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# Analysis of the Factors That Influence the Clinical Outcome of Severe Acute Respiratory Syndrome Caused by SARS-CoV-2 in Pregnant Women

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## Abstract

**Introduction:** The new coronavirus (SARS-CoV-2) pandemic has shown to cause even more severe problems among pregnant women, increasing the incidence of complications before and after childbirth, especially cardiorespiratory problems, such as the Severe Acute Respiratory Syndrome (SARS). **Objectives:** To describe the clinical outcome of SARS caused by SARS-CoV-2 in Brazilian pregnant women and to compare the rates of morbidity and mortality from other causes in this group, stratified by the following variables: gestational age and age group. **Methodology:** Observational, analytical study based on documents whose data were collected from the 2020 Epidemiological Report No. 40 in the database of the Brazilian Department of Health, from which morbidity and mortality data were extracted to calculate the lethality rate and compare rates using a binomial test with a significance level of 0.05. **Results:** Of the total number of pregnant women hospitalized for SARS, 4,467 (46.6%) were confirmed for COVID-19 and, of these, 233 died, corresponding to a lethality rate of 5.2%. Morbidity was higher in the third trimester of pregnancy, but the disease was more severe in the second trimester (7%), being worse in women aged 40 years and older (40–49; 8.7% and 50–59; 15.3%). A significant difference was observed in the rate of cases between the COVID-19 SARS group and the group with other causes in all gestational strata and age groups. As for deaths, a significant difference was found in the rates between the first and third trimesters, and in pregnant women aged 10 to 19 years. **Conclusion:** Considering the variables under analysis, evidence shows that pregnant women at an advanced age and in the second trimester of pregnancy contribute to the lethal outcome of the disease. Other variables associated with the presence of comorbidities and quality of care for pregnant women should be considered in the model in future studies.

**Keywords:** SARS, COVID-19, pregnant women, lethality, complications

## **1. Introduction**

Originating in the province of Wuhan (China) in December 2019, the coronavirus known as SARS-CoV-2 became a worldwide public concern, as warned by the World Health Organization, for its ability to cause severe respiratory tract infections. COVID-19, a disease caused by such etiologic agent, presents fever, cough, expectoration, headache, myalgia or fatigue, and diarrhea as the most common symptoms, and may progress to Severe Acute Respiratory Syndrome (SARS) [1]. This respiratory complication signals the potential of the pathogen to cause respiratory failure, the risks of which can be lethal and exacerbated by the presence of comorbidities, such as hypertension, diabetes mellitus, and cardiovascular diseases [2].

COVID-19 has already infected 122,813,796 people and caused the death of 2,709,640, according to weekly epidemiological data provided by the World Health Organization on March 20, 2021 [3]. Also, according to the 55th Epidemiological Report released by the Brazilian Department of Health, Brazil has the second highest number of accumulated cases worldwide (11,950,459), as well as the number of accumulated deaths (292,752) [4].

Pregnant women are part of this worrying scenario. They are commonly in contact with healthcare professionals and attend medical facilities, representing one of the groups most physiologically susceptible to cardiorespiratory complications, such as hypoxia, and changes in lung volume and functional capacity, especially when they show common signs and symptoms of COVID-19 that make diagnosis difficult, such as dyspnea [5].

In Brazil, a review conducted from January 1 to March 20, 2021 (from the Epidemiological Week – EW 01/2021 to 11/2021), shows that of the 353,277 cases hospitalized due to SARS, about 2,746 individuals were pregnant women, and 1,491 pregnant women (54.3%) were affected by COVID-19. The Southeast region corresponds to the Brazilian region with the highest number of pregnant women affected by SARS (1,063 cases or 38.7%), followed by the Northeast region (519 cases or 18.9%). The most representative states in these regions are São Paulo, Ceará, Minas Gerais, and Rio de Janeiro. The most affected age group was 20–29 years (40.9%), followed by pregnant women aged 30–39 years (40.2%), with the third trimester of pregnancy being the period with the highest concentration of cases [4].

Pregnant women with SARS are at risk of death mainly because of progressive respiratory failure and severe sepsis due to the physiological susceptibility to infections during pregnancy [5]. Thus, SARS evolved to death in 3.6% of the 9,500 pregnant women covered by the Special Epidemiological Report of EW 11/2021, of which 90.2% were confirmed to have been infected with COVID-19. Also, the highest number of cases was in the Southeast and North regions (36.4 and 25.8%, respectively), affecting a larger number of pregnant women aged 30–39 years, corresponding to 42.1% [4, 6].

Given the worrisome healthcare scenario described, this study aims to describe the clinical outcomes of SARS due to SARS-CoV-2 in Brazilian pregnant women and to compare the morbidity and mortality rates due to other causes in this group, stratified by the variables: gestational age and age group.

## **2. Methodology**

This is an observational analytical study based on documents, whose data were collected in the database of the Brazilian Department of Health, precisely in the

2020 Special Epidemiological Report No. 40 ([https://www.gov.br/saude/pt-br/assuntos/media/pdf/2020/dezembro/11/boletim\\_epidemiologico\\_covid\\_40-1.pdf](https://www.gov.br/saude/pt-br/assuntos/media/pdf/2020/dezembro/11/boletim_epidemiologico_covid_40-1.pdf)). The proposed document has a consolidated report on the number of cases and deaths from COVID-19 in specific groups, including pregnant women affected by SARS, the object of analysis in this study. The information contained in the Report included data accumulated up to Epidemiological Week - EW 49 (11/29/2020 to 12/05/2020).

