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Clinical characteristics and perinatal outcomes of pregnant women with Coronavirus-19 disease

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Abstract

Objective: The aim of this study was to evaluate the maternal and perinatal outcomes of COVID-19 infection during pregnancy.

Methods: We performed a retrospective review of medical records of 37 pregnant women with the diagnosis of COVID-19. The clinical characteristics, laboratory results, perinatal and neonatal outcomes were analyzed.

Results: The majority of cases with COVID-19 were evaluated as mild (97.3%). None of the women needed intensive care unit or invasive mechanical ventilation and mortality were not observed. The most common symptoms were fever (62.2%) and cough (40.5%). Of all the pregnancies, 5.4% ended with abortion, 2.7% with stillbirth, and 10% of the infants were hospitalized in the neonatal intensive care unit. Neonatal mortality was not observed.

Conclusion: In our study, none of the pregnant women with SARS-CoV-2 infection had severe illness. Vertical transmission of SARS-CoV-2 which was possible in several studies is not observed in our patient population.

Keywords: Coronavirus-19, pregnancy outcome, newborn.

Introduction

Emerging in China, Wuhan at the end of 2019, the outbreak of novel coronavirus disease (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly spread to become a pandemic leading to a global public health crisis.[1] The spectrum of the disease severity ranges from mild to critical. Because of this pandemic, many researchers shifted their interest to investigate the possible impact of this infection on vulnerable groups like pregnant women and their fetuses.[2–4] Pregnancy is a state that is particularly susceptible to infectious diseases primarily because of an altered immune response.[5] Along with it, due to the physiologic changes in their cardiopulmonary systems, pregnant women are prone to develop severe pneumonia.[6,7]

As previously stated, infections especially of viral origin may affect pregnancy outcomes.[8,9] Most infectious diseases may increase complications during pregnancy and lead to extremely detrimental effects on the fetus and the mother.[10,11] However, there also have been studies showing that pregnant women are not found to be more susceptible to SARS-CoV-2 than non-pregnant women.[12,13] One of the largest series on both pregnancy and neonatal outcomes, including a total of 99

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SARS-CoV-2-infected pregnant women, demonstrated that this infection during pregnancy was not associated with an increased risk of adverse outcomes, such as spontaneous preterm birth.[14]

When we investigate different time frames, as seasonal flu is known to be associated with higher rates of miscarriage for the period of early pregnancy (first trimester), there is little evidence about the possible impact of SARS-CoV-2 infection on this period of pregnancy.[15] When we search for evidence about the impact of SARS-CoV-2 infection on late pregnancy (third trimester), the majority of studies have been reassuring and the risk of severe disease and mortality due to SARS-CoV-2 infection in pregnancy appears to be no greater than the general population.[16] On the other hand, considering the severity of the disease, limited data suggest that pregnant women may present with severe symptoms which can provoke fetal distress, preterm labor, miscarriage, or even fetal death.[17,18]

As for the fetus, the risk of perinatal transmission of SARS-CoV-2 infection is unknown and the risk of postnatal transmission remains to be clarified.[1,19] Yan et al. stated that none of the 100 neonates born to women with COVID-19 was infected with SARS-CoV-2.[14] However, data to date is scarce and there are conflicting results according to several case reports and studies. Until recently, 15 studies presented the neonatal test results for SARS-CoV-2[20–23] but positive cases were reported only in the minority.[20,21,23] Furthermore, significant neonatal respiratory diseases appear to be rare, even in the presence of SARS-CoV-2 positivity.

There is still a need to accumulate and analyze each data to further elucidate the course of COVID-19 infection during pregnancy and clarify possible perinatal outcomes.[24] Therefore, our study aimed to unravel meaningful factors which have a possible impact on how COVID-19 affects pregnant women and their babies.

Methods

Study design and patients

We performed a retrospective review of medical records of pregnant women with the diagnosis of COVID-19 admitted to Tepecik Training and Research Hospital, İzmir, Turkey from March 15, 2020 to January 31, 2021. Diagnosis and management of pregnant women with possible COVID-19 infection were based on the "Diagnosis and Management Guideline for COVID-19 Infection" published by the Turkish Ministry of Health. All 37 pregnant women with COVID-19 infection were tested positive for SARS-CoV-2 by the use of reverse transcriptase-polymerase chain reaction (RT-PCR) on samples from the respiratory tract. This study was reviewed and approved by the Medical Ethical Committee of Tepecik Training and Education Hospital (approval number 2021/02-27).

