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Research Article

# Clinical and laboratory differences between healthy and COVID-19 positive pregnant women and the negative effects of COVID-19 on pregnancy

Sağlıklı ve COVID-19 pozitif gebeler arasındaki klinik ve laboratuvar farklılıklar ve COVID-19'un gebelik üzerine olumsuz etkileri

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## Abstract

**Introduction**: Depending on pregnancy; physiological changes in the immune system, respiratory and circulatory systems may cause a more severe course of infection with respiratory viruses. The aim of this study is to examine the clinical and laboratory findings of our pregnant patients with and without COVID-19 and to determine whether COVID-19 disease has a negative effect on late pregnancy.

**Methods**: This study was conducted with a total of 60 pregnant patients followed in the Infectious Diseases and Clinical Microbiology Clinic and Gynecology and Obstetrics Clinic of a Training and Research Hospital. Demographic characteristics and laboratory findings of pregnant women and their fetuses were obtained from the hospital management information system.

**Results**: The mean age of the COVID-19 positive pregnant women (n:30) included in the study was 28.87±1.38 years, the mean hospitalization time was 6.33±0.35 days, and it was significantly different from the COVID-19 negative group (n:30) ($p<0.001$). The most common symptom observed in COVID-19 positive pregnant women at presentation was fever (73.3%), followed by cough (53.3%) and headache (43.3%). C-reactive protein (25.53±5.79, p: 0.005), ferritin (83.97±10.51, p: 0.005) and erythrocyte sedimentation rate (30.97± 4.59, p: 0.011) were found to be higher in COVID-19 positive pregnant women.

**Conclusion**: In conclusion; CRP, ferritin and ESR levels were found to be higher in pregnant women with COVID-19. It is important for healthcare providers to know the clinical course of COVID-19, maternofetal or obstetric outcomes in the pregnant population. Mode and timing of delivery should be individualized according to disease severity, pre-existing maternal comorbidities, obstetric history, gestational age, and fetal conditions.

**Keywords**: COVID-19, C-reactive protein, cough, pregnancy

## Öz

**Giriş**: Hamileliğe bağlı olarak; bağışıklık sistemi, solunum ve dolaşım sistemlerindeki fizyolojik değişiklikler solunum yolu virüsleri ile daha ciddi bir enfeksiyon seyrine neden olabilir. Bu araştırmanın amacı, COVID-19 olan ve olmayan gebe hastalarımızın klinik ve laboratuvar bulgularını incelemek ve COVID-19 hastalığının geç gebelik üzerinde olumsuz bir etkisi olup olmadığını belirlemektir.

**Yöntem**: Bu çalışma, bir Eğitim ve Araştırma Hastanesi Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği ile Kadın Hastalıkları ve Doğum Kliniğinde takip edilen toplam 60 gebe hasta ile yapılmıştır. Gebelerin ve fetüslerin demografik özellikleri ve laboratuvar bulguları hastane yönetim bilgi sisteminden elde edildi.

**Bulgular**: Çalışmaya alınan COVID-19 pozitif gebelerin (n:30) ortalama yaşı 28,87±1,38 yıl, ortalama hastanede kalış süresi 6,33±0,35 gün olup, COVID-19 negatif gruptan (n:30) anlamlı olarak farklıydı ($p<0,001$). COVID-19 pozitif gebelerde başvuru anında en sık görülen semptom ateş oldu (%73,3), bunu öksürük (%53,3) ve baş ağrısı (%43,3) izledi. COVID-19 pozitif gebelerde C-reaktif protein (25,53±5,79, p:0,005), ferritin (83,97±10,51, p:0,005) ve eritrosit sedimantasyon hızı (30,97±4,59, p:0,011) daha yüksek bulundu.

**Sonuç**: CRP, ferritin ve ESR düzeyleri COVID-19'lu gebelerde daha yüksek bulundu. Sağlık hizmeti sunucularının hamile popülasyonda COVID-19'un klinik seyrini, anne karnındaki veya doğumla ilgili sonuçları bilmesi önemlidir. Doğum şekli ve zamanlaması, hastalığın ciddiyetine, önceden var olan maternal komorbiditelere, obstetrik öyküye, gebelik yaşına ve fetal koşullara göre kişiselleştirilmelidir.

