Araştırma Makalesi / Research Article

COVID-19 Experience in a Pregnant Population of a Tertiary Center / *Tersiyer Bir Merkezin Gebe Populasyonunda COVID-19 Deneyimi*

Dr. Burcu TİMUR[1], Dr. Bergen LALELİ KOÇ[2], Dr. Hakan TİMUR[3]

1. Ordu University Training and Research Hospital Obstetrics and Gynecology, drburccu@gmail.com

2. Ankara City Hospital Perinatology, bergen.laleli@gmail.com

3. Ordu University Training and Research Hospital Perinatology, drhakantimur@gmail.com

Gönderim Tarihi | Recieved: 08.04.2022, Kabul Tarihi | Accepted: 23.04.2022, Yayın Tarihi | Date of Issue: 23.06.2022, DOI: https://www.doi.org/10.25279/sak.1100662

Atıf | Reference: "TİMUR, B; LALELİ KOÇ, B; TİMUR, H. (2022). COVID-19 Experience in a Pregnant Population of a Tertiary Center. Health Academy Kastamonu (HAK), 7 (Covid-19 Additional Issue), 116-124."

Abstract

Aim: This study aimed to examine the clinical features of COVID-19 infection, maternal and fetal side effects related to infection and share experiences of our clinic in this context. Materials and Methods: A total of 63 pregnant women diagnosed with COVID-19 were identified in a tertiary hospital between September-May 2021. Disease-related symptoms, laboratory parameters, maternal and fetal side effects were examined. Results: The symptoms, comorbid diseases, sociodemographic and clinical features of patients were evaluated. Fever (41.2%) was the most common patients' complaint at admission. Almost half of the patients had no accompanied comorbid disease (48%). The mean gestational week of patients who had COVID-19 was 29.55±8.33 (Mean±SD) and the mean of their ages was 30.36±6.02 (Mean±SD). Conclusion and suggestions: The COVID-19 disease has caused a pandemic that has affected the world since December 2019. High fever, cough and shortness of breath are the most common symptoms.The increased susceptibility to respiratory tract diseases during pregnancy makes this patient group more vulnerable to the devastating effects of disease factors. We obtained findings consistent with the literature in terms of symptoms, laboratory values, and obstetric prognoses of pregnant women with COVID-19 infection that we followed up in our clinic, a tertiary center.

Keywords: COVID-19, Pregnancy, Infection

Öz

Amaç: Bu çalışmadaki amaç, COVID-19 enfeksiyonunun klinik özelliklerini, enfeksiyona bağlı maternal ve fetal yan etkilerini incelemek, bu bağlamda kliniğimizin deneyimlerini paylaşmaktır. Gereç ve Yöntemler: Ordu Üniversitesi Eğitim ve Araştırma Hastanesi'nde Eylül-Mayıs 2021 tarihleri arasında COVID-19 tanısı almış toplam 63 gebe tanımlandı. Hastalığa bağlı semptomları, laboratuvar parametreleri, maternal ve fetal yan etkileri incelendi. Bulgular: Hastaların semptomları, komorbid hastalıkları, sosyodemografik ve klinik özellikleri incelendi. Hastaların en sık hastaneye başvuru şikayeti ateş (%41) idi. Hastaların neredeyse yarısının (48%) gebeliğe eşlik eden komorbid hastalığı yoktu. COVID-19 geçiren hastaların ortalama gestasyonel haftaları 29.55±8.33 (Ortalama±SS), yaş ortalaması 30.36±6.02 (Ortalama±SS) idi. Sonuç ve Öneriler: COVID-19 hastalığı Aralık 2019 tarihinden bu yana dünyayı etkisi altına alan bir pandemiye neden olmuştur. Yüksek ateş,

öksürük ve nefes darlığı en yaygın semptomlardır. Gebelikte solunum yolu hastalıklarına karşı hassasiyetin artmış olması, bu hasta grubunu hastalık etkenlerinin yıkıcı etkisine daha açık hale getirmektedir. Tersiyer bir merkez olan kliniğimizde takip ettiğimiz COVID-19 tanılı gebelerin semptomları, laboratuvar değerleri ve obstetrik prognozları açısından literatürle uyumlu bulgular elde ettik.