Data collection

Clinical characteristics, laboratory results, and treatment courses were extracted from the medical records of patients. We collected data regarding maternal age, parity, blood type, medical history of other underlying conditions, presenting signs and symptoms (fever, cough, shortness of breath, fatigue, loss of taste and smell, nausea and vomiting, and arthralgia), the timing of infection, laboratory tests, imaging results, duration of hospitalization, gestational age at delivery, intensive care unit admission and use of mechanical ventilation. We also analyzed gestational and neonatal outcomes, including mode of delivery (cesarean or vaginal delivery), miscarriage indication for cesarean delivery, the time between COVID-19 diagnosis and delivery, fetal distress, APGAR scores, birth weight of the fetus, and neonatal morbidities including respiratory distress syndrome, neonatal intensive care unit (NICU) admission, meconium aspiration syndrome, stillbirth, and mortality. Samples of nasopharyngeal and pharyngeal swabs were tested for SARS-CoV-2 by using a kit (Bioeksen, Istanbul, Turkey), following the World Health Organization guidelines for RT-PCR. Amniotic fluid, cord blood, placental swab, or human milk samples could not be analyzed for any of the patients.

Statistical analysis

Statistical analysis was done with IBM SPSS Statistics 21.0 (IBM Corp. Released 2012; IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY, USA). Continuous data are shown as mean ± standard deviation and categorical data are given as percentage (%). The Shapiro-Wilk test was used to investigate the compatibility of the data to normal distribution. For the comparison of groups showing normal distribution, independent sample t-test analysis was used for cases with two groups, and one-way analysis of vari-

ance (one-way ANOVA) for cases with three or more groups. In a comparison of the groups that did not conform to a normal distribution, the Mann-Whitney U test was used for cases with two groups and the Kruskal-Wallis H test for cases with three or more groups. Determining the direction and size of the relationship (correlation) between variables, regression analysis was performed for variables with normal distribution, and lines were drawn. Pearson chi-square, Pearson's exact chi-square, and Fisher's exact chi-square analyzes were used in the analysis of the cross tables created. A p-value of less than 0.05 was considered significant for the statistical tests.

Results

We have studied 37 pregnant women who were diagnosed with confirmed SARS-CoV-2 infection during the period of nearly 11 months. None of the pregnant women were vaccinated as data collection was carried out in the first wave of the pandemic. The median age of the women was 25 years.[22–31] Three (8.1%) of them had multiple pregnancies. Of these 37 women, 2 (15.4%) had coexisting preeclampsia, 1 (7.7%) had asthma, 2 (15.4%) had cholestasis, 5 (38.5%) had gestational diabetes, 2 (15.4%) had hypothyroidism and 1 (7.7%) had gestational hypertension. Demographic characteristics and comorbid diseases of pregnant women with confirmed SARS-CoV-2 infection are shown in **Table 1**. Thirty-four of the women had a diagnosis of SARS-CoV-2 infection during the third trimester (median: 38.0 [range 38.0–39.0] weeks) while only 2 had this diagnosis during the first trimester (median: 11.0 [range 10.5–11.5] weeks) and 1 had it during the second trimester (median: 22.0 weeks). The mean time between the time of diagnosis and delivery is 8.08±7.94 weeks (8.41±8.17 weeks for single and 4.33±3.21 weeks for multiple pregnancies). The most common symptom was fever in 23 (62.2%) patients, cough in 15 (40.5%) patients, then arthralgia in 7 (18.9%) patients, fatigue in 7 (18.9%) patients, loss of taste and smell in 7 (18.9%) patients, nausea in 3 (8.1%) patients and diarrhea in 1 (2.7%) patient. Mean white blood cell count was 9180±4100/mm^3, absolute lymphocyte count was 1320±570/mm^3, median C-reactive protein was 21.0 (range 3.40–54.0) mg/l, and D-dimer was 1120 (range 540–2860) ng/ml. No thrombocytopenia was observed. Thrombocyte values were lower (p=0.019) and ferritin values were higher (p=0.001) in multiple pregnancies. Lopinavir was used for only one case who was in the third trimester of pregnancy. Clinical characteristics, laboratory findings, pregnancy and neonatal outcomes of pregnant women are shown in **Tables 2** and **3**.

