

Severe Acute Respiratory Syndrome by COVID-19 in pregnant and postpartum women

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Abstract

Objectives: to evaluate the morbidity and mortality profile and factors associated with death due to severe acute respiratory syndrome (SARS) by COVID-19 in pregnant and postpartum women.

Methods: this is a quantitative and retrospective research that analyzed the SIVEP-gripe Database (Influenza Epidemiological Surveillance Information System), from 01/01/2020 to 04/01/2021. All pregnant women and postpartum women diagnosed with SARS caused by COVID-19 in the State of Minas Gerais were included. After the descriptive analysis of the hospitalizations profile, the association between different exposure variables and the occurrence of death was evaluated.

Results: of the 227 records obtained, 94.3% required hospitalization. Among hospitalizations in the Intensive Care Unit, 29.8% used invasive ventilatory support. Fifteen deaths were recorded. The most frequent clinical manifestations were: cough and fever; the predominant comorbidities were cardiovascular disease and diabetes mellitus. The variables “ICU stay”, “use of ventilatory support” and “heart disease” were associated with the occurrence of deaths.

Conclusions: hospitalization was necessary for most pregnant women with SARS and the presence of previous heart disease increased the risk of death. Knowing the SARS morbidity and mortality profile is important in the definition of public health strategies aimed at reducing the impacts of COVID-19 during pregnancy and the puerperium.

Key words COVID-19, Severe acute respiratory syndrome, Pregnancy, Postpartum period, Pregnancy infectious complications



Introduction

The COVID-19 pandemic, caused by the coronavirus of the Severe Acute Respiratory Syndrome 2 (SARS-CoV-2) has already affected 111 million victims in the world and was responsible for over 2.4 million deaths until February 24, 2021. Brazil is at the third rank in number of cases, with more than 10 million people with the disease, and at the second rank in number of deaths, with over 247 thousands.¹ The inexistence of effective therapy aggravates the situation even more.

Among the already known risk groups, we highlight pregnant women, once the physiological alterations of the pregnancy increase the risk of infections. The physiological dyspnea caused by the increase of maternal metabolism, with a higher oxygen consumption, aggravated by gestational anemia, should be properly evaluated in order to not to be confused with pathological dyspnea. Other alterations may also contribute to a worse prognosis, such as altered lung volumes and decrease of immunity mediated by Th1 cells, due to the dominant environment of Th2 cells.² It is worth highlighting that, initially, only high-risk pregnant women were considered at risk group, however, after epidemiological analyses and considering the increase of maternal death ratio in developing countries, all pregnant women were included.³

In Brazil, there is no exclusive system for registering and monitoring cases of COVID-19 in pregnant and puerperal women. Nevertheless, there is a national data system, the Information System of Epidemiological Surveillance of Influenza (SIVEP-Gripe – Portuguese acronym), which includes cases of Severe Acute Respiratory Syndrome (SARS), including those caused by SARS-CoV-2 and which contemplates this population. SRAS in pregnant and puerperal women is considered an aggravation of the clinical status of a patient with COVID-19 and is characterized as an influenza-like illness which meet the following criteria: (1) dyspnea or respiratory distress; (2) persistent chest pressure; (3) O₂ inferior to 95% in room air; (4) facial or lip cyanosis. It is also important to observe the presence of hypotension and oliguria.³

The follow-up of SRAS cases due to COVID-19, in puerperal and pregnant women is necessary once high lethality rates have been reported in these groups.⁴ Therefore, this study evaluated the morbimortality profile and factors associated with death by SRAS in pregnant and puerperal women with COVID-19 in the state of Minas Gerais.

