Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Pregnancy as a risk factor for severe coronavirus disease 2019 using standardized clinical criteria

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BACKGROUND: As of November 18, 2020, more than 11 million people have been infected with coronavirus disease 2019 and almost 250,000 people have died from the disease in the United States, less than 1 year since its discovery. Although literature is beginning to emerge on pregnancy as a risk factor for severe coronavirus disease 2019, these studies are heterogeneous and use primary outcomes such as intensive care unit admission or hospitalization as surrogate markers that may subject analyses to misclassification bias in pregnant patients.

OBJECTIVE: This study aimed to determine the risk of severe coronavirus disease 2019 among pregnant women with symptomatic coronavirus disease 2019 compared with nonpregnant women using nonadmission-based, standardized clinical criteria for severe disease.

STUDY DESIGN: This is a retrospective cohort study of women aged 13 to 45 years and diagnosed as having symptomatic coronavirus disease 2019 between May 28, 2020, and July 22, 2020. The primary outcome was severe coronavirus disease 2019 as defined by 2 sets of nonadmission-based, clinical criteria: the World Health Organization Ordinal Scale for Clinical Improvement and the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Adjusted risk ratios were estimated using multivariable logistic regression analyses.

RESULTS: Of 262 women aged 13 to 45 years with symptomatic coronavirus disease 2019, 22 (8.4%) were pregnant and 240 (91.6%) were nonpregnant. After adjusting for covariates potentially associated with the primary outcome, symptomatic pregnant women were at a significantly increased risk of severe coronavirus disease 2019 compared with nonpregnant women using both the World Health Organization Ordinal Scale for Clinical Improvement (adjusted relative risk, 3.59; 95% confidence interval, 1.49–7.01) and Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (adjusted relative risk, 5.65; 95% confidence interval, 1.36–17.31) criteria.

CONCLUSION: Pregnancy significantly increases the risk of severe coronavirus disease 2019 as defined by nonadmission-based, clinical criteria.

Key words: coronavirus, COVID-19, pregnancy, SARS, SARS-CoV-2, severe COVID-19

Introduction

As of November 18, 2020, more than 11 million people have been infected with coronavirus disease 2019 (COVID-19) and 247,834 have died from the disease in the United States, less than 1 year since its discovery.[1] Of the many clinical characteristics that make combating COVID-19 challenging is the varied and sometimes rapid progression of COVID-19 infection, representing a spectrum ranging from persistently asymptomatic infection to acute respiratory failure. Among pregnant women admitted for delivery, asymptomatic infection seems to be the most common presentation of COVID-19; however, up to one-third may progress to symptomatic disease, including critical illness, during a single admission.[2]

With limited therapeutic options and no vaccine yet widely available to the general population, the focus of pandemic control has been on primary prevention and identifying those at the greatest risk of severe disease. In June 2020, the Centers for Disease Control and Prevention (CDC) included pregnancy as a risk factor for severe COVID-19 based on hospitalization rates, although their data were limited, because pregnancy status was not available for 71% of patients and admission indication was not specified.[3] Recent literature continues to support pregnancy as a risk factor for severe COVID-19.[4,5] However, the diagnosis of severe COVID-19 in these studies is heterogeneous, using primary outcomes such as intensive care unit admission or hospitalization as surrogate markers that are subject to misclassification bias in pregnant patients.

Although there is no gold standard, 2 definitions of severe COVID-19 have been published previously. Shortly after the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the classification of COVID-19 as a class B notifiable disease in China, the Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (NCPERET) set specific clinical criteria defining severe disease as a way to better describe the emerging viral illness.[6] Notably, the NCPERET criteria is the same as that recommended by the Society for Maternal-Fetal Medicine to define severe disease with the exception that dyspnea is excluded.[7] More recently, the World Health Organization (WHO) proposed an ordinal scale of clinical endpoints to facilitate interpretation and combination of results across studies and trials (https://www.who.int/teams/blueprint/covid-19). Contemporary clinical studies regarding COVID-19 have widely adopted ordinal scales similar to the WHO Ordinal Scale for Clinical Improvement (WHOOSCI) to define severe disease in nonpregnant individuals.[8–11]

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AJOG MFM at a Glance

Why was this study conducted?

