths due to COVID-19 are described according to the categories of explanatory variables in relation to the total number of pregnant women reported.

Table 2 presents the crude prevalence ratios of the survey response variables according to the explanatory variables. In Table 3, the adjusted prevalence ratios are shown according to the variables that remained in the multiple model for each outcome.

There was no association between diabetes, other comorbidities and the three response variables. Obesity did not remain in the final model for the response variable hospitalization in the ward, and heart disease did not remain in the death outcome, as both presented p -value $>5\%$ (backward selection).

The deviance test applied to evaluate the quality of fit of the models obtained p -values $>5\%$, demonstrating the suitability of the proposed models for the three outcomes.

The adjusted analysis identified that pregnant women aged 35 or over were almost 1.4 times more likely to be hospitalized in a ward (95%CI 1.10–1.62) compared to patients below this age range.

Pregnant women in the third trimester were approximately five (95%CI 2.82–7.30) times more likely to be admitted to the ward compared to those in the first trimester. There was no statistically significant difference between women in the second and first trimesters for this outcome. Furthermore, having heart disease doubled (95%CI 1.43–3.05) the probability of a pregnant woman with COVID-19 requiring hospitalization in a ward.

The probability of admission to the ICU was increased by approximately two (95%CI 1.78–2.71) times among pregnant women of advanced maternal age. Compared to women in the first trimester, the probability of admission to the ICU for those in the second and third trimesters increased by almost three and six times, respectively.

Table 1. Prevalence of hospitalization in wards and intensive care units and proportions of deaths in relation to the total population of pregnant women according to the categories of independent variables. Paraná, Brazil, March 2020 to September 2021

| Characteristics | Outcomes | | | | | | Total notifications (n=4,719) |
|-----------------------|-----------------------------------|----------------|--------------------------------|----------------|--------------|----------------|-------------------------------|
| | Hospitalization in a ward (n=453) | | Hospitalization in ICU (n=240) | | Death (n=92) | | |
| | n | Prevalence (%) | n | Prevalence (%) | n | Proportion (%) | n |
| Age range (years) | | | | | | | |
| <35 | 353 | 9.01 | 159 | 4.06 | 54 | 1.38 | 3,918 |
| ≥35 | 100 | 12.48 | 81 | 10.11 | 38 | 4.74 | 801 |
| Gestational trimester | | | | | | | |
| First | 42 | 3.50 | 17 | 1.42 | 3 | 0.25 | 1,199 |
| Second | 103 | 5.72 | 71 | 3.94 | 31 | 1.72 | 1,800 |
| Third | 308 | 17.91 | 152 | 8.84 | 58 | 3.37 | 1,720 |
| Comorbidity | | | | | | | |
| Heart disease | | | | | | | |
| No | 436 | 9.36 | 221 | 4.75 | 85 | 1.83 | 4,656 |
| Yes | 17 | 26.98 | 19 | 30.16 | 7 | 11.11 | 63 |
| Diabetes | | | | | | | |
| No | 427 | 9.35 | 218 | 4.77 | 82 | 1.80 | 4,568 |
| Yes | 26 | 17.22 | 22 | 14.57 | 10 | 6.62 | 151 |
| Obesity | | | | | | | |
| No | 429 | 9.42 | 202 | 4.44 | 74 | 1.62 | 4,554 |
| Yes | 24 | 14.55 | 38 | 23.03 | 18 | 10.91 | 165 |
| Others | | | | | | | |
| No | 443 | 9.64 | 231 | 5.03 | 87 | 1.89 | 4,597 |
| Yes | 10 | 8.20 | 9 | 7.38 | 5 | 4.10 | 122 |

ICU: intensive care unit.

