Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020

Lisiane F. Leal a,*, Joanna Merckx a, Deshayne B. Fell b, Ricardo Kuchenbecker c, Angelica E. Miranda d, Wanderson K. de Oliveira e, Robert William Platt f, Lívia Antunes g, Mariângela F. Silveira h, Natália Bordin Barbieri i

a Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada
b School of Epidemiology and Public Health, University of Ottawa, Ottawa, Canada
c Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil
d Departamento de Medicina Social, Universidade Federal do Espírito Santo, Vitória, RS, Brazil
e Ministry of Defense, Armed Forces Hospital, Technical Directorate of Education and Research, Brasília, DF, Brazil
f Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal, Canada
g Instituto Brasileiro de Desenvolvimento e Sustentabilidade (IBS), Brasília, DF, Brazil
h Programa de Pós-graduação em Epidemiologia, Faculdade de Medicina, Universidade Federal de Pelotas, Pelotas, RS, Brazil
i United Nations Development Programme Brazil, UNDP Brazil, Brazil

ABSTRACT

Background: Knowledge about COVID-19 in pregnancy is limited, and evidence on the impact of the infection during pregnancy and postpartum is still emerging.

Aim: To analyze maternal morbidity and mortality due to severe acute respiratory infections (SARI), including COVID-19, in Brazil.

Methods: National surveillance data from the SIVEP-Gripe (Sistema de Informação de Vigilância Epidemiológica do Gripe) was used to describe currently and recently pregnant women aged 10−49 years hospitalized for SARI from January through November, 2020. SARI cases were grouped into: COVID-19; influenza or other detected agent SARI; and SARI of unknown etiology. Characteristics, symptoms and outcomes were presented by SARI type and region. Binomial proportion and 95% confidence intervals (95% CI) for outcomes were obtained using the Clopper-Pearson method.

Results: Of 945,460 SARI cases in the SIVEP-Gripe, we selected 11,074 women aged 10−49 who were pregnant (7964) or recently pregnant (3110). COVID-19 was confirmed in 49.4% cases; 1.7% had influenza or another etiological agent; and 48.9% had SARI of unknown etiology. The pardô race/ethnic group accounted for 50% of SARI cases. Hypertension/Other cardiovascular diseases, chronic respiratory diseases, diabetes, and obesity were the most common comorbidities. Mortality was associated with COVID-19, influenza, and other etiological agents, and was more frequent in the pardô race/ethnic group. SARI cases were also associated with respiratory failure and death in the hospital. The estimated maternal mortality rate for SARI was 0.02 per 100,000 live births.

Keywords: Pregnancy, Maternal mortality, Severe acute respiratory infections, SARS-CoV-2, Brazil, SIVEP-Gripe

* Corresponding author at: 1020 Pine Avenue West, Montreal, QC H3A 1A2, Canada.
E-mail address: Lisiane.freitasleal@mail.mcgill.ca (L.F. Leal).
https://doi.org/10.1016/j.bjid.2021.101620
1413-8670/© 2021 Sociedade Brasileira de Infectologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Please cite this article as: L.F. Leal et al., Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020, Brazilian Journal of Infectious Diseases (2021), https://doi.org/10.1016/j.bjid.2021.101620
common comorbidities. A total of 362 women with COVID-19 (6.6%; 95%CI 6.0–7.3) died. Mortality was 4.7% (2.2–8.8) among influenza patients, and 3.3% (2.9–3.8) among those with SARI of unknown etiology. The South-East, Northeast and North regions recorded the highest frequencies of mortality among COVID-19 patients. Conclusion: Mortality among pregnant and recently pregnant women with SARIs was elevated among those with COVID-19, particularly in regions where maternal mortality is already high.

© 2021 Sociedade Brasileira de Infectologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Introduction

By November 23, 2020, Brazil had more than six million confirmed cases of COVID-19 and 176,000 associated deaths. These numbers are likely underestimates. According to the Epicovid19-BR, a national serological household population-based survey, for each confirmed diagnosis, there are approximately six additional unreported cases, and for every 100 hundred infected, one dies. In addition, ethnic and regional disparities in rates of infection have been documented in Brazil. Evidence about the impact of COVID-19 during pregnancy and postpartum is still emerging. Early case series studies from China suggested that pregnant women were not at increased risk of severe disease. However, as the pandemic spread globally, evidence of increased clinical severity, including mortality, among pregnant women emerged in some high-income countries. Knowledge about the impact of COVID-19 during pregnancy in low- and middle-income countries (LMIC) is limited. A recent study of 978 pregnant and postpartum Brazilian women with COVID-19 reported 124 deaths (case fatality rate of 12.7%) by June 18, 2020. Risk factors for mortality among these cases, included obesity, diabetes, cardiovascular diseases, and postpartum period. However, no information has been reported on maternal morbidity and mortality from other/unknown severe acute respiratory illnesses (SARIs) during the same period, even though SARIs with unknown etiology have increased in Brazil since the beginning of the pandemic, and may actually reflect undiagnosed COVID-19. Understanding the treatment and clinical outcomes of pregnant and recently pregnant women with COVID-19 and other SARIs is needed to inform public health decision-making.

This manuscript analyzes maternal morbidity and mortality due to SARIs, including COVID-19, in Brazil, using data from the SIVEP-Gripe (Sistema de Informação de Vigilância Epidemiológica da Gripe) for January to November 2020.