Methods

This is a quantitative and retrospective research, which analyzed the Severe Acute Respiratory Syndrome database from SIVEP-gripe, including data from COVID-19, provided by the Department of Computing of the Unified Health System (DATASUS), regarding the period from January 1, 2020 to January 4, 2021.⁵

Pregnant women in different gestational periods and puerperal women in Minas Gerais were included, with final diagnosis of SRAS caused by COVID-19. Variables were selected, related to sociodemographic factors (age, race/color and schooling), signs and symptoms (fever, cough, sore throat, dyspnea, respiratory distress, O₂ saturation, diarrhea and vomit), presence of comorbidities (chronic cardiovascular disease, chronic hematological disease, asthma, diabetes mellitus, neurological disease, other chronic pneumopathy, immunodeficiency, chronic kidney disease and obesity), characteristics of hospitalization (hospitalization in intensive care unit, need for ventilatory support and clinical evolution) and in regard of radiography alterations (chest X-ray).

The spatial distribution of cases of SRAS by COVID-19 was presented by means of a choropleth map. The analysis of normality of quantitative variables was performed by the Shapiro-wilk test, and the comparison of medians of ages in relation to death, by means of Mann-Whitney test. Chi-squared test or Fisher's exact test, as well as the relative risks and their confidence intervals were used for the analysis of association between the studied qualitative variables and the occurrence of death. Statistical analyses were conducted in IBM SPSS® software, with a common level of significance of 5%.

Once they are secondary data, of public, unrestricted access and without identification of participants, this study is exempted of evaluation by the Research Ethics Committee, according to the resolution CNS n° 510, April 7, 2016.⁶

Results

In Brazil, 10,421 SRAS cases were registered in pregnant and puerperal women, between January 1, 2020 to January 4, 2021, according to SIVEP-gripe, and 4,765 of these had COVID-19 diagnosis. Yet, in the same database, in Minas Gerais, there was a registry of 765 pregnant and puerperal women with SRAS and 227 of these had COVID-19 diagnosis, representing 30% of cases.

Thus, the registries of 210 pregnant women

Table 1

Sociodemographic data of pregnant and puerperal women with SARS caused by COVID-19, in the state of Minas Gerais, from January 1, 2020 to January 4, 2021, n=227.

Variables	N	%
Age (years)		
10 - 19	8	3.52
20 - 34	141	62.12
Over 35	78	34.36
Total	227	100.00
Race/color		
Brown	110	53.1
White	77	37.2
Black	18	8.7
Yellow	2	1.0
Total	207	100.00
Schooling		
Elementary 1° cycle (1 st - 5 th year)	5	5.0
Elementary 2° cycle (6 th - 9 th year)	17	16.8
High School	62	61.4
University	17	16.8
Total	101	100.0
Gestational age		
1 st trimester	27	11.9
2 nd trimester	83	36.6
3 rd trimester	104	45.8
Unknown gestational age	13	5.7
Total	227	100.0

(92.4%) and 17 puerperal women (7.5%), with mean age of 32 ±9 years, with Severe Acute Respiratory Syndrome caused by COVID-19. Most of these declared themselves brown (53.1%) and completed high school (61.4%). In relation to gestational age, 45.8% (n=104) of patients with SARS caused by COVID-19 were in the 3rd trimester of pregnancy (Table 1). The criterion of diagnosis was laboratorial in 219 (96.5%) cases. For six patients, the information on the type of test that was performed was absent, however, these women had COVID-19 as final classification. The most frequent test was Reverse Transcription Polymerase Chain Reaction (RT-PCR), executed in samples of 193 (88.1%) pregnant and puerperal women. One pregnant woman (0.46%) had epidemiological diagnosis criterion, and other one (0.46%) had her diagnosis performed by image

The distribution of cases by epidemiological week is demonstrated in Figure 1, being week 28 the one with the highest number of notifications (n=17). The cities with more COVID-19 case registries in Minas Gerais were Belo Horizonte (26.9%) and