The study variables were the age group and gestational age of the pregnant women, stratified by cases and deaths in two groups: SARS caused by COVID-19 and SARS caused by other etiologic agents, such as the influenza virus, other viruses of the respiratory system, and unidentified cases. This grouping of cases caused by etiological agents is done by the Brazilian Department of Health itself. The age of the pregnant women was divided into five age groups (10–19 years, 20–29 years, 30–39 years, 40–49 years, and 50–59 years), and gestational age into four categories (first, second, third trimester, and unidentified). Cases under investigation were not included in the specified sample.

Initially, a descriptive analysis was performed to present the absolute and relative frequency of cases and deaths at the age and gestational age strata of pregnant women distributed in the two groups: SARS caused by COVID-19 and SARS caused by other etiologic agents. To learn the severity degree of the disease by the study categories (age group and gestational age), the lethality coefficient was calculated according to the following formula:

$$L(\%) = \text{Number of deaths SARS caused by COVID19} \times 100. \quad (1)$$
$$\frac{\text{Number of deaths SARS caused by COVID19}}{\text{Number of diagnosed cases of SARS caused COVID19}} \times 100.$$

The rates of cases and deaths in the referred categories were compared using the binomial test at the level of 5%, with the aid of BioEstat 5.3 software. Sample 1 size, total number of confirmed SARS cases due to COVID-19, and number of successful cases in each stratum analyzed were considered. The same was employed for sample 2 with cases of SARS caused by other agents. The same procedure was carried out for deaths.

The research respected the ethical aspects of research with human beings, described in the Resolution of the National Health Council 510/16, on the guidelines and regulatory standards for research in human and social sciences. It provides for the waiver of consideration by an Ethics Committee when using data available in the public domain [7]. The ethical criteria of the Declaration of Helsinki and international standards were observed.

### 3. Results

**Table 1** shows the number of cases and deaths of pregnant women with SARS diagnosed with COVID-19 (sample 1), as well as other causes (sample 2). In sample 1, 4,467 cases with 233 deaths were reported and in sample 2, 4,268 cases with 101 deaths. Excluding the number of pregnant women of unknown age, the stratum with the highest prevalence of cases and deaths in sample 1 was the stratum of 20–39 years (3,647 and 183, respectively), corresponding to about 82 and 78.5%, respectively. In sample 2, 3,309 cases (77.7%) and 76 deaths (75.2%) were reported in that age group, a number significantly lower than that in sample 1 ( $p < 0.05$ ). However, the highest rate of deaths occurred more significantly in the stratum of 10–19 years as a result of causes other than COVID-19 ( $p = 0.028$ ).

As for gestational age, the third trimester showed the highest prevalence of SARS, and the number of SARS cases due to SARS-CoV-2 was significantly higher ( $p < 0.0001$ ). However, the prevalence was significantly higher in the sample of pregnant women with SARS due to other causes/etiologic agents in the first and second trimesters (**Table 2**).

Concerning deaths, **Table 2** shows that the lowest rate of deaths occurred in the first trimester, excluding when gestational age was not identified in either sample, being significantly lower in sample 2 ( $p = 0.0051$ ). However, in the third trimester, it is higher in sample 1, i.e. in pregnant women with SARS due to SARS-CoV-2 (0.0147).

| Data   | Age group* | SARS by COVID-19 (4,464) – confirmed | %    | SARS by other etiologic agents (4,256) | %    | Binomial test (0.05) |
|--------|------------|--------------------------------------|------|--|------|----------------------|
| Cases  | 10–19      | 434                                  | 9.7  | 687                                    | 16.1 | $p < 0.0001$         |
|        | 20–29      | 1863                                 | 41.7 | 2003                                   | 47.1 | $p < 0.0001$         |
|        | 30–39      | 1784                                 | 40.0 | 1306                                   | 30.7 | $p < 0.0001$         |
|        | 40–49      | 311                                  | 7.0  | 218                                    | 5.1  | $p = 0.0003$         |
|        | 50–59      | 72                                   | 1.6  | 42                                     | 1.0  | $p = 0.0101$         |
| Deaths | 10–19      | 12                                   | 5.2  | 12                                     | 11.9 | $p = 0.0287$         |
|        | 20–29      | 77                                   | 33.0 | 39                                     | 38.6 | $p = 0.3264$         |
|        | 30–39      | 106                                  | 45.5 | 37                                     | 36.6 | $p = 0.1328$         |
|        | 40–49      | 27                                   | 11.6 | 6                                      | 5.9  | $p = 0.1121$         |
|        | 50–59      | 11                                   | 4.7  | 7                                      | 6.9  | $p = 0.4114$         |
| Total  | —          | 233                                  | 100  | 101                                    | 100  | —                    |

\*Three cases with unidentified age group were excluded from this analysis.

Source: Authors, 2020 [4] based on data from BRASIL (2020).