Table 2. Crude prevalence ratios of outcomes according to age group, gestational trimester, and comorbidities. Paraná, Brazil, March 2020 to September 2021.

| Characteristics | Outcomes | | | | | |
|-----------------------|---------------------------|--------|------------------------|--------|-----------------------|--------|
| | Hospitalization in a ward | | Hospitalization in ICU | | Death | |
| | PRc (95%CI) | p* | PRc (95%CI) | p* | PRc (95%CI) | p* |
| Age range (years) | | | | | | |
| <35 (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| ≥35 | 1.39 (1.10–1.72) | 0.003 | 2.49 (1.90–3.24) | <0.001 | 3.44 (2.26–5.19) | <0.001 |
| Gestational trimester | | | | | | |
| First (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Second | 1.63 (1.15–2.36) | 0.007 | 2.78 (1.68–4.88) | <0.001 | 6.88 (2.46–28.68) | <0.001 |
| Third | 5.11 (3.75–7.16) | <0.001 | 6.23 (3.89–10.68) | <0.001 | 13.48 (4.99–55.24) | <0.001 |
| Comorbidity | | | | | | |
| Heart disease | | | | | | |
| No (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Yes | 2.88 (1.70–4.52) | <0.001 | 6.35 (3.85–9.87) | <0.001 | 6.09 (2.56–12.22) | <0.001 |
| Diabetes | | | | | | |
| No (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Yes | 1.84 (1.21–2.68) | 0.002 | 3.05 (1.91–4.62) | <0.001 | 3.69 (1.79–6.77) | <0.001 |
| Obesity | | | | | | |
| No (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Yes | 1.54 (1.00–2.28) | 0.038 | 5.19 (3.62–7.25) | <0.001 | 6.71 (3.89–10.97) | <0.001 |
| Others | | | | | | |
| No (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Yes | 0.85 (0.42–1.50) | 0.612 | 1.47 (0.70–2.69) | 0.258 | 2.17 (0.76–4.81) | 0.092 |

*Regarding the Wald Test; ICU: intensive care unit; PRc: Crude prevalence ratio; 95%CI: 95% confidence interval.

Patients with obesity were more likely to be hospitalized in the ICU, with a probability practically four (95%CI 2.71–4.86) times higher than those without the comorbidity. Having heart disease increased the probability of needing intensive care by around two times (95%CI 1.46–3.87).

The probability of death was three (95%CI 2.30–4.15) times higher among pregnant women aged 35 years old or older. Being in the third trimester increased the chance of death from COVID-19 by approximately 13 (95%CI 2.90–24.23) times, however, there was no statistically significant difference with regard to the second and first trimesters of pregnancy. The adjusted analysis found an association between obesity and death, increasing the probability of the outcome by approximately five (95%CI 2.41–8.83) times.

DISCUSSION

Adjusted analysis showed an association between age equal to or over 35 years old, as well as the third trimester of pregnancy and the three severity outcomes: hospital-

ization in the ward and ICU, and death due to COVID-19. The second trimester was related to the need for intensive care. Having a heart disease increased the probability of admission to the ward and ICU. There was an association between obesity and ICU hospitalization and death.

The use of secondary data implies limitations inherent to this set of information: there was a high number of records with important elements not filled out, which resulted in purification of the study population and made it impossible to assess the impact of race/color on severe outcomes of COVID-19. Ethnic-racial disparities in relation to the risk of infection and mortality have been reported among pregnant women¹⁰, therefore, the non-inclusion of health determinants in this analysis is a limitation. The probable underreporting of asymptomatic cases is a limiting factor. This research was carried out in a limited context, the state of Paraná, therefore, generalizing the results to other locations with different socioeconomic and health characteristics must be cautious.

Table 3. Adjusted prevalence ratios of outcomes according to the variables that remained in the final model. Paraná, Brazil, March 2020 to September 2021.

| Characteristics | Outcomes | | | | | |
|-----------------------|---------------------------|----------------|------------------------|----------------|-----------------------|----------------|
| | Hospitalization in a ward | | Hospitalization in ICU | | Death | |
| | PRa* (95%CI) | p [†] | PRa* (95%CI) | p [†] | PRa* (95%CI) | p [†] |
| Age range (years) | | | | | | |
| <35 (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| ≥35 | 1.36 (1.10–1.62) | <0.001 | 2.25 (1.78–2.71) | <0.001 | 3.22 (2.30–4.15) | <0.001 |
| Gestational trimester | | | | | | |
| First (reference) | 1.00 | - | 1.00 | - | 1.00 | - |
| Second | 1.63 (0.92–2.34) | 0.028 | 2.67 (1.36–3.99) | <0.001 | 6.74 (0.88–12.61) | <0.001 |
| Third | 5.06 (2.82–7.30) | <0.001 | 6.03 (3.67–8.39) | <0.001 | 13.56 (2.90–24.23) | <0.001 |
| Comorbidity | | | | | | |
| Heart disease | | | | | | |
| No (reference) | 1.00 | - | 1.00 | - | - | - |
| Yes | 2.24 (1.43–3.05) | <0.001 | 2.66 (1.46–3.87) | <0.001 | - | - |
| Obesity | | | | | | |
| No (reference) | - | - | 1.00 | - | 1.00 | - |
| Yes | - | - | 3.79 (2.71–4.86) | <0.001 | 5.62 (2.41–8.83) | <0.001 |