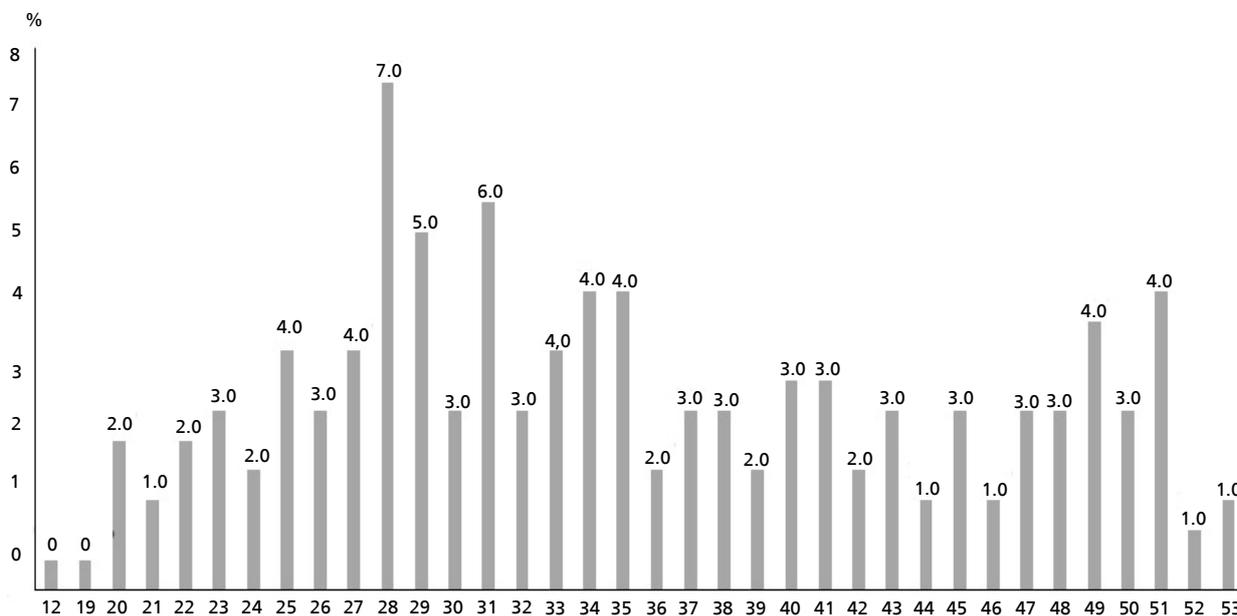
Uberlândia (12.3%) and of deaths, Contagem (20.0%) and Poços de Caldas (20.0%). Deaths occurred in nine distinct municipalities (Figure 2).

In relation to clinical manifestations, there was predominance of fever, cough and dyspnea. The most frequent comorbidities were chronic cardiovascular disease, diabetes mellitus and obesity, followed by asthma. The most frequent radiological alteration was interstitial infiltrate (Table 2). Of the total of patients, 94.3% (n=214) needed hospitalization, being 47 of these in Intensive Care Units (ICU). Invasive ventilatory support was used in 29.8% (n=14) of patients hospitalized in ICU and in nine patients that did not need intensive care, totaling 23 patients. Non-invasive ventilatory support was necessary in 66 pregnant and puerperal women (Table 2).

When evaluating the vaccine coverage against influenza, it was observed that only 63 women were immunized. In relation to the use of antiviral medication, it was observed that 47 received antiviral therapy, 44 (93.6%) with Osetalmivir and one (2.1%), Zanamivir.

Figure 1

Registries of Severe Acute Respiratory Syndrome caused by COVID-19 in the state of Minas Gerais, from January 1, 2020 to January 4, 2021, according to the epidemiological week, n=227.



Fifteen deaths (6.7%) of pregnant and puerperal women were registered. The variables “presence of comorbidities”, “hospitalization in ICU”, “use of ventilatory support” and “cardiopathy” had statistically significant association with the evolution to death ($p < 0.05$) (Table 3). There was no significant differentiation between the medians of age of women that evolved or not to death. Given that between the assessed risk factors, only “cardiopathy” was significantly associated with the occurrence of deaths, multivariate analysis of data was not performed.