**Table 1.**  
Absolute and relative frequencies of SARS cases and deaths in pregnant women notified in Brazil (2020), according to maternal age.

| Data   | Gestational age (trimesters) | SARS due to COVID-19 – confirmed | %    | SARS by other etiologic agents | %    | Binomial test (0.05) |
|--------|------------------------------|----------------------------------|------|--------------------------------|------|----------------------|
| Cases  | 1st                          | 384                              | 8.6  | 553                            | 13.0 | $p < 0.0001$         |
|        | 2nd                          | 1018                             | 22.8 | 1208                           | 28.3 | $p < 0.0001$         |
|        | 3rd                          | 2784                             | 62.3 | 2284                           | 53.5 | $p < 0.0001$         |
|        | Unidentified                 | 281                              | 6.3  | 223                            | 5.2  | $p = 0.0328$         |
| Total  | —                            | 4467                             | 100  | 4268                           | 100  | —                    |
| Deaths | 1st                          | 16                               | 6.9  | 17                             | 16.8 | $p = 0.0051$         |
|        | 2nd                          | 71                               | 30.5 | 32                             | 31.7 | $p = 0.8258$         |
|        | 3rd                          | 133                              | 57.0 | 43                             | 42.6 | $p = 0.0147$         |
|        | Unidentified                 | 13                               | 5.6  | 9                              | 8.9  | $p = 0.2596$         |
| Total  | —                            | 233                              | 100  | 101                            | 100  | —                    |

Source: Authors, 2020 [4] based on data from BRASIL (2020).

**Table 2.**  
Absolute and relative frequencies of SARS cases and deaths in pregnant women notified in Brazil (2020), according to gestational age.

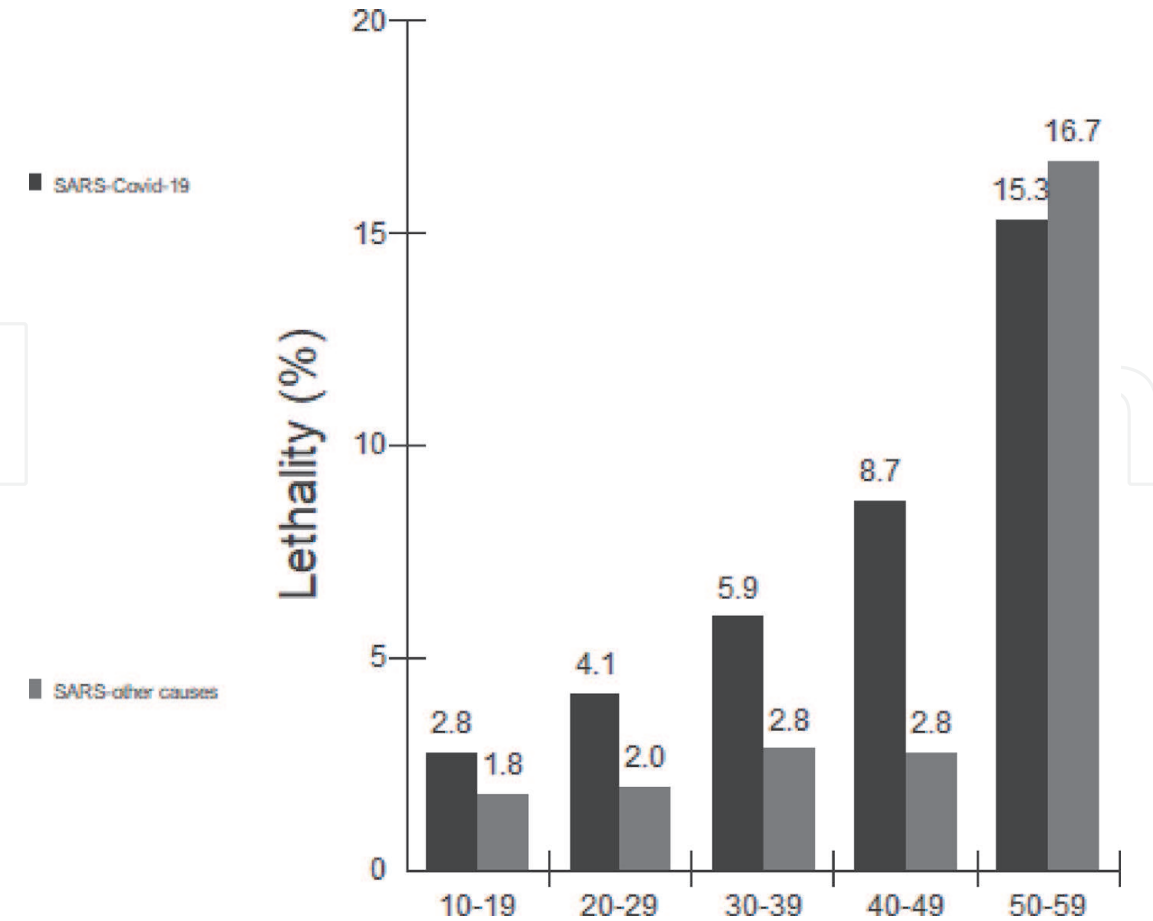


**Table 3** shows the lethality rates by gestational age. The group of pregnant women with SARS caused by COVID-19 was observed to have a higher mortality rate than that of the group of pregnant women with SARS due to other causes (5.2 and 2.3%, respectively). Considering the strata, the event was more severe in the second trimester (7%) for the first group, whereas it was more significant in the first trimester (3.1%) for the second one.