**Anahtar Kelimeler**: COVID-19, C-reaktif protein, öksürük, gebelik

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## Key Points

1. CRP, ferritin and ESR levels were found to be significantly higher in pregnant women with COVID-19.
2. D-dimer levels of pregnant women with COVID-19 were 2.3 times higher than the mean levels compared to healthy pregnant women, this rate was not statistically significant.
3. The fetal weights were lower in COVID-19 positive pregnant women.

## Introduction

It was determined that a new type of coronavirus was the cause of the pandemic, which started in Wuhan in China's Hubei province in December 2019 and then spread rapidly all over the world and turned into a very serious public health problem [1]. As a result of this infection, which swept the whole world, called COVID-19 (SARS-CoV-2), and still continues; severe lower respiratory tract infection, severe acute respiratory distress syndrome (SARS), vascular disease, myocarditis, coagulopathy, paralysis, neurological defects due to central nervous system involvement (loss of taste and smell), kidney disease, multisystem inflammatory syndrome similar to Kawasaki syndrome in the pediatric age group and many more multisystemic pathological conditions including death occurred. 81% of cases show asymptomatic/mild flu-like symptoms, 14% show severe symptoms (requiring hospitalization and oxygen support), and 5% show critical symptoms (requiring mechanical ventilation). Mortality rate varies between 2.3-3% [2,3]. The patient's age and comorbidities are related to the severity of the disease. ~44.5% of patients over 60 years of age with comorbidities such as hypertension and/or diabetes experience a severe form of the disease and have the worst prognosis [3].

Depending on pregnancy; physiological changes in the immune system, respiratory and circulatory systems may cause a more severe course of infection with respiratory viruses [4]. The pregnancy uterus causes the diaphragm to rise about 4 cm. As a result, the functional residual capacity decreases by 30%. The decrease in residual capacity during pregnancy is most common in the third trimester. Therefore, dyspnea is most commonly reported during this period. However, respiratory rate does not change in any period and tachypnea developing during pregnancy should be considered pathological until proven otherwise [5]. Some publications in the United States state that the risk of serious COVID-19 disease is higher in pregnant women than in non-pregnant women [6,7].

However, there are also ideas that immunological changes occurring during pregnancy suppress SARS-CoV-2 infection [8]. According to this theory; during pregnancy, there is a shift in favor of Th2 between T helper 1 (Th1)-related and T helper 2 (Th2)-related cytokines. The cell-mediated immune response associated with Th1 is down-regulated, while a dominant Th2-dependent humoral immune response occurs, allowing for immune tolerance of the fetus. This; contributes to increased susceptibility to viral infections (especially respiratory pathogens). COVID-19 severity may be affected by these immunological changes. Considering that a Th1-mediated immune response plays a key role in lung damage in patients with COVID-19, the predominance of Th2 immunity in pregnant women can be interpreted in their favor [9-11]. Human chorionic gonadotropin and progesterone inhibit the Th1 proinflammatory pathway by causing reduction of tumor necrosis factor-α (TNF-α). This may protect pregnant women from cytokine storm and related morbidity and mortality [12]. Studies on variations in the cytokine profile on non-pregnant patients indicate that interferon-y, IL-1β, IL-4 and IL-10 levels are increased and the differences in disease severity are related to these increases. It was also found that IL-2, IL-7, IL-10, granulocyte stimulating colony factor and TNF-α levels were found to be higher in patients with intensive care hospitalization indication [13].

In previous coronavirus pandemics known as severe acute respiratory distress syndrome virus (SARS-CoV-1) and Middle East respiratory syndrome virus (MERS), pregnant women and their fetuses have been more severely affected than non-pregnant patients. Maternal mortality rates have been reported between 25-28% for SARS-CoV-1 and MERS. It also caused higher morbidity and mortality rates in pregnant women in the 2009 H1N1 influenza pandemic [14]. However, despite all these data, the generalization of pregnancy as a state of immunosuppression or increased risk of infection is a misleading concept, and it should not be ignored that a unique immune state is modulated rather than suppressed [12].

