

## CLINICAL ARTICLE

## Obstetrics

# Updated experience of a tertiary pandemic center on 533 pregnant women with COVID-19 infection: A prospective cohort study from Turkey

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## Abstract

**Objective:** To investigate the clinical course and impact of coronavirus disease 2019 (COVID-19) infection on pregnant women.

**Methods:** A prospective cohort study was conducted on pregnant women with confirmed COVID-19 infection. Demographic features, clinical characteristics, and perinatal outcomes were prospectively evaluated.

**Results:** Of the 533 cases, 161 (30.2%) had co-morbidities and 165 (30.9%) were asymptomatic. Cough ( $n = 178$ , 33.4%) and myalgia ( $n = 168$ , 31.5%) were the leading symptoms. In total, 261 patients (48.9%) received COVID-19 therapy, 509 (95.5%) had mild disease, 7 (1.3%) were admitted to the intensive care unit (ICU), and invasive mechanical ventilation was necessary in 2 (0.4%) patients. Maternal mortality was observed in 2 (0.4%) cases. Of the patients, 297 (55.7%) were hospitalized, 39 (7.3%) had suspicious radiologic imaging findings, 66 (12.4) had pregnancy complications (preterm delivery [ $n = 22$ , 4.1%] and miscarriage [ $n = 12$ , 2.2%] were the most common pregnancy complications), 131 births occurred, and the cesarean section rate was 66.4%. All neonates were negative for COVID-19. The rate of admission to the neonatal ICU was 9.9%. One specimen of breast milk was positive for the infection.

**Conclusion:** The course of COVID-19 was mild in the majority of cases. However, increased rates of pregnancy complications and cesarean delivery were observed.

## KEYWORDS

COVID-19, pandemic, perinatal outcomes, pregnancy, SARS-CoV-2

## 1 | INTRODUCTION

Coronavirus disease 19 (COVID-19) is a highly contagious infection that can be deadly and is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).<sup>1</sup> As pregnancy is a unique condition characterized by prominent physiologic changes in the cardiovascular, respiratory, and immune systems, researchers have questions related to the impact of COVID-19 on pregnant women.<sup>2,3</sup> The current literature indicates that pregnancy may worsen the course of COVID-19 infection compared to non-pregnant women of the same age. On the other hand, the course of severe or critical COVID-19 in hospitalized pregnant women has been shown to be shorter than in the non-pregnant population.<sup>2,3</sup> It has been stated that COVID-19 may cause an increase in obstetric complications such as preterm labor and fetal distress.<sup>2,3</sup> However, international knowledge is still limited on this issue and the experience of large pandemic centers will help to achieve better results.

Ankara City Hospital is one of the leading pandemic centers in Turkey and the authors previously shared their experience on pregnant women with COVID-19 infection.<sup>4</sup> As the number of cases has increased dramatically since the initial publication of that study, the authors intend to share their updated experience on pregnant women with COVID-19. The aim of the present study was to investigate the clinical course and impact of COVID-19 infection on pregnant women at one of the biggest pandemic centers in Turkey.

## 2 | MATERIALS AND METHODS

The present prospective cohort study was conducted on pregnant women with confirmed COVID-19 infection who were followed up at the Turkish Ministry of Health Ankara City Hospital between March 11, 2020, and September 10, 2020. All consecutive pregnancies with confirmed SARS-CoV-2 positivity were included in the study. Pregnancies with negative real-time polymerase chain reaction (RT-PCR) results for SARS-CoV-2 were excluded from the study. Informed consent was obtained from all patients and the study protocol was approved by both the institutional ethics committee and the Turkish Ministry of Health (E1-20-602).

