

Title page

- Association between nutritional state and maternal and perinatal outcomes of pregnant and postpartum women with COVID-19: An original research

- Running head: COVID-19 and maternal nutrition

- Short title: Nutritional state of pregnant and postpartum women with COVID-19

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- Abstract:

Background: The disease caused by the new coronavirus, COVID-19 started in mid-December 2019 in China. The physiological changes typical of the gestational period, such as increased oxygen demand and altered lung function, included pregnant women and puerperal women as a risk group and it seems to be even greater in women with previous diseases or high-risk pregnancies, such as those with obesity, which may be associated with maternal mortality, respiratory failure and premature birth. **Objective:** To assess the nutritional status of pregnant and postpartum women with COVID-19 and to verify the association with clinical outcomes of mortality and prematurity of childbirth. **Study design:** Retrospective observational longitudinal

analysis of medical records carried out between June and September 2020 at a university hospital in Goiânia-Goiás-Brazil. Pregnant or postpartum patients with COVID-19, over 18 years old, were evaluated. The collected data refer to demographic, clinical, obstetric and neonatal and anthropometric variables. **Results:** 34 patients were evaluated (n = 29; 85.30% pregnant women, n = 5; 14.70% puerperal women), with a mean age of 28.71 ± 4.79 years. Of the total, 91.20% were overweight or obese and 8.8% were eutrophic with a current average BMI of $32.10 \pm 7.67 \text{ kg/m}^2$ vs $23.76 \pm 0.5 \text{ kg/m}^2$, respectively. The most prevalent symptoms at hospital admission were fever, cough, dyspnoea, headache or hyporexia. Of these cases, 14 (41.20%) had previous diseases, such as diabetes mellitus, hypertension, 85.70% in the overweight group, as well as the majority of these (84.60%; n = 11) had clinical complications, with ICU stay for 8.42 ± 16.29 days and use of ventilatory support via orotracheal intubation (7.61 ± 15.09 days). The clinical outcomes of mortality and premature birth accounted for 14.70% vs 68.70% of the sample, respectively, with one death in the eutrophic group and four in those with overweight/obesity (20% vs 80%; p = 0.38), as well as the 11 premature births, 90.0% occurred in this group (p = 0.47), with an average gestational age of delivery of 33.56 ± 3.98 weeks. **Conclusion:** There was no association between nutritional status and clinical outcomes, although most patients are overweight or obese, with severe clinical complications, the need for admission to the Intensive Care Unit, mechanical ventilation and unfavorable outcomes, with a high mortality rate and premature births.

Tweetable abstract: The nutritional status was not associated to perinatal outcomes, but most patients are overweight and can develop complications.

Keywords: Coronavirus; Coronavirus 2019; Nutritional status; Coronavirus infections; Pregnancy; Postpartum period; Artificial respiration; Severe acute respiratory syndrome

BACKGROUND

The disease caused by the new coronavirus, COVID-19, started in mid-December 2019 in China¹. The pathogen was recognized as SARS-CoV-2 and transmitted worldwide, and the World Health Organization (WHO) declared a pandemic situation on March 11, 2020.

The physiological changes typical of the gestational period, such as increased oxygen demand and altered lung function, included pregnant and women in the postpartum period as a risk group for complications from the new Coronavirus infection². The severity of COVID-19 in women with previous diseases or high-risk pregnancies seems to be greater, which may be associated with maternal mortality, respiratory failure and premature birth, especially in pregnancies in the third trimester^{3,4}.

Pregnant women with COVID-19 pneumonia tend to progress faster with increased involvement of the bilateral pulmonary parenchyma, predisposing to dyspnea and, when necessary, the use of mechanical ventilation². Just as overweight and obese patients are more predisposed to complications due to chronic inflammatory status⁵.

Thus, the nutritional assessment and diagnosis at the hospital admission of pregnant women and women who have recently given birth with COVID-19 can point out patients with probability of injury and may contribute to conducts that corroborate prevention and intervention strategies and establish a better prognosis. So, the aim of this study was to assess the nutritional status of pregnant women and mothers with COVID-19 and to verify the association with complications and clinical outcomes of maternal mortality and prematurity of delivery.

STUDY DESIGN

Study design and ethical aspects

This is a longitudinal observational retrospective study of medical records analysis, carried out at a University Hospital in Goiânia-Goiás-Brazil between the months of June and

September 2020, after approval by the Research Ethics Committee of the Clinical Hospital of University Federal of Goiás, under opinion number 4.298.295. The consent to participate in the research was granted through telephone contact with the patient.