Methods

Data source

The development of Brazilian reporting systems for surveillance of the COVID-19 pandemic has been described elsewhere. Briefly, in January 2020, the Ministry of Health implemented a REDCap platform to prospectively report suspected, probable and confirmed COVID-19 cases. By March, the REDCap system had been discontinued and mild COVID-19 cases began to be reported on e-SUS Vigilância Epidemiológica (e-SUS-VE), a new national COVID-19 reporting system. Meanwhile, hospitalized COVID-19 cases were recorded on the SIVEP-Gripe, which had been created in 2002 and used for surveillance of circulating viruses. In 2009, this system incorporated SARI notification for all hospitals, and has since been used to report SARIs in the Brazilian population. Both e-SUS-VE and SIVEP-Gripe include suspected and confirmed COVID-19 cases as reported by public and private health services. The two systems are inter-related on the Brazilian Ministry of Health “Portal do COVID-19” website (https://covid.saude.gov.br/), which summarizes daily aggregated counts from both platforms.

All SARI-related hospital admissions and deaths are captured in the SIVEP-Gripe, and notifications are mandatory. The SIVEP-Gripe records variables, such as notification date, onset of symptoms, hospitalization, collection of clinical specimens, detection, release of laboratory results, and case resolution (Supplementary Table S1). Access to de-identified and unduplicated data is publicly available (https://opendata.sus.saude.gov.br/dataset/bd-srag-2020).

Study design and population

This population-based case series study used surveillance data from the SIVEP-Gripe. We included all cases of currently and recently pregnant women aged 10–49 years, who were hospitalized because of SARIs (including COVID-19) between January 1 and November 23, 2020. Currently pregnant women were identified as those with a recorded gestational age, who were not simultaneously recorded as postpartum nor had had an abortion. Recently pregnant women comprised those in the postpartum or post-abortion period. Those for whom final classification of the case (final diagnosis by type of SARI) was missing were excluded.

Measures

SIVEP-Gripe classifies SARI cases as being due to influenza, other respiratory virus, other etiological agents, COVID-19, or with unknown etiology. We regrouped SARI cases into three categories:
COVID-19, defined as SARS-CoV-2 infection confirmed by laboratory testing (molecular diagnostics with real-time quantitative PCR or serology), clinical/epidemiological, clinical or clinical-imaging criteria;

- Influenza or other detected agent SARI, defined by laboratory-confirmed respiratory virus or other etiological agent; and

- SARI with unknown etiology, defined by clinically-confirmed influenza-like illnesses or SARI with no etiologic agent identified.

Maternal age was computed by the SIVEP-Gripe as the interval between the woman’s date of birth and date of the first symptoms, and was categorized as: 10−19, 20−29, 30−39, and 40−49 years.

Race/ethnicity was recorded according to the patient’s declaration. The official Brazilian classification recognizes five groups: branco (White), pardo (those who declare themselves as such or as mulatto, caboclo, caafuza, mameluca or mestizo), preto (Black), amarelo (East Asian), and indígena (Indigenous).

Education was the highest grade/year the patient declared, and was grouped into five categories: no education; elementary; high school; higher education; and missing or unknown.

Results are presented by region of residence and federation unit (state level). The regional division of Brazil consists of states (26 states and the Federal District) and municipalities grouped into five regions (North, Northeast, Southeast, South, and Central West).

We adapted the World Health Organization list of signs and symptoms and comorbidities available in the COVID-19 Data Platform for monitoring pregnancies.13

Hypertension (pre-existing or onset during pregnancy) is grouped with other cardiovascular diseases. Diabetes is a composite variable including pre-existing and gestational diabetes.

Outcomes (admission to intensive care unit [ICU], ventilatory support, and death) are presented by SARI type and region of residence.

The supplemental material contains additional details for coding of study variables (Supplementary Table S2).

Statistical analysis

We used descriptive statistics to summarize the characteristics of the study population. Categorical variables are summarized as counts and percentages; continuous variables are expressed as medians with inter-quartile ranges. Binomial proportion and 95% confidence intervals (95% CI) for outcomes were obtained using the Clopper-Pearson method.

Analyses were performed with SAS software, version 9.4 (SAS Institute, Inc., Cary, North Carolina). We used ArcGIS, version 10.6, (Environmental Systems Research Institute, Redlands, WA, USA) to plot the number of cases and deaths by region of residence. To construct maps, we used the Natural Breaks (Jenks) method for defining ranges and consolidation of classes.

Ethical statement

This study used only non-identifiable publicly available data; therefore, no ethical approval was necessary.

Results

Among 945,460 cases of SARI hospitalized between January 1 and November 23, 2020, 11,074 (1.2%) were pregnant or recently pregnant women and constituted the study population. Of these 11,074 women, 71.9% were currently pregnant (including those with trimester missing information), and 28.1% were recently pregnant.

Close to half (49.4%) were confirmed COVID-19 cases, and 48.9% had SARI of unknown etiology; the remaining 1.7% had confirmed influenza or another etiological agent.

Fig. 1 presents the flow diagram for identifying the study population.

Forty-four percent of these women were aged 20−29, and 37% were aged 30−39 (Table 1). Almost half (45.9%) reported pardo race/ethnicity, although about 20% of records were missing information on ethnic origin.