The present study is an updated version of the previously published research by Sahin et al.<sup>4</sup> A precise diagnosis of COVID-19 infection was made by the detection of SARS-CoV-2 positivity on RT-PCR analysis of nasopharyngeal and oropharyngeal specimens collected from the participants.<sup>4</sup> The following information was prospectively recorded by the researchers: maternal age; gravidity; parity; number of living children; previous miscarriages; pre-pregnancy body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters; BMI  $\geq 30$  was defined as obese); route of admission to hospital; co-morbid diseases; gestational age at diagnosis; pregnancy trimester at diagnosis; initial symptoms; close contact with a confirmed or suspected case; abnormal vital signs at admission; medications for pregnancy complications; COVID-19-related medications; disease severity; respiratory support; admission to the intensive care unit (ICU); maternal mortality;

hospitalization rate; length of hospital stay; initial laboratory test results; radiologic imaging findings; blood group; pregnancy complications; mode of delivery; and obstetric and neonatal outcomes. All cases were managed according to the national guidelines at the time of the study by a multidisciplinary team comprising obstetricians, perinatologists, radiologists, neonatologists, and infectious disease specialists.<sup>5</sup>

Statistical analyses were performed using SPSS version 22 (IBM Corp.). Mean or median values were used for descriptive variables according to the characteristics of the data. Categorical data were presented as numbers and percentages.

## 3 | RESULTS

During the study period, 533 pregnancies diagnosed with COVID-19 infection were followed up in the study institution. Demographic features and clinical characteristics of the cases are shown in Table 1. A total of 161 (30.2%) cases had co-morbidities, of which obesity was the leading one ( $n = 71$ , 44.1%). A total of 238 (44.7%) cases were diagnosed in the third trimester. One hundred and sixty-five cases (30.9%) were asymptomatic. Cough ( $n = 178$ , 33.4%) and myalgia ( $n = 168$ , 31.5%) were the leading symptoms. One hundred and twenty-eight patients (24.1%) had close contact with a confirmed or suspected case. Tachycardia ( $n = 150$ , 28.1%) and fever ( $n = 71$ , 13.3%) were the most common abnormal vital signs. Thirty-three patients (6.2%) received pregnancy-specific medications. Tocolytic agents and antenatal corticosteroids were administered in 9 (1.7%) and 24 (4.5%) cases, respectively. Two hundred and sixty-one patients (48.9%) received COVID-19 therapy. Low-molecular weight heparin was administered in 220 (41.3%) cases. Hydroxychloroquine was the most common (10.3%) and tocilizumab was the least common (0.2%) administered medication. The vast majority of the patients had mild disease ( $n = 509$ , 95.5%). Seven cases (1.3%) were admitted to the ICU and invasive mechanical ventilation was necessitated in 2 (0.4%) patients. Respiratory support was given to 22 (4.1%) patients and 2 (0.4%) were intubated.

Maternal mortality was observed in 2 (0.4%) cases. The first case of maternal mortality was a 27-year-old primigravida at 18 weeks of pregnancy who was admitted to hospital via ambulance for RT-PCR positivity. On admission, she had lymphopenia ( $540 \text{ mm}^3/\text{mL}$ ), hypokalemia ( $2.2 \text{ mmol/L}$ ), and low oxygen saturation (88%). Her close relatives were also positive for COVID-19. She had a persistent fever despite treatment with hydroxychloroquine and lopinavir-ritonavir. Her interleukin levels reached  $1000 \text{ pg/mL}$ . Admission to the ICU was needed on the third day of hospitalization. High-flow oxygen with a nasal cannula together with systemic corticosteroid and recombinant human IL-1 receptor antagonist were administered in the ICU. However, her clinical condition worsened and she was intubated. A spontaneous miscarriage ensued on the ninth day of her hospital stay. She received postdelivery intravenous oxytocin and the placenta was expelled spontaneously. No surgical intervention was necessitated. Convalescent plasma therapy and favipiravir were added to the treatment protocol. Unfortunately, the patient went

