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Initial review of pregnancy and neonatal outcomes of pregnant women with COVID-19 infection

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Abstract

Objectives: Data regarding the pathogenesis and clinical manifestations of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continue to emerge, however, there's limited data in regard to maternal and neonatal outcomes. Therefore, we conducted a retrospective analysis of all pregnant women who tested positive for SARS-CoV-2 within Nuvance Health system.

Methods: Data were abstracted from the medical records of each patient and descriptive analysis was performed. Variables included demographics, COVID testing results, symptoms, management, labor course, neonatal information, and complications.

Results: Total of 40 patients were identified. Average age was 29.6 years old, 35% were Hispanic, and approximately one in three patients had comorbidities. Of the patients who had repeated testing, the average number of days between first positive test and negative test was 36.8 days (± 19.9 days). Three out of four women reported symptoms. Of the 40 pregnant women who were positive for SARS-CoV-2, 25 of them delivered. About 84% of the women delivered after 37 weeks. Twelve percent of the women delivered under 33 and 6/7 weeks. Most patients had vaginal deliveries (68%) and the remaining had cesarean deliveries. Neonatal outcomes included: mean 1 and 5 min Apgar scores of 8 and 8.8, respectively and the

mean birth weight was 3212 g. Twenty neonates were tested for SARS-CoV-2 and were all found to be negative.

Conclusions: Overall, with routine prenatal care and preventive measures, pregnant patients and neonates in our study had good outcomes. At this time, there appears to be no evidence of vertical transmission.

Keywords: COVID-19; coronavirus; COVID in pregnancy; neonatal outcomes; COVID-19 in neonates; fetus; ethics; maternal outcomes; synthesis.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus which was initially identified in Wuhan, Hubei Province, China resulting in a pandemic. The disease produced by the virus is termed coronavirus disease (COVID-19) [1]. As of June 20, 2020, COVID-19 has affected 188 countries/regions and there have been 8,733,136 confirmed cases worldwide, with the highest proportion of cases occurring in the United States [2]. The incidence of SARS-CoV-2 cases in Connecticut continues to increase due to its proximity to New York City especially Fairfield county which has a prevalence rate of 1,741 cases per 100,000 and 1,355 total deaths, as of June 17, 2020 [3]. Dutchess and Putnam are New York counties that border Western Connecticut. The prevalence rate of COVID-19 in Dutchess and Putnam county are 1,557 and 1,469 per 100,000 cases, respectively. The Center for Disease Control and Prevention (CDC) recently reported a total of 12,969 cases and 35 deaths of pregnant women with COVID-19 in the United States [3].

Data regarding the pathogenesis and clinical manifestations of the virus continue to emerge, however, there is insufficient data on the clinical course of the disease in pregnant women. Early cases reported a range of symptoms including fever, dry cough, myalgia, fatigue, and respiratory distress [4]. Treatment options include several investigational drugs such as Remdesivir, tocilizumab, and convalescent plasma. However, the efficacy of these drugs has yet to be determined in pregnant women [5]. Of late, hydroxychloroquine and lopinavir/ritonavir are not recommended for treatment of COVID-19 except in clinical trials [6].

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The current data is limited in regard to at risk populations, maternal outcomes, neonatal outcomes, and intrapartum course. To address the information gaps regarding pregnant women and neonates, we performed a retrospective review of all pregnant women who tested positive for SARS-CoV-2 during the designated study period. This observational study aimed to identify trends in the clinical presentation and outcome of pregnant women with COVID-19 infection.

Materials and methods

Study design and participants

We conducted a retrospective cohort study of patients from four large, acute care hospitals in the Nuvance Health System. The study received exempt determination from the Biomedical Research Alliance of New York Institutional Review Board and the Vassar Brothers Medical Center Institutional Review Board.

The study included pregnant women 18 years or older with a diagnosis of COVID-19 (ICD 10 codes B97.29, J12.89, J18.9, U07.1) between March 17, 2020 and June 4, 2020 who were evaluated in several units (emergency department, outpatient clinic, inpatient, or labor and delivery). Pregnancy status was defined as a documented current 'pregnant' status in the problem list. Patients were excluded if they did not have a documented positive lab result for COVID-19. Women were identified by a data analytics weekly report in the Nuvance Health medical record system with a quality assurance review completed by a third-party research assistant. Testing for SARS-CoV-2 was performed using polymerase chain reaction (PCR) of a nasopharyngeal or nasal swab by either the hospital internal lab or Sunrise Laboratory. Testing was performed on admission to the labor and delivery unit, outpatient setting, and/or inpatient hospitalization.