*All variables were adjusted for those that remained in the multiple model; [†]Regarding the Wald Test; ICU: intensive care unit; PRa: Adjusted prevalence ratio; 95% CI: 95% confidence interval.

A study carried out with 240 pregnant women with confirmed cases of SARS-CoV-2 infection found that hospitalized patients were more likely to have at least one comorbidity, such as hypertension, type two diabetes, obesity, among others²⁹.

Similarly, advanced maternal age and the existence of any comorbidity, including obesity, chronic lung disease, and hypertension, stood out as risk factors for the moderate to severe and critical condition of COVID-19 in a cohort consisted of 7,950 pregnant women²², in agreement with the present findings. A dose-response effect was found with regard to comorbidities and severe forms of the disease²².

Two studies, which specifically evaluated ICU admission as a response variable, observed that advanced age and comorbidities increased the risk of the outcome^{23,30}. One of these analyses carried out in Brazil demonstrated that obesity and diabetes were prominent in relation to the risk of ICU admission among comorbidities²³.

Regarding death from COVID-19, the two studies cited^{23,30} corroborated the results obtained here: advanced maternal age and the presence of comorbidities were related to mortality from the disease. A second Brazilian survey reinforced that having associated clinical conditions, such as obesity, diabetes, and cardiovascular disease, increased the risk of death¹⁷.

Regarding the influence of the gestational period on the prognosis of COVID-19, a systematic review, which summa-

rized the products of 77 studies, did not observe a correlation between advanced gestational age and complications arising from the disease¹⁸.

Another longitudinal analysis found that the gestational trimester was not associated with an increased risk of developing moderate to severe and critical forms of the pathology. The authors themselves, however, highlighted that the low representation of pregnant women in the first trimester of pregnancy could restrict the understanding of the interference of this variable²².

On the other hand, a study carried out in Brazil found a predominance of deaths due to COVID-19 in the third trimester of pregnancy or in the postpartum period¹⁶. Likewise, the majority of patients hospitalized with the pathology in an analysis carried out in the United States were in the third trimester²⁹.

A cohort study developed by North American researchers found that pregnant women affected by COVID-19 were three times more likely to be admitted to the ICU compared to those without the disease, and that the risk was increased by infection during the third trimester³¹. Two review studies also indicated that the last gestational trimester was associated with the severity of the pathology^{20,21}. These results converge with those of this research.

The anatomic-functional changes observed mainly in the third trimester, such as those in the respiratory system (increased oxygen demand and limitation of lung expansion, for example)^{32,33}, could form the pathophys-

iological mechanism that would explain the increased susceptibility of pregnant women affected at the end of their pregnancy³⁴.

Furthermore, the assertion that pregnancy corresponds to a state of immunosuppression *per se* is inaccurate³⁴. In the third trimester of pregnancy until delivery, a pro-inflammatory disposition prevails in the woman's body. In this sense, it is assumed that infection by SARS-CoV-2 could worsen this process during the final phase of the gestational period³³.

The most frequent symptoms among pregnant women with COVID-19 investigated in this research were coughing, sore throat, fever, and dyspnea, similar to those identified by other authors^{23,35}.

As previously mentioned, in developing countries, the impact of COVID-19 on maternal health may be discrepant compared to developed nations³⁶. In Brazil, the significant consequences of the disease in pregnant and postpartum women can be explained, primarily, by clinical issues. In the national territory, the main cause of maternal death is hypertensive disorders¹⁹, which, combined with COVID-19, can deteriorate the prognosis during the gestational period. Added to this are the high prevalence of overweight and obesity among Brazilian pregnant women, both pro-inflammatory states^{17,37}.