**Figure 1** shows the relationship between the age of pregnant women and disease lethality. The lowest rates have been observed to occur in the first stratum (10–19 years), increasing with age. In group 1 (deaths from SARS caused by COVID-19), lethality ranged from 2.8% in the 10–19 age group to 15.3% in the 50–59 age group.

| Gestational age (trimesters) | Cases of SARS by COVID-19 | Deaths | Lethality rate (%) | Cases of SARS by other etiologic agents | Deaths | Lethality rate (%) |
|------------------------------|---------------------------|--------|--------------------|---|--------|--------------------|
| 1st                          | 384                       | 16     | 4.2                | 553                                     | 17     | 3.1                |
| 2nd                          | 1018                      | 71     | 7.0                | 1208                                    | 32     | 2.6                |
| 3rd                          | 2784                      | 133    | 4.8                | 2284                                    | 43     | 1.8                |
| Unidentified                 | 281                       | 13     | 4.6                | 223                                     | 9      | 3.8                |
| <b>Total</b>                 | 4467                      | 233    | 5.2                | 4268                                    | 101    | 2.3                |

**Table 3.**  
*Lethality in pregnant women due to SARS caused by COVID-19 and other causes, according to gestational age in Brazil (2020).*



**Figure 1.**  
*Distribution of lethality rates by age in the groups of pregnant women with SARS caused by COVID-19 and SARS due to other causes (BRASIL, 2020).*

In all age groups from group 2 (deaths from SARS due to other causes), the lethality rate was lower than in group 1, except for the 50–59 age group (16.7%).

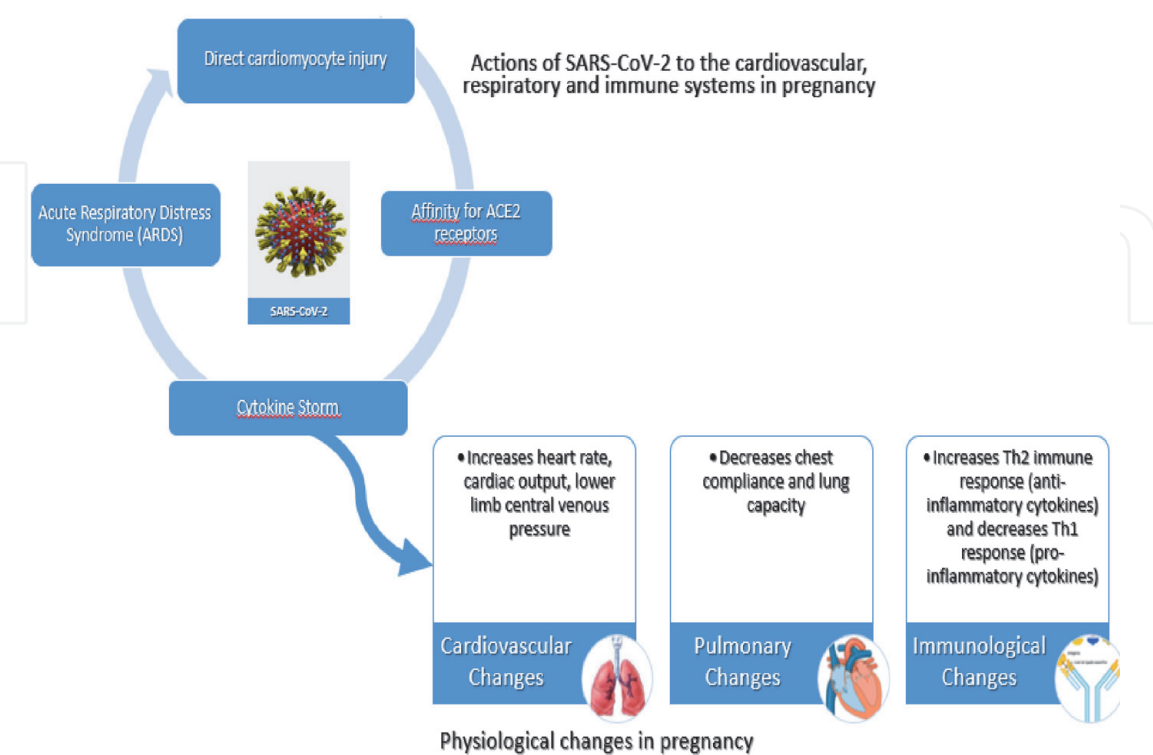
4. Discussion

Susceptibility to respiratory pathogens and severe cases of pneumonia during pregnancy occur due to immunological and cardiopulmonary changes that can make pregnant women more vulnerable to hypoxia [8]. **Figure 2** summarizes the main changes in pregnancy and its susceptibility to COVID-19.

The pulmonary system of pregnant women also undergoes complex changes due to their pregnancy status. There is a compression of the diaphragm by the uterus, leading to a decrease in thoracic compliance and total lung capacity [8]. In addition, pneumonia caused by COVID-19 rapidly progresses from focal to bilateral pulmonary consolidation, predisposing these patients to hypoxemic respiratory failure [5] (**Figure 2**). Symptoms started between 5.8 and 29.9 weeks of pregnancy and between 5.7 and 30.7 weeks of hospital stay [9].

In the cardiovascular system (**Figure 2**), the pregnant woman undergoes profound physiological changes. There is a myocardial hypertrophy with enlarged cardiac chambers, which leads to an increase in cardiac output that reaches a maximum of 30–40% between the 28th and 36th week, when it stabilizes until childbirth; there is a gradual increase in heart rate that reaches its maximum peak between the 28th and 36th weeks [10]; total peripheral resistance is reduced by up to 30% from the 8th–12th week of gestation, remaining at these levels until term [11]; finally, there is an increase in central venous pressure in the lower portions of the body, especially from the second trimester onwards, due to the action of the uterine volume on the pelvic veins and inferior vena cava [12].