This study aimed to improve the understanding of the risk of severe coronavirus disease 2019 (COVID-19) in pregnant and nonpregnant patients using nonadmission-based, clinical criteria.

Key findings

After adjusting for ethnicity and insurance type, pregnancy is associated with a substantially higher risk of severe COVID-19 among symptomatic women at the age of 13 to 45 years using 2 different sets of clinical criteria.

What does this add to what is known?

This study adds to the existing literature by applying 2 sets of widely accepted clinical criteria defining severe COVID-19 to investigate the association of pregnancy and severe disease in a cohort of inpatient and outpatient women at the age of 13 to 45 years with symptomatic COVID-19.

To better describe the relationship between pregnancy and severe COVID-19, we tested the hypothesis that pregnancy is associated with a higher risk of severe disease in symptomatic COVID-19 positive patients using 2 sets of standardized clinical criteria recommended by the NCPERET and WHO, rather than inpatient or intensive care unit admission, to define severe disease.

Materials and Methods

This is a retrospective cohort study of all women aged 13 to 45 years who had a positive SARS-CoV-2 test result by polymerase chain reaction or rapid antigen testing and were symptomatic with COVID-19 between May 28, 2020, and July 22, 2020, at a single, urban tertiary hospital. The Washington University School of Medicine Human Research Protection Office granted exemption as part of a quality improvement initiative. Patients with asymptomatic COVID-19, such as those found to have a positive test result as a part of universal testing before delivery or surgery, were excluded.

The primary outcome was severe COVID-19 defined in the following 2 ways: NCPERET criteria[6] and the WHOOSCI (https://www.who.int/teams/blueprint/covid-19). Severe COVID-19 using the NCPERET criteria is defined as dyspnea, respiratory rate of ≥30 breaths per minute, blood oxygen saturation of ≤93%, a ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2) of <300, or lung infiltrates involving >50% on imaging (Table 1). Disease severity using the WHOOSCI is determined by oxygen and organ support requirements. Scores of 5 to 7 are classified as severe disease (Table 1).

All patients with a positive SARS-CoV-2 test result during the study period were identified, and then the cohort was narrowed by sex and age. A detailed chart review of clinical notes, medical history, pregnancy status, vital signs, laboratory studies, and imaging pertaining to the index encounter after a positive test result was performed by trained staff. Patients were deemed to have severe disease based on the presence of any criteria for severe disease by either the NCPERET or WHOOSCI during the index encounter. Patients who met the criteria for severe disease were only counted once for each set of criteria, regardless of the number of criteria present for severe disease.

The primary outcome of severe disease was compared between pregnant and nonpregnant women. The presence of medical comorbidities deemed by the CDC as risk factors for severe disease (with the exception of pregnancy) was determined by chart review. Comorbidities were assessed individually, summed up to generate a composite comorbidity risk score, and compared between pregnant and nonpregnant women.[12] Baseline patient characteristics were compared using χ^2 or Fisher

TABLE 1
NCPERET and WHOOSCI criteria for severe COVID-19

NCPERET: severe disease defined as the presence of any of the following	WHOOSCI: severe disease defined as a score of ≥5–7
Dyspnea	1. No limitation of activity
Respiratory rate of ≥30 breaths/min	2. Limitation of activities
Blood oxygen saturation of ≤93%	3. Hospitalized, no oxygen therapy
PaO_2/FiO_2 ratio of <300	4. Oxygen by mask or nasal prongs
Lung infiltrates involving >50% on imaging	5. Noninvasive ventilation or high-flow oxygen use
	6. Intubation and mechanical ventilation
	7. Ventilation with additional organ support (ECMO, RRT, vasopressor use)

COVID-19, coronavirus disease 2019; *ECMO*, extracorporeal membrane oxygenation; *NCPERET*, Novel Coronavirus Pneumonia Emergency Response Epidemiology Team; *PaO2/FiO2*, arterial oxygen partial pressure to fractional inspired oxygen; *RRT*, renal replacement therapy; *WHOOSCI*, World Health Organization Ordinal Scale for Clinical Improvement.

