

A pandemic center's experience of managing pregnant women with COVID-19 infection in Turkey: A prospective cohort study

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Abstract

Objective: To evaluate the course and effect of coronavirus disease 2019 (COVID-19) on pregnant women followed up in a Turkish institution.

Methods: A prospective, single tertiary pandemic center cohort study was conducted on pregnant women with confirmed or suspected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Positive diagnosis was made on a real-time polymerase chain reaction (RT-PCR) assay of a nasopharyngeal and oropharyngeal specimen. Demographic features, clinical characteristics, and maternal and perinatal outcomes were evaluated.

Results: SARS-CoV-2 was suspected in 100 pregnant women. Of them, 29 had the diagnosis confirmed by RT-PCR. Eight of the remaining 71 cases had clinical findings highly suspicious for COVID-19. Ten (34.5%) of the confirmed cases had co-morbidities. Cough (58.6%) and myalgia (51.7%) were the leading symptoms. COVID-19 therapy was given to 10 (34.5%) patients. There were no admissions to the intensive care unit. Pregnancy complications were present in 7 (24.1%) patients. Half of the births (5/10) were cesarean deliveries. None of the neonates were positive for SARS-CoV-2. Samples of breastmilk were also negative for the virus. Three neonates were admitted to the neonatal intensive care unit.

Conclusion: The clinical course of COVID 19 during pregnancy appears to be mild in the present study.

KEYWORDS

COVID-19; Maternal outcome; Neonatal outcomes; Obstetric outcomes; Pregnancy; SARS-CoV-2

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a global health problem threatening billions of lives all over the world. It is caused by a novel coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and unfortunately, no effective treatment is available at the time of publication.^{1,2}

Healthcare systems have been deeply affected by this pandemic and there continue to be unanswered questions in the minds of clinicians regarding the impact of COVID-19 on groups of high-risk patients. Pregnancy is a unique health condition characterized by prominent physiological changes in the bodies of women and it has been long known that infections may cause severe complications during the pregnancy period.³⁻⁵ However, there are conflicting reports

in the literature about the course and effect of COVID-19 in pregnant women.^{1,2,6,7} Although the prognosis in pregnant women has been generally found to be similar to non-pregnant individuals of the same age, studies have emphasized an increased risk for certain obstetric complications such as preterm delivery and fetal compromise.^{1,2,6,7} Additionally, there are concerns about the possibility of vertical transmission.⁷ Nonetheless, knowledge is still limited on these issues and more data are urgently needed to establish more effective management protocols for pregnant women. For this reason, the experiences of tertiary referral centers are invaluable.

The aim of the present study was to evaluate the clinical course and effect of COVID-19 on pregnant women at a Turkish institution.

2 | MATERIALS AND METHODS

The present prospective cohort study was conducted on pregnant women with confirmed or suspected SARS-CoV-2 infection who were admitted to the Ministry of Health Ankara City Hospital between March 11, 2020, and June 11, 2020. All consecutive pregnancies screened for SARS-CoV-2 infection during the study period were included in the study. Written informed consent for participation in the study was obtained from all the patients and the study was conducted in accordance with the Declaration of Helsinki.⁸ Pregnant women diagnosed with other respiratory tract pathogens were excluded from the study. The information of all patients, including demographic data, clinical characteristics, laboratory parameters, and outcomes, were collected prospectively. The study protocol was approved by the Turkish Ministry of Health and the institutional ethics committee (E1-20-602).

Demographic features, clinical characteristics, and obstetric outcomes of pregnant women with suspected or confirmed SARS-CoV-2 infection were retrospectively evaluated from the hospital records. The diagnosis of SARS-CoV-2 infection was made by a positive result on a real-time polymerase chain reaction (RT-PCR) assay of a nasopharyngeal and oropharyngeal specimen.⁹ Patients with significant clinical features (for example, body temperature $\geq 38^{\circ}\text{C}$, oxygen saturation $\leq 93\%$ and/or respiratory rate $\geq 20/\text{min}$, lymphocyte count $\leq 1000/\text{mm}^3$, and a confirmed case in the household) and/or suspicious radiologic findings for COVID-19 (for example, ground-glass opacification, mixed consolidation, pleural thickening, interlobular septal thickening, air bronchograms) but with negative RT-PCR for SARS-CoV-2 were regarded as highly suspicious for COVID-19 in the present study. These cases were evaluated as a separate group.