Table 1. Demographic characteristics and baseline comorbidities of pregnant women infected with SARS-CoV-2.

Characteristics	n (%)
Maternal age, years (median, IQR)	25.0 (22.0–31.0)
Blood type	
A+	15 (40.5%)
A-	1 (2.7%)
0+	8 (21.6%)
0-	0 (0%)
B+	6 (16.2%)
B-	0 (0%)
AB+	5 (13.5%)
AB-	2 (5.4%)
Gravidity	2 (1–3)
Parity	1 (0–2)
Comorbidity	
Preeclampsia	2 (15.4%)
Asthma	1 (7.7%)
Cholestasis	2 (15.4%)
Gestational diabetes	5 (38.5%)
Hypothyroidism	2 (15.4%)
Gestational hypertension	1 (7.7%)
Single pregnancy	34 (91.9%)
Multiple pregnancy	3 (8.1%)

Out of the 37 women, 17 (47.2%) had cesarean section, 18 (47.2%) had a vaginal delivery, and 2 (5.6%) had an abortion. Cesarean section indication was mostly due to repeat cesarean section with a ratio of 70.6%. One out of 37 women had to undergo a cesarean section due to fetal distress. The mean gestational age at birth was 36.4±6.88 weeks and the mean birth weight was 3148±428 g. In 5 cases, women gave birth to a baby with a birth weight <2500 g and 1 of them was multiple pregnancy.

Median APGAR scores were 7 (IQR: 7–7) for the 1-minute and 8 (IQR: 8–8) for the 5-minute. Four (11.8%) of the babies were admitted to the neonatal intensive care unit. Three (8.8%) of them had the diagnosis of RDS, one (2.9%) of them had meconium dyed

Table 2. Clinical characteristics, laboratory findings, and gestational and neonatal outcomes of pregnant women infected with SARS-CoV-2.