**TABLE 1** Demographic features and clinical characteristics of pregnant women with COVID-19 infection (*n* = 533)<sup>a</sup>

| Variables  | Values               |
|--|----------------------|
| Maternal age (years)                             | 28.04 ± 5.84 (17–47) |
| Gravidity  | 2 (2, 0–8)           |
| Parity   | 1 (2, 0–7)           |
| Living child                                     | 1 (1, 0–7)           |
| Previous miscarriage                             | 0 (0, 0–6)           |
| Pre-pregnancy BMI (kg/m <sup>2</sup> )           | 26.49 ± 5.47 (18–40) |
| Route of admission to the hospital               |                      |
| Emergency service                                | 291 (54.6)           |
| Ambulance  | 223 (41.8)           |
| Referral from another hospital                   | 19 (3.6)             |
| Co-morbid disease                                |                      |
| Obesity  | 71 (44.1)            |
| Hypothyroidism                                   | 28 (17.4)            |
| Hypertension                                     | 23 (14.3)            |
| Diabetes mellitus type 2                         | 8 (4.9)              |
| Asthma   | 8 (4.9)              |
| Rheumatological disease                          | 7 (4.3)              |
| Cardiovascular disease                           | 5 (3.1)              |
| Diabetes mellitus type 1                         | 3 (1.9)              |
| Thalassemia minor                                | 2 (1.2)              |
| ITP  | 2 (1.2)              |
| Renal disease                                    | 2 (1.2)              |
| Epilepsy   | 2 (1.2)              |
| Gestational age at diagnosis (weeks)             | 24.97 ± 11.16 (4–41) |
| Pregnancy trimester at diagnosis                 |                      |
| First  | 130 (24.4)           |
| Second   | 165 (30.9)           |
| Third  | 238 (44.7)           |
| Initial symptoms                                 |                      |
| Asymptomatic                                     | 165 (30.9)           |
| Symptomatic                                      | 368 (69.1)           |
| Cough  | 178 (33.4)           |
| Myalgia  | 168 (31.5)           |
| Dyspnea  | 99 (18.6)            |
| Sore throat                                      | 83 (15.6)            |
| Fever  | 71 (13.3)            |
| Headache   | 65 (12.2)            |
| Anosmia  | 64 (12)              |
| Ageusia  | 46 (8.6)             |
| Nausea/vomiting                                  | 32 (6)               |
| Nasal congestion                                 | 28 (5.2)             |
| Diarrhea   | 21 (3.9)             |
| Chest pain                                       | 12 (2.2)             |
| Close contact with a confirmed or suspected case | 128 (24.1)           |

**Table 1** (Continued)

| Variables                                     | Values            |
|---|-------------------|
| Abnormal vital signs at admission to hospital |                   |
| Tachycardia (heart rate ≥100/min)             | 150 (28.1)        |
| Fever (≥38°C)                                 | 71 (13.3)         |
| Tachypnea (respiratory rate ≥20/min)          | 18 (3.4)          |
| Oxygen saturation ≤93%                        | 15 (2.8)          |
| Pregnancy-specific medications                |                   |
| Tocolytic agent                               | 9 (1.7)           |
| Antenatal corticosteroid                      | 24 (4.5)          |
| COVID-19 therapy                              |                   |
| Low-molecular weight heparin                  | 220 (41.3)        |
| Hydroxychloroquine                            | 55 (10.3)         |
| Lopinavir-ritonavir                           | 33 (6.2)          |
| Systemic corticosteroid                       | 20 (3.7)          |
| Azithromycin                                  | 17 (3.2)          |
| Favipiravir                                   | 6 (1.1)           |
| <i>N</i> -acetylcysteine                      | 5 (0.9)           |
| High-dose vitamin C                           | 3 (0.5)           |
| rHuIL-1Ra                                     | 3 (0.5)           |
| Convalescent plasma                           | 3 (0.5)           |
| Tocilizumab                                   | 1 (0.2)           |
| Antibiotherapy for other pathogens            | 102 (19.1)        |
| COVID-19 severity                             |                   |
| Mild  | 509 (95.5)        |
| Moderate                                      | 17 (3.2)          |
| Severe  | 5 (0.9)           |
| Critic  | 2 (0.4)           |
| Respiratory support                           |                   |
| Nasal oxygen therapy                          | 17 (3.2)          |
| High-flow nasal cannula                       | 3 (0.5)           |
| Invasive mechanical ventilation               | 2 (0.4)           |
| Admission to ICU                              | 7 (1.3)           |
| Maternal mortality                            |                   |
| Rate of hospitalization                       | 297 (55.7)        |
| Length of hospital stay (days)                | 4.43 ± 3.5 (1–35) |

Abbreviations: BMI, body mass index; COVID-19, coronavirus disease 19; ICU, intensive care unit; IQR, interquartile range; ITP, immune thrombocytopenic purpura; rHuIL-1Ra, recombinant human IL-1 receptor antagonist; SD, standard deviation.