The following were recorded: maternal age, gravidity, parity, number of living children, number of previous miscarriages, pre-pregnancy body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters), route of admission to hospital, comorbid diseases, gestational age and pregnancy trimester at diagnosis of COVID-19, initial symptoms, history of close contact with a confirmed or suspected case, abnormal vital signs on admission to hospital, pregnancy-specific medications, therapy for COVID-19, use of low molecular weight heparin, presence of an additional pathogen,

disease severity, rate of respiratory support, rate of admission to the intensive care unit (ICU), length of hospital stay, initial laboratory test results, radiologic imaging findings, blood group, pregnancy complications, mode of delivery, and obstetric and neonatal outcomes. Severity of disease was assessed according to current guidelines.^{10,11} Furthermore, treatment protocols were determined in accordance with the national COVID-19 guidelines.¹⁰

The RT-PCR test for SARS-CoV-2 was performed on nasopharyngeal and oropharyngeal swabs of all neonates and breastmilk samples of all mothers. Detection of SARS-CoV2 in oropharyngeal and nasopharyngeal samples was performed by the RT-PCR method targeting the RNA-dependent RNA polymerase (RdRp) gene. Sterile Dacron or rayon swabs with flexible plastic shafts were used to collect nasopharyngeal and oropharyngeal samples from patients. After collection, swabs were placed into 2 mL of sterile viral transport medium (VTM; various manufacturers). Samples were transported to the Molecular Virology Laboratory within 12 hours of collection and tested on arrival without delay. Extraction of RNA from samples was performed using the Biospeedy Viral Nucleic Acid Isolation Kit (Bioeksen, Istanbul, Turkey) according to the manufacturer's instructions; swab samples in VTM were vortexed for 15 seconds and then a 100- μL sample was transferred to a 1.5-mL microcentrifuge tube containing 100 μL viral nucleic acid extraction buffer supplied by the manufacturer. After vortexing again, the tube was ready for PCR. Real-time RT-PCR was performed using the Bio-Speedy COVID-19 RT-qPCR Detection Kit (Bioeksen). A 20- μL reaction contained 5 μL of RNA, 5 μL of Oligo Mix (RdRp gene for SARS-CoV-2 detection, Rnase P gene for internal control), 10 μL of 2 \times Primer Script Mix containing Taq Polymerase, each deoxyribo triphosphates (dNTP), reverse transcriptase, and ribonuclease inhibitor. Thermal cycling was performed at 45 $^{\circ}\text{C}$ for 10 minutes for reverse transcription, followed by 95 $^{\circ}\text{C}$ for 3 minutes, and then 45 cycles of 95 $^{\circ}\text{C}$ for 5 seconds and 55 $^{\circ}\text{C}$ for 35 seconds in the Rotor-Gene Q device (Qiagen, Hilden, Germany). Cycle threshold values under 40 were defined as positive.

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS.22, IBM SPSS Statistics for Windows, Version 22.0, IBM Corp., Armonk, NY, USA). Visual (histograms, probability plots) and analytical methods (Kolmogorov-Smirnov test) were used to determine the normality of distribution. Mean or median values were used for descriptive analysis according to the characteristics of data for normal distribution. Categorical data were presented as percentages.

3 | RESULTS

Ankara City Hospital is a new tertiary referral center in the capital of Turkey which was established in June 2019 and covers all medical and surgical disciplines. Its Department of Obstetrics and Gynecology is one of the main maternity centers in Turkey with approximately 1100 deliveries per month. The hospital has served 28 086 obstetric patients since the beginning of the pandemic. Moreover, it has been serving as one of the main national pandemic centers since the beginning of

the COVID-19 outbreak. Since the beginning of the study period, a total of 27 737 SARS-CoV-2 RT-PCR tests have been performed in our hospital and 3568 (12.8%) were found to be positive. A total of 100 pregnant women with confirmed or suspected SARS-CoV-2 were cared for by the Department of Obstetrics and Gynecology during the study period and 29 (29%) of them had an RT-PCR proven diagnosis of COVID-19. Among the remaining 71 patients, 8 (11.2%) were regarded as highly clinically suspicious for COVID-19 (Fig. 1). All cases were hospitalized until their RT-PCR results became negative on two swab tests taken 24 hours apart.

