



Severity of illness by pregnancy status among laboratory-confirmed SARS-CoV-2 infections occurring in reproductive-aged women in Colombia

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Abstract

Background: Multiple studies have described increased risk of severe coronavirus disease (COVID-19) among pregnant women compared to nonpregnant women. The risk in middle-income countries where the distributions of age groups and preexisting conditions may differ is less known.

Objectives: To determine whether pregnant women with SARS-CoV-2 infection are at increased risk for severe COVID-19 compared to nonpregnant women in Colombia.

Methods: We analysed national surveillance data from Colombia, of women aged 15–44 years with laboratory-confirmed infection with SARS-CoV-2 by molecular or antigen testing, from 6 March 2020 to 12 December 2020. An enhanced follow-up of pregnant women with COVID-19 was established to monitor pregnancy and birth outcomes.

Results: Of 371,363 women aged 15–44 years with laboratory-confirmed SARS-CoV-2 infection, 1.5% ($n = 5614$) were reported as pregnant; among those, 2610 (46.5%) were considered a complete pregnancy for reporting purposes at the time of analysis. Hospitalisation (23.9%) and death (1.3%) occurred more frequently among pregnant symptomatic women compared to nonpregnant symptomatic women (2.9% and 0.3%, respectively). Compared to nonpregnant symptomatic women, pregnant symptomatic women were at increased risk of hospitalisation (adjusted risk ratio [RR] 2.19, 95% confidence interval [CI] 2.07, 2.32) and death (RR 1.82, 95% CI 1.60, 2.07), after adjusting for age, type of health insurance and presence of certain underlying medical conditions. Among complete pregnancies, 55 (2.1%) were pregnancy losses, 72 (2.8%) resulted in term low birthweight infants and 375 (14.4%) were preterm deliveries.

Conclusions: Although pregnant women were infrequently reported with laboratory-confirmed SARS-CoV-2 infection, pregnant symptomatic women with COVID-19 were at increased risk for hospitalisation and death compared to nonpregnant symptomatic

women. Almost all infections we reported on were third-trimester infections; ongoing follow-up is needed to determine pregnancy outcomes among women infected earlier in pregnancy. Healthcare providers should counsel pregnant women about preventive measures to protect from SARS-CoV-2 infection and when to seek care.

KEYWORDS

birth outcomes, congenital infection, COVID-19, pregnancy, SARS-CoV-2

1 | BACKGROUND

Studies from multiple countries have described increased risk of severe illness of coronavirus disease 2019 (COVID-19) in pregnant people compared to nonpregnant people,¹⁻³ and pregnant people with COVID-19 are at increased risk of adverse pregnancy outcomes, such as preterm birth and stillbirth.^{2,4} However, the risk in pregnancy and the overall burden is less known in middle-income countries, where the distribution of age groups and preexisting conditions as well as standards of care are different.⁵ The first COVID-19 laboratory-confirmed case in Colombia was identified on 6 March 2020. As of 10 May 2021, Colombia has reported 3,002,758 confirmed cases of COVID-19 and 77,854 COVID-19-related deaths, among an estimated total population of 48 million.⁶ In 2019, there were 650,000 births in Colombia, with the age distribution as 47% for 15- to 24-year-olds and 41% for 25- to 34-year-olds.⁷ The majority of pregnant people attend prenatal care, regardless of socioeconomic status, with almost 80% initiating prenatal care in the first trimester of pregnancy.⁸ The burden and characteristics of pregnant people with SARS-CoV-2, the virus that causes COVID-19, infection and impact on severity of illness and adverse outcomes in Colombia have yet to be described.

Colombia has a passive national surveillance system (known as Sivigila) for over 100 public health reportable conditions. In February 2020, Colombia's Instituto Nacional de Salud (INS) published guidelines for COVID-19 surveillance,⁹ and Sivigila rapidly created a case report form and trained local health authorities on the identification and mandatory reporting of COVID-19 daily to INS. The case report form captures whether a woman is pregnant and other information such as symptoms, underlying conditions and markers of illness severity (eg hospitalisation, death). Colombia also established a protocol to conduct enhanced follow-up of pregnant women with COVID-19 and continues to monitor pregnancy and birth outcomes among this cohort to help avoid complications, disabilities and death in pregnant women and newborns.

We conducted a secondary data analysis to describe the overall burden and characteristics of women aged 15–44 years with laboratory-confirmed SARS-CoV-2 infection by pregnancy status and assess risk of severe illness among pregnant women compared to nonpregnant women reported to the national surveillance system in Colombia. Among those women with a single gestation pregnancy, SARS-CoV-2 infection and sufficient time for a complete pregnancy, we report on birth outcomes. These findings can help contribute to our understanding of the impact of COVID-19 on severity of illness

Synopsis

Study question

Are pregnant women with SARS-CoV-2-infection at increased risk for severe coronavirus disease 2019 (COVID-19) compared to nonpregnant women in Colombia?

What is already known?

Multiple studies have described an increased risk of severe COVID-19 among pregnant women compared to nonpregnant women; however, these studies do not focus on middle-income countries where the distributions of age groups and preexisting conditions may differ.

What this study adds?

Pregnant symptomatic women with COVID-19 were at increased risk for hospitalisation and death compared to nonpregnant symptomatic women in Colombia. Preliminary findings suggest that pregnancy loss and preterm birth, mostly among third-trimester infections, do not appear higher than pre-pandemic rates.

during pregnancy and adverse outcomes, particularly in a middle-income setting, and can be used to inform local efforts for public health and clinical decision-making.