<sup>a</sup>Values are given as number (percentage), mean ±SD (range), or median (IQR, range).

into cardiopulmonary arrest on the 14th day of her hospitalization and she died of multiorgan failure despite all interventions.

The second case of maternal mortality was referred from another tertiary center with suspected COVID-19 infection. She was a 30-year-old multigravida at 34 weeks of pregnancy with a history of two previous cesarean deliveries. She had a history of cardiac arrest at her last delivery, and despite investigation, the etiology could not be clearly identified by

(Continues)

**TABLE 2** Initial laboratory test results of pregnant women with COVID-19 infection ( $n = 533$ )<sup>a</sup>

| Variables   | Values                                   |
|---|--|
| Hb (g/dL)   | 11.84 ± 1.35 (5.9–15.6)                  |
| Hct (%)   | 35.74 ± 4.41 (26.2–47.1)                 |
| Hb <10 mg/dL  | 45 (8.4)                                 |
| Leukocyte ( $10^3/\text{mm}^3$ )                              | 6904.79 ± 2594.12<br>(2020–28 510)       |
| Leukocytosis (>11 000/ $\text{mm}^3$ )                        | 35 (6.6)                                 |
| Neutrophil ( $10^3/\text{mm}^3$ )                             | 5029.10 ± 2317.90<br>(1070–25 430)       |
| Neutrophil percentage (%)                                     | 71.31 ± 9.81 (62–90.8)                   |
| Neutrophilia (>7700/ $\text{mm}^3$ or >70% of leukocytes)     | 59 (11.1)                                |
| Lymphocyte ( $10^3/\text{mm}^3$ )                             | 1329.73 ± 576.61<br>(310–4650)           |
| Lymphocyte percentage (%)                                     | 23.41 ± 9.30 (3.8–51.8)                  |
| Lymphocytopenia (<1000/ $\text{mm}^3$ or <8% of leukocytes)   | 162 (30.4)                               |
| Neutrophil to lymphocyte ratio                                | 4.52 ± 3.29 (1.2–25.28)                  |
| Platelet ( $10^3/\text{mm}^3$ )                               | 223088.1 ± 62 501.53<br>(19 000–460 000) |
| ESR (mm/h)  | 40.80 ± 23.94 (2–113)                    |
| CRP (mg/dL)   | 19.90 ± 34.74 (1–419)                    |
| Procalcitonin (ng/mL)   | 0.17 ± 1.95 (0–40)                       |
| IL-6 (pg/mL)  | 25.79 ± 94.16 (0–1000)                   |
| Ferritin (ng/mL)  | 52.89 ± 406.72 (10–9130)                 |
| BUN (mmol/L)  | 16.68 ± 6.11 (9–75)                      |
| Creatinine (mg/dL)  | 0.51 ± 0.21 (0.30–4.85)                  |
| ALT (IU/L)  | 24.63 ± 26.49 (8–253)                    |
| AST (IU/L)  | 25.74 ± 34.47 (9–611)                    |
| Elevated liver enzymes (ALT and AST ≥2 times the upper limit) | 24 (4.5)                                 |
| LDH (IU/L)  | 216.10 ± 175.46<br>(125–3780)            |
| D-dimer (mcg/mL)  | 1.90 ± 2.16 (0.01–24.20)                 |
| CK-MB (ng/mL)   | 1.02 ± 1.46 (0–11)                       |
| Troponin (ng/mL)  | 2.81 ± 24.29 (0–411)                     |
| Hypokalemia ( $K < 2.5$ mmol/L)                               | 8 (1.5)                                  |
| Lipid profile results   | 85 (15.9)                                |
| Triglyceride (mg/dL)  | 239.04 ± 111.77 (47–766)                 |
| HDL (mg/dL)   | 45.83 ± 13.19 (20–75)                    |
| LDL (mg/dL)   | 104.56 ± 38.92 (32–218)                  |
| VLDL (mg/dL)  | 48.22 ± 38.92 (10–101)                   |
| Radiologic imaging  | 68 (12.7)                                |
| Chest X-ray   | 68 (12.7)                                |
| Chest CT  | 36 (6.7)                                 |
| Pulmonary CT angiography                                      | 3 (0.5)                                  |
| Radiologic imaging findings suspicious for COVID-19           | 39 (7.3)                                 |