Discussion

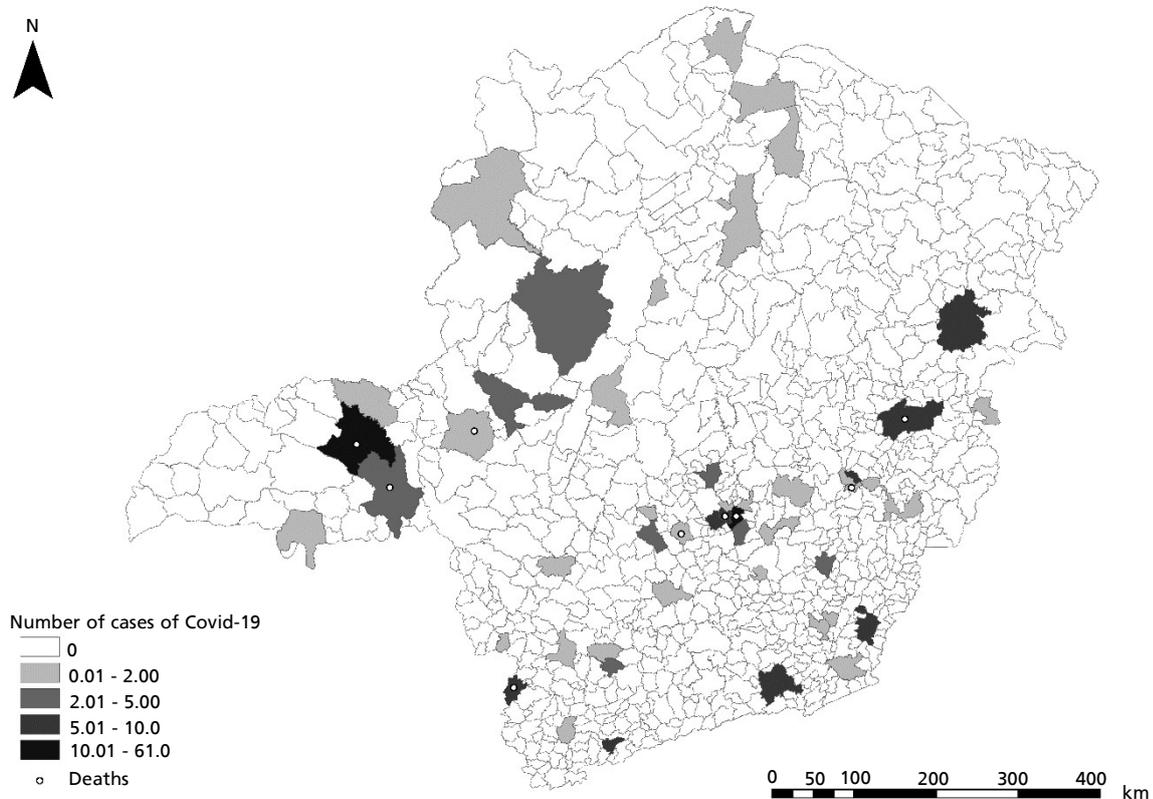
The occurrence of SRAS by COVID-19 in pregnant and puerperal women from the state of Minas Gerais was more common in brown patients, aged from 20 to 34 years, at the 3rd trimester of pregnancy and with comorbidities. COVID-19 was responsible for the death of 6.4% of pregnant and puerperal women with SRAS and the risk of death was more associated with the presence of the comorbidity “cardiopathy”, as well as the use of ventilators and intensive care. However, only cardiopathy may be considered an increased risk factor for death, being the other associated variables considered as indicators of severity of the case.