2 | METHODS

2.1 | Cohort selection

This study used national disease surveillance data from Colombia, of women aged 15–44 years with laboratory-confirmed infection with SARS-CoV-2 by molecular or antigen testing, from 6 March 2020 to 12 December 2020. INS conducts national surveillance for a wide range of reportable conditions, including acute respiratory infections (such as laboratory-confirmed SARS-CoV-2 infection), foodborne diseases, birth defects and severe maternal morbidity.¹⁰ Criteria for reporting a probable case of COVID-19 include at least one of the following symptoms: fever $\geq 38^{\circ}\text{C}$, cough, difficulty

breathing, odynophagia, fatigue, loss of taste or smell and meet at least one of the following conditions: belong to at least one high-risk group, such as healthcare or social worker, or have had close contact with a confirmed or probable case of COVID-19 in the past 14 days or have a positive serologic test specific for IgM antibodies taken 11 days (immunochromatography) or 14 days (ELISA or chemiluminescence) after symptom-onset date. Criteria for a probable death due to COVID-19 include all deaths from severe acute respiratory infection with a clinical picture of unknown aetiology and meeting any of the following conditions mentioned above for probable cases. Criteria for asymptomatic cases include close contact with a confirmed case of COVID-19 and no symptoms have occurred within seven days after exposure, or asymptomatic persons who tested positive for SARS-CoV-2 infection after screening. Cases are considered confirmed if there is a positive reverse transcription polymerase chain reaction (RT-PCR) or antigen test for SARS-CoV-2 infection, or if a probable case meets one of the following epidemiologic criteria: close contact with a confirmed case of COVID-19 between 2 and 14 days of symptom-onset date, or having a close contact who becomes a confirmed case between 1 and 14 days after last contact.¹¹ Health staff from local health authorities and agencies around the country are instructed to send information immediately on cases meeting the above criteria electronically to Sivigila using SARS-CoV-2 case report forms.¹² Reporting agencies also inform INS about the receipt of samples that will be sent to the laboratory.

An epidemiology team at INS reviews the forms daily and provides weekly feedback to reporting agencies. Linkage of the surveillance data to hospitalisation and death records is done to provide more complete data. The SARS-CoV-2 report form includes a checkbox to indicate a pregnant woman, including the gestational week at time of infection. Using the information reported to Sivigila, INS requests additional information from local authorities and health insurance companies to initiate close monitoring of the pregnancy to help avoid complications, disabilities and death in pregnant women and newborns by providing rapid referrals and conducting regular follow-up with the pregnant women. A list of pregnant women with COVID-19 is shared weekly with local health authorities to verify information, including gestational age at time of infection, and to update and send back to INS. These data are linked to laboratory testing results, birth records to obtain pregnancy and birth outcome, surveillance for maternal morbidity complications¹³ and death records to identify maternal or infant deaths.

2.2 | Exposure

The exposure for this analysis is laboratory-confirmed SARS-CoV-2 infection. INS established mandatory guidelines for SARS-CoV-2 testing for all public and private laboratories in Colombia and created a secure reporting system for local authorities and health insurance companies to review laboratory testing results electronically. Laboratories are mandated to report all positive and negative SARS-CoV-2 RT-PCR and antigen results to INS. Samples are also

processed at the INS public health laboratory. Laboratory-confirmed SARS-CoV-2 infection in this analysis includes cases with either a positive molecular test by RT-PCR or a positive antigen test.¹⁴

2.3 | Outcomes

This analysis examines hospitalisation and death among women of reproductive age with laboratory-confirmed SARS-CoV-2 infection to determine severity of illness. Since some pregnancies are ongoing, we examined birth and infant outcomes by trimester of infection among all pregnant women with SARS-CoV-2 infection by restricting the analysis to pregnancies that could have the potential for duration of 42 weeks by the end of the study period (December 12, 2020), as well as to women with a single gestation pregnancy. We excluded all pregnancies for which a hypothetical duration of 42 weeks would end after 12 December 2020, regardless of whether the pregnancy outcomes occurred prior to that date, to avoid overestimating frequency of pregnancy loss and preterm birth. Among the same subset of pregnancies, we also report on severe maternal morbidity complication (ie a severe life-threatening obstetric pregnancy complication during the pregnancy, delivery or within 42 days of delivery).¹⁵

2.4 | Statistical analysis

The analysis was limited to laboratory-confirmed SARS-CoV-2 infections among women aged 15–44 years reported to INS from 6 March to 12 December 2020. Given the difference in magnitude of cases by pregnancy status, we examined weekly number of cases by pregnancy status, using absolute frequency and logarithmic scale. We also report number of infections by department (ie state) in Colombia. To examine severity of illness, we restricted the analysis to symptomatic and SARS-CoV-2-positive women to focus on the complications related to COVID-19, but we also present the data for the entire cohort in a supplemental table. Unadjusted and adjusted (aRR) risk ratios and 95% confidence intervals (CI) were calculated using log-binomial regression to assess risk of hospitalisation and death for pregnant women compared to nonpregnant women. Overall and stratified risk ratios were adjusted for continuous age (in years), type of health insurance and presence of obesity, asthma, diabetes or cardiovascular disease. Analyses were conducted in STATA and SAS[®] 9.4 software.^{16,17}

2.5 | Missing data

Outcome measures and covariates had no missing information, except for type of health insurance which was missing for 6.5% of women in our study population. Imputation of 40 data sets was employed for the analysis of risk factors for severe COVID-19 among women with SARS-CoV-2 infection using the fully conditional specification method. Following imputation, regression models were

computed using the imputed data sets. Results were combined, taking the variation between the results of the imputed data sets into account. Frequencies presented for type of health insurance in Tables 2 and S1 are from the first imputed data set.