(Continues)

Table 2 (Continued)

| Variables  | Values     |
|------------|------------|
| Blood type |            |
| A+         | 176 (33.1) |
| A.         | 31 (5.8)   |
| B+         | 84 (15.7)  |
| B.         | 12 (2.2)   |
| AB+        | 35 (6.6)   |
| AB–        | 7 (1.3)    |
| O+         | 171 (32.1) |
| 1.         | 17 (3.2)   |

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; COVID-19, coronavirus disease 19; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; Hct, hematocrit; HDL, high-density lipoprotein; IL-6, interleukin 6; LDH, lactate dehydrogenase; LDL, low-density lipoprotein; SD, standard deviation; VLDL, very low density lipoprotein.  
<sup>a</sup>Values are given as number (percentage) or mean ± SD (range).

the study team. Her oxygen saturation was 80% upon admission and she had regular uterine contractions with new onset of rupture of membranes and leakage of amniotic fluid. An emergency cesarean delivery was planned, and the patient was transferred to the operating theatre without delay. An infant weighing 2110 g was delivered alive and the mother was transferred to the ICU. Unfortunately, a cardiopulmonary arrest occurred on arrival at the ICU. The patient responded to initial resuscitation and was intubated. Her RT-PCR test result was positive for SARS-CoV-2 and chest computed tomography (CT) scan revealed bilateral acute respiratory distress findings. Systemic corticosteroid, tocilizumab, favipiravir, and convalescent plasma therapy were added to the conventional COVID-19 treatment protocol. She had persistently rising cardiac enzymes (peak troponin T value 5963 ng/mL) and brain natriuretic peptide levels (peak value 6479 pg/mL) during her stay in the ICU. The patient died on the 11th day of admission to hospital due to multiorgan failure.

In total, 297 (55.7%) cases were hospitalized, and the mean length of hospital stay was  $4.43 \pm 3.5$  days.

The initial laboratory test results of pregnant women with COVID-19 infection are shown in Table 2. Neutrophilia and lymphocytopenia were observed in 59 (11.1%) and 162 (30.4%) cases, respectively. Elevated liver enzymes were observed in 24 (4.5%) patients. Hypokalemia was present in 8 (1.5%) cases. Radiologic imaging was performed for 68 (12.7%) patients, with chest CT and CT angiography used in 36 (6.7%) and 3 (0.5%) cases, respectively. Thirty-nine patients (7.3%) had radiologic imaging findings suspicious for COVID-19. A Rh+ and O Rh+ were the most common blood group types (33.1% and 32.1%, respectively).

The obstetric and neonatal outcomes of pregnant women with COVID-19 are shown in Table 3. Pregnancy complications were observed in 66 (12.4%) patients. Preterm delivery ( $n = 22$ , 4.1%) and miscarriage ( $n = 12$ , 2.2%) were the most common pregnancy complications. Among the 130 pregnancies in the first trimester, 12 (9.2%) resulted in miscarriage. There were three congenital anomalies: one skeletal dysplasia; one non-immune hydrops fetalis; and one