Demographic features, clinical characteristics, and obstetric outcomes of cases with SARS-CoV-2 RT-PCR positivity are shown in Table 1. Ten cases (34.5%) had clinical co-morbidities: obesity was the leading condition (50%) followed by hypothyroidism (40%). Fifteen cases (51.7%) were diagnosed in the third trimester. Cough and myalgia were the leading initial symptoms (58.6% and 51.7%, respectively).

Twenty-three cases (79.3%) had close contact with a confirmed or suspected case before admission. Fever, tachypnea, and tachycardia were the most common abnormal vital signs during admission (27.6%, 24.1%, and 27.6%, respectively). Tocolytic agents were not administered to any of the positive cases and antenatal corticosteroids for fetal lung maturity were used in only 1 (3.4%) case. Therapy for COVID-19 was given in 10 (34.5%) patients and hydroxychloroquine was the most common medication (34.5%). Low molecular weight heparin was administered in 9 (31%) cases. Adenovirus was found as an additional pathogen in 1 (3.4%) case. Twenty-five cases (86.2%) had mild COVID-19. Respiratory support was needed in 4 (13.8%) cases and all of these patients received nasal oxygen therapy. None of the cases were admitted to ICU. The mean length of hospital stay was 6 days.

Initial laboratory test results of cases positive for SARS-CoV-2 with RT-PCR are shown in Table 2. Neutrophilia ($>7700/\text{mm}^3$ or $>70\%$ of leukocytes) and lymphocytopenia ($<1000/\text{mm}^3$ or $<8\%$ of leukocytes)