Overall, hypertension or other cardiovascular diseases, chronic respiratory diseases, diabetes, and obesity were the most common comorbidities in this population (9.9%, 6.9%, 6.5%, and 4.1%, respectively). Among those with COVID-19, hypertension/other cardiovascular disease and diabetes were the leading comorbidities (10.3% and 7.7%, respectively).

Asthma/other lung diseases was the most common comorbidity among those with influenza-associated SARI (7.5%) and among those with SARI of unknown etiology (9.5%).

Four in ten (40.4%) women in the study population were in their third trimester, and 28.1% were in the postpartum or post-abortion period. Recorded abortions accounted for 0.7% of recently pregnant patients.

Based on absolute case counts, the highest burden of disease was in the Southeast region with 39.0% of the total number of SARI cases, followed by the Northeast (29.0%), Central-West (11.0%, North (10.5%), and South (10.5%). The Southeast and Northeast regions reported the highest percentages of COVID-19 cases (33.9% and 30.5%, respectively).

A large majority (93.4%) of the SARI cases were recorded as symptomatic; 1.3% had no symptoms; and 4.8% had missing information for all variables related to symptoms. Cough was the most frequently recorded symptom (64.8%), regardless of SARI type (Table 2). Compared with the other groups, those with COVID were more likely to have loss of smell or taste, headache, diarrhea, fatigue/malaise, and muscle aches. Fever, cough, sore throat, and oxygen saturation <95% were relatively more frequent among those with SARI with influenza or another etiological agent.

Maternal outcomes by SARI type are described in Table 3. ICU admission was more frequent in women with COVID-19 (19.5%, 95%CI: 18.4−20.5) than among those with SARI of unknown etiology (16.8%, 95%CI: 15.8−17.8) or influenza (15.8%, 95%CI: 10.9−21.8). For those admitted to ICU, the length of stay for COVID-19 cases was longer (median of 6...
days) than that for women with other SARIs. Most women (56.7%) did not receive invasive ventilatory support. A total of 362 deaths (6.6%; 95%CI: 6.0–7.3) were documented among women diagnosed with COVID-19. Mortality was 4.7% (95%CI: 2.2–8.8) among women with influenza, and 3.3% (95%CI: 2.9–3.8) among those with SARI of unknown etiology. Survival status was missing or unknown for 13%.

Table 4 compares the characteristics of women with COVID-19 who died with the characteristics of survivors. Higher percentages of those who died were aged 30-39 (49.7%; 180/362) and self-identified as pardo (53.6%). Hypertension/other cardiovascular diseases, diabetes, and obesity were more common among those who died than among survivors (19.1% versus 9.6%, 16.3% versus 7.4%, and 12.1% versus 4.4%, respectively). Most of the women who died were in the postpartum period (48.3%) or third trimester (29.0%); no information was available about the stage of pregnancy at which they had been infected. Admission to ICU, invasive ventilation, and longer length of ICU stay were also more frequent among those who died.

Differences in characteristics were also observed between survivors and non-survivors for other SARIs (Supplementary Tables S3 and S4).

Fig. 2 depicts the number of cases and deaths by type of SARI for each of the 27 Brazilian states. Low numbers of cases and deaths were observed for influenza-associated SARI. The absolute numbers of cases of COVID-19 and SARI with unknown etiology were similar, but their geographical distributions differed sharply. The North, Northeast and Central-West regions had higher frequencies of COVID-19 cases and deaths, particularly the Northeast and Southeast states. The supplementary material (Supplementary Tables S5-S7) shows the distribution by region and states for survivors and non-survivors for all SARI types.

Discussion

Using data from a national surveillance system in Brazil, we described the characteristics of pregnant and recently pregnant women with SARIs from January 2020 to November 2020, with special attention to COVID-19, which was confirmed in 50% of the study population. Our inclusion of comparable analyses of the characteristics, outcomes and geographical distribution of pregnancies of SARIs with influenza and those with SARIs of unknown etiology, is an approach, that to our knowledge, has not been previously applied to this population. Mortality among those with COVID-19 was elevated, compared with the other SARI groups. A total of 362 deaths were...
recorded among COVID-19 cases. To put this figure in context, 371 maternal SARI deaths were recorded during the 2009-2010 A/H1N1 influenza pandemic, 227 of which were attributed to A/H1N1. COVID-19 mortality in pregnancies is higher in Brazil than estimates from other countries for the same period.6

Table 1 - Characteristics of pregnant and recently pregnant women with SARI infections who were admitted or died, SIVEP-Gripe, Brazil, January-November 2020 (n = 11,074).

