ORIGINAL RESEARCH

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A Retrospective Analysis of Clinical Features, Maternal and Neonatal Outcomes of COVID-19 patients in an Obstetric Clinic in Ankara, Turkey

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ABSTRACT Objective: To evaluate the effects of coronavirus disease-2019 (COVID-19) infection on clinical and laboratory features; maternal and fetal outcomes. **Material and Methods:** In this retrospective study, the patients diagnosed with COVID-19 by positive severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) reverse transcription polymerase chain reaction (RT-PCR) and delivered at Koru Hospital (Ankara, Turkey) between March 2020 and February 2021 were included. We obtained demographic, clinical, laboratory features, obstetric and delivery history, maternal and perinatal outcomes from medical records. **Results:** Twelve pregnant patients were included in the study. The mean age was 32 years (range 28-43 years) and the mean gestational age at diagnosis of COVID-19 was 34 weeks (range 22 to 39 weeks 6 days), the mean gestational age at delivery was 38 weeks 4 days (range 35 to 40 weeks). All deliveries were as cesarean section. At first admission with suspicion of COVID-19, seven (58%) patients had fever, five (41%) patients had cough, two (16%) patients had dyspnea, two (16%) patients had anosmia and loss of taste, one (8.3%) patient had sore throat. None of the pregnant patients were taken to the intensive care unit before or after delivery. One neonate was tested for SARS-CoV-2 RT-PCR and the result was negative. Two neonates were admitted to neonatal intensive care unit due to preterm delivery of a twin pregnancy. **Conclusion:** COVID-19 infection has similar clinical characteristics in pregnant patients as in non-pregnants reported in the literature. The maternal, fetal and neonatal outcomes were good and vertical transmission seems unlikely.

Keywords: COVID-19; severe acute respiratory syndrome coronavirus 2; pregnancy; newborn

Pregnant women are prone to respiratory tract infections and they need more attention during the severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) pandemic. Increased angiotensin-converting enzyme 2 (ACE2) receptors, where the SARS-CoV-2 virus enters the cell, increase the risk of a more severe infection in pregnant women.[1] Despite the existence of this information, it is seen that coronavirus disease-2019 (COVID-19) infection progresses similarly in pregnant women and non-pregnant women. The clinic is mild in 95%, severe in 3% and critical in 8% of the pregnant women. In severe cases, pneumonia, severe acute respiratory infection, kidney failure, and even death may develop.[2]

As seen in any infection, COVID-19 may cause the fetus to be stressed in the intrauterine environment. While the cesarean delivery rate was 69.4% in the case series so far, the normal vaginal delivery rate was 30.6%. Sixty seven percent of deliveries were after 36 weeks. While 99% of babies were born alive, stillbirths were seen in 6 per thousand. There is no evidence of increased miscarriage or early pregnancy loss in pregnant women diagnosed with COVID-19. Transmission through the placenta, birth canal, or breastfeeding have been considered as possible transmission routes from infected mother to baby. However, there is no evidence yet of mother-to-baby transmission.[3]

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The data about the COVID-19 clinical course and treatment in pregnancy are limited and rapidly changing.[1] The aim of this study is to examine the clinical and laboratory features; maternal and fetal outcomes of pregnant patients diagnosed with COVID-19 and gave birth in our clinic.

MATERIAL AND METHODS

In this study, the patients diagnosed with COVID-19 by positive SARS-CoV-2 RT-PCR and delivered at Koru Hospital (Ankara, Turkey) between March 2020 and February 2021 were included retrospectively. Healthy pregnant women without respiratory tract infection symptoms and complaints or negative RT-PCR test for SARS-CoV-2 were excluded. We obtained demographic, clinical, laboratory and treatment features; maternal and fetal outcomes from medical records. Data were analyzed using the SPSS-21 statistical program. Informed constent was not required due to retrospectivedesign of the study. Quantitative variables were expressed as ranges; qualitative variables were expressed as percentages (%). The Ministry of Health approval number of the study is 2021-01-14T23_08_48. This study was approved by the ethics committee of Gazi University with a number of 2021/84. This study was conducted in accordance with the Helsinki Declaration principles.