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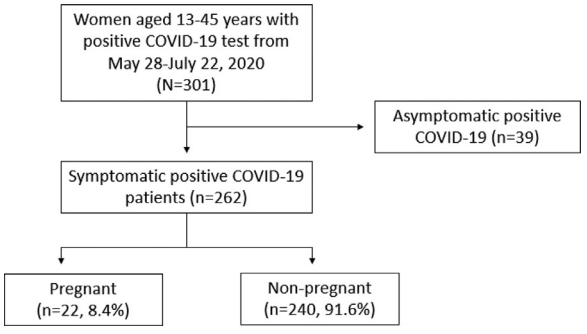
exact test for categorical variables and Student *t* test or Wilcoxon rank-sum test for continuous variables, as appropriate. The normality of distribution for continuous variables was tested using the Kolmogorov-Smirnov test. Relative risk (RR) and 95% confidence intervals (CIs) were calculated for the primary outcome using each set of clinical criteria separately. Multivariable logistic regression was used to adjust for confounders, identified as variables which had at least a 10% effect size on the RR. The Zhang method was used to approximate an adjusted RR (aRR) from the adjusted odds ratio (aOR) given the frequency of our primary outcome.[13] The final model was tested with the Hosmer-Lemeshow goodness-of-fit test. No a priori sample size estimation was performed, because all patients who met the inclusion criteria during the study period were included. Statistical analyses were performed using Stata software version 16.1 (StataCorp LLC, College Station, TX).

Results

A total of 301 patients who met the inclusion criteria had a positive test result for SARS-CoV-2 within the study period. Of those, 39 were asymptomatic (n=26, 66.6% pregnant; n=13, 33.3% nonpregnant) and excluded. Of the remaining 262 symptomatic women, 22 (8.4%) were pregnant and 240 (91.6%) were not pregnant at the time of the positive test result (Figure). Pregnant patients were more likely to be Hispanic or Latina (36.4% vs 9.6%; *P*=.001) and publicly insured (72.7% vs 38.3%; *P*=.002) (Table 2). The median gestational age of pregnant patients with symptomatic COVID-19 at diagnosis was 32.4 weeks (range, 15.7−39.6). There was no difference in gestational age between patients who had nonsevere (median, 33.1 weeks; range, 15.7−39.6) and severe COVID-19 (median, 33.2 weeks; range, 24.3−35.4; *P*=.57). There were no postpartum patients in our cohort. Nonpregnant patients were older than pregnant patients (31.0±7.8 years vs 29.4±5.9 years, respectively), although this was not statistically significant (*P*=.35). Nonpregnant patients also had a higher composite comorbidity risk score than pregnant women that did not reach statistical significance (1.0±1.1 vs 0.6±0.7; *P*=.06). The duration of clinical follow-up after a positive test result was similar between pregnant and nonpregnant patients (median and interquartile range, 15 [3−15] and 15 [0−15] days, respectively).