| Characteristics                                      | SARI with influenza or other etiological agents (n = 190) | SARI cases with unknown etiology (n = 5415) | COVID-19 cases (n = 5469) |
|------------------------------------------------------|----------------------------------------------------------|-------------------------------------------|-------------------------|
|                                                      | n             | %              | n             | %              | n             | %              |
| Age (years), median (IQR)                            | 27            | 21.32          | 27            | 22.33          | 29            | 24.34          |
| Age group (years)                                    |               |                |               |                |               |                |
| 10 to 19                                             | 33            | 17.4           | 836           | 15.4           | 534           | 9.8            |
| 20 to 29                                             | 82            | 43.2           | 2,494         | 46.1           | 2,267         | 41.4           |
| 30 to 39                                             | 70            | 36.8           | 1,766         | 32.6           | 2,264         | 41.4           |
| 40 to 49                                             | 5             | 2.6            | 319           | 5.9            | 404           | 7.4            |
| Race/ethnicity (self-reported)                       |               |                |               |                |               |                |
| White                                                | 75            | 39.5           | 1,597         | 29.5           | 1,404         | 25.7           |
| Black                                                | 12            | 6.3            | 401           | 7.4            | 281           | 5.1            |
| East Asian                                           | 2             | 1.0            | 40            | 0.7            | 46            | 0.8            |
| Pardo                                                | 78            | 41.0           | 2,374         | 43.8           | 2,633         | 48.1           |
| Indigenous                                           | 0             | 0              | 30            | 0.6            | 80            | 1.5            |
| Missing/unknown                                      | 23            | 12.1           | 973           | 18.0           | 1,025         | 18.7           |
| Education level                                      |               |                |               |                |               |                |
| No education                                         | 1             | 0.5            | 23            | 0.4            | 17            | 0.3            |
| Elementary school                                    | 38            | 20.0           | 865           | 16.0           | 704           | 12.9           |
| High school                                          | 56            | 29.5           | 1,229         | 22.7           | 1,316         | 24.1           |
| Higher education                                     | 22            | 11.6           | 314           | 5.8            | 409           | 7.5            |
| Missing/unknown                                      | 73            | 38.4           | 2,984         | 55.1           | 3,023         | 55.3           |
| Comorbidities                                        |               |                |               |                |               |                |
| Hypertension/other cardiovascular disease            | 14            | 7.4            | 522           | 9.6            | 562           | 10.3           |
| Diabetes                                             | 8             | 4.2            | 292           | 5.4            | 421           | 7.7            |
| Asthma/other chronic lung diseases                   | 14            | 7.4            | 513           | 9.5            | 241           | 4.4            |
| Obesity                                              | 7             | 3.7            | 185           | 3.4            | 264           | 4.8            |
| Immunosuppression/HIV                                | 3             | 1.6            | 114           | 2.1            | 69            | 1.3            |
| Chronic hematological diseases or anemia             | 1             | 0.5            | 77            | 1.4            | 56            | 1.0            |
| Neurological disease or depression                   | 3             | 1.6            | 58            | 1.1            | 47            | 0.9            |
| Chronic renal disease                                | 0             | 0              | 47            | 0.9            | 46            | 0.8            |
| Chronic liver disease or hepatitis                   | 0             | 0              | 29            | 0.5            | 17            | 0.3            |
| Tuberculosis                                         | 0             | 0              | 10            | 0.2            | 2             | 0.04           |
| Other comorbidities                                  | 12            | 6.3            | 274           | 5.1            | 238           | 4.3            |
| Smoking (former or current)                          | 5             | 2.6            | 79            | 1.5            | 19            | 0.3            |
| Gestational age                                      |               |                |               |                |               |                |
| First trimester                                      | 16            | 8.4            | 531           | 9.8            | 378           | 6.9            |
| Second trimester                                     | 48            | 25.3           | 1,102         | 20.3           | 985           | 18.0           |
| Third trimester                                      | 86            | 46.3           | 1,914         | 35.3           | 2,475         | 45.3           |
| Trimester ignored                                    | 9             | 4.7            | 182           | 3.4            | 238           | 4.3            |
| Postpartum or post-abortion                          | 31            | 16.3           | 1,686         | 31.1           | 1,393         | 25.5           |
| Imaging (X-ray or CT)                                |               |                |               |                |               |                |
| Not performed                                        | 69            | 36.3           | 2,078         | 38.4           | 2,039         | 37.3           |
| Performed                                            | 64            | 33.7           | 1,519         | 28.0           | 1,596         | 29.2           |
| Missing/unknown                                      | 57            | 30.0           | 1,818         | 33.6           | 1,834         | 33.5           |
| Region of residence*                                 |               |                |               |                |               |                |
| Southeast                                            | 58            | 30.5           | 2,412         | 44.5           | 1,852         | 33.9           |
| Northeast                                            | 56            | 29.5           | 1,487         | 27.5           | 1,668         | 30.5           |
| Central-West                                         | 26            | 13.7           | 487           | 9.0            | 701           | 12.8           |
| North                                                | 12            | 6.3            | 360           | 6.6            | 792           | 14.5           |
| South                                                | 38            | 20.0           | 669           | 12.3           | 454           | 8.3            |

* Two missings on region not computed here.

To develop and target public health interventions, it is important to understand why the pandemic is affecting this segment of Brazil’s population. Despite substantial improvements, maternal health remains a major concern in LMICs. Morbidity and mortality due to non-communicable and infectious diseases affecting pregnancies are far higher in LMICs...
than in more affluent countries. Thus, when a pandemic reaches a population already at high risk, the health consequences tend to be greater.

A systematic review has synthesized characteristics of and outcomes for pregnant women affected by COVID-19. Brazilian authorities are adopting international recommendations, but these guidelines may not reflect the unique characteristics, social context, and health care reality of Brazil. Our study, by contrast, used data from the national surveillance system to focus on pregnant and recently pregnant Brazilian women affected by SARIs.

Age and underlying conditions (notably, chronic hypertension and pre-existing diabetes) have been identified as risk factors for severe COVID-19 in pregnant women. We observed elevated mortality among those with COVID-19 aged 30-39 or who had hypertension/other cardiovascular diseases or diabetes, when compared with their counterparts with other SARIs. However, it was not possible to determine if these conditions were pre-existing or pregnancy-related.