Variables

Data were obtained through medical record abstraction. The variables included age, race, body mass index (BMI), positive COVID-19 status before delivery, rapid testing upon admission for delivery, retest COVID-19 information, known negative COVID-19 tests, viral symptoms, respiratory symptoms, COVID-19 related medications and illness complications, imaging results and obstetrics history. Race/ethnicity was defined as White, Black or African American, Hispanic, or other (undefined in medical chart). Treatment-related variables included the need for hospital admission, mechanical ventilation, oxygen requirements, biologic infusions, and treatment with antibiotics. For patients who delivered, we collected data regarding the mode of delivery, delivery course, neonatal birth weight, Apgar score, and neonatal SARS-CoV-2 test results.

Statistics

We computed descriptive statistics as percentages of the total for dichotomous and categorical variables and mean with standard deviation for continuous variables

Results

About 1,246 pregnant women delivered during the study timeframe. Forty women were identified as 18 years or older, pregnant, and positive for SARS-CoV-2. Descriptive statistics for the full sample is shown in Table 1. Among women who tested positive, the mean age was 29.6 years and with the highest proportion of women reporting Hispanic (35%) or non-Hispanic White (27.5%) race/ethnicity. The average body mass index (BMI) was 31.8. Over half of the women were multiparous (62.5%), 22.5% were nulliparous, and parity was unknown in 15% of patients due to evaluation and treatment occurring in an emergency room without a complete obstetrics history performed. During the study period, 32.5% of women presented with comorbidities with the most common diagnosis being pre-existing diabetes (10%) and gestational diabetes A1 (10%). Two women had preeclampsia without severe features and an additional two were asthmatic.

Within this population of COVID-19 positive patients, 12 had repeat testing for COVID-19 either during their delivery admission or on an outpatient basis. Of these 12, 11 tested negative and the average number of days between re-testing was 36.8 days with a range of 15–74 days. One woman received the PCR nasopharyngeal swab five times and was positive each test spanning 48 days. Seventy five percent of women reported at least one symptom due to COVID-19, with the remaining 25% being asymptomatic. The symptoms experienced by pregnant women included loss of smell and taste, nausea, vomiting, body aches, chills, headache, fever, dry cough, shortness of breath, abdominal pain, difficulty breathing, and chest pain. Results of chest imaging by radiograph or computed tomography results were reported for nine women, with findings of lower lobe opacity (n=1), linear opacity in lower lung (n=1), bilateral infiltrate (n=3), bilateral opacification (n=2), and pneumonia (n=2). In reviewing the lab results of the women, lymphocytopenia was a common finding on admission in 44% of patients, and additionally there were elevated levels of C-reactive protein (CRP) in a similar number of patients.

Notable treatment courses for pregnant women with COVID-19 include two patients who received convalescent plasma and four who received supplemental oxygen due to respiratory distress. Both women who received convalescent plasma also received supplemental oxygen and were found to have bilateral opacification on chest imaging. In this study, there were no women requiring intubation or ICU admission. COVID-19 medications prescribed for this population include seven women

Table 1: Demographic characteristics of COVID-19 pregnant patients.

Characteristics	Mean (SD)
Total pregnant positive patients, n=40	
Age, years	29.6 (6.03)
BMI, kg/m ²	31.8 (6.63)
Characteristics	No. (%)
BMI	
< 18.5	0
18.5–24.9	6 (15.0)
25–29.9	12 (30)
≥30	22 (55)
Age, years	
<30	20 (50.0)
30–34	8 (20.0)
≥ 35	12 (30.0)
Race	
Hispanic	14 (35)
White	11 (27.5)
Black/African American	5 (12.5)
Other ^a	10 (25)
Parity	
Nulliparous	9 (22.5)
1–3	23 (57.5)
>3	2 (5.0)
Unknown	6 (15.0)
Medical history	
No comorbidities	24 (60.0)
Asthma	2 (5.0)
Chronic hypertension	1 (2.5)
Preeclampsia w/o severe features	2 (5)
Pre-existing diabetes	4 (10.0)
Gestational diabetes A1	4 (10.0)
Gestational diabetes A2	1 (1.25)
Sarcoidosis	1 (2.5)
Anemia	1 (2.5)
Hashimoto's disease	1 (2.5)

Total COVID-19 positive pregnant women=40. SD, standard deviation.