This overload of the cardiovascular system becomes dangerous as the pregnant woman faces the potential aggressions of COVID-19 (**Figure 2**). According to the



**Figure 2.** *Actions of SARS-CoV-2 to the cardiovascular, respiratory and immune systems and their physiological alterations in pregnancy. Source: Authors (2021).*

literature, regardless of being pregnant or not, it is postulated that SARS-CoV-2 causes myocardial damage by at least three mechanisms: (I) Hyperexpression of ACE2 receptors (Angiotensin II receptor) in the cardiovascular system – it would lead to a greater affinity of the virus for the cells of the cardiac system, causing direct damage to the cells by SARS-CoV-2; (II) Myocardial damage caused by the “Cytokine Storm” – with aggression from the immune system directly to the cardiomyocyte cells; and (III) the Severe Acute Respiratory Distress syndrome (ARDS) would cause hypoxemia, leading to myocardial ischemia [13]. Thus, pregnant women, due to the physiological overload of the cardiovascular system, theoretically, would have more severe cases of COVID-19.

Additionally, in the case of pregnant women, another factor should be considered: the immunotolerance changes in the innate and adaptive systems caused by pregnancy (**Figure 2**). In the gestational immune system [14] there is a complex humoral response in signaling. What happens is an alteration in the signaling pattern, especially in CD4+ T lymphocytes. In this context, there is an important decrease in the immune response by Th1 lymphocytes and an increase in the response mediated by Th2 lymphocytes. In practice, this contributes to increased maternal susceptibility to intracellular pathogens and viral infections, which causes an increase in gestational morbidity in a broad and general way [15]. Thus, Th1 type cytokines are pro-inflammatory agents that contain interleukins (IL-1a, IL-1b, IL-6, IL-12) and interferon-gamma (IFN- $\gamma$ ), while Th2 type cytokines are anti-inflammatory drugs agents that contain interleukins (IL-4, IL-10, IL-13) and transforming growth factor-beta (transforming growth factor  $\beta$ , TGF- $\beta$ ). Patients with SARS-CoV-2 demonstrated preferential activation of Th1 immunity, resulting in a considerable increase in pro-inflammatory cytokines for at least two weeks after the onset of the disease, which would cause severe lung damage [13].

Consistent with literature data, pregnancy with the presence of Acute Respiratory Syndrome is more associated with maternal and neonatal complications such as premature birth, intrauterine growth restriction, spontaneous abortion, orotracheal intubation, ICU admissions, disseminated intravascular coagulation and acute renal failure [16, 17]. A North American cohort that evaluated 8,207 pregnant women with 83,205 women of childbearing age (15–44 years), both groups with laboratory confirmation for SARS-CoV-2 showed a mortality rate lower than 1% (0.2% - being 16 pregnant and 208 not pregnant). The authors further report that pregnant women had higher admission rates than their controls (31.5% vs. 5.8%, respectively). In addition, pregnant women had a higher incidence of ICU admissions compared to non-pregnant women (1.5% vs. 0.9%, respectively) and also had greater need to use invasive mechanical ventilation (0.5% vs. 0.3%) [18]. A prospective cohort conducted in Mexico through the “COVID-19 National Data Registry of Mexico” compared 5,183 pregnant women with 175,905 non-pregnant women with COVID-19 confirmed by RT-PCR. According to the authors, pregnant women had higher odds ratios (OR) for deaths (1.84; 95% CI, 1.26–2.69), pneumonia (1.86; 95% CI, 1.60–2.16), and ICU admissions (1.86; 95% CI, 1.41–2.45) compared to non-pregnant women [19].

In the context of SARS-COV-2, it seems that the clinical consequences caused by COVID-19 are influenced by the patient's age and pre-existing comorbidities [20]. Sentilhes et al. observed that women had one or more known maternal characteristics associated with severe maternal morbidity, such as: age over 35 years, overweight, gestational hypertension, diabetes and preexisting asthma, which are warning aspects for monitoring and managing pregnant women infected with COVID-19 [21]. Study by Knight et al. showed that almost half (41% - 175) of pregnant women with SARS-CoV-2 admitted to UK hospitals and evaluated in their prospective cohort were at the age of 35 or over [22].



A systematic review carried out in 2021 reported that, in general, patients with non-communicable chronic diseases such as obesity, diabetes mellitus and systemic arterial hypertension have higher morbidity and mortality rates when they acquire COVID-19 compared to the general population [23]. In our study, approximately 80 and 50% of the pregnant patients were overweight or obese, respectively, before pregnancy and had associated conditions, such as systemic arterial hypertension (SAH). Obesity is considered an aggravating factor because it weakens lung function through mechanical and inflammatory pathways. In synergy with COVID-19, obesity, asthma, and mechanical stress caused by high uterine volume can increase the risk of premature birth [24]. Another study pointed out that 18.5% of pregnant women had at least one comorbidity before pregnancy: asthma, SAH, or obesity [21]. A cohort carried out in the United Kingdom based on the “UK Obstetric Surveillance System” showed that of the 427 pregnant women admitted to hospital units with SARS-CoV-2 infection, 69% (281) were overweight or obese and 34% (145) had other pre-existing comorbidities. Around 10% of the admitted pregnant women needed O2 support and 1% died [22]. However, it is not always possible to determine the relationship between COVID-19 complications and the comorbidities of pregnant women. In a study of 116 cases, of which nine patients (7.8%) had gestational diabetes and five (4.3%) presented hypertensive disorders, including pre-eclampsia, the authors indicated that there is not necessarily a direct relationship between comorbidities and pregnancy complications associated with COVID-19 [25].