Obesity, another risk factor for unfavorable COVID-19 outcomes, has an estimated prevalence of 18.6% in Brazilian women aged 20-49. The prevalence of obesity in our study population was only 5%, but obesity was the third most frequent comorbidity among women with COVID-19 who died. Because of natural changes in weight associated with pregnancy, this relationship needs to be more carefully quantified.

For cases of SARIs with influenza or other etiological agents, the most common age range for deaths was 20-29, not 30 or older. Also, deaths in this group occurred more frequently among those with asthma or other chronic lung diseases rather than cardiovascular diseases or obesity.

A previous study of mortality among COVID-19 patients, also based on SIVEP-Gripe data, revealed disparities by ethnic/racial group. We found similar patterns when the analysis was confined to pregnant and recently pregnant women. In our study, pardos, who are concentrated in specific regions, accounted for the largest percentage of infections and deaths. Inequities related to race/ethnicity are well known in Brazil. Whereas 15% of white people live below the poverty line, this is the case for almost 33% of blacks or pardos, which may partially explain their lack of access to the health care. Menezes et al. hypothesized that increased morbidity and mortality are related to lack of access and delays in seeking care. This needs to be considered in evaluations of health care access, particularly access to prenatal care.

Since the 2009 A/H1N1 pandemic, the SIVEP-Gripe has monitored outbreaks in Brazil. However, the data have limitations, including substantial underreporting and poor quality in recording variables such as education, race/ethnicity, and comorbidities. Multiple issues indeed apply with the current system in place for monitoring pregnancies for which no data are recorded. These shortcomings hinder timely reporting and analyses of infectious disease outbreaks, information that is essential for informed policymaking.

Unlike other countries, Brazil does not have registries or surveillance systems designed to include pregnant and recently pregnant women. In recent months, initiatives have

### Table 2 - Signs and symptoms of pregnant and recently pregnant women with SARI infections who were admitted or died, SIVEP-Gripe, Brazil, January-November 2020 (n = 11,074).

| Signs and symptoms         | SARI with influenza or other etiological agents (n = 190) | SARI cases with unknown etiology (n = 5415) | COVID-19 cases (n = 5469) |
|----------------------------|----------------------------------------------------------|--------------------------------------------|--------------------------|
| Symptomatic cases, n (%)   |                                                          |                                            |                          |
| Fever                      | 134 (70.5)                                               | 2,727 (50.4)                               | 3,107 (56.8)             |
| Cough                      | 162 (85.3)                                               | 3,466 (64.0)                               | 3,550 (64.9)             |
| Sore throat                | 80 (42.1)                                                | 1,122 (20.7)                               | 1,180 (21.6)             |
| Shortness of breath       | 113 (59.5)                                               | 2,541 (46.9)                               | 2,593 (47.4)             |
| Oxygen saturation < 95%   | 61 (32.1)                                                | 1,281 (23.7)                               | 1,351 (24.7)             |
| Vomiting or nausea        | 22 (11.6)                                                | 637 (11.8)                                 | 557 (10.2)               |
| Runny nose or nasal congestion | 20 (10.5)                                           | 567 (10.5)                                 | 566 (10.3)               |
| Headache                  | 22 (11.6)                                                | 592 (10.9)                                 | 828 (15.1)               |
| Muscle aches              | 18 (9.5)                                                 | 384 (7.1)                                  | 731 (13.4)               |
| Diarrhea                  | 13 (6.8)                                                 | 473 (8.7)                                  | 545 (10.0)               |
| Fatigue/malaise           | 12 (6.3)                                                 | 352 (6.5)                                  | 503 (9.2)                |
| Loss of smell             | 2 (1.0)                                                  | 214 (3.9)                                  | 850 (15.5)               |
| Loss of taste             | 3 (1.6)                                                  | 156 (2.9)                                  | 565 (10.3)               |
| Chest pain                | 3 (1.6)                                                  | 104 (1.9)                                  | 107 (2.0)                |
| Abdominal pain            | 6 (3.2)                                                  | 189 (3.5)                                  | 181 (3.3)                |
| Joint pain (arthralgia)    | 0 (0)                                                    | 18 (0.3)                                   | 18 (0.3)                 |
| Conjunctivitis            | 0 (0)                                                    | 6 (0.1)                                    | 1 (0.02)                 |
| Skin rash or skin ulcers  | 0 (0)                                                    | 9 (0.2)                                    | 8 (0.1)                  |
| Bleeding (hemorrhage)     | 0 (0)                                                    | 6 (0.1)                                    | 12 (0.2)                 |
| Lymphadenopathy           | 0 (0)                                                    | 2 (0.04)                                   | 2 (0.04)                 |
| Other symptoms            | 15 (7.9)                                                 | 366 (6.8)                                  | 337 (6.2)                |

Please cite this article as: L.F. Leal et al., Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020, Brazilian Journal of Infectious Diseases (2021), https://doi.org/10.1016/j.bjid.2021.101620
been implemented to monitor health outcomes in women affected by COVID-19 around the world, some of them in Latin America. The United Kingdom Obstetric Surveillance System, which aims to describe the epidemiology of a variety of uncommon disorders of pregnancy, now monitors outcomes in women with COVID-19. The United States Centers for Disease Control and Prevention has adapted the Surveillance for Emerging Threats to Mothers and Babies Network to monitor those affected by COVID-19 and releases weekly reports. A European project, “Covid-19 infectION and mediciNes in preGNaNcy” aims to provide guidance to regulators in the management of COVID-19-positive pregnant women. Networks and initiatives like COVI-preg (International COVID-19 and Pregnancy Registry) have been established to determine best practices worldwide.