RESULTS

Twelve pregnant patients diagnosed with COVID-19 and delivered between 11 March and 11 February 2021, were included in the study. Three patients were primiparous and nine were multiparous. The mean age was 32 years (range 28-43 years) and the mean gestational age at diagnosis of COVID-19 was 34 weeks (range 22 to 39 weeks 6 days), the mean gestational age at delivery was 38 weeks 4 days (range 35 to 40 weeks). Two (15%) patients had hypertension and one (7.6%) patient had hypertension with gestational diabetes. At first admission with suspicion of COVID-19, seven (58%) patients had fever, five (41%) patients had cough, two (16%) patients had dyspnea, two (16%) patients had anosmia and loss of taste, one (8.3%) patient had sore throat (Table 1).

In laboratory tests, leukocytosis (33%) and lymphopenia (33%) were found in three patients of tested nine patients. Platelet counts were normal in all tested patients. D-dimer was above 0.5 µg/mL in all three patients tested. As acute phase reactants; C-reactive protein levels were above 5 mg/dL in four patients, lactate dehydrogenase levels were above 255 U/L in one patient. Only one patient had pulmonary graphy which showed signs of viral pneumonia. Three patients had antibiotics as cephalosporins and beta-lactams, two of them had anticoagulant treatment also. Seven patients had antipyretic treatment during fever. No patient used antivirals and needed oxygen therapy. Cesarean section was the route of delivery in all patients. In four cases, cesarean was performed during active infection. Spinal anesthesia was used in all patients.

None of the pregnant women were taken to the intensive care unit during active infection or after delivery. All patients had discharged from the hospital on the postoperative second day. The neonatal birthweights and Apgar scores were normal. None of the fetuses had fever or any other symptom of a viral infection. Only two neonates were admitted to the neonatal intensive care unit due to the preterm birth of a twin pregnancy. Postpartum nasopharyngeal swab RT-PCR test of a newborn delivered at 39 weeks from a mother diagnosed with COVID-19 at 34 weeks, was negative. Maternal nasopharyngeal swab RT-PCR test was also negative postpartum. Umbilical cord, amnion, placenta and vaginal secretions were negative for SARS-CoV-2. One mother has a positive blood anti SARS-CoV-2 immunoglobulin G (IgG) and a positive colostrum anti SARS-CoV-2 immunoglobulin (IgA). One month later, colostrum was tested negative for SARS-CoV-2 but IgG levels were still positive in maternal blood.

DISCUSSION

This retrospective study investigated the clinical and laboratory features, maternal and neonatal outcomes of pregnant women infected with SARS-CoV-2. We demonstrated good maternal and neonatal outcomes in twelve pregnant patients with COVID-19 (Table 2).

TABLE 1: Maternal characteristics of twelve patients with COVID-19.

Patients	1	2	3	4	5	6	7	8	9	10	11	12
Age (years)	34	34	28	29	43	34	37	31	30	29	30	30
Gravida (parity)	3 (2)	1 (0)	3 (2)	3 (1)	2 (1)	2 (1)	5 (2)	2 (1)	1 (0)	5 (1)	2 (1)	1 (0)
Gestational age at diagnosis of COVID-19 (weeks+day)	37	22	35	35	34	38	38 w 5 days	39	39 w 6 days	38	25	26
Chronic illness	No	No	HT	No	No	HT	No	No	No	GDM HT	No	No
Pregnancy complications	No	No	No	No	No	No	No	No	No	No	No	PTE
Symptoms												
Fever	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No
Soar throat	Yes	No	No	No	No	No	No	No	No	No	No	No
Cough	Yes	Yes	No	No	Yes	Yes	Yes	No	No	No	No	No
Dispnea	No	No	No	No	No	Yes	Yes	No	No	No	No	No
Anosmia	No	No	No	No	No	Yes	No	No	No	Yes	No	No
Loss of taste	No	No	No	No	No	Yes	No	No	No	Yes	No	No
Laboratory												
WBC	5.13	NT	NT	NT	5.8	8.37	11.8	12.1	9.5	6.43	8.97	11.5
Lymphocyte	1.69	NT	NT	NT	1.12	0.94	1.03	1.5	1.67	0.82	1.76	1.08
Platelet	118	NT	NT	NT	208	154	174	346	221	116	268	286
CRP	22	NT	NT	NT	NT	9.2	NT	36	NT	NT	17	3.08
D-dimer	6.5	NT	NT	NT	NT	NT	NT	1.01	NT	NT	NT	1.3
Creatinine	0.44	NT	NT	NT	0.54	0.51	NT	0.63	NT	NT	NT	NT
CK	NT	NT	NT	NT	NT	32	NT	NT	NT	NT	60	59
LDH	NT	NT	NT	NT	NT	267	NT	NT	NT	NT	172	201
Ferritin	41	NT	NT	NT	NT	NT	NT	71	NT	NT	NT	20
PCR	+	+	+	+	+	+	+	+	+	+	+	+
Radiological findings	+	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
Treatment	AB AP AC	No	AP	AP	AP	AP	AP	AB AP AC	No	AB	No	No