2.6 | Ethics approval

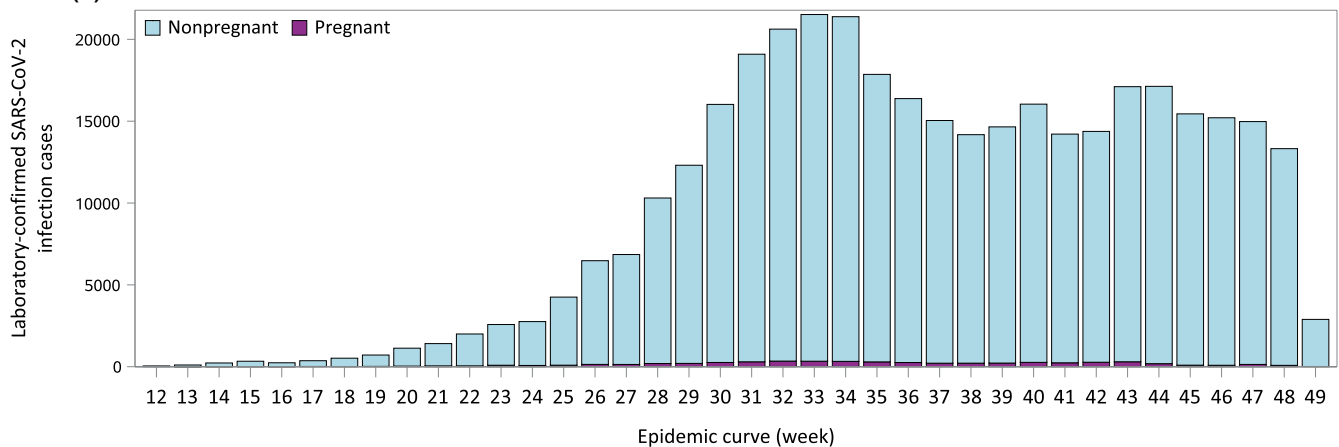
Per Colombian resolution 08430 of 1993, the study is considered minimal risk, since retrospective documentary techniques and methods were used and no intervention or intentional modification of the biological, physiological, psychological or social variables were carried out.¹⁸ This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¹⁹

3 | RESULTS

From 6 March to 12 December 2020, among 371,363 women aged 15–44 years with laboratory-confirmed SARS-CoV-2 infection, 1.5% ($n = 5614$) were reported as pregnant. Among pregnant women,

85% of laboratory-confirmed infections were confirmed by RT-PCR; among nonpregnant women, 79% were confirmed by RT-PCR. Laboratory-confirmed infections peaked in August 2020 for women of reproductive age with a plateauing of infections at about 15,000 per week until November 2020 (Figure 1, Panel A). Although cases in pregnant women were a small proportion of total cases, the timing of infection over the year was comparable (Figure 1, panel B). The highest counts of SARS-CoV-2 infection occurred in the most populous departments: Bogotá, Antioquia, Valle del Cauca and Atlántico (Figure 2). Pregnant women with confirmed SARS-CoV-2 infection were more likely to be younger, of lower socioeconomic stratum and have subsidised health insurance compared to SARS-CoV-2-positive nonpregnant women (Table 1). The proportion of asymptomatic cases was 23.7% in pregnant women compared to 29.0% in nonpregnant women. The most frequent symptoms reported among pregnant women were cough (51.4%), fever (33.1%), fatigue (28.9%), sore throat (29.3%) and headache (21.0%), which were similar to nonpregnant women. Pregnant women reported a higher percentage of any underlying condition compared to nonpregnant women (33.1% vs 13.2%), but a substantial portion of pregnant women indicated other conditions (25.9%), compared to nonpregnant women (5.9%).

Panel (A)



Panel (B)

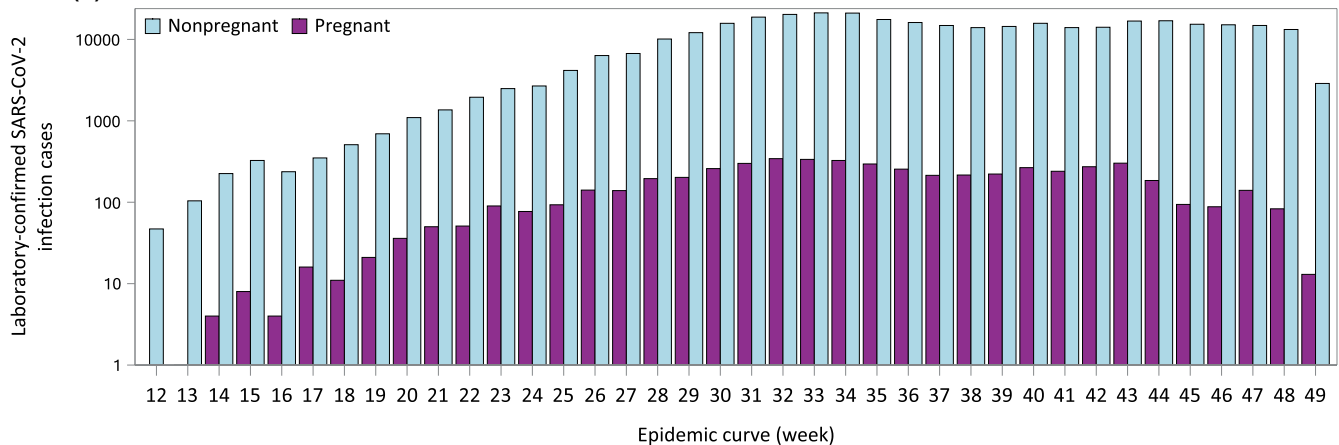


FIGURE 1 Epidemic curve of laboratory-confirmed SARS-CoV-2 infections among reproductive-aged women by pregnancy status, with cases presented on linear scale (panel A) and logarithmic scale (panel B), Colombia