Among symptomatic women, 7 pregnant (31.8%) and 17 nonpregnant patients (7.1%) were classified as having severe COVID-19 using the NCPERET criteria. Using the WHOOSCI criteria, 3 pregnant (13.6%) and 6 nonpregnant patients (2.50%) were classified as having severe COVID-19. Composite comorbidity, ethnicity, and insurance type were selected as covariates for the multivariable logistic regression model given clinical and statistical significance; however, only when ethnicity and insurance remained in the final model did the Hosmer-Lemeshow goodness-of-fit test reach *P*>.05, meaning there was no significant difference between observed and expected values within the final model. After adjusting for these covariates, pregnant patients were significantly more likely to have severe disease than nonpregnant patients using both the NCPERET criteria and the WHOOSCI (aRR, 3.59; 95% CI, 1.49−7.01; and aRR, 5.65; 95% CI, 1.36−17.31, respectively) (Table 3). Although there was no significant difference in the length of stay between pregnant and nonpregnant patients, more pregnant patients with severe COVID-19 were admitted to an intensive care unit (7 [100%] vs 9 [50%], *P*=.03, and 3 [100%] vs 5 [83.3%], *P*=1.00, by the NCPERET and WHOOSCI criteria, respectively). There were no deaths in either group.

FIGURE
Flowchart of study participants



COVID-19, coronavirus disease 2019.

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Discussion

Principal finding

Among women presenting with symptomatic COVID-19, pregnancy was associated with a greater risk of severe disease by standardized NCPERET and WHOOSCI criteria than nonpregnant counterparts.

Results

Our results mirror the described clinical course of pregnant women infected with both COVID-19 and other respiratory viral illnesses (ie, influenza).[2,5,14−17] During the 2009 influenza pandemic (H1N1), pregnant women accounted for 5% of all deaths yet only represented 1% of the population, a marked disproportion in the distribution of severe disease.[15] In a systematic review of H1N1, pregnancy was demonstrated to be a risk factor for hospitalization, intensive care unit admission, and death compared with nonpregnant women of similar age.[16] Although many pregnant women with H1N1 had severe disease, pregnant women with additional comorbidities identified by the Advisory Committee on Immunization Practices as risk factors for severe disease were more likely to develop severe disease than those without additional risk factors. This is in contrast to findings from a recently

TABLE 2
Background characteristics of pregnant and nonpregnant patients with symptomatic COVID-19

Characteristic	Symptomatic pregnant patients with COVID-19 (n=22)	Symptomatic nonpregnant patients with COVID-19 (n=240)	*P* value[a]
Age, y	29.4±5.9	31.0±7.8	.35
Race			.56
White	10 (45.4)	99 (41.3)	
Black	11 (50.0)	124 (51.7)	
Asian or Pacific Islander	1 (4.6)	2 (0.8)	
American Indian	0	1 (0.4)	
Other	0	1 (0.4)	
Unable to obtain	0	13 (5.4)	
Ethnicity			.001[b]
Non-Hispanic or Latina	14 (63.6)	194 (80.8)	
Hispanic or Latina	8 (36.4)	23 (9.6)	
Unable to obtain	0	23 (9.6)	
Insurance type			.002[b]
Public	16 (72.7)	92 (38.3)	
Private	6 (27.3)	148 (61.7)	
Area deprivation index,[4] decile	6.3±2.9	5.9±3.3	.60
Obese[c]	8 (36.4)	119 (49.6)	.23
Cancer	0	4 (1.7)	.70
Renal disease[d]	1 (4.5)	7 (2.9)	.51
Transplant	0	4 (1.7)	.70
Cerebrovascular disease[e]	0	3 (1.2)	.77
Cardiovascular disease[f]	2 (9.1)	36 (15.0)	.35
Sickle cell disease	0	2 (0.8)	.84
Thalassemia	0	1 (0.4)	.92
Diabetes mellitus	1 (4.5)	17 (7.1)	.54
HIV	0	1 (0.4)	.92
Liver disease[g]	0	1 (0.42)	.92
Pulmonary disease[h]	1 (4.5)	44 (18.3)	.08
Tobacco use	0	13 (5.4)	.31
Composite comorbidity risk score	0.6±0.7	1.0±1.1	.06
Duration of follow-up, d	15 (3–15)	15 (0–15)	.06
Gestational age at diagnosis, wk	32.4 (15.7–39.6)	N/A	
Nonsevere COVID-19	33.2 (24.3–35.4)		
Severe COVID-19	33.1 (15.7–39.6)		

Data are presented as number (percentage), mean±standard deviation, or median (range).