COVID-19: Coronavirus disease-2019; WBC: White blood cell; CRP: C-reactive protein; CK: Creatine kinase; LDH: Lactate dehydrogenase; PCR: Polymerase chain reaction; HT: Hypertension; GDM: Gestational diabetes mellitus; PTE: Pulmonary thromboembolism; NT: Non-tested; AB: Antibiotic; AP: Antipyretic; AC: Anticoagulant.

TABLE 2: Maternal and neonatal outcomes of twelve patients with COVID-19.

Patients	1	2	3	4	5	6	7	8	9	10	11	12
Delivery week	38	40	37	38 w 6 days	39	39	39	39	40	38	38	35
Neonatal outcome	N	N	N	N	N	N	N	N	N	N	N	N
Birthweight (g)	3,160	3,390	2,800	3,460	2,820	3,450	3,760	3,420	3,300	3,800	3,600	2,420/2,240
Apgar score (1 min)	9	8	9	9	9	9	9	9	9	9	9	8
Apgar score (5 min)	10	9	10	10	10	10	10	10	10	10	10	9
Neonatal intensive care unit admission	No	No	No	No	No	No	No	No	No	No	No	Yes
Neonatal PCR	NT	NT	NT	NT	(-)	NT	NT	NT	NT	NT	NT	NT
Neonatal complication	No	No	No	No	No	No	No	No	No	No	No	No

COVID-19: Coronavirus disease-2019; PCR: Polymerase chain reaction; N: Normal; NT: Non-tested.

The most common symptoms demonstrated in literature are fever, cough, shortness of breath, sore throat, diarrhea and vomiting, and the most common laboratory findings were increased white blood cells, acute phase reactants and a decrease in lymphocytes.[1] In our study, the most common symptoms were fever

and cough and the less common ones were sore throat, dyspnea, anosmia and loss of taste. The main findings in laboratory tests were leukocytosis, lymphopenia, elevation of C-reactive protein and D-dimer. Our patients had characteristics similar to non-pregnant patients with COVID-19 and also similar to COVID-19 infected pregnant patients as demonstrated in the literature.[2,4] It was shown that in 85% of the cases, there may be pulmonary findings typically as ground glass image with multilobar retention in the acute period. In non-severe cases, no finding may be found on computerized tomography.[1] In our study, none of the patients needed computerized tomography, but one had a pulmonary graphy with findings of viral pneumonia. It was suggested that maternal temperature, blood oxygen saturation, respiration rate, pulse, blood pressure and fetal cardiac activity should be followed closely.[1] In our follow up, maternal vital signs and fetal cardiac activity did not deteriorate in patients.

There is not an established treatment of COVID-19 in pregnant patients yet and still under investigation. In literature, chloroquine and azithromycin were defined as safe for treatment and remdesivir, ribavirin and other antiviral drugs were used despite the unproven efficiency and safety.[1,2] Due to prothrombotic state of pregnancy, thromboprophylaxis is advised for pregnant patients with COVID-19.[5] In our records, no patient was given antivirals, three patients had antibiotics as cephalosporins and beta-lactams, two of them also had anticoagulant treatment. Seven patients had antipyretic treatment during the period of fever.