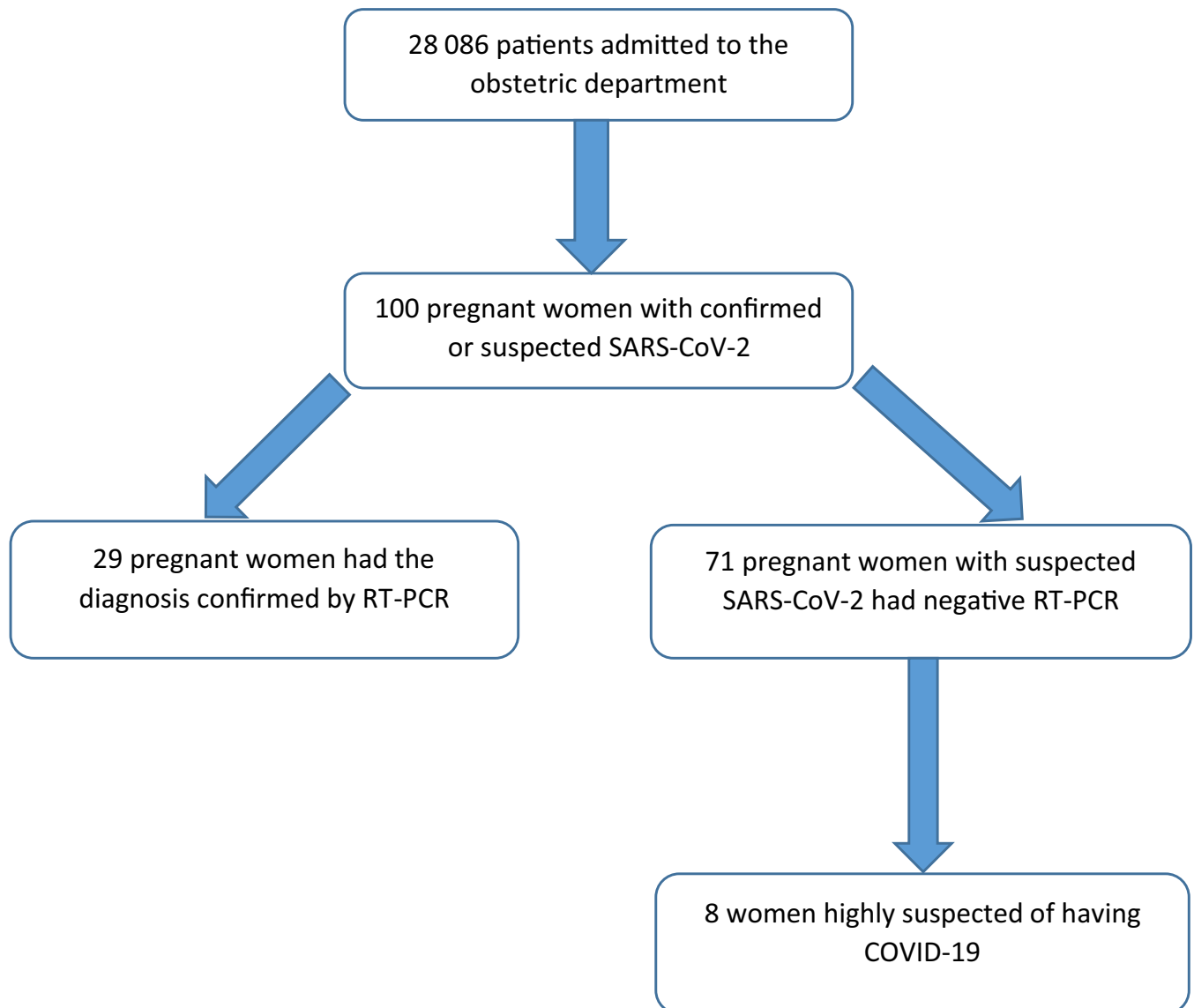


FIGURE 1 Flowchart of the study. Abbreviations: COVID-19, coronavirus disease 2019; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

TABLE 1 Demographic features and clinical characteristics of cases positive for SARS-CoV-2 with RT-PCR (n=29).^a

Variables	Values
Maternal age (years)	26.38 ± 5.52 (17–40)
Gravidity	2 (2, 0–5)
Parity	1 (1.5, 0–4)
Living child	1 (1.5, 0–4)
Previous miscarriage	0 (0, 0–2)
Pre-pregnancy BMI (kg/m ²)	26.40 ± 5.34 (18–38)
Route of admission to the hospital	
Emergency service	11 (37.9)
Ambulance	11 (37.9)
Referral from another hospital	7 (24.1)
Co-morbid disease	10 (34.5)
Obesity	5 (50)
Hypothyroidism	4 (40)
Asthma	1 (10)
Gestational age at diagnosis (weeks)	26.93 ± 1.96 (5–39)
Pregnancy trimester at diagnosis	
First	6 (20.7)
Second	8 (27.6)
Third	15 (51.7)
Initial symptoms	
Fever	8 (27.6)
Cough	17 (58.6)
Dyspnea	10 (34.5)
Chest pain	1 (3.4)
Myalgia	15 (51.7)
Nasal congestion	4 (13.8)
Sore throat	11 (37.9)
Anosmia	9 (31)
Ageusia	6 (20.7)
Headache	7 (24.1)
Nausea/vomiting	6 (20.7)
Diarrhea	1 (3.4)
Close contact with a confirmed or suspected case	23 (79.3)
Abnormal vital signs at admission to hospital	
Fever (body temperature ≥38°C)	8 (27.6)
Tachypnea (respiratory rate ≥20/min)	7 (24.1)
Tachycardia (heart rate ≥100/min)	8 (27.6)
Oxygen saturation ≤93%	4 (13.8)
Pregnancy-specific medications	1 (3.4)
Tocolytic agent	0 (0)
Antenatal corticosteroid	1 (3.4)
COVID-19 therapy	10 (34.5)
Hydroxychloroquine	10 (34.5)

(Continues)

TABLE 1 (Continued)

Variables	Values
Azithromycin	3 (10.3)
Lopinavir-ritonavir	1 (3.4)
Oseltamivir	0 (0)
Low molecular weight heparin	9 (31)
Additional pathogen	1 (3.4)
COVID-19 severity	
Mild	25 (86.2)
Moderate	1 (3.4)
Severe	3 (10.3)
Critical	0 (0)
Respiratory support	4 (13.8)
Nasal oxygen therapy	4 (13.8)
Non-invasive ventilation	0 (0)
Invasive mechanical ventilation	0 (0)
ICU admission	0 (0)
Length of hospital stay (days)	6.30 ± 0.70 (1–20)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; ICU, intensive care unit; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aValues are given as number (percentage), mean ± standard deviation (range), or median (interquartile range, range).