	All pregnant women (n=37)	Single pregnancy (n=34)	Multiple pregnancy (n=3)	p-value
Gestational age at diagnosis, weeks (median, IQR)	38.0 (38.0–39.0)	38.0 (38.0–39.0)	38.0 (34.0–38.0)	<0.001
Duration of hospitalization, days (mean, SD)	4.43±7.60	14.0±18.5	4.33±3.21	0.478
Drug therapy - lopinavir	1 (2.7%)	0 (0%)	1 (100.0%)	0.317
Symptoms				
Fever	23 (62.2%)	21 (61.8%)	2 (66.7%)	1.000
Loss of smell	7 (18.9%)	5 (14.7%)	2 (66.7%)	0.152
Arthralgia	7 (18.9%)	6 (17.6%)	1 (33.3%)	1.000
Cough	15 (40.5%)	15 (44.1%)	0 (0%)	0.38
Malaise	7 (18.9%)	6 (17.6%)	1 (33.3%)	1.000
Nausea	3 (8.1%)	3 (8.8%)	0 (0%)	1.000
Diarrhea	1 (2.7%)	1 (2.9%)	0 (0%)	1.000
Asymptomatic	0 (0%)	0 (0%)	0 (0%)	1.000
Symptomatics				
Single symptom	16 (43.2%)	14 (41.2%)	2 (66.7%)	0.393
Multiple symptoms	21 (56.8%)	20 (58.8%)	1 (33.3%)	
Laboratory findings				
White blood count, $\times 10^9$/mL, (median, IQR)	8300 (6700–10700)	8350 (6700–10,500)	8300 (7250–9600)	0.198
Lymphocyte, $\times 10^9$/mL, (median, IQR)	1300 (900–1600)	1250 (900–1580)	1300 (1050–1950)	0.095
Neutrophil, $\times 10^9$/mL, (median, IQR)	6300 (4500–7500)	6300 (4500–7500)	7200 (5550–7350)	0.120
Platelet, $\times 10^9$/mL, (median, IQR)	223,000 (181,000–249,000)	224,000 (186,000—470,000)	180,000 (180,000–224,000)	0.019
CRP, mg/mL, (median, IQR)	21.0 (3.40–54.0)	16.8 (3.33–47.7)	55.4 (45.3–80.2)	0.948
Procalcitonin, ng/mL, (median, IQR)	0.0200 (0.0100–0.0300)	0.0200 (0.0100–0.0300)	0.0300 (0.0200–0.0300)	0.93
ALT, U/L, (median, IQR)	19.0 (14.0–28.0)	18.5 (14.0–27.5)	19.0 (16.0–33.5)	0.839
AST, U/L, (median, IQR)	27.0 (19.0–34.0)	26.5 (18.3–33.8)	27.0 (24.0–38.0)	0.799
Lactate dehydrogenase, U/L, (median, IQR)	200 (150–220)	191 (150–212)	252 (228–260)	0.903
D-Dimer, ng/mL, (median, IQR)	1120 (540–2860)	1090 (526–2810)	2370 (1950–4230)	0.471
Blood urea nitrogen, mol/L, (median, IQR)	15.0 (14.0–18.0)	15.0 (14.0–17.5)	18.0 (16.5–21.0)	0.898
Albumin, g/dL, (median, IQR)	3.10 (2.73–3.14)	3.10 (2.74–3.14)	2.90 (2.00–3.00)	0.499
Creatinine, mg/dL, (median, IQR)	0.600 (0.510–0.800)	0.600 (0.503–0.700)	0.800 (0.700–1.41)	0.804
Ferritin, mL/ng, (median, IQR)	55.0 (36.0–122)	51.4 (33.3–121)	70.0 (57.5–153)	0.001
Gestational age at birth, weeks, (median, IQR)	38.0 (38.0–39.0)	38.0 (38.0–39.0)	38.0 (34.0–38.0)	0.793
Week between diagnosis and birth, (median, IQR)	5.00 (3.00–8.00)	5.50 (3.25–8.75)	3.00 (2.50–5.50)	0.478
Delivery method				
Cesarean section (C/s)	17 (47.2%)	15 (44.1%)	2 (66.7%)	
Vaginal delivery	18 (47.2%)	17 (50%)	1 (33.3%)	0.512
Abortion	2 (5.6%)	2 (5.9%)	0 (0.0%)	
Indication for C/s				
Fetal distress	1 (5.9%)	1 (6.7%)	0 (0.0%)	
Repeat C/s	12 (70.6%)	11 (73.3%)	1 (50.0%)	0.515
Cephalopelvic disproportion	3 (17.6%)	2 (13.3%)	1 (50.0%)	
Labor arrest	1 (5.9%)	1 (6.7%)	0 (0.0%)	
Birth weight <2500 g	5 (13.5%)	4 (11.8%)	1 (33.3%)	0.171
Birth weight ≥2500 g	32 (86.5%)	30 (88.2%)	2 (66.7%)	
Birth weight, g (mean, SD)	3148±428	3119±601	2543±748	0.059
APGAR score (median, IQR) 1-min	7 (7-7)	7 (7-7)	7 (7–7)	0.650
APGAR score (median, IQR) 5- min	8 (8-8)	8 (8-8)	8 (8–8)	0.556
Neonatal morbidity				
NICU admission	4 (11.8%)	3 (9.7%)	1 (33.3%)	0.783
RDS	3 (8.8%)	2 (6.5%)	1(33.3%)	1.000
Meconium aspiration syndrome	1 (2.9%)	1 (3.2%)	0 (0%)	1.000
Mortality	0 (0%)	0 (0%)	0 (0%)	1.000
Stillbirth	1 (2.7%)	1 (2.9%)	0 (0%)	1.000

Table 3. Clinical characteristics, laboratory findings, and gestational and neonatal outcomes of pregnant women infected with SARS-CoV-2 (according to the time of diagnosis).