In this study; It was aimed to examine the clinical and laboratory findings of our pregnant patients with or without COVID-19, and to determine whether the disease has a negative effect on late pregnancy.

## Methods

Our study was conducted with 30 COVID-19 positive and 30 COVID-19 negative pregnant women (60 pregnant women in total) who were in the last trimester and were followed in the Infectious Diseases and Clinical Microbiology Clinic and Gynecology and Obstetrics Clinic of a Training and Research Hospital. Demographic characteristics and laboratory findings of pregnant women and their fetuses were obtained from the hospital management information system. COVID-19 positive pregnant patients include patients between March 2020, when the epidemic started in Turkey, and February 2021, when vaccination started. Patients with COVID-19 symptoms but negative polymerase chain reaction (PCR) tests and pregnant women with any additional disease (diabetes, chronic lung, kidney, liver disease, rheumatologic, cardiac, malignancy, etc.) were not included in the study.

For the detection and isolation of patients infected with COVID-19; PCR test was performed using Bio-speedy SARS-Cov-2 real-time PCR detection kit (Bioksen, Istanbul, Turkey) from the nasopharyngeal swabs of the patients.

### Ethical approval

This research was approved by İzmir Katip Çelebi University Ethics Committee (Non-Invasive Clinical Research Ethics Committee Decision Form: 0053/24.02.2022).

### Statistical analysis

Statistical analysis was done with SPSS (SPSS Inc., Chicago, IL, USA,) version 21.0 program. The conformity of the variables to the normal distribution was evaluated with Kolmogorov-Smirnov and Shapiro-Wilk tests. In the comparisons between groups, t-test was used in independent groups for normally distributed continuous variables, and Mann Whitney U test was used for continuous variables that did not show normal

distribution. All measurements are shown as "mean ± standard deviation". Non-continuous variables with normal distribution were evaluated using the Chi-square test, and non-continuous variables without normal distribution were evaluated using Fisher's exact probability test. The significance level of $p<0.05$ was taken as basis.

## Results

**Clinical, Demographic and Obstetric Characteristics**

All patients were hospitalized during delivery and treatment. The mean age of the COVID-19 positive pregnant women included in the study was 28.87±1.38 years, the mean hospitalization time was 6.33±0.35 days, and it was significantly different from the COVID-19 negative group ($p<0.001$) (Table 1). The highest number of gravida in all pregnant women: 2 (38.3-n:23), the highest parity number: 1 (41.7%-n:25), cesarean delivery rate 58.3% (n:35) and premature birth rate (<37 weeks) was found to be 20.1% (n:12). Birth weight ranged between 1650-4570 g, low birth weight (<2500 g) and average fetal weight of 3192 g were observed in 13 (21.6%) newborns.

The rates of gravida (p: 0.002) and parity (p: 0.012) were significantly lower in COVID-19 positive pregnant women. The average birth weight of the newborns was found to be 2994.33±87.64 g in COVID-19 positive pregnant women and this was lower than the newborns of healthy pregnant women (p:0.019). There was no difference between the groups in terms of week of birth and postpartum hemoglobin (PPHgb). The rate of cesarean section was 48.6% (n:17) in COVID-19 positive pregnant women and 51.4% (n:18) in negative pregnant women. There was no statistical difference between the two groups in terms of delivery type and fetal growth retardation (FGR) (Table 2). The most common symptom observed in COVID-19 positive pregnant women at presentation was fever (73.3%), followed by cough (53.3%) and headache (43.3%). Less reported and other observed symptoms are given in Table 3.