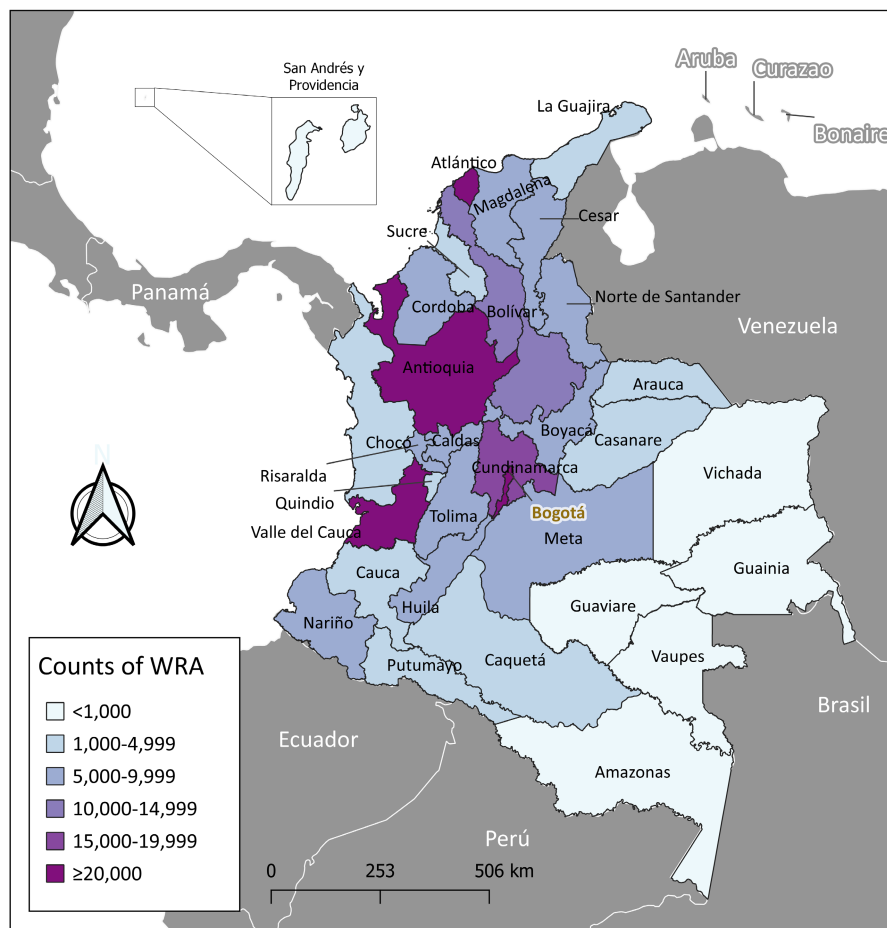


FIGURE 2 Counts of laboratory-confirmed SARS-CoV-2 infections among women of reproductive age (WRA) by department, Colombia

Other conditions include but are not limited to arthritis, anaemia and seizures.

Compared to nonpregnant symptomatic SARS-CoV-2-positive women, pregnant symptomatic women were at increased risk of hospitalisation and death accounting for age, type of health insurance and presence of obesity, asthma, diabetes and cardiovascular disease (Table 2). Risk of hospitalisation and death was higher for pregnant women in all age groups compared to nonpregnant women. Risk of hospitalisation was higher for pregnant women within all insurance groups, and risk of death was higher among pregnant women with employer-based or subsidised health insurance compared to nonpregnant women. Pregnant women with obesity, asthma, diabetes and cardiovascular disease were at an increased risk for hospitalisation compared to nonpregnant women with these medical conditions. Pregnant women with asthma were also at greater risk for death compared to nonpregnant women with asthma. These associations held true for all SARS-CoV-2-positive pregnant women compared to SARS-CoV-2-positive nonpregnant women (Table S1).

Of 5614 SARS-CoV-2-positive pregnant women, the median gestational age at the time of infection was 27 weeks (interquartile range=18), with 15.7%, 29.0%, 44.6% or 10.8% infected in the first, second and third trimesters of pregnancy, or missing timing of infection, respectively (Table 1). Among all SARS-CoV-2-positive pregnant women, 2610 (46.5%) had a single gestation pregnancy and the

opportunity for at least a 42-week observation and are included in the reporting of birth and infant outcomes; of these, 2,278 (87.3%) had a pregnancy outcome reported (Figure S1). Among SARS-CoV-2-positive pregnant women with at least a 42-week observation period and a single gestation pregnancy, 82.1% had infection in the third trimester (Table 3); 55 (2.1%) had pregnancy losses reported. After excluding pregnancy losses, 2.8% of infants were reported to be term low birthweight and 14.7% of infants were preterm. A higher frequency of preterm deliveries was reported in symptomatic compared to asymptomatic women (15.7% vs 11.4%) (Table S2). In the maternal morbidity surveillance, 14.2% of pregnant women with SARS-CoV-2 infection presented with severe life-threatening complications during the pregnancy, and frequency by symptom status was similar (Table S2).