Vaginal delivery is not contraindicated in COVID-19 patients and should be allowed in patients in whom labor begins spontaneously and progresses actively. However, the second phase should be shortened to prevent active straining. Emergency cesarean section is required in the presence of septic shock, acute organ failure or fetal distress. Although the duration of vaginal delivery is longer and the droplet output is higher, COVID-19 is not an indication for cesarean delivery alone and the delivery method should be decided according to the patient's clinic, gestational week and fetal condition.[1-6] In our clinic, all deliveries were performed as cesarean section in COVID-19 infected pregnant patients at term with an aim of decreasing droplet output. The mean time from beginning of symptoms to delivery was four weeks and it was shorter when the pregnancy week was advanced at first admission of diagnosis. Regional anesthesia with epidural or spinal block were preferred in pregnant women with confirmed COVID-19 at delivery as advised in literature. Late clamping of the cord was not performed as recommended.[1,3]

Vertical transmission of COVID-19 is a controversial issue and seems to be a low probability according to published articles. Dong et al. and Zeng et al. determined positive immunoglobulin M (IgM) and negative RT-PCR in a neonate born from an infected mother.[7,8] Because the high gravity of IgM, this result could be a placental variation or a false negative result. Zeng et al. also demonstrated low expression of ACE2 receptors at maternal-fetal interface that coronavirus uses to enter the cell.[8] In literature; amnion, placenta and cord blood were negative for SARS-CoV-2 RT-PCR in cases.[6,9-11] First RT-PCR positive neonates were detected postpartum 30th hours in February 2020.[6,9] Perinatal transmission was not ruled out in these cases due to insufficient isolation precautions. And in another case, newborn borned to a SARS-CoV-2 RT-PCR positive mother had a positive nasopharyngeal swab RT-PCR test, negative immunoglobulin IgM and IgG for SARS-CoV-2 at postpartum 16th hour.[10] Vertical transmission becomes suspicious in these cases due to long interval of testing. It was speculated that the negative neonatal serology could be a result of immature immune system in neonates.[10] In our records, only one neonate born to a mother who had RT-PCR positivity at 34 weeks and gave birth at 39 weeks tested with nasopharyngeal swab RT-PCR and after delivery both mother and baby were negative. Umbilical cord, amnion, placenta and vaginal secretions were negative for SARS-CoV-2. One mother has a positive blood anti COVID-19 IgG and a positive colostrum anti COVID-19 IgA. One month later, colostrum was tested negative for COVID-19 but IgG levels were still positive in maternal blood.

LIMITATIONS

Limitations of this study are the small sample size and retrospective design. Because all patients were in

their second or third trimester, the effect of virus on maternal and neonatal outcomes at first trimester can not be discussed. Large sample sized, long interval of follow up studies that compare long term outcomes and vertical transmission are needed. This study demonstrates the experience of a single center in pregnant women who are infected with COVID-19 and their neonates in Ankara, Turkey. The clinical course of SARS-CoV-2 infection in the second and third trimester, maternal and neonatal outcomes are good.

CONCLUSION

The clinical course of COVID-19 during pregnancy is similar to those mentioned in literature. The maternal, fetal and neonatal outcomes of COVID-19 infection in second and third trimester are good. Long term outcomes and vertical transmission need to be further researched.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *İlknur Selvi, Aydan Biri;* ***Design:*** *İlknur Selvi;* ***Control/Supervision:*** *Aydan Biri;* ***Data Collection and/or Processing:*** *İlknur Selvi;* ***Analysis and/or Interpretation:*** *İlknur Selvi, Funda Cevher;* ***Literature Review:*** *İlknur Selvi, Funda Cevher;* ***Writing the Article:*** *İlknur Selvi;* ***Critical Review:*** *Aydan Biri, Funda Cevher.*

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