The results of this study should be considered in the context of several limitations. First, we present only data from the SIVEP-Gripe, which collects information on hospitalized cases. This yielded a more severely ill study population, and likely generated a higher case fatality rate than would data that included a broader range of clinical severities. The SIVEP-Gripe is not linked with Brazil’s surveillance system for mild influenza, influenza-like and Covid-19 cases (e-SUS); linkage would permit assessment of the impact of COVID-19 on a larger, less selective group of pregnant women.

Second, the data were not validated, so misclassification of characteristics of the study population, such as comorbidities or type of SARI, cannot be ruled out. In addition, during the study period, changes occurred in definitions (for example, the use of images in the diagnosis was implemented in August 2020) (Supplementary Table S8).

Third, the SIVEP-Gripe contained no confirmed diagnosis for 1,332 cases, which had to be excluded from the analysis. More specifically, data were missing differentially for underrepresented and vulnerable populations, such as pregnant women and residents of disadvantaged regions.

Fourth, the category “other viral etiologies and co-infection” was ambiguous. If results between laboratory methodologies diverged, the final diagnosis prioritized the RT-PCR and disregarded infections that occurred simultaneously. However, COVID-19 patients can be infected by another respiratory virus, a factor that should be considered when evaluating disease severity.

Finally, the SIVEP-Gripe does not indicate whether the observed deaths were directly attributed to COVID-19 or other SARIs, or how changes in practice of care and delays in seeking access to care might affect the pregnant population.

Limitations notwithstanding, our analysis has notable strengths. It is one of the few studies based on national surveillance data, and the first to use the SIVEP-Gripe to describe pregnant and recently pregnant women with COVID-19 or other SARIs. We show the absolute burden that COVID-19 imposes on pregnant and recently pregnant women in Brazil.

As previously mentioned, international guidelines for managing pregnancies affected by COVID-19 may not reflect the situation in Brazil. Takemoto et al. predicted that this would be the case, and our analysis supports their expectation. Our study describes characteristics of women hospitalized with COVID-19 or other SARIs in Brazil and the uneven...
In the effort to avoid more deaths and evaluate the short- and long-term effects of the pandemic, specific regions should be targeted, mainly those where maternal mortality rate is high\textsuperscript{15} and where prenatal care is known to be limited.\textsuperscript{31} Projections using previous estimates of live births (Supplementary Figure S1), a proxy for the number of pregnancies, and linkage with the Mortality Information System and the National Live Birth Information System would be beneficial, as would transparent analysis.

In summary, this study provides estimates of maternal morbidity and mortality due to SARIs generally, and COVID-19 specifically, in Brazil. Marked differences in absolute distributions of infections and deaths were observed by region and state. However, higher numbers of reported cases did not necessarily translate into more deaths. Rather, geographic differences were associated with differences in structural socio-economic vulnerability within a diverse, but racialized, country.

The results reinforce the need to collect and rigorously analyze data on trends, possible causes, risk factors, and excess morbidity and mortality in pregnant and recently pregnant women, preferably with governmental support.

### Table 4 – Characteristics of survivors and non-survivors among COVID-19 cases, SIVEP-Gripe, Brazil, January-November 2020 (n = 5,469).