4 | COMMENT

4.1 | Principal findings

Using national population-based surveillance data from Colombia in 2020, pregnant women with laboratory-confirmed SARS-CoV-2 infection had an increased risk of COVID-19 hospitalisation and death. Stratified analyses reveal an increased risk for hospitalisation for all age groups, all types of health insurance and obesity, asthma, diabetes and

TABLE 1 Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infections by pregnancy status, Colombia^a

	Pregnant women n = 5614	Nonpregnant women n = 365,749	Total N = 371,363
	Number (%)	Number (%)	Number (%)
Age (years)			
15–24	1713 (30.5)	84,131 (23.0)	85,844 (23.1)
25–34	2955 (52.6)	157,280 (43.0)	160,235 (43.2)
35–44	946 (16.9)	124,338 (34.0)	125,284 (33.7)
Socioeconomic stratum^b			
Lower	3464 (61.7)	197,481 (54.0)	200,945 (54.1)
Middle	1004 (17.9)	95,565 (26.1)	96,569 (26.0)
Upper	68 (1.2)	6680 (1.8)	6748 (1.8)
Missing	1078 (19.2)	66,023 (18.1)	67,101 (18.1)
Health insurance			
Employer-based	3360 (59.9)	276,330 (75.6)	279,690 (75.3)
Subsidised	1404 (25.0)	44,465 (12.2)	45,869 (12.4)
Other	341 (6.1)	21,177 (5.8)	21,518 (5.8)
Missing	509 (9.1)	23,777 (6.5)	24,286 (6.5)
Residence			
Urban	5327 (94.9)	358,429 (98.0)	363,756 (98.0)
Non-urban	254 (4.5)	7320 (2.0)	7574 (2.0)
Missing	33 (0.6)	0	33 (0.0)
Occupation			
Healthcare worker	382 (6.8)	31,138 (8.5)	31,520 (8.5)
Symptoms			
Asymptomatic	1333 (23.7)	105,880 (29.0)	107,213 (28.9)
Symptomatic ^c	4281 (76.3)	259,869 (71.1)	264,150 (71.1)
Cough	2883 (51.4)	176,658 (48.3)	179,541 (48.4)
Fever	1858 (33.1)	107,994 (29.5)	109,852 (29.6)
Sore throat	1643 (29.3)	128,294 (35.1)	129,937 (35.0)
Fatigue	1621 (28.9)	118,352 (32.4)	119,973 (32.3)
Headache	1176 (21.0)	84,208 (23.0)	85,384 (23.0)
Nasal discharge	682 (12.2)	38,509 (10.5)	39,191 (10.6)
Loss of smell or taste	611 (10.9)	45,666 (12.5)	46,277 (12.5)
Difficulty breathing	573 (10.2)	29,565 (8.1)	30,138 (8.1)
Diarrhoea	213 (3.8)	18,331 (5.0)	18,544 (5.0)
Conjunctivitis	35 (0.6)	4065 (1.1)	4100 (1.1)
Other symptoms	253 (4.5)	16,622 (4.5)	16,875 (4.5)
Underlying medical conditions			
Any medical condition	1857 (33.1)	48,141 (13.2)	49,998 (13.5)
No underlying medical condition	3757 (66.9)	317,608 (86.8)	321,365 (86.5)
Obesity	212 (3.8)	9261 (2.5)	9473 (2.6)
Asthma	143 (2.6)	8809 (2.4)	8952 (2.4)
Diabetes	121 (2.2)	2895 (0.8)	3016 (0.8)
Cardiovascular disease ^d	109 (1.9)	6154 (1.7)	6263 (1.7)
Tobacco smoker	52 (0.9)	4116 (1.1)	4168 (1.1)

(Continues)

TABLE 1 (Continued)

	Pregnant women n = 5614	Nonpregnant women n = 365,749	Total N = 371,363
	Number (%)	Number (%)	Number (%)
Cancer	16 (0.3)	1272 (0.4)	1288 (0.4)
Malnutrition	16 (0.3)	561 (0.2)	577 (0.2)
HIV	14 (0.3)	350 (0.1)	364 (0.1)
Renal disease	13 (0.2)	853 (0.2)	866 (0.2)
Chronic obstructive pulmonary disease	6 (0.1)	354 (0.1)	360 (0.1)
Immunosuppressive medication	9 (0.2)	787 (0.2)	796 (0.2)
Tuberculosis	4 (0.1)	253 (0.1)	257 (0.1)
Other	1451 (25.9)	21,422 (5.9)	22,873 (6.2)
Median gestational week (IQR) at infection	27.0 (18)	NA	NA
Trimester of infection			
First (0–13 weeks)	880 (15.7)	NA	NA
Second (14–27 weeks)	1628 (29.0)	NA	NA
Third (28–42 weeks)	2502 (44.6)	NA	NA
Missing	604 (10.8)	NA	NA

Abbreviation: IQR, Interquartile range; NA, Not applicable.

^aIncludes women who tested positive for SARS-CoV-2 by either a positive molecular test by reverse transcription polymerase chain reaction (RT-PCR) or a positive antigen test.