In this study, characteristics of 227 pregnant and puerperal women with Severe Acute Respiratory Syndrome caused by COVID-19 were assessed in Minas Gerais. After the first registration, at epidemiological week 12, there was an increase of cases with peak at week 28 (n=17), although with a remarkable reduction and stabilization after week 36 (n=4), returning to an increase in weeks 49 (n=9) and 51 (n=10), with progressive reduction in the other weeks. Compared to data from hospitalizations by SRAS in the state, the peak period is accordant, once the period with more registries was between epidemiological weeks 27 and 30.7. These data confirm the findings in other viral outbreaks and endemics, in which the risk of viral pneumonia was significantly higher between pregnant women compared to the general population.^{8,9}

In relation to the distribution of cases per city, the two cities with the highest number of inhabitants of the state, Belo Horizonte and Uberlândia, were responsible for the registry of 39.2% of cases of SRAS by COVID-19 in pregnant and puerperal women. Betim and Contagem, two cities among five with the highest number of inhabitants in the state, and Muriaé were responsible for 13.2% of cases, with 10 registries each. However, Muriaé city is only at the 29th position in the rank of most populous cities in Minas Gerais.¹⁰ In relation to deaths,

Figure 2

Distribution of cases of Severe Acute Respiratory Syndrome caused by COVID-19 in pregnant and puerperal women, in the state of Minas Gerais, by city of occurrence, from January 1, 2020, to January 4, 2021, n=227.



Contagem and Poços de Caldas were responsible for 40% of cases, with three registries each, followed by Governador Valadares and Uberaba, with two registries each. It is worth highlighting that Poços de Caldas is only at the 15th position in that rank.¹⁰ These data suggest that there is no direct relationship between the number of cases and death by SRAG caused by COVID-19 in pregnant and puerperal women with the local population.

The gold-standard test for COVID-19 diagnosis is the RT-PCR and this was the most used test in this population. However, since July 2020, the MH (Ministry of Health) emphasized the need for expansion of RT-PCR tests in priority groups, in which pregnant and puerperal women are embedded.³ Nevertheless, the proportion of individuals tested with RT-PCR is defined according to the capability of collection of each municipality.

The great loss of information in relation to schooling of users may have influenced the result of non-association between schooling and aggravation

of cases of SRAS by COVID-19 in the studied population. However, other studies demonstrated that socio-economic status and low schooling level may accelerate the aggravation of maternal health status, given that these variables influence in self-care and interfere in the quality of prenatal consultation and effectiveness of treatment, thus being directly related to maternal lethality.^{11,12}

Most patients in the study were hospitalized and 23.4% of these needed to be admitted in Intensive Care Units, and even invasive ventilatory support in some cases. In 2009, during H1N1 pandemics, 12% to 25% of hospitalized pregnant women needed hospitalization in ICUs and 6% to 19% used mechanical ventilation.^{13,14}

In relation to clinical manifestations, the most frequent in this study were cough (76.1%), fever (63.9%) and dyspnea (58.4%), corroborating with a previous study, which observed that pregnant women with COVID-19 are less prone to have fever compared to non-pregnant women, although in

Table 2

Clinical data from pregnant and puerperal women with SRAS caused by COVID-19 in the state of Minas Gerais, between January 1, 2020 to January 4, 2021.

Clinical manifestations	N	%
Cough (n= 222)	169	76.1
Fever (n= 219)	140	63.9
Dyspnea (n= 219)	128	58.4
Respiratory distress (n= 212)	98	46.2
O ₂ saturation< 95% (n= 213)	68	31.9
Sore throat (n= 214)	53	24.8
Loss of smell (n=147)	29	19.7
Loss of taste (n= 146)	26	17.8
Diarrhea (n= 211)	34	16.1
Vomit (n= 211)	32	15.2
Comorbidities		
Chronic cardiovascular disease (n= 137)	24	17.5
Diabetes mellitus (n= 137)	22	16.1
Obesity (n= 135)	19	14.1
Asthma (n= 135)	15	11.1
Immunodeficiency (n= 135)	5	3.7
Chronic kidney disease (n= 134)	4	3.0
Chronic hematologic disease (n=135)	3	2.2
Other chronic lung disease (n= 132)	2	1.5
Chronic neurological disease (n= 135)	1	0.7
Characteristics of hospitalization(n= 201)		
Hospitalization in ICU	47	23.4
Use of ventilatory support (n= 89)		
Non-invasive	66	74.2
Invasive	23	25.8
Radiological alterations (n= 39)		
Interstitial infiltrate	17	43.6
Others	8	20.5
Consolidation	4	10.3
Mixed	1	2.6