| Characteristics | Survivors (n = 4349) | Non-survivors (n = 362) | Without outcome\* (n = 758) |
|-----------------|----------------------|-------------------------|--------------------------|
|                 | n        | %       | n        | %       | n        | %       |
| **Age group (years)** | | | | | | |
| 10 to 19        | 441      | 10.1    | 21       | 5.8     | 72       | 9.5     |
| 20 to 29        | 1,820    | 41.8    | 121      | 33.4    | 326      | 43.0    |
| 30 to 39        | 1,771    | 40.7    | 180      | 49.7    | 313      | 41.3    |
| 40 to 49        | 317      | 7.3     | 40       | 11.0    | 47       | 6.2     |
| **Race/ethnicity (self-reported)** | | | | | | |
| White           | 1,174    | 27.0    | 85       | 23.5    | 145      | 19.1    |
| Black           | 216      | 5.0     | 30       | 8.3     | 35       | 4.6     |
| East Asian      | 35       | 0.8     | 4        | 1.1     | 7        | 0.9     |
| Pardo           | 2,023    | 46.5    | 194      | 53.6    | 416      | 54.9    |
| Indigenous      | 68       | 1.6     | 2        | 0.5     | 10       | 1.3     |
| Missing/unknown | 833      | 19.1    | 47       | 13.0    | 145      | 19.1    |
| **Education level** | | | | | | |
| No education    | 9        | 0.2     | 2        | 0.5     | 6        | 0.8     |
| Elementary school | 557   | 12.8    | 40       | 11.0    | 107      | 14.1    |
| High school     | 1,024    | 23.5    | 90       | 24.9    | 202      | 26.6    |
| Higher education | 330     | 7.6     | 23       | 6.3     | 56       | 7.4     |
| Missing/unknown | 2,429    | 55.8    | 207      | 57.2    | 387      | 51.1    |
| **Comorbidities** | | | | | | |
| Hypertension or other cardiovascular disease | 417 | 9.6 | 69 | 19.1 | 76 | 10.0 |
| Diabetes        | 322      | 7.4     | 59       | 16.3    | 40       | 5.3     |
| Asthma or other chronic lung diseases | 183 | 4.2 | 19 | 5.2 | 39 | 5.1 |
| Obesity         | 193      | 4.4     | 44       | 12.1    | 27       | 3.6     |
| Immunosuppression/HIV | 48 | 1.1 | 9 | 2.5 | 12 | 1.6 |
| Chronic hematological diseases or anemia | 42 | 1.0 | 8 | 2.2 | 6 | 0.8 |
| Neurological disease or depression | 40 | 0.9 | 3 | 0.8 | 4 | 0.5 |
| Chronic kidney disease | 27 | 0.6 | 6 | 1.7 | 13 | 1.7 |
| Chronic liver disease or hepatitis | 13 | 0.3 | 3 | 0.8 | 1 | 0.1 |
| Tuberculosis    | 0        | 0       | 2        | 0.6     | 0        | 0       |
| Other comorbidities | 182 | 4.2 | 31 | 8.6 | 25 | 3.3 |
| Smoking (former or current) | 13 | 0.3 | 1 | 0.3 | 5 | 0.7 |
| **Gestational age** | | | | | | |
| First trimester | 304      | 7.0     | 12       | 3.3     | 62       | 8.2     |
| Second trimester | 770     | 17.7    | 61       | 16.8    | 154      | 20.3    |
| Third trimester | 2,040    | 46.9    | 105      | 29.0    | 330      | 43.5    |
| Trimester ignored | 203     | 4.7     | 9        | 2.5     | 26       | 3.4     |
| Postpartum or post-abortion | 1,032 | 23.7 | 175 | 48.3 | 186 | 24.5 |
| Admission to intensive care unit (ICU) | 686 | 15.8 | 245 | 67.7 | 194 | 25.7 |
| ICU Length of stay | 5 (n = 377) | 2;10 | 11 (n = 139) | 4;19 | 4 (n = 24) | 2;15.5 |
| **Ventilatory support** | | | | | | |
| Not artificially ventilated | 2,594 | 59.6 | 39 | 10.8 | 389 | 51.3 |
| Non-invasive ventilation | 1,001 | 23.0 | 64 | 17.7 | 158 | 20.8 |
| Invasive ventilation | 191 | 4.4 | 213 | 58.8 | 51 | 6.7 |
| Missing | 563 | 12.9 | 46 | 12.7 | 160 | 21.1 |

\* Missing or still in hospital.

\** The sum of the presence of comorbidity may exceed the total of the column, since several comorbidities per woman might apply.\
Fig. 2 – Distribution of cases and deaths due to SARIs among pregnant and recently pregnant women, by state, SIVEP-Gripe, Brazil, January-November 2020 (n = 11,074)

A. SARI with influenza or other etiological agents (A1-Number of confirmed cases; A2-Number of reported deaths). B. SARI cases with unknown etiology (B1-Number of confirmed cases; B2-Number of reported deaths). C. COVID-19 cases (C1-Number of confirmed cases; C2-Number of reported deaths).
Data sharing

SIVEP-Gripe data are publicly available. De-identified and unduplicated individual data are available indefinitely at https://opendatasus.saude.gov.br/dataset/bd-srg-2020.

Authors’ contributions

LFL, JM, DBF, RK, AEM, WKO, MFS, LA, RWP, and NBB contributed to the conception and design of the study; to the acquisition, analysis, and interpretation of data; and to the draft of the manuscript. LFL and NBB analyzed and reviewed results.

All authors have approved the submitted version.

Conflicts of interest

JM is an employee of bioMérieux. The other authors have no competing interests to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjid.2021.101620.