**Table 1.** Demographic and obstetric characteristics of pregnant women

| | Group | Mean | Standard error | p[b] value |
|---|---|---|---|---|
| Age | Non-COVID | 28.93 | 1.03 | 0.969 |
| | COVID | 28.87 | 1.38 | |
| Gravida | Non-COVID | 3.17 | 0.34 | **0.002*** |
| | COVID | 1.97 | 0.17 | |
| Parity | Non-COVID | 2.10 | 0.33 | **0.012*** |
| | COVID | 1.13 | 0.17 | |
| Birth weight | Non-COVID | 3391.17 | 139.18 | **0.019*** |
| | COVID | 2994.33 | 87.64 | |
| Birth week | Non-COVID | 38.23 | 0.36 | 0.690 |
| | COVID | 38.03 | 0.35 | |
| PPHgb[a] | Non-COVID | 10.94 | 0.31 | 0.075 |
| | COVID | 10.20 | 0.27 | |
| Duration of hospitalization | Non-COVID | 2.73 | 0.11 | **<0.001*** |
| | COVID | 6.33 | 0.35 | |

[a] PPHgB: postpartum hemoglobin [b] Comparisons were made using the t-test and Mann Whitney U test in independent groups

**Table 2.** Mode of delivery and FGR values

| | | Group | | p[b] value |
|---|---|---|---|---|
| | | Non-COVID | COVID | |
| Birth Type | Normal birth | 12 (48.0%) | 13 (52.0%) | 0.793 |
| | Cesarean | 18 (51.4%) | 17 (48.6%) | |
| FGR[a] | No | 26 (55.3%) | 21 (44.7%) | 0.117 |
| | Yes | 4 (30.8%) | 9 (69.2%) | |

[a] FGR: Fetal growth retardation [b] Comparisons were made using the Chi-square test and Fisher's exact probability test

**Table 3.** Distribution of symptoms of COVID-19 + pregnant women

| Symptoms | COVID (+) Pregnants |
|---|---|
| Fever | 73.3% |
| Cough | 53.3% |
| Headache | 43.3% |
| Myalgia | 30% |
| Chills/Trembling | 26.6% |
| Loss of taste/smell | 23.3% |
| Fatigue/Weakness | 20% |
| Dyspnea | 16.6% |
| Nausea/ Vomiting | 13.3% |
| Sore throat/ runny nose | 6.6% |
| Diarrhea | 3.3% |
| Asymptomatic | 3.3% |

**Laboratory Findings**

Tables 4 and 5 describe laboratory findings at admission. A significant difference was found between COVID-19 positive and negative pregnant women in terms of creatinine and lactate dehydrogenase (LDH) values (p<0.001). No difference was observed in terms of liver enzymes. 80% of patients had elevated C-reactive protein (CRP) levels. CRP (25.53±5.79, p: 0.005), ferritin (83.97±10.51, p: 0.005) and erythrocyte sedimentation rate (ESR) (30.97± 4.59, p: 0.011) were found to be higher in COVID-19 positive pregnant women. The mean D-dimer level was found to be 1025.67±322.94 in positive pregnant women and 445.13±58.73 in negative pregnant women (p:0.08) (Table 4).

Mean lymphocyte count (1.77±0.10, p: 0.016), erythrocyte count (3.94±0.08, p: 0.045) and hematocrit value (32.89±0.58, p: 0.005) in COVID-19 positive pregnant women was found to be significantly lower. There was no difference between the two groups in terms of other whole blood parameters (p>0.05) (Table 5).

**Table 4.** Biochemical findings of pregnant women

| | Group | Mean | Standard error | p[a] value |
|---|---|---|---|---|
| Urea | Non-COVID | 7.90 | 0.67 | 0.201 |
| | COVID | 6.87 | 0.43 | |
| Creatinine | Non-COVID | 0.73 | 0.03 | **<0.001*** |
| | COVID | 0.60 | 0.02 | |
| Aspartate aminotransferase (AST) | Non-COVID | 22.60 | 2.80 | 0.949 |
| | COVID | 22.37 | 2.36 | |
| Alanine aminotransferase (ALT) | Non-COVID | 16.43 | 2.76 | 0.605 |
| | COVID | 18.86 | 3.77 | |
| LDH | Non-COVID | 253.97 | 14.41 | **<0.001*** |
| | COVID | 168.20 | 11.64 | |
| Creatinine kinase (CK) | Non-COVID | 98.40 | 28.03 | 0.628 |
| | COVID | 84.13 | 8.50 | |
| CRP | Non-COVID | 8.46 | 1.20 | **0.005*** |
| | COVID | 25.53 | 5.79 | |
| D-DIMER | Non-COVID | 445.13 | 58.73 | 0.08 |
| | COVID | 1025.67 | 322.94 | |
| Ferritin | Non-COVID | 38.57 | 11.51 | **0.005*** |
| | COVID | 83.97 | 10.51 | |
| ESR | Non-COVID | 17.57 | 2.27 | **0.011*** |
| | COVID | 30.97 | 4.59 | |