Funding

This research had no funding.

Sample

42 pregnant or postpartum patients, over 18 years old, with a suspected or confirmed diagnosis of COVID-19. Of these, 34 were included in the study and 8 were excluded (Figure 1), 3 with a negative diagnosis for COVID-19, 4 for not accepting to participate in the study and 1 with incomplete data in medical records.

Data collect

Data were collected from medical records. Informations such as age, previous diseases, obstetric data, feeding, anthropometry (pre-gestational and current weight and height), symptoms at hospital admission, days of hospital stay, respiratory function, gestational age and type of delivery, weight of birth and its classification according to gestational age⁶.

Anthropometric assessment

The anthropometric evaluation was obtained by means of pre-gestational weight, current weight, height, followed by the calculation of the pre-gestational and current Body Mass Index (BMI), which were classified according to the parameters proposed by WHO⁷ and Atalah⁸.

The classification of the patients current nutritional status was established according to the BMI result on the day of hospital admission. The total gestational weight gain was obtained by the difference between the pre-gestational weight (kg) and the current one, being classified according to IOM⁹.

Clinical outcomes

Clinical outcomes were based on results obtained during in-hospital treatment. The following outcomes were considered: maternal mortality and premature birth¹⁰.

Statistical analysis

The analyzes were performed using the SPSS version 19.0 statistical program. Continuous variables were tested for normality by the Kolmogorov Smirnov test, considered normal $p \geq 0.05$ and estimates of mean and standard deviation were obtained.

Comparisons of means for parametric data were performed using the Student's t-test or non-parametric equivalent, Mann-Whitney U test. Categorical variables were expressed in absolute (n) and relative (%) values and the groups' homogeneity in relation to proportions was tested using Pearson's Chi-square test or two-tailed Fischer Exact test. A significance level of 5% ($p < 0.05$) was considered.

RESULTS

34 patients were evaluated, with a mean age of 28.71 ± 4.79 years, 11 white (32.35%) and 23 (67.65%). Of the total number of women evaluated, 29 were admitted pregnant women (85.30%) and 14.70% in the postpartum period ($n = 5$) with 7 ± 8.08 postpartum days, being one case of spontaneous abortion at 11 weeks of gestation. The mean pre-gestational BMI was 28.11 ± 7.55 kg/m² and the average gestational weight gain was 9 ± 9.73 kg. There was no difference between the classification of nutritional status in terms of pre-pregnancy and current BMI, with three eutrophic patients (8.80%) and 31 overweight or obese (91.20%), with a mean current BMI of $23.76 \pm 0,5$ kg/m² vs 32.10 ± 7.67 kg/m², respectively (Table 1).

Upon hospital admission, most patients (85.30%) had symptoms associated with or isolated from fever, cough, dyspnoea, headache or hyporexia and the others (14.70%), symptoms such as vomiting, diarrhea, dysgeusia and anosmia. Almost 50% of patients had previous diseases, such as arterial hypertension and gestational diabetes mellitus, 85.70% of

whom were overweight. As for the feeding route, around one third needed a nasogastric tube, all from the overweight or obesity group (Table 1).

Although not statistically significant, two eutrophic and 11 overweight patients evolved with clinical complications and, only those with overweight / obesity, required mechanical ventilation, staying around seven days on this support and hospitalized in the ICU for approximately nine days. Hospitalization of patients was around 10 days for eutrophic patients and 17 days for those with overweight / obesity ($p = 0.807$) (Table 1). The studied group had 14.70% ($n = 5$) deaths and 68.70% ($n = 11$) premature births with 80% and more than 90%, respectively, referring to the group of overweight / obese women (Table 2).

During hospitalization, of the 29 pregnant patients admitted, 12 (41.38%) performed delivery with an average of 6 ± 8.62 days after hospital admission. In addition, the admitted mothers ($n = 4$), performed their deliveries in another Hospital in Goiânia, via cesarean section, with an average gestational age of 34 weeks and 1 twin case. Three of these mothers, when admitted to the institution where the study was conducted, were admitted to the Intensive Care Unit (ICU), with a stay of 12 ± 8.34 days and 1 (33.34%) died after 39 days of delivery.