	1st trimester (n=2)	2nd trimester (n=1)	3rd trimester (n=34)	p-value
Gestational week at diagnosis, (median, IQR)	11.0 (10.5–11.5)	22.0 (22.0–22.0)	38.0 (38.0–39.0)	-
Single pregnancy	2 (100%)	1 (100%)	31 (91.2%)	1.000
Multiple pregnancy	0 (0%)	0 (0%)	3 (8.8%)	
Duration of hospitalization, days (mean, SD)	3.00±4.24	3.00±0.0	4.56±7.89	0.021
Drug therapy - lopinavir	0 (0%)	0 (0%)	1 (2.9%)	1.000
Symptoms				
Fever	1 (50%)	1 (100%)	21 (61.8%)	1.000
Loss of smell	1 (50%)	0 (0%)	6 (17.6%)	0.481
Arthralgia	2 (100%)	1 (100%)	33 (97.1%)	1.000
Cough	2 (100%)	1 (100%)	19 (55.9%)	0.511
Malaise	1 (50.0%)	0 (0%)	6 (17.6%)	0.481
Nausea	2 (100%)	1 (100%)	31 (91.2%)	1.000
Diarrhea	2 (100%)	1 (100%)	33 (97.1%)	1.000
Asymptomatic	0 (0%)	0 (0%)	0 (0%)	1.000
Symptomatics				
Single symptom	1 (50%)	1 (100%)	14 (41.2%)	0.712
Multiple symptoms	1 (50.0%)	0 (0.0%)	20 (58.8%)	
Laboratory findings				
White blood count, $\times10^9$/mL, (median, IQR)	4900 (4850–4950)	13,400 (13,400–13,400)	8400 (6730–10,500)	0.759
Lymphocyte, $\times10^9$/mL, (median, IQR)	500 (300–700)	1100 (1100-1100)	1300 (950–1680)	0.450
Neutrophil, $\times10^9$/mL, (median, IQR)	3600 (3550–3650)	11500 (11,500-11,500)	6550 (4580–7500)	0.859
Platelet, $\times10^9$/mL, (median, IQR)	213,000 (189,000–236,000)	87,000 (87,000-87,000)	224,000 (186,000–247,000)	0.748
CRP, mg/mL, (median, IQR)	26.8 (19.1–34.4)	31.2 (31.2–31.2)	19.8 (3.33–55.1)	0.327
Procalcitonin, ng/mL, (median, IQR)	0.0150 (0.0125–0.0175)	0.0200 (0.0200–0.0200)	0.0200 (0.0100–0.0300)	0.742
ALT, U/L, (median, IQR)	17.5 (16.3–18.8)	26.0 (26.0–26.0)	18.5 (13.3–33.3)	0.931
AST, U/L, (median, IQR)	17.5 (16.3–18.8)	33.0 (33.0–33.0)	27.0 (19.0–34.0)	0.953
Lactate dehydrogenase, U/L, (median, IQR)	174 (155–194)	210 (210–210)	198 (150–222)	0.223
D-Dimer, ng/mL, (median, IQR)	495 (473–518)	560 (560–560)	1330 (960–3170)	0.375
Blood urea nitrogen, mol/L, (median, IQR)	16.0 (15.0–17.0)	14.0 (14.0–14.0)	15.0 (14.0–18.0)	0.156
Albumin, g/dL, (median, IQR)	3.07 (3.05–3.08)	3.51 (3.51–3.51)	3.03 (2.72–3.13)	0.216
Creatinine, mg/dL, (median, IQR)	0.550 (0.525–0.575)	0.600 (0.600–0.600)	0.600 (0.518–0.800)	0.384
Ferritin, mL/ng, (median, IQR)	361 (293–428)	56.0 (56.0–56.0)	46.9 (33.3–114)	0.735
Week between diagnosis and birth, (median, IQR)	3.00 (2.50–3.50)	2.00 (2.00–2.00)	6.00 (3.25–8.75)	0.401
Delivery method				
Cesarean section (C/s)	0 (0%)	0 (0%)	17 (50%)	
Vaginal delivery	0 (0%)	1 (100%)	17 (50%)	0.615
Abortion	2 (100%)	0 (0%)	0 (0%)	
Indication for C/s				
Fetal distress	0 (0%)	0 (0%)	1 (5.9%)	
Repeat C/s	0 (0%)	0 (0%)	12 (70.6%)	1.000
Cephalopelvic disproportion	0 (0%)	0 (0%)	3 (17.6%)	
Labor arrest	0 (0%)	0 (0%)	1 (5.9%)	
Birth weight, g				
<2500 g	0 (0%)	1 (100%)	2 (94.1%)	0.086
≥2500 g	0 (0%)	0 (0%)	32 (5.9%)	
Mean (SD), g	-	-	3148±428	-
APGAR score (median, IQR) 1-min	-	-	7 (7–7)	-
APGAR score (median, IQR) 5-min	-	-	8 (8–8)	-
Neonatal morbidity				
NICU admission	0 (0%)	0 (0%)	4 (11.7%)	-
RDS	0 (0%)	0 (0%)	3 (8.8%)	-
Meconium aspiration syndrome	0 (0%)	0 (0%)	1 (2%)	-
Mortality	0 (0%)	0 (0%)	0 (0%)	-
Stillbirth	0 (0%)	1 (100%)	0 (0%)	-