**TABLE 3** Obstetric and neonatal outcomes of pregnant women with COVID-19 ( $n = 533$ )<sup>a</sup>

| Variables   | Values                         |
|---|--------------------------------|
| Pregnancy complications                             | 66 (12.4)                      |
| Threatened abortion                                 | 2 (0.3)                        |
| Miscarriage   | 12 (2.2)                       |
| Hiperemesis gravidarum                              | 2 (0.3)                        |
| Cholestasis of pregnancy                            | 5 (0.9)                        |
| Fetal anomaly                                       | 3 (0.5)                        |
| Intrauterine fetal demise                           | 1 (0.2)                        |
| Fetal growth restriction                            | 5 (0.9)                        |
| Gestational diabetes                                | 3 (0.5)                        |
| Gestational hypertension                            | 4 (0.7)                        |
| Preterm delivery                                    | 22 (4.1)                       |
| Pre-eclampsia                                       | 5 (0.9)                        |
| Placental abruption                                 | 1 (0.2)                        |
| Deep vein thrombosis                                | 1 (0.2)                        |
| Delivery status                                     |                                |
| Pregnancy loss                                      | 13 (2.4)                       |
| Ongoing pregnancy                                   | 389 (73.1)                     |
| Delivered   | 131 (24.5)                     |
| Time interval between diagnosis and delivery (days) | 4.76 ± 2.73 (1–12)             |
| Route of delivery                                   |                                |
| Normal spontaneous vaginal delivery                 | 43 (32.9)                      |
| Cesarean delivery                                   | 87 (66.4)                      |
| Vaginal birth after cesarean delivery               | 1 (0.7)                        |
| Cesarean indications                                |                                |
| Previous cesarean delivery                          | 38 (43.6)                      |
| Maternal health condition                           | 16 (18.4)                      |
| Cephalopelvic disproportion                         | 14 (16.1)                      |
| Fetal distress                                      | 12 (13.8)                      |
| Macrosomia  | 5 (5.7)                        |
| Multiple pregnancy                                  | 2 (2.3)                        |
| Labor anesthesia                                    |                                |
| None  | 43 (32.9)                      |
| General   | 5 (3.8)                        |
| Regional  | 82 (62.6)                      |
| Spontaneous labor                                   | 90 (68.7)                      |
| Gestational age at delivery (weeks)                 | 37.39 ± 4.23 (28–42)           |
| Birth weight (g)                                    | 3100.80 ± 626.62<br>(900–4350) |
| Apgar 1st min                                       | 8 (1, 6–9)                     |
| Apgar 5th min                                       | 9 (1, 8–10)                    |
| Admission to NICU                                   | 13 (9.9)                       |
| Neonatal SARS-CoV-2 positivity                      | 0 (0)                          |

(Continues)

**Table 3** (Continued)

| Variables                            | Values  |
|--------------------------------------|---------|
| SARS-CoV-2 positivity in breast milk | 1 (0.2) |

Abbreviations: COVID-19, coronavirus disease 19; IQR, interquartile range; NICU, neonatal intensive care unit; RT-PCR, real-time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SD, standard deviation.

<sup>a</sup>Values are given as number (percentage), mean ± SD (range), or median (IQR, range).

congenital cardiac anomaly (atrioventricular septal defect, truncus arteriosus, and right isomerism). A total of 131 deliveries occurred (129 singleton and two twin pregnancies). The rate of cesarean delivery was 66.4%, and 1 (0.7%) vaginal birth after cesarean delivery occurred due to immediate delivery upon admission to hospital. Previous cesarean delivery was the most common indication for cesarean delivery ( $n = 38$ , 43.6%). Spontaneous labor occurred in 90 (68.7%) deliveries. Regional anesthesia ( $n = 82$ , 62.6%) was the preferred method in the majority of the cases with cesarean deliveries. The mean gestational age at delivery and birth weight were  $37.39 \pm 4.23$  weeks and  $3100.80 \pm 626.62$  g, respectively. Thirteen neonates (9.9%) were admitted to the neonatal ICU (NICU) due to prematurity. The RT-PCR study of nasopharyngeal and oropharyngeal samples obtained from all neonates were negative on the first, third, and 14th day of life. One of the samples of breast milk obtained from the mothers was positive for SARS-CoV-2.<sup>15</sup>

## 4 | DISCUSSION

The management of pregnancies complicated by COVID-19 infection is challenging for physicians as there is still no consensus on issues such as optimal treatment modality, indications for hospitalization, selection of the most appropriate imaging modality, timing, and route of delivery.<sup>6,7</sup> The experience of major pandemic centers in dealing with a large case load is valuable to improve people's knowledge on pregnant women with COVID-19 infection.