[a] Comparisons were made using the t-test and Mann Whitney U test in independent groups

**Table 5.** Whole blood parameters of pregnant women

| | Group | Mean | Standard error | p value |
|---|---|---|---|---|
| WBC | Non-COVID | 10.62 | 0.51 | 0.806 |
| | COVID | 10.43 | 0.56 | |
| NEU | Non-COVID | 7.58 | 0.45 | 0.620 |
| | COVID | 7.93 | 0.52 | |
| NEU % | Non-COVID | 70.61 | 1.55 | 0.072 |
| | COVID | 74.58 | 1.51 | |
| LYM | Non-COVID | 2.17 | 0.13 | **0.016*** |
| | COVID | 1.77 | 0.10 | |
| LYM % | Non-COVID | 21.22 | 1.26 | 0.071 |
| | COVID | 18.02 | 1.20 | |
| MONO | Non-COVID | 0.73 | 0.05 | 0.128 |
| | COVID | 0.63 | 0.03 | |
| MONO % | Non-COVID | 6.90 | 0.33 | 0.428 |
| | COVID | 6.44 | 0.47 | |
| RBC | Non-COVID | 4.19 | 0.10 | **0.045*** |
| | COVID | 3.94 | 0.08 | |
| HGB | Non-COVID | 11.82 | 0.31 | 0.183 |
| | COVID | 11.28 | 0.25 | |
| HCT | Non-COVID | 35.83 | 0.83 | **0.005*** |
| | COVID | 32.89 | 0.58 | |
| PDW | Non-COVID | 12.70 | 0.35 | 0.923 |
| | COVID | 12.64 | 0.56 | |
| RDW | Non-COVID | 15.16 | 0.56 | 0.218 |
| | COVID | 14.14 | 0.59 | |
| PLT | Non-COVID | 250.93 | 11.32 | 0.272 |
| | COVID | 230.90 | 14.06 | |
| PCT | Non-COVID | 0.27 | 0.01 | 0.721 |
| | COVID | 0.26 | 0.02 | |

[a] Comparisons were made using the t-test and Mann Whitney U test in independent groups

## Discussion

Due to changes in respiratory, circulatory and immunological systems as a result of some physiological effects during pregnancy, more susceptibility to viral infections may increase [15]. In a review examining the effects of COVID-19 on pregnancy; reported that high maternal age, body mass index, and pre-existing comorbidities were correlated with the severity of infection [16]. In the report of Lokken et al. [17] on the clinical features of pregnant women who are positive for SARS-CoV-2, they determined that pregnant women with pre-pregnancy overweight/obesity or concomitant chronic diseases such as asthma had a 15% more severe COVID-19 infection. In another study supporting these publications, it was found that the probability of developing any complications in pregnant women with comorbidities who had COVID-19 was higher than those who did not [18].