The symptomatology of pregnant women with COVID-19 is not different from that observed in the general population. A review study summarizes in **Figure 3** the main clinical manifestations of COVID-19 in pregnant women in epidemiological studies:

|   | Cases | Fever   | Cough   | Sore throat | Diarrhea | Dyspnea |
|---|-------|---------|---------|-------------|----------|---------|
| Chen et al  | 9     | 78%     | 44%     | 22%         | 11%      | 11%     |
| Zhu et al   | 7     | 100%    | 42%     | 14%         | 14%      | NA      |
| Liu et al <span style="border: 1px solid black; padding: 0 2px;">*</span> | 11    | 86%     | 59%     | 6%          | 6%       | 6%      |
| Yu et al  | 7     | 85%     | 14%     | NA          | 14%      | 14%     |
| Chen et al  | 5     | 0%      | 0%      | NA          | NA       | 0%      |
| Lee et al   | 1     | Present | Present | Present     | NA       | NA      |
| Liu et al   | 13    | 77%     | NA      | NA          | NA       | 23%     |

Abbreviations: NA, Not available.

*\* data including three puerperal patients.*

**Figure 3.**  
Main clinical manifestations of pregnant women with COVID-19 [adapted]. Source: Castro et al. [26].

The data in **Figure 3** are compatible with subsequent studies. A meta-analysis carried out by an Italian group showed that the most common symptoms of pregnant women with SARS-CoV-2, MERS and SARS were fever (82.6%), cough (57.1%) and dyspnea (27.0%) [27]. Rasmussen et al. reported that the most common symptoms of COVID-19 are fever, cough, myalgia, headache, and diarrhea [28].

After analyzing 46 pregnant women with COVID-19 in a retrospective study, most cases were treated in outpatient settings (78.3%, 36/46) or were asymptomatic (6.5%, 3/46), with dyspnea being the main symptom. However, seven pregnant patients (15.2%) were hospitalized due to COVID-19, one of whom was admitted to the intensive care unit (ICU). The authors believe that pregnant women should be considered a high-risk population for the severe form of COVID-19, particularly in the second and third trimesters of pregnancy, especially if they are obese [24]. A cross-sectional, descriptive and quantitative study carried out in the city of Wuhan, China and published in the New England Journal of Medicine in April 2020, reports that of the pregnant women who acquired COVID-19, 55 out of 106 (52%) were nulliparous and 75 out of 118 (64%) had been infected with SARS-CoV-2 in the third trimester. The most common symptoms in 112 women were fever (75%) and cough (73%). Most (92%) had the disease in its mild form and 8% had hypoxemia and severe forms, and of these patients one required intensive care support with mechanical ventilation. Interestingly, COVID-19 was more severe among patients in the immediate postpartum period [29].

The findings by Pierce-Williams et al. pointed out that, within the sample universe analyzed, 73% of the pregnant women with severe manifestations of COVID-19 required O<sub>2</sub> supplementation, and 95% were intubated. Among women with the severe form of the disease, 70% developed acute respiratory distress syndrome (ARDS), 20% were placed in a prone position (in gestational ages at 26 to 31 weeks), and 20% required reintubation [9]. Systematic review conducted by Juan et al. refers to seven maternal deaths, four intrauterine fetal deaths (one with twin pregnancy) and two neonatal deaths (twin pregnancy) reported in a non-consecutive case series of nine cases with severe COVID-19. In the case reports, two maternal deaths, one neonatal death and two cases of neonatal SARS-CoV-2 infection were stated [30].

However, these findings are not unanimous in the literature. A cross-sectional, descriptive and prospective study conducted in Utah, India, which analyzed 65 pregnant women with positive RT-PCR for COVID-19, showed that 88.4% were asymptomatic [31]. An Iranian review study points out that pregnant women with comorbidities are more likely to have more severe clinical pictures of COVID-19, although it is inconclusive for the authors that COVID-19 alone can increase maternal-fetal risk [32]. A second review study published in 2021 comparing outcomes between pregnant and non-pregnant women with SARS-CoV-2, MERS (Middle East respiratory syndrome coronavirus) and SARS (Severe acute respiratory syndrome coronavirus) concluded that there is no evidence that pregnant women are more susceptible to coronavirus infection in general, or that those infected with these viruses are more likely to develop severe pneumonia. Similar to non-pregnant women, pregnant women with MERS had the highest mortality, followed by those with SARS and COVID-19 [33]. These findings are corroborated by a retrospective and multicentric cohort carried out in 2020 [34] in which it was observed that the mortality rate among pregnant women (110 patients) compared to non-pregnant women (224 patients) did not show statistically significant differences. However, pregnant women had lower saturation rates and global lymphocyte counts than their peers in a statistically significant way.

The prospective cohort study by Prabhu et al. analyzed 675 women admitted for delivery, 10.4% tested positive for COVID-19, of whom 21.4% had at least one symptom, demonstrating that there are significant outcome differences between pregnant women who tested positive and negative for SARS-CoV-2 and symptomatic and asymptomatic ones. The rate of cesarean section was 15% higher among women who were infected with the virus, in addition to demonstrating that post-partum complications, including fever and hypoxia, occurred in 12.9% of the women infected versus 4.5% of the women not infected. In that same study, placental perfusion diseases, possibly thrombi in fetal vessels, were frequent in approximately 48% of the infected women [35].

The worsening of the clinical condition of pregnant women with COVID-19 raises great concern with potential outcomes that include spontaneous abortion, premature birth, and fetal morbidity and mortality [24]. The severe consequences for the fetus result from the oxygen supply deficit caused by maternal respiratory disease, leading to hypoxemia due to the reduction of the partial pressure of oxygen [14]. The study by Allotey J et al. showed that among pregnant women and recently pregnant women with COVID-19, the chance of premature births was high compared to pregnant women who did not have the disease [36].