COVID-19, coronavirus disease 2019; *N/A*, not available.

[a] Based on χ^2 or Fisher exact test for categorical variables and Student *t* test for parametric continuous variables; [b] Significant values; [c] Obese, body mass index of ≥30 kg/m^2; [d] Renal disease or chronic kidney disease; [e] Cerebrovascular disease, stroke, or dementia; [f] Cardiovascular disease, heart failure, coronary artery disease, cardiomyopathy, pulmonary hypertension, or hypertension; [g] Liver disease, alcohol-related liver disease, nonalcoholic fatty liver disease, or cirrhosis; [h] Pulmonary disease, moderate to severe asthma, chronic obstructive pulmonary disease, cystic fibrosis, pulmonary fibrosis, or other chronic lung disease.

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TABLE 3
Comparison of severe disease between pregnant and nonpregnant patients with symptomatic COVID-19

Clinical criteria for severe disease	Symptomatic pregnant patients with COVID-19 (n=22)	Symptomatic nonpregnant patients with COVID-19 (n=240)	RR (95% CI)	aRR[a] (95% CI)
Novel Coronavirus Pneumonia Emergency Response Epidemiology Team (NCPERET) criteria[6]	7 (31.8)	17 (7.1)	4.49[b] (2.09−9.64)	3.59[b] (1.49−7.01)
Dyspnea	7	18		
Respiratory rate of >30 breaths/min	7	15		
Blood oxygen saturation of ≤93%	6	15		
PaO_2/FiO_2 ratio of <300[c]	2	8		
Lung infiltrates of >50% on imaging	6	15		
WHO Ordinal Scale for Clinical Improvement (WHOOSCI)[d]	3 (13.6)	6 (2.50)	5.45[b] (1.46−20.32)	5.65[b] (1.36−17.31)
Score 5: noninvasive ventilation or high-flow oxygen	1	4		
Score 6: intubation and mechanical ventilation.	0	0		
Score 7: ventilation with additional organ support (extracorporeal membrane oxygenation, renal replacement therapy, vasopressors)	2	2		
			P value[e]	
Length of stay, d	5 (1−15)	6 (1−25)	.77	
Severe COVID-19 (NCPERET)	8 (1−15)	7 (1−29)	.94	
Severe COVID-19 (WHOOSCI)	11 (8−15)	16 (1−29)	.70	
ICU admission	8 (36.4)	9 (3.75)	<.01[b]	
Severe COVID-19 (NCPERET)	7 (100.0)	9 (50.0)	.03[b]	
Severe COVID-19 (WHOOSCI)	3 (100.0)	5 (83.3)	1.00	
Death	0	0	—	

Data are presented as number (percentage) or median (range).

aRR, adjusted relative risk; *CI*, confidence interval; *COVID-19*, coronavirus disease 2019; *ICU*, intensive care unit; *PaO_2/FiO_2*, arterial oxygen partial pressure to fractional inspired oxygen; *RR*, relative risk; *WHO*, World Health Organization.

[a] Determined using multivariable logistic regression adjusting for ethnicity and insurance type; [b] Significant values; [c] Values not available for 4 pregnant (4 of 22, 18.1%) and 8 nonpregnant patients (8 of 240, 3.3%); [d] https://www.who.int/teams/blueprint/covid-19; [e] Based on Wilcoxon rank-sum or Fisher exact test, as appropriate.

