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.

Examining the impact of trimester of diagnosis on COVID-19 disease progression in pregnancy

Rachel C. Schell, MD; Devin A. Macias, MD; W. Holt Garner, BA; Alesha M. White, MD; Donald D. McIntire, PhD; Jessica Pruszynski, PhD; Emily H. Adhikari, MD

BACKGROUND: COVID-19 infection is associated with increased morbidity in pregnancy and adverse maternal and neonatal outcomes. Little is currently known about how the timing of infection during pregnancy affects these outcomes.

OBJECTIVE: This study aimed to evaluate the effect of trimester of COVID-19 infection on disease progression and severity in pregnant patients.

STUDY DESIGN: This was a prospective cohort study of pregnant patients diagnosed with COVID-19 infection who delivered at a single urban hospital. Universal testing for SARS-CoV-2 was performed at hospital admission and for symptomatic patients in inpatient, emergency department, and outpatient settings. Disease severity was defined as asymptomatic, mild, moderate, severe, or critical on the basis of National Institutes of Health criteria. We evaluated disease progression from asymptomatic to symptomatic infection and from asymptomatic or mild infection to moderate, severe, or critical illness, and stratified by trimester of COVID-19 diagnosis. Primary outcomes included progression of COVID-19 disease severity and a composite obstetrical outcome, which included delivery at <37 weeks, preeclampsia with severe features, abruption, excess blood loss at delivery (>500 mL for vaginal or >1000 mL for cesarean delivery), and stillbirth.

RESULTS: From March 18, 2020 to September 30, 2021, 1326 pregnant patients were diagnosed with COVID-19 and delivered at our institution, including 103 (8%) first-, 355 (27%) second-, and 868 (65%) third-trimester patients. First-trimester patients were older and had more medical comorbidities; 86% of patients in all trimesters were Hispanic. Among patients admitted within 14 days of a positive test, 3 of 18 (17%) first-trimester, 20 of 47 (43%) second-trimester, and 34 of 574 (6%) third-trimester patients were admitted for the indication of COVID-19 illness. Across all trimesters, 1195 (90%) of 1326 COVID-19 infections were asymptomatic or mild, and 45 (10%) of 436 initially asymptomatic patients developed symptoms. Of patients with asymptomatic or mild symptoms at diagnosis, 4 (4%) of 93 first-, 18 (5%) of 337 second-, and 49 (6%) of 836 third-trimester patients developed moderate, severe, or critical illness (P=.80). There was no significant difference in composite obstetrical outcome with respect to trimester of COVID-19 diagnosis (24% first-trimester, 28% second-trimester, 28% third-trimester patients; P=.69).

CONCLUSION: Moderate, severe, or critical illness develops in almost 10% of pregnant patients. The frequency of COVID-19 disease progression in pregnancy does not differ by trimester of diagnosis.

Keywords: COVID-19 disease progression, COVID-19 in pregnancy, maternal morbidity, neonatal morbidity, pandemic, SARS-CoV-2 in pregnancy, trimester of infection

Introduction

Since the outbreak of the COVID-19 pandemic in the United States in early 2020, >79 million cases have been documented with over 955,000 deaths.[1,2] An estimated 182,000 cases have been diagnosed among pregnant patients through February 2022, with 285 maternal deaths.[3] Normal pregnancy is accompanied by physiological changes that include decreased pulmonary functional residual capacity by approximately 20% to 30%, and increased oxygen consumption by 20%, leading to postulation that lower respiratory infections may be poorly tolerated, particularly in the third trimester.[4,5] Pregnant patients are known to be at increased risk of morbidity associated with influenza infection, such as the development of pneumonia, hospitalization, and need for intensive care unit admission.[5–8] It is now known that pregnant patients are at increased risk of severe to critical COVID-19–related illness compared with nonpregnant females of similar age.[9–12] This disparity seems to have been exacerbated by the recent Delta (B.1.617.2) variant surge.[13,14] Furthermore, severe COVID-19 infection in pregnancy is associated with increased risk for adverse maternal and neonatal outcomes.[15,16] However, little is currently known about how the timing of infection during pregnancy may affect these risks. With relatively low vaccine acceptance among the pregnant population compared with other demographic groups,[17] we sought to understand risks of severe illness at different gestational ages. In this study, we evaluated the effect of trimester of COVID-19 infection on disease progression. We hypothesized that the frequency of COVID-19 disease progression is increased with advancing gestational age.