^aOther includes Asian or does not identify.

receiving lovenox for venous thromboembolism prophylaxis, five women receiving azithromycin, and four receiving hydroxychloroquine. Two of the four women on hydroxychloroquine also received lopinavir/ritonavir (Table 2).

Obstetrical outcomes

Of the 40 pregnant women who were positive for SARS-CoV-2, 25 delivered during the study time frame, with one woman having no labor and delivery information available (Table 3). Of the 25 women that delivered, 80%

Table 2: COVID-19 clinical features and testing trends of all pregnant patients.

COVID-19 clinical characteristics	no. (%)
Symptomatic patients	30 (75)
Asymptomatic patients	10 (25)
Medical treatment	
Supplemental oxygen	4 (10)
Convalescent plasma	2 (5)
Azithromycin	5 (12)
Hydroxychloroquine	4 (10)
Lopinavir/Ritonavir	2 (5)
Lovenox	7 (17.5)
Vitamin C	1 (2.5)
Ceftriaxone	2 (5)
SARS-CoV-2 testing trends	
Patients with repeat SARS-CoV-2 testing	n=12
Repeat test result	
Positive	1
Negative	11
Days between first positive and negative test, mean (SD)	36.8 (19.9)

^aPatients may be on multiple medications.

were COVID-19 positive at the time of admission. While the remaining 20% had a recent history of a positive COVID-19 test, however they tested negative during their labor hospitalization. Eighteen out of the 25 (72%) women were asymptomatic on admission to the labor and delivery unit. On admission for delivery, 7 (28%) women experienced active symptoms of SARS-CoV-2 and 21 of the 25 women (84%) delivered after 37 and 0/7 weeks gestation. One patient delivered between 34 and 0/7 weeks and 36 and 6/7 weeks. Three patients delivered under 33 and 6/7 weeks. Two patients had spontaneous second trimester fetal loss. The cases included fetal demise at 17 and 4/7 weeks and demise of twins at 20 and 4/7 weeks.

Seventeen of the 25 women (68%) had vaginal deliveries. The remaining eight women (32%) had cesarean deliveries. Of the women with cesarean deliveries, 4 (50%) women tested positive on admission, 2 (25%) experienced symptoms at the time of admission, and one needed supplemental oxygen due to the risk of respiratory decompensation. The indication for cesarean delivery was primarily due to non-reassuring fetal heart tracing (NRFHT) (37.5%) and history of previous cesarean delivery (50%). One patient had cesarean section for risk of respiratory decompensation. All three patients who had a cesarean delivery for NRFHT were asymptomatic during their labor. Furthermore, the modes of delivery were similar between the women that had symptoms and those without symptoms at the time of delivery. There were 9 (36%) women that had a vaginal delivery and were symptomatic while there were 8 (32%) women who were

Table 3: Obstetrical outcomes of COVID-19 positive women who delivered.

Outcomes	no. (%)
Covid-19 positive women who delivered, n=25	
Positive COVID-19 test prior to delivery ^a	13 (52)
Gestational age at delivery	
≥41 0/7	1 (4)
37 0/7 to 40 6/7	20 (80)
34 0/7 to 36 6/7	1 (4)
<33 6.7	3 (12)
Mode of delivery	
Vaginal delivery	17 (68)
Cesarean delivery	8 (32)
Indication for cesarean delivery	
Non-reassuring fetal heart tracing	3 (37.5)
History of previous cesarean delivery	4 (50)
Risk of respiratory decompensation	1 (12.5)
Complications	
Postpartum hemorrhage	2 (8)
Second trimester fetal loss	2 (8)

^aSome patients tested positive prior to delivery and testing was repeated during delivery hospitalization or initial testing was performed during delivery hospitalization.

asymptomatic with a vaginal delivery. Alternatively, 6 (24%) of the women who had a cesarean section were symptomatic, while 2 (8%) women were asymptomatic at the time of the cesarean section. Two patients were reported to have deliveries complicated by postpartum hemorrhage.