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published multicenter case-control study, in which pregnant women were found to have a greater risk of severe COVID-19 independent of select comorbidities.[17]

Our finding of pregnancy as a risk factor for severe COVID-19 is similar to several recently published studies.[5,17] In a multicenter matched case-control study, Badr et al[5] found that, compared with nonpregnant controls, pregnant women were significantly more likely to require oxygen supplementation (36.04% vs 17.24%; *P*=.006) and endotracheal intubation (10.16% vs 1.67%; *P*=.022). Although these select endpoints differ from our study, we note a similar proportion of pregnant and nonpregnant women requiring ventilation with organ support in our study, which is classified as WHOOSCI score 7 (9.1% and 1.3%, respectively). In a multicenter case-control study, Debolt et al[17] found that pregnant women were more likely to experience the composite primary outcome of death and the need for intubation, extracorporeal membrane oxygenation, noninvasive positive pressure ventilation, or supplemental oxygen via high-flow nasal cannula than nonpregnant women (aOR, 4.6; 95% CI, 1.2−18.2). Importantly, the authors highlight that although nonpregnant controls had a higher prevalence of select comorbidities, pregnancy still emerged as a risk factor for the composite primary outcome. Similarly, in our study, nonpregnant women had a higher composite comorbidity risk score than pregnant women (1.0±1.1 vs 0.6±0.7; *P*=.06).

Although this was not included in the final multivariable logistic regression model, we conclude that pregnancy is a risk factor for severe COVID-19 in symptomatic women that is likely independent of other comorbidities.

Our results add to the growing body of literature describing pregnancy as a risk factor for severe disease; however, there are important distinctions to consider. The primary outcome of severe COVID-19 was defined by 2 sets of clinical criteria in our study. Although similar findings are noted, using admission to an intensive care unit as the primary outcome for severe disease may have subjected results from previously published studies to misclassification bias given the inability to account for obligatory hospitalization during pregnancy for delivery and differential hospital protocols for admitting pregnant patients with COVID-19 to an intensive care unit.[5,18] We see this reflected in our own data, with a greater proportion of pregnant patients with severe COVID-19 defined by either the NCPERET or WHOOSCI criteria being admitted to an intensive care unit than nonpregnant patients without a significant difference in the length of stay.

In addition, most pregnant women who had a positive test result for COVID-19 during our study period were asymptomatic compared with nonpregnant patients (54.2% vs 5.1%, respectively). This is consistent with findings of previous observational studies of pregnant patients with COVID-19, likely attributed to the widespread universal testing policies on obstetrical units.[19–23] We specifically included only women symptomatic with COVID-19 in our study to minimize the risk of sampling bias, which may have affected previous studies.[5]

Clinical implications

One of the major challenges in the management of the COVID-19 pandemic is the wide spectrum in the severity of disease and the urgent need to better predict risk factors for progression.[2] The biologic plausibility of our finding of pregnancy as an independent risk factor for severe COVID-19 can be drawn from known immunologic and physiological modulations in pregnancy. The number of CD3+ T lymphocytes (CHD4+ and CD8+) and Th1 and Th2 responses to mitogenic or antigenic lymphocyte stimulation decrease during pregnancy.[24,25] After infection and replication within cells infected with SARS-CoV-2, pyroptosis (inflammation-mediated programmed cell death in response to a pathogenic stimulus) occurs, releasing damage-associated molecular proteins and stimulating a proinflammatory response.[26] T cells are attracted to the site of infection; however, because the response is modulated in the context of pregnancy, altered clearance of infected cells may favor severe disease.

Furthermore, the immunomodulatory properties of progesterone may also be implicated in the increased risk of severe disease in pregnancy. Progesterone has been shown to suppress the maternal immune response and alter the balance between Th1 and Th2 responses.[27] This shift to Th2-dominant, cell-mediated immunity is thought to be implicated in the increased severity of respiratory viral illnesses. In a mouse model of influenza A infection, treatment with progesterone resulted in a decrease of both virus-specific antibody levels and circulating CD8 + T cells.[28] When challenged with influenza A after progesterone treatment, increased severe disease was noted. In addition, physiological changes of the maternal respiratory system complicate the response to infection. Increases in minute ventilation, oxygen consumption, and chest wall compliance; reduction in expiratory reserve volume, functional residual capacity, and residual volume; and upward displacement of the maternal diaphragm all result in a decreased ability to compensate for respiratory disease.[29,30]

Together, these decreases in adaptive immunity and physiological changes of pregnancy help to explain the observed increase risk of severe COVID-19. Because the rising number of cases continues to put a strain on the demands of healthcare providers, refining the prediction of which patients are at a high risk of the development of severe disease is ever important. Pregnant women who develop symptoms from COVID-19 should be closely monitored given the risk of severe disease.