Materials and Methods

This was a prospective cohort study of pregnant patients diagnosed with SARS-CoV-2 infection at a single urban healthcare system. This study was approved by the institutional review board, and a waiver of informed consent was granted because the research involved minimal risk to the patients.

Patients were included if they tested positive for COVID-19 during pregnancy and delivered at our institution between March 18, 2020 and September 30, 2021. Before May 14, 2020, testing for COVID-19 was performed on the

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AJOG MFM at a Glance

Why was this study conducted?

Little is known about whether the risk of COVID-19 disease progression is different according to trimester of diagnosis.

Key findings

The frequency of COVID-19 disease progression does not differ by trimester of infection. Moderate, severe, or critical illness develops in almost 10% of pregnant patients.

What does this add to what is known?

This study provides insight into the natural course of asymptomatic and mild COVID-19 disease in pregnancy, which may be used to effectively counsel patients. Given that patients in all trimesters of pregnancy are susceptible to infection and to severe respiratory illness from COVID-19, these findings add urgency to the need for vaccination of all pregnant individuals.

basis of symptoms or specific risk criteria, including contact with a confirmed or suspected case, incarceration or residence in a group home setting, homelessness, outside hospital transfers, or unknown results from COVID-19 testing performed at an outside facility. Beginning May 14, 2020, a universal testing protocol was implemented in our labor and delivery unit. Universal COVID-19 polymerase chain reaction (PCR) testing was performed at hospital admission, and for symptomatic patients in inpatient, emergency department (ED), and outpatient settings. Diagnosis was made by the detection of SARS-CoV-2 nucleic acid in nasal or nasopharyngeal specimens using reverse transcriptase PCR. Patients presenting for care with external positive antigen or molecular test results were included in the study cohort without repeated testing unless the patient was admitted, in which case confirmatory molecular (PCR) testing was performed. For patients with >1 documented COVID-19 infection during pregnancy, only the index infection was included in this study.

Disease severity was defined as asymptomatic, mild, moderate, severe, or critical on the basis of National Institutes of Health (NIH) criteria.[18] The gestational week of initial diagnosis was recorded, and categorized by trimester (first, <14 weeks; second, 14 to <28 weeks; or third, ≥28 weeks). Symptom severity was recorded at the time of diagnosis and followed to determine the maximum severity throughout the disease course. Outpatients were evaluated using telemedicine virtual visits with scripted evaluation of symptoms and protocol-based management including referral to the ED for worsening respiratory symptoms or obstetrical concerns. For patients admitted to the hospital within 14 days of diagnosis, the primary indication for admission was recorded as obstetrical (unrelated to COVID-19 illness), nonobstetrical (unrelated to COVID-19 illness), or COVID-19 −related illness (based on maternal symptoms). Patients admitted with multiple indications were classified as COVID-19−related if maternal symptoms alone would warrant admission (moderate, severe, or critical illness), regardless of coexistent obstetrical indications.

Management of severe or critical COVID-19 infection evolved over the study period in accordance with extant NIH therapeutic guidelines, availability of emergency use-authorized or approved therapies, and according to recommendations by specialists at our institution (Supplemental Table 1).[18] In patients with severe or critical COVID-19 infection at or near term, delivery was considered for new or worsening oxygen requirements. COVID-19 infection was not considered an indication for cesarean delivery, except as indicated by nonreassuring fetal status, or worsening maternal respiratory status with anticipated need for intubation and immediate prone positioning in the third trimester.

Among patients with SARS-CoV-2 infection during pregnancy, we evaluated disease progression, maximum disease severity, and indication for hospitalization according to trimester of diagnosis. Demographic and baseline medical characteristics were compared between patients infected in the first, second, and third trimesters of pregnancy. Maternal, obstetrical, and neonatal outcomes were obtained by matching maternal medical records to our institutional obstetrical quality database and similarly compared according to trimester. Primary outcomes included progression of COVID-19 disease severity and a composite obstetrical outcome, which included delivery at <37 weeks, preeclampsia with severe features, abruption, excess blood loss at delivery (>500 mL for vaginal or >1000 mL for cesarean delivery), and stillbirth. Secondary outcomes included preeclampsia with severe features, abruption, stillbirth, excess blood loss at delivery (>500 mL for vaginal or >1000 mL for cesarean delivery), transfusion, cesarean delivery, gestational age <37 weeks at delivery, birthweight <3rd centile, birthweight <10th centile, 5-minute Apgar <4, umbilical cord blood pH <7.0, and the need for neonatal respiratory support (ventilator or continuous positive airway pressure). A subgroup analysis was performed comparing disease severity and outcomes between patients with COVID-19 infection who were diagnosed before (March 18, 2020−May 31, 2021) and during (June 1, 2021−September 31, 2021) the Delta variant surge.