^bSocioeconomic strata are based on residences that should receive public services. Those of higher SES strata pay more for public services and help to subsidise those of lower strata. <https://www.dane.gov.co/index.php/servicios-al-ciudadano/servicios-informacion/estratificacion-socioeconomica>.

^cIncludes indication of symptomatic status at time of report and if individual symptom was reported.

^dCardiovascular disease also includes presence of hypertension.

cardiovascular disease and increased risk of death for all age groups, women with employer-based and subsidised health insurance, and for women with asthma. These findings are consistent with other large cohort studies and results from systematic reviews.^{1–4} Other studies have noted a higher risk of hospitalisation, which could be explained by the detection of asymptomatic cases through universal COVID-19 testing practices at labour and delivery. Although about half of pregnant cases were identified in the third trimester, Colombia does not conduct universal testing of all pregnant women upon admission to labour and delivery. The proportion of asymptomatic cases are similar for pregnant and nonpregnant women in the cohort.

4.2 | Strengths of the study

Strengths of this report include that the data come from national surveillance, representing Colombia's diverse population. By including women with positive antigen testing which has high specificity and is more easily accessible outside of a hospital setting, we likely captured more mild cases making our study population more representative of pregnant women with acute infection. In addition, we excluded 8% of pregnancies with reported outcomes as they did not meet our criteria of the 42-week observation period by 12 December 2020. This was done to avoid overestimating frequency of pregnancy loss and preterm birth as those with pregnancies that were still ongoing have yet to be reported. This study provides further

evidence from an additional setting, in particular a middle-income country with different population characteristics and transmission patterns, that pregnant women are at increased risk of severe illness of COVID-19.

4.3 | Limitations of the data

There are some limitations to note. First, only 1% of COVID-19 patients were indicated as being pregnant; based on national data, it is expected that approximately 4% of women of reproductive age are pregnant at a given time.⁷ Although INS contacted local providers regarding the enhanced surveillance of pregnant women, pregnancy status may not have been as completely ascertained as possible, introducing potential misclassification. Given that pregnant women have frequent encounters for care and there might be heightened monitoring, pregnant women who were asymptomatic or who had more mild disease may be detected over nonpregnant women. However, we attempted to address this issue by limiting analysis of illness severity to symptomatic individuals. Second, hospitalisation results should be interpreted with caution due to pregnant women being more likely to be hospitalised out of an abundance of caution. Third, outcomes were missing for 13% of pregnant women with infections that met the inclusion criteria to be included in this report. However, we included them in our denominator when calculating birth and infant outcomes, but these estimates are preliminary and should be interpreted with caution. Fourth, preterm

TABLE 2 Hospitalisation and death among symptomatic women of reproductive-aged with laboratory-confirmed SARS-CoV-2 infection, Colombia^a

Outcome/Characteristic ^b	Pregnant women n = 4281	Nonpregnant women n = 259,869	Unadjusted risk ratio (95% CI) ^c	Adjusted risk ratio (95% CI) ^{c,d}
	Number (%)	Number (%)		
Hospitalisation				
All	1023 (23.9)	7500 (2.9)	8.28 (7.81, 8.77)	2.19 (2.07, 2.32)
Age (years)				
15–24	385/1293 (29.8)	1300/56,839 (2.3)	13.02 (11.80, 14.40)	2.76 (2.50, 3.04)
25–34	479/2251 (21.3)	2756/113,521 (2.4)	8.77 (8.03, 9.57)	2.29 (2.08, 2.53)
35–44	159/737 (21.6)	3444/89,509 (3.9)	5.61 (4.87, 6.46)	1.98 (1.73, 2.27)
Health insurance ^e				
Employer-based	432/2892 (14.9)	4183/217,148 (1.9)	7.75 (7.05, 8.51)	2.53 (2.41, 2.66)
Subsidised	495/1100 (45.0)	2719/28,438 (9.6)	4.66 (4.31, 5.03)	2.17 (2.00, 2.35)
Other	96/289 (33.2)	598/14,283 (4.2)	8.11 (6.73, 9.77)	2.83 (2.34, 3.42)
Underlying medical conditions				
Obesity	66/164 (40.2)	833/6990 (11.9)	3.38 (2.77, 4.11)	1.65 (1.44, 1.88)
Asthma	28/123 (22.8)	402/7634 (5.3)	4.32 (3.08, 6.07)	1.72 (1.50, 1.97)
Diabetes	36/104 (34.6)	428/2419 (17.7)	1.96 (1.48, 2.58)	1.36 (1.22, 1.52)
Cardiovascular disease ^f	27/95 (28.4)	476/5035 (9.5)	3.01 (2.16, 4.18)	1.38 (1.22, 1.55)
Death				
All	54 (1.3)	715 (0.3)	4.58 (3.48, 6.04)	1.82 (1.60, 2.07)
Age (in years)				
15–24	12/1293 (0.9)	73/56,839 (0.1)	7.23 (3.93, 13.27)	1.98 (1.46, 2.68)
25–34	28/2251 (1.2)	201/113,521 (0.2)	7.03 (4.74, 10.41)	1.88 (1.55, 2.27)
35–44	14/737 (1.9)	441/89,509 (0.5)	3.86 (2.28, 6.53)	1.52 (1.20, 1.93)
Health insurance ^e				
Employer-based	24/2892 (0.8)	267/217,148 (0.1)	6.50 (4.22, 10.00)	2.53 (2.04, 3.12)
Subsidised	28/1,100 (2.6)	397/28,438 (1.4)	1.87 (1.28, 2.72)	1.57 (1.30, 1.89)
Other	2/289 (0.7)	51/14,283 (0.4)	1.94 (0.47, 7.93)	1.63 (0.81, 3.29)
Underlying medical conditions				
Obesity	5/164 (3.1)	161/6990 (2.3)	1.32 (0.55, 3.18)	1.10 (0.71, 1.70)
Asthma	5/123 (4.1)	40/7634 (0.5)	7.76 (3.12, 19.32)	2.98 (1.89, 4.69)
Diabetes	- ^g	99/2419 (4.1)	-	-
Cardiovascular disease ^f	- ^g	97/5035 (1.9)	-	-