Neonatal outcomes

Of the 25 women who had a live birth, 23 had viable neonates (Table 4). The mean 1 and 5 min Apgar scores were 8 and 8.8, respectively. The mean birth weight was 3212 g. Of the 23 neonates, 20 were tested for SARS-CoV-2 and were all found to be negative. Three of the neonates were not tested. Preterm delivery at 28 and 2/7 weeks with apnea of prematurity and hyperbilirubinemia requiring phototherapy were the two neonatal complications noted.

Discussion

As of this publication there have been over 2.3 million cases of SARS-CoV-2 infections in the United States and over 120,000 deaths [2]. As the global pandemic develops, more research on maternal, fetal and obstetric outcomes is vitally important due to the novel nature of this virus and the disease it causes. Detailed here is a retrospective

Table 4: Neonatal outcomes of neonates born to women with COVID-19 infection.

Outcomes	Mean (SD)
1-min Apgar score	8.0 (1.6)
5-min Apgar score	8.8 (0.67)
Birthweight (g)	3212.0 (582.2)
Neonatal testing for COVID-19	no.
Negative	20
Positive	0
Not tested	3
Complications	no.
Preterm delivery, apnea of prematurity	1
Hyperbilirubinemia	1

Total viable neonates, n=23. SD, standard deviation.

descriptive review of these outcomes across a diverse regional medical system in Connecticut and New York states. This review, like others on COVID-19 infection during pregnancy, are advantageous for describing clinical findings but are limited in their ability to determine causation.

Clinical features of COVID-19 infection in all pregnancies

Current evidence on the impact of COVID-19 in pregnant women and on neonatal outcomes is limited by the emergent nature of the pandemic and the comparatively limited number of SARS-CoV-2 positive patients as demonstrated in our study. Notable patient characteristics in our study of pregnant women with COVID-19 infection include young maternal age, high BMI, and Hispanic ethnicity. About one third of the pregnant women identified as Hispanic were COVID-19 positive. The CDC also reported similar rates in which 5,141 of the 12,969 (39.6%) pregnant women with COVID-19 in the nation were Hispanic or Latino [3]. The high prevalence may be related to inequities in social determinants of health and essential work occupations in the Hispanic population. Furthermore, half of the patients were less than 30 years old, which is likely due to average childbearing age in our study population. Large-scale empirical research will lead to the identification of risk factors for poor outcomes for pregnant women.

The most commonly reported symptom was dry cough, fever, and shortness of breath, which was similar to symptoms reported by Yan et al [7]. Several of the women with respiratory distress received hydroxychloroquine and two women received convalescent plasma. Hydroxychloroquine was used in this study prior

to the recent recommendation to avoid use of the medication unless in a hospital or clinical trial because the efficacy is unclear at this time and due to the adverse effects of arrhythmia. In our study, two of the patients' symptoms improved after starting hydroxychloroquine and lopinavir/ritonavir and there were no arrhythmias noted on electrocardiogram (EKG). Additionally, evidence for convalescent plasma therapy is emerging. A systematic review showed that convalescent plasma use may decrease viral load and increase levels of neutralizing antibodies [8].

Previous case series have noted that the clinical course of patients with COVID-19 infection were similar to their non-pregnant counterparts [7]. In one of the largest expanded case series on pregnant patients with COVID-19, 8 of 116 patients developed severe pneumonia requiring ICU admission and two of these patients required mechanical ventilation [7]. There were no maternal deaths in this study. In our study, we noted no cases of severe COVID-19 infection requiring ICU admission and no patients required mechanical ventilation. The women presenting with respiratory distress were treated promptly with oxygen and plasma therapy leading to avoidance of admission to the ICU. Furthermore, lymphocytopenia was a common finding, and additionally there were elevated levels of C-reactive protein (CRP) in a similar number of patients. Lymphopenia may be due to viral infection of lymphocytes or apoptosis by inflammatory cytokines [9]. CRP is a marker of inflammation and has been found to be elevated in patients with COVID-19 infection which may be a biomarker for disease severity [10].