Statistics used included the Pearson chi-square and analysis of variance. Because there were >2 groups, pairwise comparisons were made including the chi-square test for categorical measures and the Student−Newman−Keuls multiple comparison test for continuous measures. Effect sizes are presented as relative risks (RRs) with 95% confidence intervals (CIs) for categorical measures. For subgroup analysis of the pre-Delta and Delta variant epochs, we used the

Cochran–Mantel–Haenszel test of the strength of association between epoch and outcome across strata of trimesters and the Breslow–Day test to evaluate the homogeneity (measured by odds ratio) of the association of epoch and outcome across trimesters. Statistical significance is achieved for *P* values <.05. Statistical analysis was performed using SAS, version 9.4 (SAS Institute, Cary, NC).

Results

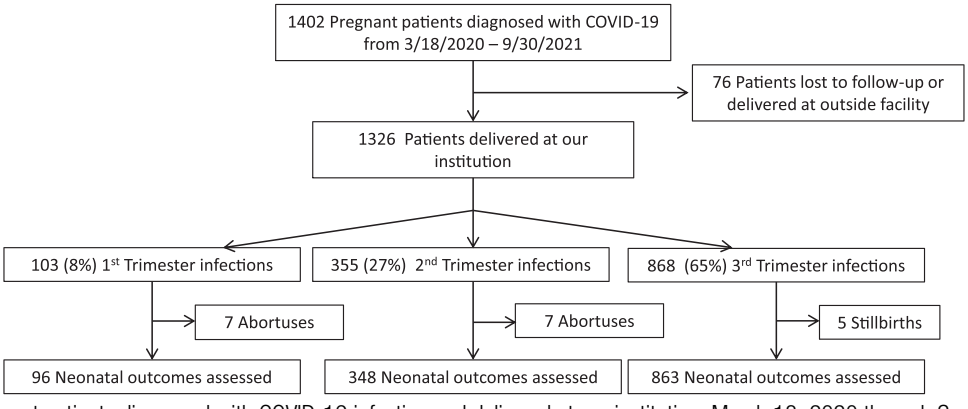
From March 18, 2020 to September 30, 2021, 20,872 pregnant patients delivered at our institution, including 1326 who tested positive for SARS-CoV-2 infection during pregnancy. At the initial positive test, there were 103 (8%) first-, 355 (27%) second-, and 868 (65%) third-trimester patients (Figure). There were no differences in race, body mass index, or parity between the trimester groups; 86% of patients in all trimesters were Hispanic. Patients diagnosed with COVID-19 in the first and second trimesters were older and more likely to have chronic hypertension or pregestational diabetes mellitus compared with patients diagnosed in the third trimester (Table 1). Among patients with COVID-19, admission within 14 days of the positive test was most frequent in patients diagnosed in the third trimester, most commonly for obstetrical indications. After excluding patients admitted for obstetrical indications, there was no difference in the frequency of admission within 14 days of diagnosis for COVID-19 among first- (3/5, 60%), second- (20/28, 74%), or third-trimester (34/56, 61%) patients (*P*=.62).

Across all trimesters, 1195 (90%) of 1326 patients with COVID-19 remained asymptomatic or mild, and 45 (10%) of 436 initially asymptomatic patients developed symptoms. Of patients with asymptomatic or mild symptoms at diagnosis, 4 (4%) of 93 first-, 18 (5%) of 337 second-, and 49 (6%) of 836 third-trimester patients developed moderate, severe, or critical illness (*P*=.80) (Table 2). Progression of symptoms from asymptomatic or mild to more severe lower respiratory tract illness (including moderate, severe, or critical illness) occurred in approximately 6% of patients overall, and was not significantly different with regard to trimester of infection.

