

ASSOCIATION BETWEEN NUTRITIONAL STATE AND MATERNAL AND PERINATAL OUTCOMES OF PREGNANT AND POSTPARTUM WOMEN WITH COVID-19

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Abstract

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. **Design:** Retrospective observational longitudinal study. **Setting:** University hospital in Goiânia-Goiás-Brazil. **Population or sample:** 34 patients with confirmed diagnosis of COVID-19, between June and September 2020. **Methods:** Medical records was analysed. All eligible cases was included. The collected data refer to demographic, clinical, obstetric and neonatal and anthropometric variables. **Main outcome measures:** Maternal deaths and prematurity of childbirth. **Results:** 34 patients were evaluated (n=29 pregnant and n=5 postpartum women), with a mean age of 28.71 ± 4.79 years. Of the total, 91.20% were overweight or obese with a current average BMI of 32.10 ± 7.67 kg/m². Of these cases, 14 had previous diseases, as well as the majority of these are in the overweight group (n=11) and had clinical complications, with ICU stay and use of ventilatory support. 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 (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 maternal and perinatal outcomes, although most patients are overweight or obese, with severe clinical complications.

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1 *Title page*

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

4 ● Running head: COVID-19 and maternal nutrition

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

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17 ● Abstract:

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

26 analysis of medical records carried out between June and September 2020 at a university
27 hospital in Goiânia-Goiás-Brazil. Pregnant or postpartum patients with COVID-19, over 18
28 years old, were evaluated. The collected data refer to demographic, clinical, obstetric and
29 neonatal and anthropometric variables. **Results:** 34 patients were evaluated (n = 29; 85.30%
30 pregnant women, n = 5; 14.70% puerperal women), with a mean age of 28.71 ± 4.79 years. Of
31 the total, 91.20% were overweight or obese and 8.8% were eutrophic with a current average
32 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
33 hospital admission were fever, cough, dyspnoea, headache or hyporexia. Of these cases, 14
34 (41.20%) had previous diseases, such as diabetes mellitus, hypertension, 85.70% in the
35 overweight group, as well as the majority of these (84.60%; n = 11) had clinical complications
36 , with ICU stay for 8.42 ± 16.29 days and use of ventilatory support via orotracheal intubation
37 (7.61 ± 15.09 days). The clinical outcomes of mortality and premature birth accounted for
38 14.70% vs 68.70% of the sample, respectively, with one death in the eutrophic group and four
39 in those with overweight/obesity (20% vs 80%; $p = 0.38$) , as well as the 11 premature births,
40 90.0% occurred in this group ($p = 0.47$), with an average gestational age of delivery of
41 33.56 ± 3.98 weeks. **Conclusion:** There was no association between nutritional status and
42 clinical outcomes, although most patients are overweight or obese, with severe clinical
43 complications, the need for admission to the Intensive Care Unit, mechanical ventilation and
44 unfavorable outcomes, with a high mortality rate and premature births.

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

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

49 **BACKGROUND**

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

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

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

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

70 **STUDY DESIGN**

71 *Study design and ethical aspects*

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

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

77 *Funding*

78 This research had no funding.

79 *Sample*

80 42 pregnant or postpartum patients, over 18 years old, with a suspected or confirmed
81 diagnosis of COVID-19. Of these, 34 were included in the study and 8 were excluded (Figure
82 1), 3 with a negative diagnosis for COVID-19, 4 for not accepting to participate in the study
83 and 1 with incomplete data in medical records.

84 *Data collect*

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

89 *Anthropometric assessment*

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

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

98 *Clinical outcomes*

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

101 *Statistical analysis*

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

105 Comparisons of means for parametric data were performed using the Student's t-test or
106 non-parametric equivalent, Mann-Whitney U test. Categorical variables were expressed in
107 absolute (n) and relative (%) values and the groups' homogeneity in relation to proportions was
108 tested using Pearson's Chi-square test or two-tailed Fischer Exact test. A significance level of
109 5% ($p < 0.05$) was considered.

110 **RESULTS**

111 34 patients were evaluated, with a mean age of 28.71 ± 4.79 years, 11 white (32.35%)
112 and 23 (67.65%). Of the total number of women evaluated, 29 were admitted pregnant women
113 (85.30%) and 14.70% in the postpartum period ($n = 5$) with 7 ± 8.08 postpartum days, being one
114 case of spontaneous abortion at 11 weeks of gestation. The mean pre-gestational BMI was
115 28.11 ± 7.55 kg/m² and the average gestational weight gain was 9 ± 9.73 kg. There was no
116 difference between the classification of nutritional status in terms of pre-pregnancy and current
117 BMI, with three eutrophic patients (8.80%) and 31 overweight or obese (91.20%), with a mean
118 current BMI of $23.76 \pm 0,5$ kg/m² vs 32.10 ± 7.67 kg/m², respectively (Table 1).

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

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

125 Although not statistically significant, two eutrophic and 11 overweight patients evolved
126 with clinical complications and, only those with overweight / obesity, required mechanical
127 ventilation, staying around seven days on this support and hospitalized in the ICU for
128 approximately nine days. . Hospitalization of patients was around 10 days for eutrophic patients
129 and 17 days for those with overweight / obesity ($p = 0.807$) (Table 1). The studied group had
130 14.70% ($n = 5$) deaths and 68.70% ($n = 11$) premature births with 80% and more than 90%,
131 respectively, referring to the group of overweight / obese women (Table 2).

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

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

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

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

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

152 **DISCUSSION**

153 *Principal findings*

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

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

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

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

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

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

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

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

207 In this context, overweight / obese pregnant women and puerperal women with COVID-
208 19 are more susceptible to complications, the need for mechanical ventilation and premature
209 delivery^{34, 35}, as observed in the present study, which can lead to sequelae, especially in cases
210 where there were clinical complications serious. The recovery of this woman in post-intensive
211 care requires multidisciplinary attention, since the late effects of the virus remain under study.

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

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

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

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

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

233 *Strengths and limitations*

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

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

245 *Interpretation*

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

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

252 **CONCLUSION**

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

259 **Contribution to Authorship**

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

263 **Funding**

264 This research had no funding.

265 **Disclosure of interest**

266 The authors report no conflict of interest.

267 **Patient and public involvement**

268 Patients were not involved in the development of the research.

269 **Patient consent**

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

272 **Ethics approval**

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

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277 especially thank the patients who recovered from COVID-19 and their families to accept and
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279 and all victims of this disease, especially brazilian.

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408

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

412

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

415

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

418

419 Figure 1: Flowchart of the sample.