A meta-analysis conducted by Mascio et al., which outlined complications caused by coronavirus diseases, such as SARS, MERS, and COVID-19, in pregnant women, found that those with COVID-19 had the highest incidence of premature birth, achieving 41% against 24% for SARS. However, this group had the lowest mortality rate (7%) [27, 35]. This low fetal mortality rate was corroborated by studies such as that by Wong et al., in which SARS had a mortality rate of 25% and induced abortions in up to 57% of the whole sample [17].

Furthermore, literature shows that advanced maternal age can be considered a risk factor for the severe form of the disease during pregnancy [36]. In this scenario, pregnant women over 35 years of age affected by COVID-19 require special attention [7, 37]. According to our data, the lethality rate among pregnant women with SARS caused by COVID-19 in the 30–39 age group is 5.8%, increasing to 8.7% in the 40–49 age group, and exceeding 15% in the 50–59 age group.

#### **4.1 Limitations**

As biases in this study, those inherent in the secondary nature of the data should be highlighted. First, the underreporting of cases - only people who sought health services were notified. Consequently, mild or asymptomatic cases were not counted; secondly, the dependence on correctly filling out the notification forms; and, finally, the limited availability of information in the Brazilian Government's databases.

#### **5. Conclusion**

Comparing the lethality rate observed in pregnant women with SARS caused by COVID-19 with that caused by other etiologic agents shows the severity of SARS-CoV-2 in this group and that its potential for lethality is greater in the second trimester of pregnancy. Likewise, it indicates that the older the age group, the greater the lethality of the virus. In addition to the variables analyzed, other variables related to the presence of comorbidities and quality of care for pregnant women should be considered in the model in future studies to determine the risk level for these women and the required specialized conduct.



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## References

- [1] Zhai P, Ding Y, Wu X, Long J, Zhong Y, Li Y. The epidemiology, diagnosis and treatment of Covid-19. *International Journal Of Antimicrobial Agents*, [S.L.], 2020; 55(5):1-11 <http://dx.doi.org/10.1016/j.ijantimicag.2020.105955>.
- [2] Al-qahtani, A.A. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): emergence, history, basic and clinical aspects. *Saudi Journal Of Biological Sciences*, 2020; 27(10): 2531-2538.
- [3] World Health Organization. Weekly operational update - 14 December 2020: emergency situation updates. Emergency Situation Updates. 2020. Disponível em: <https://www.who.int/publications/m/item/weekly-epidemiological-update—14-december-2020>. Acesso em: 14 dez. 2020.
- [4] Brasil. Ministério da saúde. Boletim Epidemiológico Especial: doença pelo coronavírus Covid-19. Doença pelo Coronavírus Covid-19. 2020. Disponível em: [https://www.gov.br/saude/pt-br/media/pdf/2020/dezembro/11/boletim\\_epidemiologico\\_Covid\\_40-1.pdf](https://www.gov.br/saude/pt-br/media/pdf/2020/dezembro/11/boletim_epidemiologico_Covid_40-1.pdf). Acesso em: 14 dez. 2020.
- [5] Dashraath P et al. Coronavirus disease 2019 (Covid-19) pandemic and pregnancy. *American Journal Of Obstetrics And Gynecology*, [S.L.], 2020; 222 (6): 521-531, jun. 2020. Elsevier BV. <http://dx.doi.org/10.1016/j.ajog.2020.03.021>.
- [6] Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. Gestação de alto risco: Manual técnico. 5ª ed. Brasília: Editora do Ministério da Saúde; 2010.
- [7] Brasil. Ministério da Saúde. Conselho Nacional de Saúde. Resolução no 510, de 7 de abril de 2016. Trata sobre as diretrizes e normas regulamentadoras de pesquisa em ciências humanas e sociais. Diário Oficial da União, Brasília, DF, 24 maio 2016.
- [8] Hegewald MJ. Respiratory physiology in pregnancy. *Clinics in Chest Medicine*. 2011; 32(1):1-13. <https://doi.org/10.1016/j.ccm.2010.11.001>.
- [9] Pierce-williams R et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a united states cohort study. *American Journal Of Obstetrics & Gynecology* 2020;2(3): 1-12. <http://dx.doi.org/10.1016/j.ajogmf.2020.100134>.
- [10] Reis GFF. Alterações Fisiológicas Maternas da Gravidez. *Revista Brasileira de Anestesiologia*. 1993; 43: 1: 3- 9.
- [11] Mathias R S, Carvalho JCA. Anestesia em Obstetrícia - Curso de Atualização – SAESP, 1990.
- [12] Bonica JJ. Principles and Practice of Obstetric Analgesia and Anesthesia. Davis, Philadelphia, 1967.
- [13] Marques Santos et al. Posicionamento sobre COVID-19 e Gravidez em Mulheres Cardiopatas – Departamento de Cardiologia da Mulher da Sociedade Brasileira de Cardiologia – 2020. *Arquivos Brasileiros de Cardiologia*. 115(5):975-986. <https://doi.org/10.36660/abc.20201063>.
- [14] Zenclussen AC. Adaptive immune responses during pregnancy. *American Journal of Reproductive Immunology*. 2013 Apr; 69(4): 291-303. <https://doi.org/10.1111/aji.12097>.
- [15] Liu H, Wang L, Zhao S, Kwak-Kim J, Mor G, Liao A. Why Are Pregnant Women Susceptible to COVID-19? *An*

Immunological Viewpoint. Journal of Reproductive and Immunology. 2020 Jun; 139:103122. <https://doi.org/10.1016/j.jri.2020.103122>.