Pregnancy loss among those with COVID-19 was more likely to occur among first- than among second-trimester patients (7 [7%] of 103 first- and 7 [2%] of 355 second-trimester; RR, 3.45; 95% CI, 1.24–9.60). Pregnancy loss occurred at a mean gestational age of 7 weeks in the first trimester and 17 weeks in the second trimester. One patient with asymptomatic COVID-19 infection in the second trimester presented 10 days later with an intrauterine fetal demise and was found to have evidence of placental SARS-CoV-2 infection on pathologic evaluation. Stillbirth occurred in 5 (0.6%) of 868 third-trimester patients; no stillbirths occurred following recovery after first- or second-trimester infection. Stillbirths occurred at a mean gestational age of 33 weeks to women with asymptomatic or mild COVID-19 illness, and were attributed to either placental abruption or vascular malperfusion. One (0.1%) patient in whom placental abruption was diagnosed was also found to have evidence of placental SARS-CoV-2 infection by immunohistochemistry.

After excluding first- and second-trimester pregnancy losses, there were no significant differences in maternal or neonatal outcomes according to trimester of COVID-19 diagnosis (Table 3). The composite obstetrical outcome (delivery at <37 weeks' gestation, preeclampsia with severe features, abruption, stillbirth, and excess blood loss [>500 mL for vaginal or >1000 mL for cesarean delivery]) occurred in 23 (24%) of 96 first-, 96 (28%) of 348 second-, and 244 (28%) of 868 third-trimester patients (*P*=.69). These rates were not significantly different when compared with patients without

FIGURE
Study cohort



Flow diagram of pregnant patients diagnosed with COVID-19 infection and delivered at our institution, March 18, 2020 through September 30, 2021.

Schell. Progression of COVID-19 by trimester. Am J Obstet Gynecol MFM 2022.

TABLE 1
Demographic characteristics among women diagnosed with COVID-19 infection in pregnancy

Characteristic	Trimester of COVID-19 diagnosis			
n	First (<14 wk) 103	Second (14–27 wk) 355	Third (>28 wk) 868	*P* value
Age, y	29.1±6.3	28.3±6.6	27.5±6.6	.01
Race/ethnicity				.82
Black, non-Hispanic	10 (10)	31 (9)	91 (10)	
White, non-Hispanic	3 (3)	9 (3)	24 (3)	
Hispanic	90 (87)	308 (87)	739 (85)	
Other	0 (0)	7 (2)	15 (2)	
Nulliparous	25 (24)	98 (28)	234 (26)	.80
Body mass index at first visit, kg/m^2	34.4±6.5	34.0±6.4	33.5±6.4	.30
Chronic hypertension	7/96 (7)	23/348 (7)	31/868 (4)	.03
Pregestational diabetes mellitus	6/96 (6)	13/348 (4)	14/868 (2)	.005
Admission within 14 d of positive test	18 (17)	46 (13)	574 (66)	<.001
Indication for admission				<.001[a]
Obstetrical	13 (72)	19 (41)	518 (90)	
COVID-19 illness	3 (17)	20 (43)	34 (6)	
Medical or surgical (non–COVID-19)	2 (11)	8 (17)	22 (4)	
Severity of symptoms at diagnosis[b]				<.001
Asymptomatic	13 (13)	42 (12)	381 (44)	
Mild	80 (78)	295 (83)	455 (52)	
Moderate	10 (10)	11 (3)	27 (3)	
Severe	0 (0)	6 (2)	5 (1)	
Critical	0 (0)	1 (0)	0 (0)	
Maximum severity of symptoms[b]				<.001
Asymptomatic	11 (11)	36 (10)	344 (40)	
Mild	78 (76)	283 (80)	443 (51)	
Moderate	11 (11)	21 (6)	35 (4)	
Severe	1 (1)	7 (2)	37 (4)	
Critical	2 (2)	8 (2)	9 (1)	

Data are shown as number (percentage) or mean±standard deviation, as appropriate.

RR, respiratory rate.

[a] When obstetrical admissions are excluded for all trimesters, *P*=.62; [b] Severity Scale: Mild: flu-like illness, such as fever, cough, myalgias, and new loss of smell/taste without clinical lung findings; RR <30 and no lower respiratory tract involvement; Moderate: lower respiratory tract disease on clinical assessment (objective dyspnea, crackles, chest x-ray findings); persistent fever of ≥39.0°C; SpO2 >93% and RR <30 on room air; Severe: RR >30/min; SpO2 ≤93% on room air; oxygen requirement; arterial blood gas ratio of PaO_2:FiO2 < 300; Critical: high-flow nasal cannula; mechanical ventilation; multiorgan failure or dysfunction.