Furthermore, the so-called indirect effects of the pandemic on maternal health should also be mentioned³⁸. Measures implemented around the world to prevent, control, and treat COVID-19 have resulted in difficulties in transportation and access to healthcare, discontinuity of maternal care services and shortages of human and material resources, such as personal protective equipment and medicines³⁹.

Responses to the pandemic, particularly in developing countries, may have intensified pre-existing social disparities and exacerbated chronic deficits in health systems^{37,39}. Thus, in Brazil, it is suggested that the significant impact of COVID-19 on maternal health is also linked to precarious obstetric care, access impairment, and social risk¹⁷.

This research found that around 13% of pregnant women hospitalized in the ICU did not receive ventilatory support; 9.2% of those hospitalized who died did not use the therapy, with the majority of these women being admitted to the hospital in the first half of 2021, between March and June, a period in which there was a significant increase in confirmed cases and deaths due to COVID-19 and, consequently, overload of the Brazilian health system⁴⁰. Five patients who did not survive the disease did not receive hospital care. This highlights that obstacles to accessing intensive care can contribute to the mortality of pregnant and postpartum women¹⁷.

This study used secondary data from epidemiological surveillance databases for an entire state with a significant sample of women. It is considered that the large representation of patients in the three trimesters of pregnancy con-

tributed to the understanding that pregnant women at the end of the gestational period may be more likely to develop severe cases of COVID-19. Furthermore, this analysis emphasized that pregnant women of advanced maternal age, and equally patients with comorbidities, should receive special attention in the pandemic context.

Identifying vulnerable women by the team involved in maternal and child care enables to develop intervention strategies that can prevent or alleviate injuries resulting from COVID-19. Finally, these findings can contribute to the construction of approaches to the continuing education of health professionals, policy formulation, organization of services, tracking of pregnant women, in addition to contributing to the development of future studies.

REFERENCES

1. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 — 11 March 2020 [Internet]. 2020 [cited on Aug 8, 2023]. Available at: <https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>
2. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020; 5: 536-44. <https://doi.org/10.1038/s41564-020-0695-z>
3. Gupta A, Madhavan MV, Sehgal K, Nair N, Mahajan S, Sehrawat TS, et al. Extrapulmonary manifestations of COVID-19. *Nat Med.* 2020; 26(7): 1017-32. <https://doi.org/10.1038/s41591-020-0968-3>
4. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Guia de vigilância epidemiológica: emergência de saúde pública de importância nacional pela doença pelo coronavírus 2019 [Internet]. Brasília: Ministério da Saúde; 2022 [cited on Aug 8, 2023]. Available at: <https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/guia-de-vigilancia-epidemiologica-covid-19/view>
5. Chen L, Li Q, Zheng D, Jiang H, Wei Y, Zou L et al. Clinical characteristics of pregnant women with Covid-19 in Wuhan, China. *N Engl J Med.* 2020; 382(25): e100. <https://doi.org/10.1056/NEJMc2009226>
6. Brasil. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Departamento de Ações Programáticas e Estratégicas. Manual de recomendações para a assistência à gestante e puérpera frente à pandemia de Covid-19 [Internet]. Brasília: Ministério da Saúde; 2021 [cited on Aug 8, 2023]. Available at: https://bvsm.sau.gov.br/bvs/publicacoes/manual_assistencia_gestante_puerpera_covid-19_2ed.pdf
7. Wong YP, Khong TY, Tan GC. The effects of COVID-19 on placenta and pregnancy: what do we know so far? *Diagnostics (Basel).* 2021; 11(1): 94. <https://doi.org/10.3390/diagnostics11010094>