R E F E R E N C E S

1. Coronavirus Brasil. Available at: https://covid.saude.gov.br/ [Accessed December 4, 2020].
2. Hallal PC, Hartwig FP, Horta BL, et al. SARS-CoV-2 antibody prevalence in Brazil: results from two successive nationwide serological household surveys. Lancet Glob Health. 2020;8:e1390-8. https://doi.org/10.1016/S2214-109X(20)30387-9.
3. Basu P, Bica I, Marra V, Ercole A, van der Schaaf M. Ethnic and regional variations in hospital mortality from COVID-19 in Brazil: a cross-sectional observational study. Lancet Glob Health. 2020;8:e1018-26. https://doi.org/10.1016/S2214-109X(20)30385-0.
4. Chen L, Li Q, Zheng D, et al. Clinical characteristics of pregnant women with COVID-19 in Wuhan, China. N Engl J Med. 2020;382:e100. https://doi.org/10.1056/NEJMoa200226.
5. Knight M, Bunch K, Voudsen N, et al. Characteristics and outcomes of pregnant women admitted to hospital with confirmed SARS-CoV-2 infection in UK: national population based cohort study. BMJ. 2020: m2107. https://doi.org/10.1136/bmj.m2107.
6. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status — United States, January 22—October 3, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1641-7. https://doi.org/10.15585/mmwr.mm6944e3.
7. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ. 2020: m3320. https://doi.org/10.1136/bmj.m3320.
8. Takemoto M, Menezes M, Andreucci C, et al. Clinical characteristics and risk factors for mortality in obstetric patients with severe COVID-19 in Brazil: a surveillance database analysis. BJOG: Int J Obstet Gyn. 2020. https://doi.org/10.1111/1471-0528.16470. 1471-0528.16470.
9. de Souza WM, Buss LF, Candido D da S, et al. Epidemiological and clinical characteristics of the COVID-19 epidemic in Brazil. Nat Hum Behav. 2020;4:856-65. https://doi.org/10.1038/s41562-020-0928-4.
10. Cavalcante JR, Cardoso-dos-Santos AC, Bremm JM, et al. COVID-19 no Brasil: evolução da doença até a semana 19 e 29 de junho de 2020. Epidemiologia e Serviços de Saúde. 2020;29. https://doi.org/10.5123/S1679-4974202000040010.
11. SRAG 2020. Rastreamentos residenciais de Síndrome Respiratória Aguda Grave - incluindo doenças da COVID-19 - Open Data. Available at: https://opendatasus.saude.gov.br/dataset/bd-srg-2020 Accessed September 21.
12. Definição de Caso e Notificação. Available at: https://coronavirus.saude.gov.br/definico-de-caso-e-notificacao [Accessed August 11, 2020].
13. Global COVID-19 Clinical Platform: Pregnancy Case Report Form (CRF). Available at: https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-Pregnancy_CRF-2020-5 accessed September 21.
14. Souza LR de O. Mortalidade e Gestantes por Influenza A (H1N1)PD09 no Brasil nos anos de e 2010. 2013.
15. Institute for Health Metrics and Evaluation (IHME). GBD Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2017 2019.
16. Ferreira RAB, Benicio MHD. Obesidade em mulheres brasileiras: associação com paridade e nível socioeconômico. Rev Panam Salud Publica. 2015;37:337-42.
17. Pena SDJ, Di Pietro G, Fuchsshuber-Moraes M, et al. The genomic ancestry of individuals from different geographical regions of Brazil is more uniform than expected. PLoS ONE. 2011;6:e17063. https://doi.org/10.1371/journal.pone.0017063.
18. IBGE | Biblioteca | Detalhes | Desigualdades sociais por cor ou raça no Brasil. Available at: https://biblioteca.ibge.gov.br/index.php/biblioteca-catalogo?view=detalhes&id=2101681 accessed October 22.
19. de Freitas, CM, Barcellos, C, Villela, DAM, Matta, GC, Reis, LC, Portela, MCB. Observatório COVID-19 após 6 meses de pandemia no Brasil. n.d. 2021
20. de Oliveira RG, da Cunha AP, Gadelha AG, et al. Desigualdades raciais e a morte como horizonte: considerações sobre a pandemia at endo o Brasil. n.d. 2021. Available at:https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/special-epidemiol.html accessed September 21.
21. IBGE | Serviço COVID-19 apo detalizado posteri. Available at: https://www.mn.gov.br/pt-g/decio/Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2017 2019.
22. Registro Internacional de Exposição a Coronavirus na Gravidez. Available at: https://corona.pregistry.com/?locale-pt accessed September 21.
23. UK Obstetric Surveillance System (UKOSS) | NPEU. Available at: https://www.npeu.ox.ac.uk/ukoss Accessed October 22.
24. Magee LA, Khalil A, von Dadelszen P. Covid-19: UK Obstetric Surveillance System (UKOSS) report. Available at: https://www.cdc.gov/ncbddd/aboutus/postpartum-women-with-acute-respiratory-distress-syndrome-factors-for-adverse-outcomes-among-pregnant-and-postpartum-women-with-acute-respiratory-distress-syndrome-due-to-COVID-19-in-Brazil.Int J Gynecol Obstet. 2020;2015;415– 23. https://doi.org/10.1016/j.ijo.201407.
25. IBGE | Serviço COVID-19 apo detalizado posteri. Available at: https://www.mn.gov.br/pt-g/decio/Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2017 2019.
26. IBGE | Service COVID-19 apo detalizado posteri. Available at: https://www.mn.gov.br/pt-g/decio/Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2017 2019.
27. CONSIGN. Covid-19 InfectiOn and Medicines in Pregnancy. Department of Pharmacy; 2020. Available at: https://www.mn.gov.br/pt-g/decio/Compare Data Visualization. Seattle, WA: IHME, University of Washington; 2017 2019.
28. Panchaud A, Favre G, Pomar L, et al. An international registry for emergent pathogens and pregnancy. Lancet. 2020;395:1483–4. https://doi.org/10.1016/S0140-6736(20)30981-8.

29. COVI-PREG. CHUV. Available at: https://www.chuv.ch/fr/dfme/dfme-home/recherche/femme-mere/materno-fetal-and-obstetrics-research-unit-prof-baud/covi-preg Accessed September 21, 2020.

30. World Health Organization Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance. Pediatr Med Rodz. 2020;16:9–26. https://doi.org/10.15557/PiMR.2020.0003.

31. Leal M do C, Esteves-Pereira AP, Viellas EF, Domingues RMSM, da Gama SGN. Prenatal care in the Brazilian public health services. Rev Saúde Pública. 2020;54:8. https://doi.org/10.11606/s1518-8787.2020054001458.