Schell. Progression of COVID-19 by trimester. Am J Obstet Gynecol MFM 2022.

COVID-19 who delivered at our institution during the same period (30%; *P*=.14). Risk of neonatal birthweight <third percentile for gestational age did not differ for patients diagnosed in the second vs third trimester (RR, 1.10; 95% CI, 0.55–2.20).

Following the initiation of COVID-19 vaccination at our institution in January 2021, 6% of patients were vaccinated before being diagnosed with COVID-19, accounting for 7% of asymptomatic or mild infections and 4% of moderate, severe, or critical disease. This difference in vaccination status was not significant (*P*=.75). Overall, 83% of patients diagnosed with COVID-19 were not vaccinated before delivery (Supplemental Table 2).

A subgroup analysis comparing disease severity and outcomes between

TABLE 2
Progression of COVID-19 illness diagnosed during pregnancy

	Maximum severity of symptoms[a]					
Symptoms at initial positive test	Asymptomatic	Mild	Moderate	Severe	Critical	Total
Asymptomatic	391 (90)	31 (7)	3 (0.6)	7 (1.6)	4 (0.9)	436
Mild	—	773 (93)	31 (3.7)	21 (2.5)	5 (0.6)	830
Moderate	—	—	33 (69)	11 (23)	4 (8)	48
Severe	—	—	—	6 (55)	5 (45)	11
Critical	—	—	—	—	1 (100)	1
Total	391 (29)	804 (61)	67 (5)	45 (3)	19 (1)	1326

	Trimester of COVID-19 diagnosis				
Progression of symptoms	First (<14 wk)	Second (14–27 wk)	Third (≥28 wk)	All	*P* value
Asymptomatic to any symptoms	2/13 (15)	6/42 (14)	37/381 (10)	45/436 (10)	.54
Asymptomatic/mild to moderate/severe/critical	4/93 (4)	18/337 (5)	49/836 (6)	71/1266 (6)	.80
Total	67	309	716	1092	

Data are shown as number (percentage).

RR, respiratory rate.

[a] Severity Scale: Mild: flu-like illness, such as fever, cough, myalgias, and new loss of smell/taste without clinical lung findings; RR <30 and no lower respiratory tract involvement; Moderate: lower respiratory tract disease on clinical assessment (objective dyspnea, crackles, chest x-ray findings); persistent fever of ≥39.0°C; SpO2 >93% and RR <30 on room air; Severe: RR >30/min; SpO2 ≤93% on room air; oxygen requirement; arterial blood gas ratio of PaO_2:FiO2 <300; Critical: high-flow nasal cannula; mechanical ventilation; multiorgan failure or dysfunction.

Schell. Progression of COVID-19 by trimester. Am J Obstet Gynecol MFM 2022.

patients with COVID-19 diagnosed before (March 18, 2020–May 31, 2021) and during (June 1, 2021–September 30, 2021) the recent Delta variant surge revealed an increased prevalence of severe or critical illness during the Delta epoch (4.4% pre-Delta vs 7.9% Delta; *P*=.02). This difference was most pronounced in patients diagnosed in the third trimester (4.6% pre-Delta vs 8.5% Delta; *P*=.05). Although not statistically significant, the progression of symptoms from asymptomatic or mild to moderate, severe, or critical illness was increased in the Delta epoch (5% pre-Delta vs 9% Delta; *P*=.059). The risk of progression was not altered by trimester of diagnosis. There were no statistically significant differences in the composite obstetrical outcome between epochs (27.0% pre-Delta vs 34.0% Delta; *P*=.09). No stillbirths occurred among patients delivering at our institution following diagnosis during the Delta variant surge, although not all patients diagnosed during the Delta surge have delivered.

Comment

Principal findings

The risk of COVID-19 disease progression in pregnancy did not differ by trimester of diagnosis. Overall, moderate, severe, or critical illness developed in nearly 10% of pregnant patients in a primarily urban Hispanic cohort. Among patients who were asymptomatic at the time of diagnosis, 10% developed symptoms of any severity. Of patients who were initially asymptomatic or had mild symptoms, approximately 5% developed moderate, severe, or critical symptoms.