Although the study population in the present study was mostly young, 30% had significant co-morbidities. The association between COVID-19 infection and co-morbid conditions has long been known.<sup>8</sup> Although the course of COVID-19 was mild in the majority of the cases, having a chronic disease or being overweight may possibly ease viral transmission.

Nearly half of the patients were in the third trimester, consistent with the current literature.<sup>2,3</sup> Of the cases, 30% were asymptomatic on admission to hospital. Cough and myalgia were the most frequently presenting symptoms. The status of initial symptoms in pregnant women has varied between studies, depending on regional, social, and clinical factors.<sup>9,10</sup> Only one-quarter of cases in the present study had a history of close contact with a suspected or confirmed case. For this reason, clinicians should suspect COVID-19

infection in the presence of possible clinical findings even if the history of a significant contact is absent. Additionally, most of the patients had normal vital signs on admission to hospital. Thus, all suspected cases should be evaluated comprehensively and they should be closely followed up until RT-PCR results are available.

The administration of tocolytic therapies as well as antenatal corticosteroids for fetal lung maturation in pregnant women with COVID-19 has not yet been standardized. The current literature suggests balancing the benefits with possible adverse effects.<sup>6,7</sup> An individualized approach should be preferred and the management decision made according to the severity of COVID-19. The approach in the present study was mostly conservative and these medications were administered only in a small number of cases.

Both physicians and patients have concerns related to the safety of COVID-19 medications during pregnancy. However, it has been reported that starting medications in the early stages of the disease process may decrease the rate of severe disease and mortality.<sup>11,12</sup> Approximately half of the cases in the present study received COVID-19-specific treatment. Low-molecular weight heparin, hydroxychloroquine, and lopinavir-ritonavir were the most common drugs used in the study population. Hydroxychloroquine and azithromycin have been widely used since the early days of the pandemic. Lopinavir-ritonavir and systemic corticosteroids were generally preferred in cases with a worse prognosis.<sup>13</sup> Venous thromboembolism prophylaxis is recommended for hospitalized pregnant women with COVID-19.<sup>14</sup> Although no fetal toxicity was reported in the use of remdesivir against the Ebola and Marburg viruses, knowledge is limited on this drug and it is therefore not recommended for pregnant and breastfeeding women with COVID-19 infection.<sup>15</sup> Convalescent plasma, tocilizumab, and recombinant human IL-1 receptor antagonist were rarely used in pregnant women.<sup>13</sup> However, they were used for severe cases in the present study along with favipiravir. Non-invasive oxygen support has become the optimal modality for patients with COVID-19 infection experiencing respiratory distress.<sup>11</sup> In parallel with the literature, non-invasive methods have been performed as a first-line approach in the study institution.

In the early days of the pandemic in Turkey, all patients were followed up in hospital settings.<sup>4</sup> However, due to the growing experience of COVID-19 and the rapidly increasing number of cases, the Turkish Ministry of Health changed its protocol. Only patients needing medical therapy have been hospitalized since the new normalization period.<sup>5</sup> Other cases were isolated at home for at least 14 days under the supervision of expert community teams. On the other hand, the rate of severe cases and maternal mortality were lower than the reported rates in the current literature.<sup>16,17</sup>