^aIncludes women who tested positive for SARS-CoV-2 by either a positive molecular test by reverse transcription polymerase chain reaction (RT-PCR) or a positive antigen test.

^bPercentages calculated among total in characteristic group.

^cUnadjusted and adjusted risk ratios were not calculated for cell sizes <5.

^dUnstratified models adjusted for age as a continuous variable, type of health insurance, and presence of obesity, asthma, diabetes and cardiovascular disease. Stratified age models adjusted for type of health insurance and presence of obesity, asthma, diabetes and cardiovascular disease; stratified models for type of health insurance adjusted for age as a continuous variable and any presence of obesity, asthma, diabetes and cardiovascular disease; stratified model for obesity adjusted for asthma, type of health insurance and age as a continuous variable; stratified model for asthma adjusted for presence of obesity, diabetes and cardiovascular disease, type of health insurance and age as a continuous variable; stratified model for diabetes adjusted for asthma and cardiovascular disease, type of health insurance and age as a continuous variable; stratified model for cardiovascular disease adjusted for asthma and diabetes, type of health insurance and age as a continuous variable.

^eAll reported frequencies are from the first imputed data set.

^fCardiovascular disease also includes presence of hypertension.

^gSuppressed data because of small cell size <5.

birth outcomes are not restricted to women infected at <37 weeks of gestation; however, if this exclusion is applied, our denominator decreases by nearly 40%, showing a prevalence of preterm birth in

23.6% of pregnant women with SARS-CoV-2 infection, which is higher than the national estimate. Fifth, pregnant women had higher documentation of other underlying conditions than nonpregnant women,

Outcome	Second trimester n = 456	Third trimester n = 2142	Total ^b n = 2610
	Number (%)	Number (%)	Number (%)
Pregnancy outcome (n = 2610)			
Pregnancy outcome not reported	66 (14.5)	259 (12.1)	332 (12.7)
Pregnancy loss	20 (4.4)	35 (1.6)	55 (2.1)
Live birth	370 (81.1)	1848 (86.3)	2223 (85.2)
Infant outcome (n = 2555) ^c			
Pregnancy outcome not reported	67 (15.4)	260 (12.3)	334 (13.1)
Term not low birthweight	294 (67.4)	1475 (70.0)	1774 (69.4)
Term low birthweight	14 (3.2)	58 (2.8)	72 (2.8)
Preterm	61 (14.0)	314 (14.9)	375 (14.7)
Infant death (n = 2555) ^c			
Neonatal death	10 (2.3)	33 (1.6)	43 (1.7)
Severe pregnancy complications ^d (n = 2610)	43 (9.4)	328 (15.3)	371 (14.2)

TABLE 3 Birth outcomes among pregnant women with laboratory-confirmed SARS-CoV-2 infection by trimester of infection^a, Colombia

^aAnalysis restricted to single gestation pregnancies that could have potential for duration of 42 weeks by the end of the study period (12 December 2020) based on reported gestational week at the time of SARS-CoV-2 infection. Trimester of infection was defined as 0 to 13 w + 6 d (first), 14–27 w + 6 d weeks (second), and 28 w to 41 w + 6 d (third).

^bOf 2610 pregnancies, 12 were infected in the first trimester or were missing timing of infection, and are not presented in the table.

^cExcludes pregnancy losses.

^dSevere life-threatening obstetric pregnancy complication during the pregnancy, delivery or within 42 days of delivery.

perhaps because of the enhanced follow-up of these cases or because they were under medical care. Sixth, differences in findings from other studies could be due to differences in testing and reporting of cases, lower number of cases to detect differences for rare outcomes and differences in healthcare systems to manage and treat persons with severe COVID-19 illness.

4.4 | Interpretation

Pregnant women in Colombia with laboratory-confirmed SARS-CoV-2 infection had an increased risk of COVID-19 hospitalisation and death, which is consistent with findings from other large cohort studies in other countries. Almost all birth and infant outcomes reported from this cohort are third-trimester infections, and preliminary findings suggest that pregnancy loss and preterm birth (2% and 14%) do not appear to be higher than pre-pandemic published rates of 5.8% and 17%, respectively.^{7,20} Based on two systematic reviews, pregnant women with COVID-19 were at increased risk of having a preterm birth and stillbirth compared to pregnant women without COVID-19.^{2,4} It is important to understand the impact of COVID-19 in pregnant woman and their infants to inform clinical care decisions. The Colombian Ministry of Health and Social Protection published COVID-19 public health guidelines for the health care of pregnant and lactating women and their babies in June 2020.²¹ The guidelines recommended telemedicine or home visits for periconceptional care

that included SARS-CoV-2 laboratory testing, and in-person care for ultrasounds and delivery plan visits. For newborns of mothers with suspected or confirmed COVID-19, the guidelines recommended testing within 24 h after birth for COVID-19. The guidelines help support the surveillance system of pregnant woman and their infants, and the surveillance system will provide useful information to update the guidelines when necessary.