8. Liu H, Wang LL, Zhao SJ, Kwak-Kim J, Mor G, Liao AH. Why are pregnant women susceptible to COVID-19? An immunological viewpoint. *J Reprod Immunol.* 2020; 139: 103122. <https://doi.org/10.1016/j.jri.2020.103122>
9. Galang RR, Chang K, Strid P, Snead MC, Woodworth KR, House LD, et al. Severe coronavirus infections in pregnancy: a systematic review. *Obstet Gynecol.* 2020; 136(2): 262-72. <https://doi.org/10.1097/aog.0000000000004011>
10. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status – United States, January 22–October 3, 2020. *MMWR Morb Mortal Wkly Rep.* 2020; 69(44): 1641-7. <https://doi.org/10.15585/mmwr.mm6944e3>
11. Khan DSA, Pirzada AN, Ali A, Salam RA, Das JK, Lassi ZS. The differences in clinical presentation, management, and prognosis of laboratory-confirmed COVID-19 between pregnant and non-pregnant women: a systematic review and meta-analysis. *Int J Environ Res Public Health.* 2021; 18(11): 5613. <https://doi.org/10.3390/ijerph18115613>
12. Ellington S, Strid P, Tong VT, Woodworth K, Galang RR, Zambrano LD, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status – United States, January 22–June 7, 2020. *MMWR Morb Mortal Wkly Rep.* 2020; 69(25): 769-75. <https://doi.org/10.15585/mmwr.mm6925a1>
13. Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, Torres-Torres J, Espino Y Sosa S, Sandoval-Mandujano K, et al. Pregnant women with SARS-CoV-2 infection are at higher risk of death and pneumonia: propensity score matched analysis of a nationwide prospective cohort (COV19Mx). *Ultrasound Obstet Gynecol.* 2021; 57(2): 224-31. <https://doi.org/10.1002/uog.23575>
14. Observatório Obstétrico Brasileiro. OOB Br SRAG: Síndrome respiratória aguda grave em gestantes e puérperas [Internet]. 2021 [cited on Aug 8, 2023]. Available at: https://observatorioobstetrico.shinyapps.io/covid_gesta_puerp_br
15. Gajbhiye RK, Sawant MS, Kuppusamy P, Surve S, Pasi A, Prusty RK et al. Differential impact of COVID-19 in pregnant women from high-income countries and low- to middle-income countries: a systematic review and meta-analysis. *Int J Gynecol Obstet.* 2021; 155: 48-56. <https://doi.org/10.1002/ijgo.13793>
16. Scheler CA, Discacciati MG, Vale DB, Lajos GJ, Surita F, Teixeira JC. Mortality in pregnancy and the postpartum period in women with severe acute respiratory distress syndrome related to COVID-19 in Brazil, 2020. *Int J Gynaecol Obstet.* 2021; 155(3): 475-82. <https://doi.org/10.1002/ijgo.13804>
17. Takemoto MLS, Menezes MO, Andreucci CB, Knobel R, Sousa L, Katz L, et al. Clinical characteristics and risk factors for mortality in obstetric patients with severe COVID-19 in Brazil: a surveillance database analysis. *BJOG.* 2020; 127(13): 1618-26. <https://doi.org/10.1111/1471-0528.16470>
18. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ.* 2020; 370: m3320. <https://doi.org/10.1136/bmj.m3320>
19. Brasil. Ministério da Saúde. Secretaria de Atenção Primária à Saúde. Manual de gestação de alto risco [Internet]. Brasília: Ministério da Saúde; 2022 [cited on Aug 8, 2023]. Available at: <http://aps.saude.gov.br/biblioteca/visualizar/MjA4Ng==>
20. Turan O, Hakim A, Dashraath P, Jeslyn WJL, Wright A, Abdul-Kadir R. Clinical characteristics, prognostic factors, and maternal and neonatal outcomes of SARS-CoV-2 infection among hospitalized pregnant women: a systematic review. *Int J Gynaecol Obstet.* 2020; 151(1): 7-16. <https://doi.org/10.1002/ijgo.13329>
21. Boushra MN, Koyfman A, Long B. COVID-19 in pregnancy and the puerperium: a review for emergency physicians. *Am J Emerg Med.* 2021; 40: 193-8. <https://doi.org/10.1016/j.ajem.2020.10.055>
22. Galang RR, Newton SM, Woodworth KR, Griffin I, Oduyebo T, Sancken CL, et al. Risk factors for illness severity among pregnant women with confirmed severe acute respiratory syndrome coronavirus 2 infection-surveillance for Emerging Threats to Mothers and Babies Network, 22 State, Local, and Territorial Health Departments, 29 March 2020–5 March 2021. *Clin Infect Dis.* 2021; 73(Suppl 1): S17-S23. <https://doi.org/10.1093/cid/ciab432>
23. Menezes MO, Takemoto MLS, Nakamura-Pereira M, Katz L, Amorim MMR, Salgado HO, et al. Risk factors for adverse outcomes among pregnant and postpartum women with acute respiratory distress syndrome due to COVID-19 in Brazil. *Int J Gynecol Obstet.* 2020; 151(3): 415-23. <https://doi.org/10.1002/ijgo.13407>
24. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Int J Surg.* 2014; 12(12): 1495-9. <https://doi.org/10.1016/j.ijsu.2014.07.013>
25. Instituto Brasileiro de Geografia e Estatística. Censo 2022. Panorama. Indicadores. Ranking por UF. Paraná. [Internet]. 2022 [cited on Oct 2, 2023]. Available at: <https://censo2022.ibge.gov.br/panorama/indicadores.html?localidade=41>
26. Instituto Brasileiro de Geografia e Estatística. Índice de Desenvolvimento Humano. Ranking. Brasil, Paraná [Internet]. 2021 [cited on Oct 2, 2023]. Available at: <https://cidades.ibge.gov.br/brasil/pr/pesquisa/37/0?tipo=ranking>
27. Brasil. Ministério da Saúde. Painel coronavírus [Internet]. 2023 [cited on Aug 8, 2023]. Available at: <https://covid.saude.gov.br/>
28. Brasil. Ministério da Saúde. Secretaria de Vigilância em Saúde. Guia de vigilância epidemiológica: emergência de saúde pública de importância nacional pela doença pelo coronavírus 2019 [Internet]. Brasília: Ministério da Saúde; 2022 [cited on Aug 8, 2023]. Available at: <https://www.gov.br/saude/pt-br/coronavirus/publicacoes-tecnicas/guias-e-planos/guia-de-vigilancia-epidemiologica-covid-19/view>