amniotic fluid and there was no neonatal death. One (2.7%) woman experienced stillbirth. All the live-born babies were tested negative for SARS-CoV-2 and none of the mothers needed intensive care unit admission. There was a positive correlation between the time of diagnosis and the time of birth. This correlation was more prominent in multiple pregnancies (**Fig. 1**).

Discussion

The present study is a descriptive study on both maternal and neonatal clinical features as well as outcomes of pregnancies complicated with SARS-CoV-2 infection. We found that the most common symptoms in our patient population were fever and cough. This finding is concordant with the findings of previous studies that found fever and cough as the most common symptoms in pregnant women having the diagnosis of COVID-19.[19,24–26] But on the contrary, one study revealed that the majority of women were asymptomatic at presentation.[27] As we did not perform routine screening for all the pregnant women except the ones who had signs and symptoms of SARS-CoV-2 infection or who were admitted to the hospital for a planned cesarean delivery, we could not diagnose most of the asymptomatic cases. We speculate that, in a cross-sectional study where all the pregnant women are screened at once in a population, different results regarding signs and symptoms would be observed.

In our study, the most common comorbidity in pregnant women with COVID-19 was gestational diabetes. 13.5% of the pregnant women with COVID-19 were associated with gestational diabetes. The International Diabetes Federation suggests that 1 in 6 (16.8%) preg-