were present in 6 (20.7%) and 9 (31%) patients, respectively. The mean neutrophil to lymphocyte ratio was 4:1. Radiologic imaging was performed in 8 (27.6%) cases and findings suspicious for COVID-19 were found in 5 (17.2%) cases. A Rhesus positive was the most common blood group (48.3%). It has been reported that there was a higher risk for COVID-19 infection with blood group A compared with non-A blood groups.^{12,13}

Obstetric and neonatal outcomes of cases positive for SARS-CoV-2 with RT-PCR are shown in Table 3. Pregnancy complications were observed in 7 (24.1%) patients. The only fetal abnormality detected in the present study was a skeletal dysplasia. Ten patients (34.5%) delivered during the study period and half were delivered by cesarean section. Regional anesthesia was the most common method of anesthesia for cesarean delivery (80%). Two cesarean sections (40%) were performed due to the maternal health conditions and fetal compromise was observed in 1 (20%) case. Normal spontaneous vaginal deliveries were managed by obstetricians with a unique institutional personal protective equipment: the delivery table shield.¹⁴ During the study period, none of the neonates delivered from mothers positive for SARS-CoV-2 showed any clinical symptoms. The RT-PCR study of nasopharyngeal and oropharyngeal samples obtained from all neonates were negative on the first, third, and 14h day of postnatal age. Only three neonates (born at 27, 30, and 31 weeks of gestation, respectively) experienced respiratory distress due to prematurity and required respiratory support in the neonatal ICU (NICU). Breastmilk specimen samples from all women were negative for SARS-CoV-2.

TABLE 2 Initial laboratory test results of cases positive for SARS-CoV-2 with RT-PCR (n=29).^a

Variables	Values
Hb (g/dL)	11.38 ± 0.20 (9.5–13.4)
Hct (%)	33.5 ± 0.65 (27.3–41.3)
Hb <10 mg/dL	3 (10.3)
Leukocyte (10 ³ /mm ³)	6900.68 ± 2879 (2850–12270)
Leukocytosis (>11 000/mm ³)	5 (17.2)
Neutrophil (10 ³ /mm ³)	4996.20 ± 2420.10 (1650–9540)
Neutrophil percentage (%)	57.17 ± 27.20 (62–80.6)
Neutrophilia (>7700/mm ³ or >70% of leukocytes)	6 (20.7)
Lymphocyte (10 ³ /mm ³)	1317.24 ± 542.40 (590–2830)
Lymphocyte percentage (%)	20.55 ± 8.20 (8.2–39.4)
Lymphocytopenia (<1000/mm ³ or <8% of leukocytes)	9 (31)
Neutrophil to lymphocyte ratio	4.10 ± 2.10 (1.2–10.5)
Platelet (10 ³ /mm ³)	210 931.1 ± 50 235.1 (135 000–328 000)
ESR (mm/h)	24.10 ± 23.10 (2–76)
CRP (mg/dL)	15.5 ± 20.5 (1–81)
Procalcitonin (ng/mL)	0.20 ± 0.70 (0–0.4)
IL-6 (pg/mL)	3.28 ± 4.34 (0–20)
Ferritin (ng/mL)	29.70 ± 50.71 (10–238)
BUN (mmol/L)	17.58 ± 4.78 (9–26)
Creatinine (mg/dL)	0.45 ± 0.16 (0.30–0.90)
ALT (IU/L)	27.75 ± 37.22 (8–180)
AST (IU/L)	26.96 ± 28.26 (9–126)
LDH (IU/L)	214.90 ± 80.20 (125–476)
D-Dimer (mcg/mL)	2.08 ± 2.94 (0.01–13.60)
Radiologic imaging	8 (27.6)
Radiologic imaging findings suspicious for COVID-19	5 (17.2)
Blood group	
A+	14 (48.3)
A-	2 (6.9)
B+	6 (20.7)
B-	0 (0)
AB+	0 (0)
AB-	0 (0)
O+	7 (24.1)
O-	0 (0)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; IL-6, interleukin 6; LDH, lactate dehydrogenase; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aValues are given as number (percentage) or mean ± standard deviation (range).