29. Lokken EM, Huebner EM, Taylor GG, Hendrickson S, Vanderhoeven J, Kachikis A, et al. Disease severity, pregnancy outcomes, and maternal deaths among pregnant patients with severe acute respiratory syndrome coronavirus 2 infection in Washington State. *Am J Obstet Gynecol.* 2021; 225(1): 77.e1-77.e14. <https://doi.org/10.1016/j.ajog.2020.12.1221>
30. Torres-Torres J, Martinez-Portilla RJ, Espino-Y-Sosa S, Estrada-Gutierrez G, Solis-Paredes JM, Villafan-Bernal JR, et al. Comorbidity, poverty and social vulnerability as risk factors for mortality in pregnant women with confirmed SARS-CoV-2 infection: analysis of 13 062 positive pregnancies including 176 maternal deaths in Mexico. *Ultrasound Obstet Gynecol.* 2022; 59(1): 76-82. <https://doi.org/10.1002/uog.24797>
31. Doyle TJ, Kiros GE, Schmitt-Matzen EN, Propper R, Thompson A, Phillips-Bell GS. Maternal and perinatal outcomes associated with SARS-CoV-2 infection during pregnancy, Florida, 2020–2021: a retrospective cohort study. *Clin Infect Dis.* 2022; 75(Suppl 2): S308-S316. <https://doi.org/10.1093/cid/ciac441>
32. Wastnedge EAN, Reynolds RM, van Boeckel SR, Stock SJ, Denison FC, Maybin JA, et al. Pregnancy and COVID-19. *Physiol Rev.* 2021; 101(1): 303-18. <https://doi.org/10.1152/physrev.00024.2020>
33. Ferrer-Oliveras R, Mendoza M, Capote S, Pratcorona L, Esteve-Valverde E, Cabero-Roura L, et al. Immunological and physiopathological approach of COVID-19 in pregnancy. *Arch Gynecol Obstet.* 2021; 304(1): 39-57. <https://doi.org/10.1007/s00404-021-06061-3>
34. Thompson JL, Nguyen LM, Noble KN, Aronoff DM. COVID-19-related disease severity in pregnancy. *Am J Reprod Immunol.* 2020; 84(5): e13339. <https://doi.org/10.1111/aji.13339>
35. Knight M, Bunch K, Vousden N, Morris E, Simpson N, Gale C, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. *BMJ.* 2020; 369: m2107. <https://doi.org/10.1136/bmj.m2107>
36. Amorim MMR, Takemoto MLS, Fonseca EBD. Maternal deaths with coronavirus disease 2019: a different outcome from low- to middle-resource countries? *Am J Obstet Gynecol.* 2020; 223(2): 298-9. <https://doi.org/10.1016/j.ajog.2020.04.023>
37. Nakamura-Pereira M, Amorim MMR, Pacagnella RC, Takemoto MLS, Penso FCC, Rezende-Filho J, et al. COVID-19 and maternal death in Brazil: an invisible tragedy. *Rev Bras Ginecol Obstet.* 2020; 42(8): 445-7. <https://doi.org/10.1055/s-0040-1715138>
38. Lucas DN, Bamber JH. Pandemics and maternal health: the indirect effects of COVID-19. *Anaesthesia.* 2021; 76(Suppl 4): 69-75. <https://doi.org/10.1111/anae.15408>
39. Kingsley JP, Vijay PK, Kumaresan J, Sathiakumar N. The changing aspects of motherhood in face of the COVID-19 pandemic in low- and middle-income countries. *Matern Child Health J.* 2021; 25(1): 15-21. <https://doi.org/10.1007/s10995-020-03044-9>
40. Fundação Oswaldo Cruz. Um balanço da pandemia em 2021 em um cenário de incertezas e falta de dados [Internet]. *Boletim do Observatório Covid-19; 2021* [cited on Oct 9, 2023]. Available at: https://portal.fiocruz.br/sites/portal.fiocruz.br/files/documentos/boletim_covid_2021-retrospectiva.pdf