The results of pregnancy and neonates are described in Table 3. Most women realize cesarean delivery, compared to vaginal delivery (87.5% vs 12.5%). The indication for cesarean section was justified by the worsening of the woman's clinical condition, 10 (71.4%) of whom were admitted to the ICU.

The average gestational age was 33.56 ± 3.98 weeks, with no significant difference in terms of nutritional status ($p = 0.98$), with a total of three twin pregnancy cases, one of them with a gestational age of delivery of 28 weeks and 4 days, with the first twin weighing 885 grams and progressing to death after birth and the lowest gestational age of 26 weeks, with a newborn weight of 520 grams and neonatal and maternal death outcome.

As for the other cases of maternal death, which occurred on average 23 days after

hospital admission, 1 pregnant woman with 24 weeks and 3 postpartum women from preterm births, with twin births with a gestational age of 31 weeks and birth weights of 1,310 1,105 kilograms. In all these other cases, babies remained hospitalized to treat complications of prematurity and there was no confirmed case of vertical transmission.

DISCUSSION

Principal findings

In this longitudinal observational study in which the nutritional status was related to maternal mortality and preterm delivery in pregnant women and puerperal women diagnosed with COVID-19, admitted to a tertiary care university hospital, the current nutritional status was not associated with complications and studied clinical outcomes. It is believed that the very characteristic of the hospital in receiving high-risk pregnant women, culminated in a homogeneous public and did not allow showing statistical differences between the two groups, in addition to our sample not having been large enough to demonstrate the influence of nutritional status in front of COVID-19. However, the results found show that this population group is leaning to develop clinical complications¹¹, high mortality and premature births.

According to the epidemiological bulletin released by the Brazilian Ministry of Health¹², the majority of confirmed cases of pregnant women with COVID-19 in Brazil are in the age group of 20 to 29 years, corresponding to 44.4% of the total cases, as shown in this study.

The present study demonstrated a high mortality rate in the studied patients¹³. Similarly, previous studies in pregnant women with SARS due to viral infection caused by Coronavirus demonstrated a high mortality rate in small samples (14.7% vs 40%¹⁴ vs 25%¹⁵), as it seems to happen in the context of COVID-19. Clinical complications, such as the use of mechanical ventilation and admission to ICUs, were also demonstrated in the study by Lumbreras-Marquez et al¹⁶, conducted with Latin American women.

This study found a higher mortality rate, compared to a Brazilian study that took into account the maternal mortality rate across the country by COVID-19 (14.7% vs 12.7%), considering the cases until mid-2020¹⁷. This finding was probably the result of the university hospital's characteristic of admitting high-risk patients. Likewise, obese patients had a higher mortality rate than those who recovered from the disease (21.3% vs 10.3%)¹⁸.

The nutritional status of the studied patients was predominantly overweight and obesity. This situation is an additional factor of concern, considering that the prevalence of overweight and obesity in women aged 25 to 39 years in Brazil is 57% and 27.9%, respectively¹⁹. Our study did not find a statistical association between nutritional status at hospital admission and the clinical outcomes studied, however, it is known that overweight represents a problem in relation to COVID-19, as it is related to high risk of hospitalization, serious cases and deaths²⁰, which demonstrates the urgent need for public health measures worldwide to combat overweight and obesity.

This study also revealed a high prevalence of complications and premature birth. A series of published cases reported critical patients who progressed to severe respiratory failure, the need for mechanical ventilation, maternal death and neonatal complications, such as premature birth and intrauterine fetal death^{21, 22, 23}. The findings emphasize the risk factors related to complications²⁰ and how pregnant women are leaning to prolonged hospitalizations and invasive ventilation, especially those with obesity²³, considering the impairment in lung function and oxygenation levels due to high central adiposity^{25, 26}.

As there are currently few studies on pre-gestational and current nutritional status and stratifying it according to clinical outcome and pregnancy complications, our study sought to emphasize that pregnant women may represent a potential for clinical worsening, contradicting the initial studies^{27, 28, 29}, with no record of serious cases in pregnant women, as well as the risk factors associated with such cases.

Pregnant women are ready for physiological body changes, such as changes in the cardiopulmonary and immune systems and an increase in susceptibility to serious infections, such as viral infections². Thus, there is a detrimental impact on the course of pregnancy and neonatal outcomes, which in the context of COVID-19, are not yet known. However, when assessing nutritional status, the influence of excess weight on the clinical results of a pregnancy is proven^{30, 31}, which makes these women at risk for hypertension and / or diabetes mellitus. Due to the chronic inflammatory condition, there is a deficit in the immune system and worsening of pulmonary function³², which, especially in infections that affect the upper respiratory system, represents a worse prognosis³³.