Obstetrical outcomes of patients who delivered

A total of 25 patients with COVID-19 infection delivered. Two of the patients had preterm deliveries at 28 and 2/7 weeks and 35 and 0/7 weeks. Two of the patients had a spontaneous second trimester loss. It cannot be confirmed if the loss of the fetuses was related to COVID-19. Both patients were asymptomatic and the fetuses were not tested. Furthermore, one of the patients had no prenatal care. A study by Schwartz reported cases of preterm delivery in COVID-19 patients; however, there is no current evidence that COVID-19 increases risk of miscarriages [11]. In regard to the mode of delivery, most patients in our study had vaginal deliveries while 32% of the patients had cesarean deliveries. The indications for cesarean delivery were primarily for non-reassuring fetal heart tracing and previous cesarean delivery. One patient had a cesarean delivery secondary to acute hypoxic

respiratory failure requiring supplemental oxygenation and convalescent plasma therapy. This patient was nulliparous and presented at 37 and 3/7 weeks with eight days shortness of breath, fever along with significant transaminitis, and the chest X-ray showed bilateral opacifications. Fetal status was reassuring at the time, however cesarean delivery was performed due to worsening dyspnea and remote from delivery. Plasma therapy was initiated due to hypoxia and concern for respiratory decompensation especially given risk factors including morbid obesity and diabetes. In a study of seven pregnant women with COVID-19 pneumonia in Wuhan, China all patients had cesarean deliveries [12]. The indication for cesarean delivery in that study is unclear however all the patients required oxygen and antiviral therapy. The Society of Maternal Fetal Medicine (SMFM) recommends that mode of delivery should be based on routine indications [5]. However, cesarean delivery may be warranted if maternal status is deteriorating and the patient is remote from delivery. Currently, there is no data comparing obstetrical complications between pregnant women with COVID-19 and pregnant women without COVID-19 infection. However, there's no evidence at this time that pregnant women are susceptible to severe pneumonia in comparison to non-pregnant women [7]. However, pregnant women are more likely to be hospitalized than non-pregnant women and the risk of death is similar for both [3].

Neonatal outcomes

There is limited data on the effect of COVID-19 on neonates. To date, there is no evidence of vertical transmission of COVID-19. There is one case report of a woman with COVID-19 whose neonate tested positive for SARS-CoV-2 [13]. However, the neonate was swabbed at about 30 hours old. It is unclear if horizontal transmission occurred via exposure to respiratory droplets while breastfeeding. Also, there was no testing of cord blood or placenta therefore intrauterine transmission cannot be confirmed. Our study demonstrated that all 20 neonates tested negative which is similar to prior studies [14, 15]. Furthermore, placental pathology did not detect COVID-19 infection. At this time, vertical transmission is unlikely, however it is inconclusive and further efforts are needed to analyze amniotic fluid, breast milk, and umbilical cord for the presence of SARS-CoV-2.

The Apgar scores and birth weights of the neonates in our study were reassuring and within normal limits. Neonatal complications were also minimal which included

apnea of prematurity and hyperbilirubinemia. Both of the neonates with complications were born by women who were asymptomatic. It is unclear if these complications are associated with COVID-19 infection or are unrelated events. A case report of pregnant women with COVID-19 infection showed that none of the three infants developed serious symptoms [16]. Two infants had a rash that spontaneously resolved and one had mild dyspnea. Overall, the neonates in our study had similarly good outcomes.

Conclusions

Limitations of this study include small sample size due to limited numbers of COVID-19 positive pregnant patients in the health system. Nevertheless, our study presents a retrospective cohort study with valuable information on maternal, neonatal and obstetric outcomes related to COVID-19. In our study, we note a higher prevalence of COVID-19 infection in Hispanic pregnant women similar to rates reported by the CDC. Furthermore, with routine intrapartum care and preventive measures, women with COVID-19 infection had overall good maternal outcomes. Neonatal outcomes were also good without evidence of vertical transmission of COVID-19. However, further studies are needed to analyze amniotic fluid, breast milk, and umbilical cord samples. Long-term follow-up is warranted to determine if pregnant women are more susceptible to COVID-19 infection and comparison of outcomes between pregnant women with and without COVID-19 infection.

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