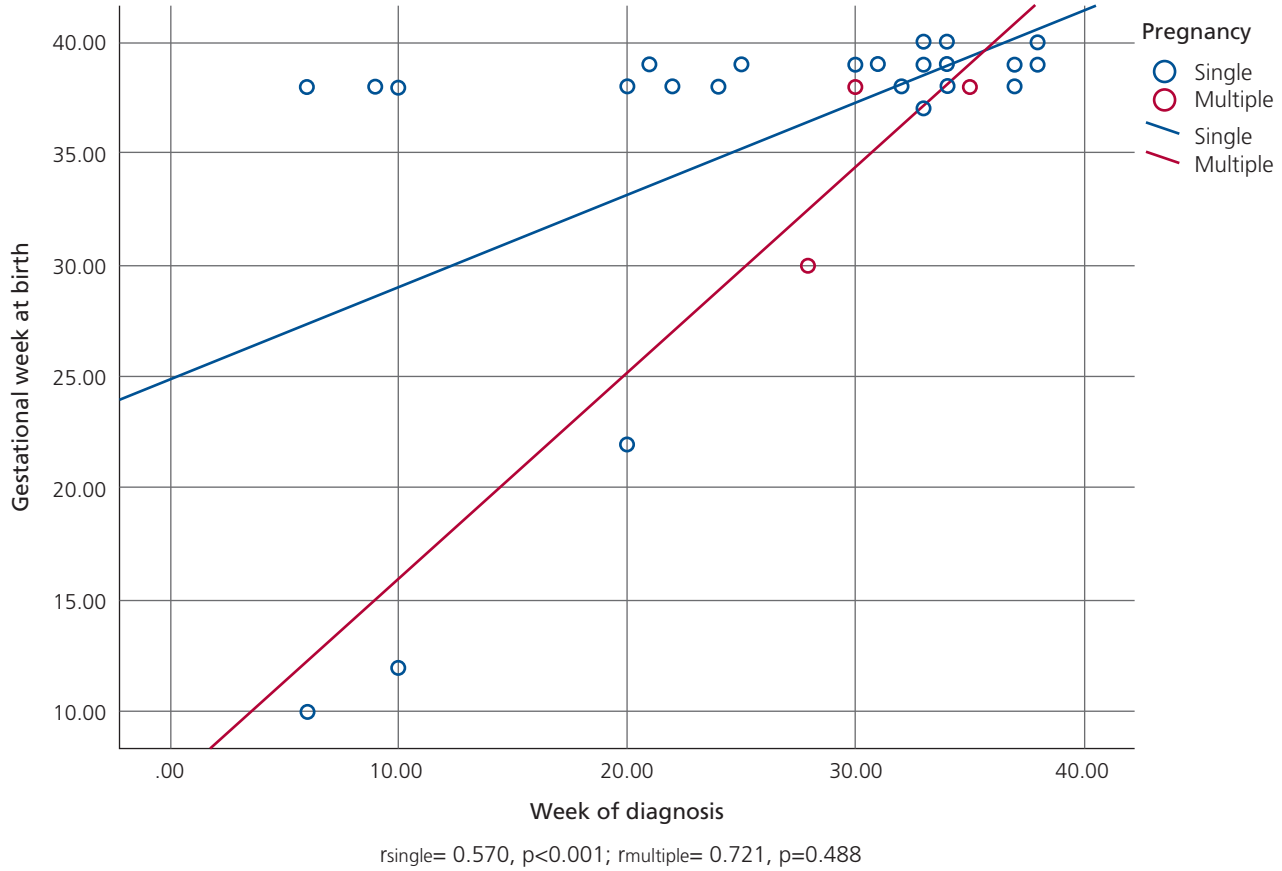

Fig. 1. Correlation between the time of diagnosis and time of birth in single and multiple pregnancies.

nancies are affected by diabetes. 13.6% of them are pregestational diabetes and 86.4% are gestational diabetes. Although the relationship between gestational diabetes and SARS-CoV-2 infection during pregnancy has been documented in many studies, SARS-CoV-2 infection did not increase the frequency of gestational diabetes in our cases and was consistent with the gestational diabetes prevalence rate in the literature.[25] The majority of the pregnant women (40.5%) had a blood type of A (+) which was concordant with the general population (39%).[28]

Previous studies showed that most of pregnant women with COVID-19 were diagnosed during the late second or third trimester of pregnancy.[19,26] Besides, a prospective cohort study found that pregnant women hospitalized were in their third trimester of pregnancy.[25] When we evaluated our findings according to the time of diagnosis, the majority of cases were diagnosed during the third trimester of pregnancy. This was partly attributed to the fact that most of the pregnant women in the early trimester remain undiagnosed as they may prefer not to search for medical assistance in case of minor signs of COVID-19. Moreover, some of the pregnant women were diagnosed by routine PCR testing just when they were admitted to the hospital for delivery. Cosma et al. recruited 138 pregnant women attending the first-trimester screening in Italy and found 10.1% of cumulative COVID-19 incidence during the first trimester with a high prevalence of asymptomatic patients (42.8%).[29] Therefore, our study, as well as many other similar studies, most probably underestimate both the real incidence of SARS-CoV-2 infection in pregnancy and also the real distribution of COVID-19 incidence according to different trimesters of pregnancy.

In the present study, the pregnant women who had the diagnosis during the first trimester had slightly lower total lymphocyte values but this did not reach statistical significance. Pregnant women in the third trimester had higher values of CRP compared to other trimesters of pregnancy and those with multiple gestations also had higher values of CRP compared to the singleton pregnancies, none of which approached statistical significance. The same association was also observed for D-dimer values. Therefore, due to the hypercoagulable state in pregnancy, monitoring of D-dimer should be included in the management of pregnant women with COVID-19.[30]

In our study, none of the women required intensive care unit or invasive mechanical ventilation and the majority had a mild form of COVID-19. This result was similar to the course of the disease in non-pregnant adults.[29] Previous studies show similar results regarding intensive care unit admission and mortality rates for both pregnant women and the general population with COVID-19.[14,25] In contrast, a systematic review of 108 cases of pregnancies complicated with confirmed SARS-CoV-2 infection reported the possibility of increased risk of severe disease among pregnant women.[31] In our study, we found favorable outcomes for pregnant women with SARS-CoV-2 infection. Maternal mortalities have been rarely reported so far in the literature.[32] D'Antonio et al. reported that the rate of critical care need in pregnant women over 35 years of age with SARS-CoV-2 infection was 7.7%.[33] This difference in results is attributed to the variations in sample sizes and characteristics of different centers.