5 | CONCLUSION

In conclusion, the findings in this report provide evidence of the increased risk of severe illness of COVID-19 among pregnant women in Colombia. As most pregnancies are still ongoing, continued longitudinal surveillance of pregnancy and infant outcomes are needed. Colombia's public health surveillance incorporated monitoring of pregnant women rapidly, which provided information for clinical decision-making. Medical and public healthcare teams need to consider known risk factors for severe illness such as increased maternal age and underlying medical conditions when counselling about preventive measures for COVID-19.

DISCLAIMER

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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CONFLICT OF INTEREST

All authors have no conflicts of interest.

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REFERENCES

- 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(44):1641-1647. <https://doi.org/10.15585/mmwr.mm6944e3>
- 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;370:m3320. <https://doi.org/10.1136/bmj.m3320>
- Martinez-Portilla RJ, Sotiriadis A, Chatzakis C, 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 Obstetrics Gynecol.* 2021;57(2):224-231. <https://doi.org/10.1002/uog.23575>
- Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *Can Med Assoc J.* 2021;193(16):E540-E548. <https://doi.org/10.1503/cmaj.202604>
- Sola A, Rodríguez S, Cardetti M, Dávila C. Perinatal COVID-19 in Latin America TT - COVID-19 perinatal en América Latina. *Rev Panam Salud Publica.* 2020;44:e47. <https://doi.org/10.26633/RPSP.2020.47>
- Instituto Nacional de Salud. COVID-19 en Colombia. <https://www.ins.gov.co/Noticias/paginas/coronavirus.aspx>. Published 2021. Accessed 10 May, 2021.
- Departamento Administrativo Nacional de Estadística (DANE). Datos de nacimientos en Colombia. <https://www.dane.gov.co/index.php/estadisticas-por-tema/salud/nacimientos-y-defunciones/nacimientos>. Accessed 1 April, 2021.
- Ministerio de Salud y Protección Social y Profamilia. Colombia Encuesta Nacional de Demografía y Salud 2015. <https://dhsprogram.com/publications/publication-fr334-dhs-final-reports.cfm>. Accessed 15 June, 2021.
- Instituto Nacional de Salud. Circular No.005 de 2020- Directrices detención temprana Control Coronavirus (20189-nCov). <https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/ED/VSP/circular-externa-005-de-2020.pdf>. Published 2020. Accessed 2 March, 2021.

- Instituto Nacional de Salud. SIVIGILA. <https://www.ins.gov.co/Direcciones/Vigilancia/Paginas/SIVIGILA.aspx>. Accessed 20 May, 2021.
- Instituto Nacional de Salud. Instructivo para la Vigilancia en Salud Pública Intensificada de Infección Respiratoria Aguda y la Enfermedad Asociada al Nuevo Coronavirus 2019 (COVID-19). http://www.saludcapital.gov.co/CTDLab/Publicaciones/Vigilancia_intensificada_COVID-19.pdf. Published 2020. Accessed 10 May, 2021.
- Instituto Nacional de Salud. Protocolo de Vigilancia en Salud Pública - Infección Respiratoria Aguda (IRA). http://www.ins.gov.co/buscador-eventos/Lineamientos/Pro_Infeccionrespiratoriaaguda.pdf. Published 2020. Accessed 30 March, 2021.
- Ministerio de Salud. Protocolo de Vigilancia en Salud Pública - Morbilidad Materna Extrema. http://www.ins.gov.co/buscador-eventos/Lineamientos/Pro_Morbilidadmaternaextrema.pdf. Published 2017. Accessed 20 April, 2021.
- Centers for Disease Control and Prevention. Interim Guidance for Antigen Testing for SARS-CoV-2. <https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html>. Published 2020. Accessed 20 May, 2021.
- Say L, Souza JP, Pattinson RC. Maternal near miss - towards a standard tool for monitoring quality of maternal health care. *Best Pract Res Clin Obstetrics Gynaecol.* 2009;23(3):287-296. <https://doi.org/10.1016/j.bpobgyn.2009.01.007>
- StataCorp. *Stata Statistical Software: Release 17*. StataCorp LLC. 2021.
- SAS Institute Inc 2013. *SAS/ACCESS® 9.4 Interface to ADABAS: Reference*. SAS Institute Inc.
- Ministerio de Salud. Resolución Numero 8430 de 1993. https://www.hospitalsanpedro.org/images/Comite_Investigacion/Resolucion_8430_de_1993.pdf. Published 1993. Accessed 30 March, 2021.
- Department of Health and Human Services. 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq. <https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/ohrpregulations.pdf>. Accessed 4 February, 2021.
- Chawanpaiboon S, Vogel JP, Moller A-B, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. *Lancet Global Health.* 2019;7(1):e37-e46. [https://doi.org/10.1016/S2214-109X\(18\)30451-0](https://doi.org/10.1016/S2214-109X(18)30451-0)
- Ministerio de Salud. Lineamientos Provisionales para la Atención en Salud de las Gestantes, Recién Nacidos y para la Lactancia Materna, en el Contexto de la Pandemia de COVID-19 en Colombia. <https://www.minsalud.gov.co/Ministerio/Institucional/Procesosyprocedimientos/GIPS14.pdf>. Published 2020. Accessed 30 March, 2021.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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