TABLE 3 Obstetric and neonatal outcomes of cases positive for SARS-CoV-2 with RT-PCR (n=29).^a

Variables	Values
Pregnancy complications	7 (24.1)
Threatened abortion	1 (3.4)
Cholestasis of pregnancy	2 (6.9)
Fetal anomaly	1 (3.4)
Preterm delivery	2 (6.9)
Pre-eclampsia	1 (3.4)
Delivery status	
Ongoing pregnancy	19 (65.5)
Delivered	10 (34.5)
Time between diagnosis and delivery (days)	3.66 ± 2.51 (1–6)
Route of delivery	
Normal spontaneous vaginal delivery	5 (50)
Cesarean section	5 (50)
Cesarean indications	
Maternal health condition	2 (40)
Macrosomia	1 (20)
Cephalopelvic disproportion	1 (20)
Fetal distress	1 (20)
Labor anesthesia	
None	24 (82.8)
General	1 (3.4)
Regional	4 (13.8)
Spontaneous labor	6 (60)
Gestational age at delivery (weeks)	37.70 ± 2.66 (31–40)
Birth weight (g)	3127.00 ± 720.20 (1630–4010)
Apgar 1st minute	8 (1.25, 6–9)
Apgar 5th minute	9 (1, 8–10)
Admission to NICU	3 (30)
Neonatal SARS-CoV-2 positivity	0 (0)
Breastmilk positive for SARS-CoV-2	0 (0)

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 2019; NICU, neonatal intensive care unit; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aValues are given as number (percentage), mean ± standard deviation (range), or median (interquartile range, range).

A summary of 8 (11.2%) cases with high clinical suspicion for COVID-19 but negative RT-PCR for SARS-CoV-2 is shown in Table 4. Computed tomography (CT) was consistent with COVID-19 in 7 (87.5%) cases. Three patients (37.5%) were in the postnatal period. Co-morbid diseases were observed in 3 (37.5%) cases and obstetric complications were present in 6 (75%) patients. COVID-19 therapy was administered to 7 (87.5%) patients. Two patients (25%) were still

TABLE 4 Summary of cases with high clinical suspicion for COVID-19 but negative RT-PCR for SARS-CoV-2 (n=8).^a

Variables	Values
Maternal age (years)	32.62 ± 2.56 (21–40)
Gravidity	2 (2.5, 1–7)
Parity	1 (2.5, 0–4)
Living child	1 (1.75, 0–4)
Previous miscarriage	0 (0.75, 0–2)
Pre-pregnancy BMI (kg/m ²)	25.30 ± 2.85 (19–28)
Route of admission to the hospital	
Emergency service	3 (37.5)
Ambulance	3 (37.5)
Referral from another hospital	2 (25)
Co-morbid disease	
ITP	1 (25)
CHF	1 (25)
CKD	1 (25)
HT	1 (25)
Gestational age at diagnosis (weeks)	28.4 ± 17.8 (5–40)
Pregnancy trimester at diagnosis	
First	1 (12.5)
Second	1 (12.5)
Third	3 (37.5)
Postpartum period	3 (37.5)
Initial symptoms	
Fever	5 (62.5)
Cough	4 (50)
Dyspnea	5 (62.5)
Myalgia	2 (25)
Anosmia	1 (12.5)
Close contact with a confirmed or suspected case	3 (37.5)
Abnormal vital signs at admission to hospital	
Fever (body temperature ≥38 °C)	5 (62.5)
Tachypnea (respiratory rate ≥20/min)	1 (12.5)
Tachycardia (heart rate ≥100/min)	1 (12.5)
Oxygen saturation ≤93%	4 (50)
COVID-19 therapy	7 (87.5)
Hydroxychloroquine	7 (87.5)
Azithromycin	6 (75)
Oseltamivir	4 (50)
Low molecular weight heparin	4 (50)
Respiratory support	4 (50)
Admission to ICU	0 (0)
Length of hospital stay (days)	4.37 ± 1.5 (3–7)

(Continues)