Results in the context of what is known

It has previously been demonstrated that pregnant patients are at greater risk of developing severe illness in the setting of COVID-19 infection compared with their nonpregnant counterparts.[9–12] Although rates of severe or critical illness in our cohort (10%) are comparable with rates reported by Metz et al[16] (20%), and with those of previous studies in our population (9%),[19] our rates were lower than those reported by others whose studies included only hospitalized patients or those with symptomatic illness.[9,10,12,14] By including asymptomatic infections and patients diagnosed in the outpatient setting or with an external positive test, our cohort may be more representative of generalized community transmission. The increase in severe and critical illness during the Delta surge is consistent with previous studies from our institution and other centers.[13,14] The difference in absolute numbers likely reflects patient ascertainment and inclusion: our cohort included outpatients and asymptomatic patients while excluding those who were diagnosed but remained undelivered during the study period. Importantly, the rates of disease progression did not differ significantly with regard to the trimester of infection, highlighting the susceptibility of pregnant patients to severe COVID-19–related illness throughout pregnancy.

Ethnic disparity in diagnosed cases was evident, with 86% of pregnant

TABLE 3
Obstetrical and neonatal outcomes among pregnancies complicated by COVID-19 infection during first, second, and third trimesters

Characteristic, n	First trimester (<14 wk), 96	Second trimester (14-27), 348	Third trimester (≥28 wk), 868	*P* value
Composite[a]	23 (24)	96 (28)	244 (28)	.69
Maternal				
Preeclampsia with severe features	10 (10)	41 (12)	95 (11)	.89
Abruption	0 (0)	1 (0)	4 (0)	.74
Stillbirth	0 (0)	0 (0)	5 (0.6)	.28
Excess blood loss at delivery	15 (16)	44 (13)	116 (13)	.75
Transfusion	5 (5)	14 (4)	40 (5)	.85
Cesarean delivery	23 (24)	128 (37)	285 (33)	.06
Neonatal				
Gestational age <37 wk	8 (8)	44 (13)	102 (12)	.51
Birthweight <3rd centile	1 (1)	11/341 (3)	25/849 (3)	.52
Birthweight <10th centile	4 (4)	34/341 (10)	86/849 (10)	.17
5-min Apgar <4	0 (0)	0/341 (0)	1/849 (0)	.77
Umbilical cord blood pH <7.0	0/88 (0)	3/321 (1)	5/790 (1)	.62
Respiratory support (ventilator or CPAP)	6 (6)	12/341 (4)	31/849 (4)	.43
Infant positive for COVID-19[b]	0 (0)	0 (0)	20 (2.3)	.005

Data are shown as number (percentage) or mean±standard deviation, as appropriate.

CPAP, continuous positive airway pressure.

[a] Includes delivery at <37 weeks, preeclampsia with severe features, abruption, stillbirth, and excess blood loss (>500 mL for vaginal or >1000 mL for cesarean delivery); [b] Infants were tested if maternal infection was diagnosed within 4 weeks of delivery, or for other clinical suspicion.

Schell. Progression of COVID-19 by trimester. Am J Obstet Gynecol MFM 2022.

patients with COVID-19 of Hispanic ethnicity, compared with 75% of the pregnant population at our institution.[19] This racial disparity was similarly reported by Zambrano et al[12] and is consistent with nationwide data on racial and ethnic disparities in COVID-19 cases and deaths.[20]

COVID-19 infection in pregnancy has been associated with an increased risk of maternal and neonatal complications.[14–16] Previously reported rates of stillbirth, cesarean delivery, and preterm birth were higher than those reported in our study.[14–16] Furthermore, we demonstrated no increased risk of adverse maternal and neonatal outcomes in patients with COVID-19 infection. Again, differences in these reported outcomes are likely related to differences in the cohort, with previous studies focused on hospitalized or symptomatic patients. The stillbirth rate of 0.6% in our cohort with COVID-19 infection is consistent with general population rates of stillbirth. Although lower than the stillbirth rate of 1.26% reported by DeSisto et al,[15] our cohort included patients who recovered from COVID-19 before the delivery hospitalization. The rate of adverse maternal and neonatal outcomes was not affected by the trimester of COVID-19 infection, suggesting that infection early in pregnancy does not affect delivery outcomes except in rare cases. We did not stratify morbidity by severity of COVID-19 infection in this study because numbers of patients with severe illness are small, and the threshold for delivery changes as gestation advances.