Lymphocytopenia, neutrophilia, increased levels of acute phase reactants, ferritin, D-dimer, lactate dehydrogenase, liver enzymes, cardiac enzymes, and decreased levels of lipid levels are the most commonly reported laboratory findings for COVID-19 in the literature.<sup>18</sup> Ground-glass opacifications, mixed consolidations, pleural/interlobular septal thickening, and air bronchograms were the most common radiologic findings in previous studies.<sup>18</sup> The findings of the present study were mostly consistent with the current literature. However, although

they were measured in only 15% of cases, mean lipid levels were within normal limits. Another important point is the association between electrolyte imbalance and poor outcome in COVID-19.<sup>19</sup> Only a small number of cases had hypokalemia in the present study. On the other hand, hypokalemia was one of the initial findings in one of the cases of maternal mortality. The relationship between ABO blood types and the course of COVID-19 was investigated in various studies.<sup>20</sup> Blood types A and B were found to be associated with higher rates of SARS-CoV-2 positivity compared to blood group O.<sup>20</sup> A+ and O+ were the most common blood types in the present study.

Increased rates of obstetric complications, fetal distress, and cesarean delivery for pregnant women with COVID-19 infection have been reported in the literature.<sup>2,3</sup> Rates for both spontaneous and iatrogenic preterm deliveries were found to be increased in pregnancies complicated by COVID-19. Furthermore, low oxygen saturation and subsequent impaired perfusion to the fetus may lead to fetal distress, resulting in increased rates of cesarean delivery.<sup>2,3</sup> The association between loss of pregnancy, congenital anomalies, and COVID-19 infection was also investigated in some studies.<sup>21,22</sup> Although there is no study that clearly shows that COVID-19 causes congenital anomalies, suspicions about miscarriages are increasing among clinicians. However, it is hard to find the exact etiologic factors behind obstetric complications. Fewer antenatal visits and/or the possible hazardous effect of the virus on the growing fetus may cause these poor outcomes. Pregnancy complications were observed in only 12% of the cases in the present study, with preterm delivery and miscarriage being the most common. Congenital anomalies were present in only three cases. Two-thirds of the deliveries were by cesarean delivery, consistent with the current literature.<sup>2,3</sup> Another point discussed in the literature is the possibility of vertical transmission of the virus.<sup>23</sup> Although isolation of the newborn from the mother during the active infection was recommended previously, encouraging breastfeeding with appropriate precautions is the usual approach at present.<sup>24</sup> The Turkish Ministry of Health has also updated its guidelines and mothers have been breastfeeding their babies since June 2020 at the study institution. No vertical transmission was found in the present study and samples of breast milk were found to be negative for SARS-CoV-2 except for in one case. All admissions to the NICU occurred due to prematurity and no complications relating to COVID-19 were observed in the neonates.

The Turkish Ministry of Health has been actively fighting against COVID-19 since the early days of the pandemic. All healthcare providers were reorganized according to emergency conditions and comprehensive pandemic hospitals were established over a short period of time. Strict triage protocols, one-on-one filiation programs, and updated treatment modalities were successfully carried out by special teams. Patients could easily access health care and every patient requiring medical care was hospitalized. The number of ICUs and mechanical ventilation devices remained sufficient for the number of serious cases during the pandemic period. The whole organization was conducted together with a national scientific committee consisting of experts in their fields.<sup>4,5,25</sup> Ankara City Hospital has been serving in this context for months, and thanks to the dedication of healthcare

professionals, outcomes were generally favorable for pregnant women with COVID-19 infection.

The strengths of the present study were the prospective design, high number of study parameters, and the single-center experience. However, a lack of information related to the final outcomes of ongoing pregnancies is the main limitation.

In conclusion, the course of COVID-19 was mild in the majority of cases at Ankara City Hospital. However, increased rates of pregnancy complications and cesarean section were observed. There were no cases of vertical transmission.

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#### CONFLICT OF INTEREST

The authors have no conflicts of interest.

#### AUTHOR CONTRIBUTIONS

DS: conceptualization, methodology, visualization, reviewing, and editing; AT: original draft preparation, writing, data collection; SAE, ATA, and FDYY: data collection; HLK: analysis/interpretation; NO, EGYE: reviewing and editing; ASO-E and ES: visualization, reviewing, and editing; AY: literature search, manuscript writing; CT and SU: data collection; BD: resources, analysis/interpretation; AAS: supervision; OMT: project development.

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