According to our results, 47.2% of neonates were delivered by cesarean section. These findings are similar to the findings of previous studies.[19] Previous cesarean delivery was the most common cesarean indication (70.6%). Of our patients, which are unrelated and/or not specific to COVID-19 infection, only one mother underwent cesarean delivery because of fetal distress and one for labor arrest. Several studies reported that the majority of pregnant women delivered by cesarean section to prevent neonatal transmission of the virus.[1,17] Pierce-Williams et al. revealed higher cesarean delivery rates for pregnant women with COVID-19 (53% for severe and 94% for critical cases) compared to the general pregnant population.[34] Another review about the outcomes of COVID-19 disease in pregnancy showed that cesarean delivery rates are 80% in total in observational studies.[35] Our study emphasized that maternal SARS-CoV-2 infection itself is not an absolute contraindication for vaginal delivery.

Among the neonates of 37 women with confirmed COVID-19 infection, none of them were diagnosed with SARS-CoV-2 infection. Even if there are studies with similar results, this does not support the findings of previous studies suggesting vertical and intrapartum transmission.[1,16] On the other hand, a case report showed that virus-specific antibodies were detected in serum samples of some neonates born to pregnant

women with COVID-19, although SARS-CoV-2 infection was undetected by PCR tests.[36] As IgM is known to be too large to cross the placenta, detection of IgM was interesting and this may imply the possible vertical transmission of SARS-CoV-2 infection from mother to fetus.[37] However, in another study, transplacental passage of IgM was detected in cases of severe COVID-19.[38] So, detection of IgM in neonates may not precisely mean that IgM in neonates was produced by fetuses after vertical transmission. It may also be transferred from the mother due to severe COVID-19.

In this study, 5.4% of pregnancies resulted in abortion, and 2.7% resulted in stillbirth. Although 10% of infants were hospitalized in the NICU, infant mortality was not observed. A multinational cohort study of all consecutive pregnant women with COVID-19 from 22 different countries and 73 centers analyzed 251 newborns born to women with SARS-CoV-2 infection and found the neonatal mortality rate 2%.[39] A comprehensive meta-analysis by Allotey et al. reported that stillbirth incidence was 0.9%, NICU admission was 25.6% and neonatal death was 0.4%.[16] In a systemic review in which nine studies and 92 cases were analyzed, Smith et al. declared that 76.9% of newborns born to mothers diagnosed with COVID-19 infection required admission to NICU.[25] As most newborns are expected to be asymptomatic, this number may vary quite a lot according to the individual guidelines of each hospital. There still is not a universal consensus about how the newborn born from a SARS-CoV-2 infected or suspected mother should be followed up right after the delivery. In our hospital, newborns are admitted to an isolation room in NICU if they have any indication for hospitalization in level I-II or III NICU, and asymptomatic newborns are followed up in an isolated room in the Obstetrics ward with a healthy attendant. If the mother is asymptomatic, we also recommend placing the newborn at least 2 meters away from the mother with a barrier in between or in an incubator. If the mother is clinically symptomatic and there is no healthy attendant in the family, then the newborn is admitted to NICU as well. Neonates whose mothers have confirmed or suspected SARS- CoV-2 infection must be isolated and clinically monitored, but this does not necessarily require NICU admission. These newborns might be followed up in a single room without full NICU capabilities according to local settings.[40]

The retrospective nature of the study design and small sample size are the main limitations of our study which limit the capability to generalize the results. Furthermore, only oropharyngeal and nasal swabs were collected for the detection of COVID-19 from newborns. Antibody testing for SARS-CoV-2 may prevent incorrect COVID-19 diagnoses. However, our study provides essential information about the prognosis of COVID-19 both for pregnant women and their fetuses.

Conclusion

Our study demonstrated that clinical and laboratory findings in pregnant women with COVID-19 are mild as non-pregnant women. Furthermore, we did not observe mother-to-fetus vertical transmission of SARS-CoV-2 infection, which was possible in several studies, in our patient population. This study may help healthcare professionals to better deal with the disease in this vulnerable population. Besides, it will also contribute to the continuous update in guidance for SARS-CoV-2-positive pregnant women and their neonates about complications of COVID-19 in pregnancy as well as the possibility of vertical transmission and perinatal complications.

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