Laboratory results of pregnant women with COVID-19 should be interpreted more carefully because of the physiological changes that have already developed during pregnancy. Leukocytosis, lymphocytopenia or thrombocytopenia are changes that can actually occur during pregnancy [19]. In addition, it is known that CRP values increase during pregnancy compared to the normal population and may increase even more during delivery [20]. In the study of Huang et al. [13] in which they examined the general population with COVID-19; detected lymphopenia, leukopenia and thrombocytopenia (63%, 25% and 5%, respectively) in cases. Normal procalcitonin levels were detected in 69% of patients, with 73% having elevated LDH levels, creatinine, CK, and AST in 37%, 10%, and 33% of patients, respectively. In addition to these, neutrophil count, hemoglobin, albumin, D-dimer, prothrombin time, ALT, sodium and potassium were found to be normal. In a study examining women of reproductive age who had COVID-19, lymphopenia (47%) and increased liver enzymes (17%) were observed in pregnant women [21]. In a meta-analysis examining 385 pregnant women with COVID-19; D-dimer elevation was found in 22.3% of the patients, high CRP in 18.7%, lymphopenia in 14%, moderate increase in liver enzymes (AST: 5.7%, ALT: 5.45%) and thrombocytopenia in 1% [22]. In a systematic review of pregnant women with COVID-19; Leukocytosis was found in 27%, leukopenia in 25.5%, thrombocytopenia in 18%, and increased CRP in 52% [23]. Yet in another study; CRP increase was found in 48% of pregnant women and lymphopenia was found in 46% [24].

In our study, CRP, ferritin and ESR levels were found to be significantly higher in pregnant women with COVID-19. In whole blood parameters, lymphocyte, erythrocyte and hematocrit levels were observed to be lower than the pregnant women who did not have the disease.

Pregnancy is a prone to clotting and studies have shown a marked increased risk of thrombosis in critically ill patients infected with SARS-CoV-2 as well [25]. The risk of thrombosis during pregnancy and after delivery is three to five times greater than in the absence of pregnancy [26]. The Royal College of Obstetricians and Gynecologists recommended that hospitalized COVID-19 positive pregnant women receive prophylactic low molecular weight heparin to minimize the risk of pulmonary embolism because COVID-19 infection increases the risk of venous thromboembolism [27]. Cases of disseminated intravascular coagulopathy (DIC) with elevated D-dimer are not uncommon. There is emerging evidence that some of the symptoms of COVID-19 are associated with a systemic thrombotic and microvascular injury [28].

In a study conducted; the levels of D-dimer and fibrin degradation products were found to be much higher in pregnant women with COVID-19 than in healthy pregnant women. Therefore, it has been reported that COVID-19 infection increases the high risk of hypercoagulation and hyperfibrinolysis, even potential DIC in late pregnancy [29]. In our study, although the D-dimer levels of pregnant women with COVID-19 were 2.3 times higher than the mean levels compared to healthy pregnant women, this rate was not statistically significant (p:0.08) (Table 4).

Selim et al. [8] reported that SARS-CoV-1 infection is associated with a higher risk for preterm delivery, miscarriage, and intrauterine growth retardation. In a meta-analysis of 13 publications (n=114), premature birth, neonatal pneumonia, and respiratory distress syndrome were reported in infants born to COVID-19 positive mothers [30]. In another study; although maternal complications in COVID-19 positive mothers mostly include pneumonia, other reported complications include preterm delivery, premature rupture of membranes, increased cesarean deliveries, fetal distress, high CRP values, lymphopenia, diabetes, gestational hypertension, placenta previa, preeclampsia, polyhydramnios, oligohydramnios, hypothyroidism, abnormal umbilical cord, and sinus tachycardia [31]. In another study examining the neonatal outcomes of COVID-19; fetal distress (43%), preterm delivery (39%), intrauterine growth retardation (10%), perinatal death (7%), and miscarriage (2%) were found [9]. Allotey et al. [16] reported the spontaneous preterm delivery rate as 6% in women with COVID-19. The probability of preterm birth was found to be higher in those with the disease compared to COVID-19 negative pregnant women. In a study involving Scandinavian countries; women hospitalized for COVID-19 were more obese ($p<0.001$) and had a migrant background ($p<0.001$) compared to the total population who gave birth in 2018. Premature delivery (25%, $p<0.001$) and cesarean section (43.8%, $p<0.001$) were more common in women with COVID-19 than women who gave birth in 2018 (pre-pandemic). No maternal death, stillbirth, or neonatal death were reported in this study [32]. There is no data on termination of pregnancy due to COVID-19 infection. Pregnancy can be continued with adequate care, appropriate treatment and follow-up. Pregnancy may be terminated by emergency delivery with the consent of the patient's family, as the mother and fetus in critical condition are in danger. Clinicians should protect themselves and be aware of the severity of the risk when dealing with patients in childbirth. The time and mode of delivery depend on the condition of the mother and fetus [33]. In a multicenter study examining pregnant women and newborns with COVID-19 in Turkey; cesarean section, premature and low birth weight infant rates were 71.2%, 26.4% and 12.8%, respectively [34].