RESUMO

Objetivo: Analisar os fatores associados à hospitalização em enfermaria e unidade de terapia intensiva (UTI), e ao óbito pela COVID-19 em gestantes com caso confirmado. **Métodos:** Pesquisa observacional, transversal, realizada com dados de gestantes com caso confirmado para COVID-19 provenientes do Sistema de Informação de Vigilância Epidemiológica da Gripe e do Sistema Estadual Notifica COVID-19, do Paraná. Investigou-se a associação entre variáveis independentes e dependentes (hospitalização em enfermaria e UTI, e óbito) pelo modelo de regressão de Poisson com variância robusta. **Resultados:** 4.719 gestantes compuseram a população do estudo; 9,6 e 5,1% foram hospitalizadas em enfermaria e UTI, respectivamente; 1,9% evoluíram para óbito. Houve associação entre a idade materna avançada e internação em enfermaria (RP=1,36; IC95% 1,10–1,62) e UTI (RP=2,25; IC95% 1,78–2,71), e óbito (RP=3,22; IC95% 2,30–4,15). Verificou-se associação entre o terceiro trimestre gestacional e hospitalização em enfermaria (RP=5,06; IC95% 2,82–7,30) e UTI (RP=6,03; IC95% 3,67–8,39) e óbito (RP=13,56; IC95% 2,90–24,23). O segundo trimestre associou-se à internação em UTI (RP=2,67; IC95% 1,36–3,99). Gestantes com cardiopatia apresentaram maior frequência de hospitalização em enfermaria (RP=2,24; IC95% 1,43–3,05) e UTI (RP=2,66; IC95% 1,46–3,87). A obesidade foi associada à admissão em UTI (RP=3,79; IC95% 2,71–4,86) e ao óbito (RP=5,62; IC95% 2,41–8,83). **Conclusão:** A idade materna avançada, o final do período gestacional e comorbidades foram fatores associados a quadros graves de COVID-19.

Palavras-chave: COVID-19. Estudos transversais. Gestantes. Hospitalização. Unidades de terapia intensiva. Mortalidade materna.

AUTHORS' CONTRIBUTIONS: Bergantini, L.S.: Project administration, Conceptualization, Writing – original draft, Writing – review & editing, Investigation, Methodology, Validation, Visualization. Ichisato, S.M.T.: Project administration, Conceptualization, Writing – original draft, Writing – review & editing, Methodology, Supervision, Visualization. Salci, M.A.: Conceptualization, Writing – review & editing, Methodology, Visualization. Birolim, M.M.: Writing – review & editing, Methodology, Validation, Visualization. Santos, M.L.A.: Formal analysis, Data curation, Writing – review & editing, Investigation, Methodology, Validation. Hóring, C.F.: Formal analysis, Data curation, Writing – review & editing, Investigation, Methodology, Validation, Visualization. Rossa, R.: Methodology, Validation, Visualization. Facchini, L.A.: Conceptualization, Writing – review & editing, Methodology, Supervision, Validation, Visualization.

FUNDING: This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel – Brazil (*Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil – CAPES*) – Financing Code 001.