Research implications

Larger, prospective studies are needed to continue to understand the implications of severe COVID-19 in pregnancy on both maternal and neonatal outcomes. Currently, clinical criteria for defining severe COVID-19 are not universal and not specific to pregnancy. A 2-fold difference in the absolute number of patients classified as having severe disease between the NCPERET and WHOOSCI (7 vs 3 and 17 vs 6, respectively) in both the pregnant and nonpregnant groups underscores the importance of developing universally standardized definitions inclusive of pregnant women to determine the true prevalence of severe COVID-19 and to better interpret and combine results of future studies. Notably, certain NCPERET parameters were unavailable for almost half of the patients otherwise defined as having severe disease by some other criteria. The WHOOSCI was specifically introduced as criteria that do not require extensive laboratory data or radiologic information for the assessment of disease severity. Pragmatically, using such an ordinal scale will likely lead to better uniform clinical classification and thus could be more widely utilized across many populations.

Strengths and limitations

Our study used clinical criteria, not admission data, to determine severe COVID-19. We included symptomatic women with COVID-19 women who were followed up both in the inpatient and outpatient setting, improving the generalizability of our findings. We assessed for the presence of all comorbidities considered to be risk factors for severe disease by the CDC in evaluating the characteristics of our cohort. Most women were followed up for >14 days, which decreased the likelihood of misclassification bias.

This study has potential limitations that should be considered. Although the generation of results from a single, tertiary care center decreased the variability in the management of women with severe COVID-19 in our study, this may limit the broad application of our findings. Given the retrospective nature of the study design, all cases that met the inclusion criteria were included in the analyses. Although we detected a difference in the primary outcome using both sets of clinical criteria between pregnant and nonpregnant women, larger studies are needed to validate our findings.

Both the NCPERET and WHOOSCI have been applied to diverse populations in the literature; however, these clinical criteria are not without their limitations.[7–11] Lower scores on the WHOOSCI involve subjective assessment (eg, score 2, limitation of activity); however, we limited our assessment to women with scores of ≥5, which do not include assessment of activity limitation or hospitalization without requiring oxygen. The NCPERET criteria partially rely on laboratory data and radiologic assessment in qualifying severe disease, which not every patient underwent. Notably, 4 of 22 pregnant women (18.1%) had missing PaO_2/FiO_2 ratio information vs only 8 of 240 nonpregnant women (3.3%). The missing data, owing to the lack of arterial blood gas results, demonstrate a limitation of using the NCPERET criteria broadly to define severe disease. Using available data, there was a significant difference with more pregnant women having a PaO_2/FiO_2 ratio of <300 (11.1% vs 3.4%; P=.04), suggesting that pregnant women are more likely to have severe COVID-19 by the NCPERET criteria. Furthermore, the application of both sets of criteria to the same population allowed for a detailed investigation of the relationship between pregnancy and severe COVID-19. Larger studies are needed to analyze the 2 sets of criteria for convergent validity.

Conclusions

Pregnancy is an independent risk factor for severe COVID-19 in symptomatic women aged 13 to 45 years using clinical criteria irrespective of admission status. The results from this study highlight the need of careful surveillance for the development of COVID-19 symptoms in pregnant patients diagnosed as having COVID-19 and close clinical follow-up if symptoms develop for progression to severe disease. Future work in developing and validating universal criteria for the classification of severe disease, inclusive of pregnant women, is critically needed. ■

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