In our study, it was observed that the fetal weights were lower in COVID-19 positive pregnant women. There was no significant difference between the groups in terms of preterm birth, cesarean section rate, PPHgb and FGR.

As a result, pregnant women with COVID-19 may experience worse perinatal outcomes than healthy pregnant women. Physiological and immunological changes during pregnancy can lead women to complications from respiratory tract infections and systemic effects leading to maternal and fetal mortality and morbidity [35,36].

### Strengths and limitations

Only the registration of pregnant women with laboratory-confirmed SARS-CoV-2 infection and the follow-up of themselves and their babies even after delivery are the strengths of the study. The presence of a control group consisting of pregnant women without COVID-19 makes it easier to assess the risk of maternal and perinatal outcomes related to COVID-19. Conducting the study with pregnant women before vaccination presents

the effect of the virus on the pregnant and fetus more objectively, and this can be regarded as another strength of the study. Generalization of maternal and perinatal outcomes to the entire population may lead to biases because the income level of the patients was not examined. In addition, the pregnant women who made up the patient group mostly consisted of patients who applied with the suspicion of COVID-19 due to symptoms or exposure. Therefore, the rate of asymptomatic women in our study was low. Assuming that the number of SARS-CoV-2 positive and asymptomatic pregnant women is substantial, maternal and perinatal outcomes may actually be better. The higher numbers in the group of our study, which was planned as a case-control study, could have provided us with more reliable results. In addition, it is possible that the unknown vertical transmission and the fact that health care providers avoid longer-lasting normal birth due to more excuses have increased the rates of cesarean section all over the world.

## Conclusion

In this study conducted with pregnant women in the last trimester, we observed that acute phase reactants and D-dimer (indicating the risk of coagulation) parameters, which can also increase during normal pregnancy, are higher in COVID-19 positive patients. This finding supports the need for prophylactic anticoagulant initiation in COVID-19 positive pregnant women like other non-pregnant COVID-19 positive patients. In addition, lower birth weights were detected, and this finding suggests that pregnancy follow-ups should be performed more frequently, regardless of the gestational period in which the disease was detected.

Changes in the immune system during pregnancy are not fully understood and may theoretically cause dilemmas for clinicians. It is important for healthcare providers to know the clinical course of COVID-19, maternofetal or obstetric outcomes in the pregnant population. Mode and timing of delivery should be individualized according to disease severity, pre-existing maternal comorbidities, obstetric history, gestational age, and fetal conditions. As if compared to previous pandemics, COVID-19 positive pregnant women without comorbidities do not seem to be at an increased risk compared to negative pregnant women.

Nevertheless, considering that COVID-19 is a little more likely to predispose to preterm birth, the importance of vaccination and protection from disease emerges once again. In addition, it is a fact that more studies are needed on the effect of infection on maternal and fetal health in the first and second trimesters. Data on vertical transmission of the disease are also limited, and future data on a sequela, developmental problem, or any other health problem that may develop with long-term follow-up of the newborn will shed light on the data we have identified now.

**Conflict of Interest:** The authors declared no conflict of interest regarding this article.

| | **Author Contributions** | **Author Initials** |
|---|---|---|
| SCD | Study Conception and Design | KK, DK, MS |
| AD | Acquisition of Data | KK, MS |
| AID | Analysis and Interpretation of Data | KK, DK, MS |
| DM | Drafting of Manuscript | KK |
| CR | Critical Revision | KK, DK, MS |

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