TABLE 4 (Continued)

Variables	Values
Nasal oxygen therapy	4 (50)
Neutrophilia (>7700/mm ³ or >70% of leukocytes)	6 (75)
Lymphocytopenia (<1000/mm ³ or <8% of leukocytes)	4 (50)
Radiologic imaging	7 (87.5)
Radiologic imaging findings suspicious for COVID-19	7 (87.5)
Blood group	
A+	3 (37.5)
A-	0 (0)
B+	1 (12.5)
B-	0 (0)
AB+	2 (25)
AB-	0 (0)
O+	2 (25)
O-	0 (0)
Patients with pregnancy complications	6 (75)
Pregnancy complication types	
Fetal growth restriction	3 (37.5)
Preterm delivery	3 (37.5)
Intrauterine fetal demise	1 (12.5)
Oligohydramnios	1 (12.5)
Pre-eclampsia	1 (12.5)
Preterm premature rupture of membranes	1 (12.5)
Delivery status	
Ongoing pregnancy	2 (25)
Delivered	6 (75)
Route of delivery	
Normal spontaneous vaginal delivery	3 (50)
Cesarean section	3 (50)
Cesarean indications	
Fetal distress	3 (100)
Labor anesthesia	
None	3 (50)
General	2 (33.3)
Regional	1 (16.6)
Spontaneous labor	2 (33.3)
Gestational age at delivery (weeks)	34.2 ± 4.55 (28–40)
Birth weight (g)	2350 ± 993.73 (1400–3700)
Apgar 1st minute	6 (4, 3–9)
Apgar 5th minute	8 (3.5, 5–10)
Admission to NICU	3 (37.5)

(Continues)

TABLE 4 (Continued)

Variables	Values
Neonatal SARS-CoV-2 positivity	0 (0)
Breastmilk positive for SARS-CoV-2	0 (0)

Abbreviations: BMI, body mass index; CHF, chronic heart failure; CKD, chronic kidney disease; COVID-19, coronavirus disease 2019; HT, hypertension; ICU, intensive care unit; ITP, immune thrombocytopenic purpura; NICU, neonatal intensive care unit; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^aValues are given as number (percentage), mean \pm standard deviation (range), or median (interquartile range, range).

pregnant in this group during the study period and the rate of cesarean delivery was 50% in the remaining cases.

4 | DISCUSSION

The findings of the present study indicate that the course of COVID-19 during pregnancy was favorable in the study population. On the other hand, relatively high rates of pregnancy complications were observed.

The Turkish Ministry of Health has been effectively fighting SARS-CoV-2 since the early days of the pandemic. Establishment of a competent scientific committee, identification of suspected cases by well-organized filiation teams, hospitalization of all cases of COVID-19, administration of medications in the early stages of the disease, and specific intensive care protocols resulted in better patient outcomes than in many other countries.^{10,15}

The course of COVID-19 during pregnancy has been investigated in various studies.^{2,6,7,16-18} Although the course of the disease was found to be similar to non-pregnant women in most publications, severe complications such as prolonged ventilator support, need for extracorporeal membrane oxygenation, cardiovascular events, and multi-organ failure were also reported.^{2,6,7,16-18} Fortunately, no maternal death or serious morbidity was observed in the present study. No cases were admitted to the ICU and only nasal oxygen therapy was necessitated in a small number of patients.

It has been reported that individuals with co-morbid diseases are more susceptible to COVID-19.^{19,20} Approximately one-third of confirmed cases in the present study had co-morbid diseases consistent with the literature.^{19,20} Therefore, we can conclude that physicians should be cautious in the management of pregnancies complicated by maternal disease.

Fever, cough, myalgia, and dyspnea were the most common symptoms of COVID-19 described in the literature and this is consistent with the results of the present study.²¹

The majority of the women in the present study were in the third trimester of pregnancy and approximately one-third of them delivered during the study period. The current literature indicated increased rates of cesarean section and a preference for regional anesthesia. Furthermore, the decision for delivery due to maternal health conditions and increased rates of fetal distress were discussed in other

publications.^{11,17,22,23} Half of the cases in the present study were delivered via cesarean section, mostly under regional anesthesia. These findings were consistent with the literature.