Clinical implications

This study investigated the impact of the trimester of SARS-CoV-2 diagnosis on both disease progression and adverse maternal and neonatal outcomes. Although the adaptive changes to respiratory physiology evolve as pregnancy advances and likely contribute to potential respiratory failure in the setting of third-trimester pulmonary infection, it is less clear to what degree immunologic mechanisms (both normal and pathologic) may also contribute to severe pneumonia or acute respiratory distress syndrome even in the first trimester.[21] Pregnant patients are susceptible to COVID-19 infection throughout pregnancy, emphasizing the importance of preventive measures (eg, masking, hand hygiene, and social distancing) and vaccination as early as possible in pregnancy or before conception.[22–24]

Furthermore, although much of the current literature focuses on hospitalized patients with COVID-19 infection and those with severe or critical illness, our study provides important

information regarding the natural history of initially asymptomatic or mild COVID-19 infection. This information is important for counseling both patients diagnosed with COVID-19 infection in pregnancy, and those with vaccine hesitancy but no evidence of infection.

Research implications

Our study was not able to assess the impact of severe or critical illness in each trimester on overall pregnancy outcomes, and larger sample sizes would be required to evaluate these effects. As vaccination rates increase in the pregnant population, further research is needed to understand the progression of disease in breakthrough cases. Similarly, disease severity and progression should be studied further in the setting of evolving medical therapies and the evolution of new SARS-CoV-2 variants and recurrent infection.

Strengths and limitations

Our study has limitations. First, potential ascertainment bias exists for any study where diagnosis is dependent on testing practices and where infection may be asymptomatic. As in other institutions with universal testing at delivery, third-trimester patients had increased opportunities for testing and diagnosis of asymptomatic SARS-CoV-2 infection.[9,16] In addition, although we included patients with external tests who delivered, we did not include patients initially diagnosed in our system who delivered at other area hospitals. Therefore, underascertainment of severe or critical illness or of adverse pregnancy outcomes was possible. This may be balanced by potential underascertainment of mild infections never diagnosed or reported, particularly in the first and second trimesters. Thus, it is possible that disease progression may have actually been lower than observed in the first and second trimesters.

Differences in age and baseline medical comorbidities between trimester groups likely reflect increased medical management needs in early pregnancy, but also may have contributed to type 2 error, or failure to detect a true difference in frequency of disease progression. However, although we were unable to determine whether risk factors for infection differed between these trimester groups in our patient population, other demographic characteristics such as ethnicity were remarkably similar between groups, which may suggest similar social practices and thus transmission risks. Furthermore, type 2 error may have also occurred because of relatively low numbers of adverse outcomes in this observational cohort.

Finally, patients infected with the Delta variant who did not deliver before September 30, 2021 were not included in the study. Patients diagnosed in the third trimester in both epochs were more likely delivered within the same epoch, and therefore more likely to represent true pre-Delta and Delta variant differences.

Strengths of our study include large numbers from a single institution with consistent testing practices, and inclusion of outpatients, those with external tests, and those diagnosed in the ED. Treatment protocols in place at our institution allow for consistent practices for managing pregnant women with both mild and severe disease, making potential differences in outcomes more likely to be owing to measurable factors rather than erratic management practices.

Conclusions

The frequency of COVID-19 disease progression does not differ by trimester of diagnosis. Moderate, severe, or critical illness develops in almost 10% of pregnant patients infected with the SARS-CoV-2 virus. These results highlight the importance of preventive measures, including COVID-19 vaccination before or as early as possible during pregnancy. ■

Supplementary materials

Supplementary material associated with this article can be found in the online version, at doi:10.1016/j.ajogmf.2022.100729.

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Author and article information

From the Department of Obstetrics and Gynecology, The University of Texas Southwestern Medical Center, Dallas, TX (Drs Schell, Macias, White, McIntire, Pruszynski, and Adhikari); Parkland Health, Dallas, TX (Drs Schell, Macias, White, and Adhikari); School of Medicine, The University of Texas Southwestern Medical Center, Dallas, TX (Mr Garner).

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Corresponding author: Rachel C. Schell, MD. Rachel.Schell@UTSouthwestern.edu