ICU= Intensive Care Units.

reproductive age, with COVID-19.¹⁵ The comorbidities that stood out were chronic cardiovascular disease (17.5%), diabetes mellitus (16.1%) and obesity (14.1%), whilst in radiological alterations, interstitial infiltrate (43.6%) was more frequent. A French study that assessed 33 maternity hospitals between March 1 and April 14, 2020, revealed that the most severe COVID-19 cases were related to maternal ages over 35 years old and presence of comorbidities.¹⁶

Regarding gestational age, 45.8% of pregnant women were at the third trimester, although the entirety of effects of SARS-CoV-2 infection to pregnant women and their fetuses is still unknown. Some infections such as influenza, malaria, hepatitis and herpes simplex may be more severe when occur at

more advanced gestational ages.¹⁷ Nevertheless, there are reports of cases in which hospitalization occurred with hospital discharge and gestational course without interurrences or unknown course, as well as reports of gestational loss after such infection at the first gestational trimester and beginning of second trimester.¹⁸

At the time of assessment of influenza vaccine coverage of these women, it was noticed that only 63 (50.8%) users were immunized. The vaccine against H1N1 was offered initially for pregnant women in 2010.¹⁹ Although, due to the COVID-19 pandemic and in order to support the differential diagnosis of other respiratory infections, the pregnant women were encouraged to receive the immunization earlier.²⁰ A study demonstrated that pregnant women

Table 3

Analysis of association of variables of patients with SRAS caused by COVID-19 in the state of Minas Gerais, between January 1, 2020 to January 4, 2021, n=227.

Variables	Recovered		Deaths		RR (CI95%)	p
	n	%	n	%		
Comorbidities					3.40 (0.78-14.70)	0.09
No	76	97.4	2	2.6		
Yes	136	91.3	13	8.7		
Cardiopathy*					3.07 (1.06-8.90)	0.05
No	192	94.6	11	5.4		
Yes	20	83.3	4	16.7		
Asthma*					2.17 (0.53-8.76)	0.22
No	199	93.9	13	6.1		
Yes	13	86.7	2	13.3		
Diabetes					2.32 (0.71-7.62)	0.16
No	193	94.1	12	5.9		
Yes	19	86.4	3	13.6		
O ₂ Saturation<95% *					2.04 (0.77-5.41)	0.14
No	151	95.0	8	5.0		
Yes	61	89.7	7	10.3		
Dyspnea*					2.12 (0.69-6.47)	0.19
No	95	96.0	4	4.0		
Yes	117	91.4	11	8.6		
Use of ventilator					3.10 (1.09-8.77)	0.02
No	133	96.4	5	3.6		
Yes	79	88.8	10	11.2		
ICU*					15.31 (4.50-52.08)	<0.001
No	177	98.3	3	1.7		
Yes	35	74.5	12	25.5		
Gestational age						
Others*	189	94.5	11	5.5		
1 st trimester	23	85.2	4	14.8	2.69 (0.92-7.86)	0.08
Others	134	93.1	10	6.9		
2 nd Trimester	78	94.0	5	6.0	0.86 (0.30-2.45)	0.78
Others	113	91.9	10	8.1		
3 rd trimester	99	95.2	5	4.8	0.59 (0.20-1.67)	0.31

* Variables in which the Fisher's statistical test was applied.

that were immunized against Influenza A had a mean reduction of 40% of the risk of hospitalization by influenza, besides offering secondary protection for babies during the first months of life.²¹ In Minas Gerais, in the year 2020, 29,504 puerperal women and 153,764 pregnant women were immunized, with an estimated coverage of 101.8% of this population in the state.²²