In this context, overweight / obese pregnant women and puerperal women with COVID-19 are more susceptible to complications, the need for mechanical ventilation and premature delivery^{34, 35}, as observed in the present study, which can lead to sequelae, especially in cases where there were clinical complications serious. The recovery of this woman in post-intensive care requires multidisciplinary attention, since the late effects of the virus remain under study.

Patients with prolonged hospitalization in the ICU due to a systemic inflammatory condition lose weight, suffer microlesions in multiple organs and can suffer damage by polypharmacy, even in young people under 30³⁶. With pregnant and postpartum women in this condition, quality of life, personal care, breastfeeding and baby care can be severely compromised.

The patients who presented worsening of pulmonary function due to the influence of COVID-19 were predominantly overweight and obese and evolved to the unfavorable outcome of pregnancy. Premature births represent more than half of the sample and are a clinical challenge, considering fetal survival in the face of a severe maternal condition and the likelihood of improvement in maternal lung function after delivery³⁷.

Studies with larger samples are necessary, and it is important to consider the data of

pregnant women and puerperal women seen in other hospital units, basic health units and who did not require hospitalization, to confirm the results of this research and determine whether the nutritional status does not really influence the outcome clinical or if, due to the characteristics of the sample and the hospital, the results did not show significance.

It is not yet known whether mother-to-child vertical transmission occurs, despite controversial results^{38, 39, 40}. Cohort studies are needed to monitor women after discharge in order to investigate their clinical recovery, possible late effects of viral infection and the impact on the mother-baby relationship^{41,42}, as well as studies to determine whether intrauterine exposure to SARS-CoV-2 in any way influenced the development of these newborns and the complications resulting from prematurity^{43,44}.

Strengths and limitations

As a strong point, we emphasize that this study is a pioneer in including the assessment of the nutritional status of pregnant and postpartum women with COVID-19 at hospital admission and assessing the relationship with death, respiratory function, length of stay, clinical complications and premature delivery. The limiting factors were the size and homogeneity of the studied sample regarding BMI and the characteristic of the hospital where these patients were admitted.

In Brazil, university hospitals are characterized by their service to the highly complex Unified Health System⁴⁵ and acute complications of chronic diseases. Therefore, the characteristic of patients admitted to this Hospital Unit with COVID-19 implies some type of complication or worsening of the previous clinical picture, a factor that may have influenced the results of this study.

Interpretation

In this study with cases of pregnant and postpartum women admitted to a university hospital, almost all were classified as overweight and obesity, with severe complications, need

for ICU and ventilatory support. Although there is no statistically association between nutritional status and the complications and clinical outcomes studied, our data suggest that pregnant and postpartum women, especially those who are overweight, may evolve with complications resulting from COVID-19, resulting in high mortality and premature birth.

CONCLUSION

The study showed that almost the entire sample of pregnant and postpartum women was classified as overweight and had severe clinical complications, with ICU admissions, the need for mechanical ventilation, unfavorable neonatal outcomes and maternal deaths, although with no statistical association between nutritional status and outcome of mortality and premature birth. The need for further studies is evident, with larger samples and, mainly, that elucidate possible consequences and / or implications of late viral infection for mother and baby.

Contribution to Authorship

M. N. C. was responsible for conceptualization, methodology and database and writing. A. T. V. S. F. was responsible for formal analysis, writing and supervision. A. P. P. F. C. and M. L. F. S. were responsible for review and supervision.

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Disclosure of interest

The authors report no conflict of interest.

Patient and public involvement

Patients were not involved in the development of the research.

Patient consent

The patient's consent to participate in the research was obtained through a free and informed consent term and provided via telephone recording.

Ethics approval

The data collection was approved by the Research Ethics Committee of the Clinical Hospital of University Federal of Goiás.

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Table 1: General characteristics, associated comorbidities and clinical evolution of pregnant and postpartum women with COVID-19, according to the classification of the current nutritional status.

Table 2: Clinical outcomes of pregnant and postpartum women with COVID 19 according to the classification of the current nutritional status.

Table 3: Pregnancy and perinatal results of pregnant and postpartum women with COVID 19.

Figure 1: Flowchart of the sample.