[16] Lam CM, Wong SF, Leung TN, et al. A case-controlled study comparing clinical course and outcomes of pregnant and non-pregnant women with severe acute respiratory syndrome. BJOG: An International Journal of Obstetrics and Gynaecology 2004;111 (8):771–774. doi:10.1111/j.1471-0528.2004.00199.x.

[17] Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. American Journal of Obstetrics and Gynecology 2004;191(1): 292–297. <https://doi.org/10.1016/j.ajog.2003.11.019>.

[18] Ellington S, Strid P, Tong VT, 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. Morbidity and Mortality Weekly Report.2020;69(25): 769–775. doi:10.15585/mmwr.mm6925a1.

[19] Martínez-Portilla 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 in Obstetrics and Gynecology. 2021; 57(2): 224- 231. <https://doi.org/10.1002/uog.23575>

[20] Huntley B et al. Taxas de mortalidade materna e perinatal e transmissão vertical em gestações complicadas por síndrome respiratória aguda infecção por Coronavírus 2 (SARS-Co-V-2), Obstetrícia e Ginecologia: 2020 136 (2): 303-312. doi: 10.1097 / AOG.0000000000004010

[21] Sentilhes L et al. Coronavirus disease 2019 in pregnancy was

associated with maternal morbidity and preterm birth. American Journal Of Obstetrics And Gynecology, 2020; 223 (6): 914.1-914.15. <http://dx.doi.org/10.1016/j.ajog.2020.06.022>.

[22] Knight M, Bunch K, Vousden N, et al. UK obstetric surveillance system SARS-CoV-2 infection in pregnancy collaborative group characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. British Medical Journal. 2020;369:m2107

[23] Gonçalves-Júnior J, Cândido EL, Oliveira GF, Rolim-Neto ML. Cardiovascular system and SARS-CoV-2 – etiology, physiopathology and clinical presentation: a systematic review. Fighting the COVID-19 Pandemic. Ed.1: IntechOpen: United Kingdom. P.1-15. 2021. DOI: <http://dx.doi.org/10.5772/intechopen.97076>

[24] Lokken EM et al. Clinical characteristics of 46 pregnant women with a severe acute respiratory syndrome coronavirus 2 infection in Washington State. American Journal Of Obstetrics And Gynecology, 2020; 223 (6): 911.1-911.14. <http://dx.doi.org/10.1016/j.ajog.2020.05.031>.

[25] Yan J et al. Coronavirus disease 2019 in pregnant women: a report based on 116 cases. American Journal Of Obstetrics And Gynecology, [S.L.], 2020; 223 (1): 111.1-111.14. <http://dx.doi.org/10.1016/j.ajog.2020.04.014>.

[26] Castro P et al. Covid-19 and Pregnancy: An Overview. Revista brasileira de ginecologia e obstetrícia. 2020; 42(07): 420-426. <https://doi.org/10.1055/s-0040-1713408>

[27] Mascio D et al. Outcome of coronavirus spectrum infections (SARS, MERS, Covid-19) during pregnancy: a systematic review and meta-analysis. American Journal Of Obstetrics &

Gynecology Mfm, 2020; 2(2): 1-37.  
<http://dx.doi.org/10.1016/j.ajogmf.2020.100107>

[28] Rasmussen SA et al. Coronavirus Disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. American Journal of Obstetrics and Gynecology. 2020; 222(5): 415–426

[29] Chen et al. Clinical Characteristics of Pregnant Women with Covid-19 in Wuhan, China. New England Journal of Medicine. <https://doi.org/10.1056/NEJMc2009226>

[30] Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. Ultrasound in Obstetrics and Gynecology. 2020; 56(1): 15-27. <https://doi.org/10.1002/uog.22088>

[31] Agarwal N, Garg R, Singh S, Agrawal A. Coronavirus disease 2019 in pregnancy: Maternal and perinatal outcome. Journal of Education and Health Promotion. 2021; 10(1): 194. [https://doi.org/10.4103/jehp.jehp\\_954\\_20](https://doi.org/10.4103/jehp.jehp_954_20)

[32] Salem D, Katranji F, Bakdash T. COVID-19 infection in pregnant women: Review of maternal and fetal outcomes. International Journal of Gynecology and Obstetrics. 152(3): 291-298. <https://doi.org/10.1002/ijgo.13533>

[33] Fan S, Yan S, Liu X, Liu P, Lei H, Wang S. Human Coronavirus Infections and Pregnancy. Matern Fetal Med. 2021 Jan; 3(1): 53–65. <https://doi.org/10.1097/FM9.0000000000000071>

[34] Vizheh M et al. Characteristics and outcomes of COVID-19 pneumonia in pregnancy compared with infected nonpregnant women. International Journal of Gynecology and Obstetrics. 153(3): 462-468; 2021. <https://doi.org/10.1002/ijgo.13697>

[35] Prabhu M et al. Pregnancy and postpartum outcomes in a universally tested population for SARS-CoV-2 in New York City: a prospective cohort study. Bjog: An International Journal of Obstetrics & Gynaecology, 2020; 127(12): 1548-1556. <http://dx.doi.org/10.1111/1471-0528.16403>.

[36] Allotey J et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ (Clinical research ed.), 2020; 370, m3320. <https://doi.org/10.1136/bmj.m3320>

[37] Alves NCC et al. Complicações na gestação em mulheres com idade maior ou igual a 35 anos. Revista Gaúcha de Enfermagem, [S.L.], 2018; 38(4): 12-15. <http://dx.doi.org/10.1590/1983-1447.2017.04.2017-0042>.