In relation to antiviral therapy, it was observed that 47 (24.1%) users have used these medications, with highlight for Oseltamivir (93.6%). The MH recommends that pregnant and puerperal women

with influenza-like syndrome and at risk for COVID-19, even if immunized, be treated with Oseltamivir in the usual dose in order to reduce maternal morbimortality.²³ According to Centers for Disease Control and Prevention (CDC), the antiviral therapy started early has more probability of benefits to users.²⁴ It is worth highlighting that Oseltamivir and other antiviral used by the study population, although with less frequency, Zanamivir, is approved by the Brazilian Health Regulatory Agency (ANVISA – Portuguese acronym) for chemoprophylaxis of influenza.²³

Regarding lethality, 6.6% of pregnant and puerperal women with SRAS by COVID-19 in the analyzed period died. During H1N1 pandemic in 2009, lethality rate was between 1% and 4.3%,^{13,14} and more unfavorable outcomes may be explained partially by the changes of respiratory and immunological physio-modulation during pregnancy.²⁵ The greater risk of death was associated with the time of hospitalization in an intensive care unit. In this perspective, a study in New York City (USA) demonstrated that maternal lethality was 15% and the mean of days of ICU stay due to COVID-19 was of eight days.²⁶ In this study, the mean of days of ICU stay was six days, with considerable hospital lethality (25%).

In this study, we also confirmed that pregnant women with cardiopathies presented 3.07 times more risk of death compared to pregnant women without cardiopathy. These data comply with other studies in which pregnant women with heart disease presented greater risk of severe cardiologic complications.^{27,28}

Even during pandemic, studies about the impacts of COVID-19 infection in the clinical presentation and perinatal and/or puerperal outcomes are still being developed. However, data are still limited and inconclusive in regard of the risk of increase of severe forms of COVID-19 associated with pregnancy. Nevertheless, due to physiological alterations of gestational and puerperal period, these women may be seriously affected by infections. Therefore, it is important to adopt measures of caution against COVID-19 and the systematic follow-up of pregnant women, yet this follow-up occurs in non-presential attendance, mainly those whose profile is similar to the high risk one described in this study.^{16,29,30} The morbimortality profile of SRAS by COVID-19 in pregnant and puerperal women, in Minas Gerais, obtained in this study, may support the definition of

public health policies aiming the study population. Besides that, the results shown may contribute to the development of new studies that assess the direct impact of this infection in pregnancy and puerperium. It is still worth to highlight that this study has limitations, once it comprises only the Severe Acute Respiratory Syndrome Database and it may exist subnotification due to the strategies of testing in the state. Furthermore, the possibility of errors in data registry cannot be excluded, and those ignored were treated as negative. However, we believe that these limitations did not impaired the validation of obtained results, once they were not frequent in the assessed database and, during the pandemic, SIVEP-gripe is the main source of data in the country.

Thus, we conclude that hospitalization was necessary to most pregnant women with SRAS and the presence of previous heart diseases increased the risk of death. Thus, the attendance to pregnant and puerperal women with SRAS by COVID-19 should be prioritized mainly in cases in which patients have comorbidities. Furthermore, early diagnosis and monitoring may aid in the reduction of severity of cases, diminishing the necessity and time of hospitalization in ICU, and, consequently, reducing the risk of death.

Author's contribution

Nogueira AP, Bernardes GCS, Almeida NA, Nogueira LS and Pinheiro MB participated in the conceptualization, data curation, formal analysis, investigation, writing of the original draft and writing of the review/edition of the manuscript. Melo SN and Belo VS participated in the formal analysis, methodology, software and writing of the review/edition of the manuscript. All authors approved the final version of the article.

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- envolvam a utilização de dados diretamente obtidos com os participantes ou de informações identificáveis ou que possam acarretar riscos maiores do que os existentes na vida cotidiana. Brasília2016).
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