Another important issue is the use of medications during pregnancy. The safety and efficacy of treatments for COVID-19 during pregnancy are equivocal. Moreover, the effect of pregnancy-specific medications during COVID-19 infection is also questionable.^{24,25} Venous thromboembolism prophylaxis was recommended for pregnant hospitalized patients unless there was a contraindication.²⁶ Approximately one-third of cases received COVID-19 therapy and low molecular weight heparin. This relatively low rate of medication was due to the high number of mild cases in the present study. On the other hand, administration of antenatal corticosteroids was observed in only one case and no tocolysis was performed in the present study.

Although there is no specific laboratory test alteration in COVID-19 infection, neutrophilia, lymphocytopenia, increased neutrophil to lymphocyte ratio, interleukin 6, D-dimer, hepatic function tests, and acute phase reactants are the most common findings in the general population.^{2,27} However, at present, the authors' knowledge is limited to pregnant women. Lymphocytopenia and neutrophilia were the main findings in the present study. Additionally, radiologic imaging has been widely used as an ancillary test since the beginning of the pandemic.^{28,29} Chest CT was performed in approximately one-quarter of the confirmed cases in the present study and more than half of them had findings consistent with COVID-19 infection. These results indicated that radiologic imaging might be useful in appropriately selected cases.

Increased rates of preterm delivery, fetal compromise, and cesarean section have been reported in pregnancies complicated by COVID-19.^{1,2,6,7} Complications in pregnancy were observed in approximately one-quarter of cases in the present study, consistent with the literature.^{1,2,6,7}

Some publications claimed that blood group A was associated with a higher risk of acquiring COVID-19 and blood group O was associated with a lower risk of infection.^{30,31} Although it was also found that blood group A was more common in positive cases, there was no case with an AB group unlike in the previous studies.

There are increasing concerns about vertical transmission of COVID-19 and possible infection of the newborn during breastfeeding.^{32,33} However, no virus was detected in the nasopharyngeal and/or oropharyngeal swabs nor in the breast milk samples in the present study.

The unique part of the present study was a comprehensive evaluation of patients with high clinical suspicion. Even though their RT-PCR tests were negative, some cases in the study were managed as if they were positive for SARS-CoV-2. It has been reported that the sensitivity of testing depends on the precise assay, the type of specimen obtained, the quality of the specimen, and the duration of illness at the time of testing. Thus, physicians should be cautious in the management of cases with high clinical suspicion of COVID-19.^{34,35}

It is believed that one of the most successful healthcare policies of the Turkish Ministry of Health is the meticulous management of cases of COVID-19 and the application of an individualized approach.

Although it is controversial, when there was high clinical suspicion of COVID-19, the evaluation of a patient by chest CT played a key role in the management of the cases in the study cohort. Timely management of suspected cases provides optimal control of the disease and prevention of serious disease-related complications.

The strengths of the present study were the relatively high number of study parameters and the inclusion of clinically suspected cases. On the other hand, the lack of information relating to the final obstetric and neonatal outcomes of patients who had not delivered by the end of the study period was the main limitation.

In conclusion, the clinical course of COVID-19 during pregnancy appears to be mild in the present study. RT-PCR positivity as well as clinical findings should be considered in the management of COVID-19 during pregnancy. The hospitalization of all pregnant women with confirmed and suspected COVID-19 infection, the provision of an individualized approach, the appropriate use of medications, and the management of cases within the framework of a multidisciplinary team seem to be associated with favorable outcomes.

AUTHOR CONTRIBUTIONS

All the authors had substantial contributions to the concept and design, the execution of the work, or the analysis and interpretation of data, drafting or revising the manuscript, and have read and approved the final version of the paper. DS: Conceptualization, methodology, visualization, reviewing, and editing. AT: Original draft preparation, writing, data collection. SAE: Data collection. ATA: Data collection. EGYE: Reviewing and editing. ASO-E: Visualization, reviewing, and editing. AY: Literature search. reviewing and editing. HLK: Analysis/interpretation. CT: Data collection. SU: Data collection. FK: Resources, analysis/interpretation. BD: Resources, analysis/interpretation. IS: Supervision. UMP: Supervision. AAS: Supervision. OMT: Project development.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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