Anahtar kelimeler: COVID-19, Gebelik, Enfeksiyon

1. Introduction

Coronaviruses (CoVs) are enveloped, positive-stranded RNA viruses in the family Coronaviridae. A new type of coronavirus (COVID-19) was first detected in Wuhan, the capital of China's Hubei province, in December 2019 and continues to spread globally (Huang et al., 2020). COVID-19 causes severe respiratory diseases. It occurs in the form of bronchitis, bronchiolitis, or pneumonia, especially in individuals with chronic diseases, immunocompromised individuals, and the elderly. The novel coronavirus disease (COVID-19) caused by SARS-CoV-2 was defined as a global pandemic. The virus can be transmitted by contact with droplets from coughing and sneezing. No increased susceptibility has been demonstrated in pregnant women compared to the general population, and management is parallel to non-pregnant populations. There are limited data on the course of the disease during pregnancy and its effects on the fetus. However, it is a known fact that there is an increased susceptibility to respiratory tract diseases and pneumonia and decreased tolerance to hypoxia during pregnancy due to physiological changes in the immune system and decreased lung capacity during pregnancy. In the first trimester of pregnancy (the first 12 weeks), there is a proinflammatory process that allows trophoblastic invasion. In the second trimester (between weeks 13-27), a physiological anti-inflammatory process is entered to ensure fetal growth and prevent premature birth. When the third trimester of pregnancy begins (weeks 28-42), the proinflammatory process is activated again in preparation for birth. Physiological harmony in these three stages may be impaired by viral infections that may cause maternal and fetal complications (Mor, Aldo, & Alvero, 2017). Clinical findings related to COVID-19 infection are similar in pregnant and non-pregnant patient groups. A study involving a large pregnant population identified cough (50.3%), headache (42.7%), muscle pain (36.7%), and fever (32.0%) as the most common symptoms (Zambrano et al., 2020). A large-scale meta-analysis conducted in 2020 found higher rates of hospitalization in the intensive care unit (ICU), being connected to a mechanical ventilator, and mortality in pregnant women compared to non-pregnant women (Allotey et al., 2020). As an obstetric complication, it is known that COVID-19 infection increases the rates of preterm birth and first trimester miscarriage in pregnancy. However in the some studies it is found that COVID-19 infection did not affect the rates of early pregnancy loss (Yilmaz et al., 2021). Data on vertical transmission from the mother to the infant are not clear. However, it is important for maternal and infant health that pregnant women do not skip their routine pregnancy follow-ups even during the pandemic.

For all these reasons mentioned, the COVID-19 disease process should be addressed more closely and carefully during pregnancy. In this study, we aimed to share the COVID-19 experience during pregnancy at Training and Research Hospital of Ordu University between September 2020 and May 2021.

2. Materials and Methods

2.1. Type of Research

This is a descriptive observational study.

2.2. Place and Time of Research

Data collected at the Gynecology and Obstetrics Clinic of Ordu University Training and Research Hospital between September 2020 and May 2021.

2.3. Population, Sample and Sampling Method of Research

Sixty-three pregnant women hospitalized with the diagnosis of COVID-19. Consultations were taken from the infectious diseases and pulmonology departments. Patient data were obtained by asking patients personally and examining their files.

2.4. Data Collection Tools

All patients underwent transabdominal obstetric ultrasonography, and fetal well-being, fetal biometrics, estimated fetal weights, amniotic fluid amounts, and placenta were examined. They were evaluated for the presence of obstetric complications. Complete blood count, liver function tests, CRP levels as an inflammatory marker, coagulation parameters, and d-dimer levels were analyzed by taking serum venous blood from all patients.

2.5. Data Collection

The patients' ages, sociodemographic characteristics, gestational weeks, smoking and alcohol consumption, systemic diseases, and drugs they used were noted. The patients' contact histories and their symptoms related to COVID-19 were questioned. Gestational dates were calculated according to the date of the last menstrual period (LMP). The patients' status of receiving antiviral and anticoagulant therapy and their oxygen support needs were noted. The Apgar scores and birth weights of newborn infants of pregnant women with COVID-19 infection and whether they were followed up in the neonatal intensive care unit (NICU), and whether they experienced maternal and fetal morbidity were investigated.

2.6. Ethical Considerations

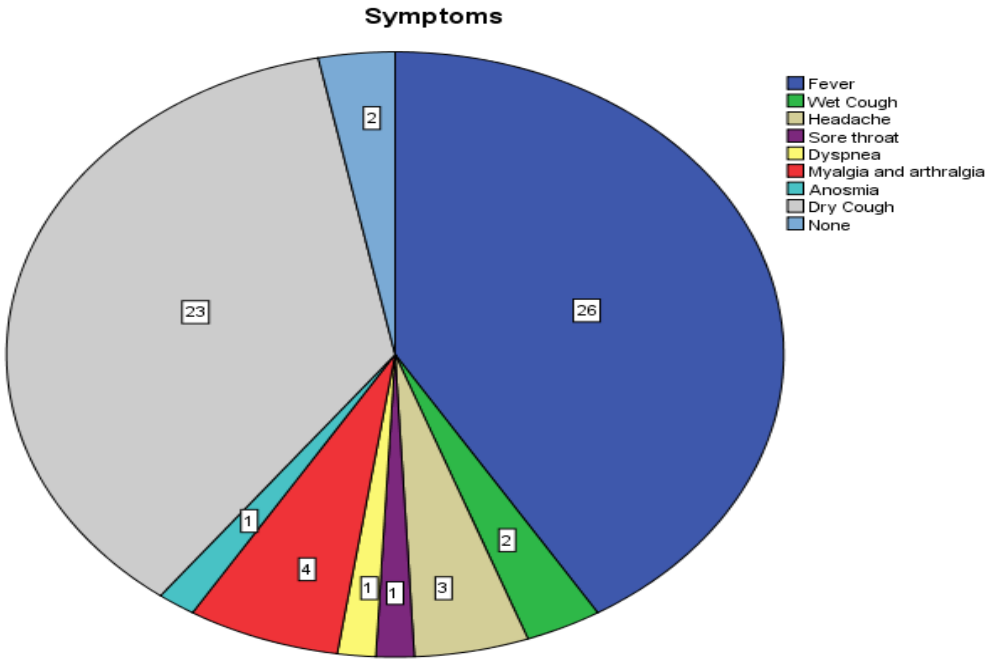
This study was approved by the clinical research ethics committee of Gümüşhane University (date: 23.03.2022 decision no: E-95674917-108.99-86712).

2.7. Statistical Analysis

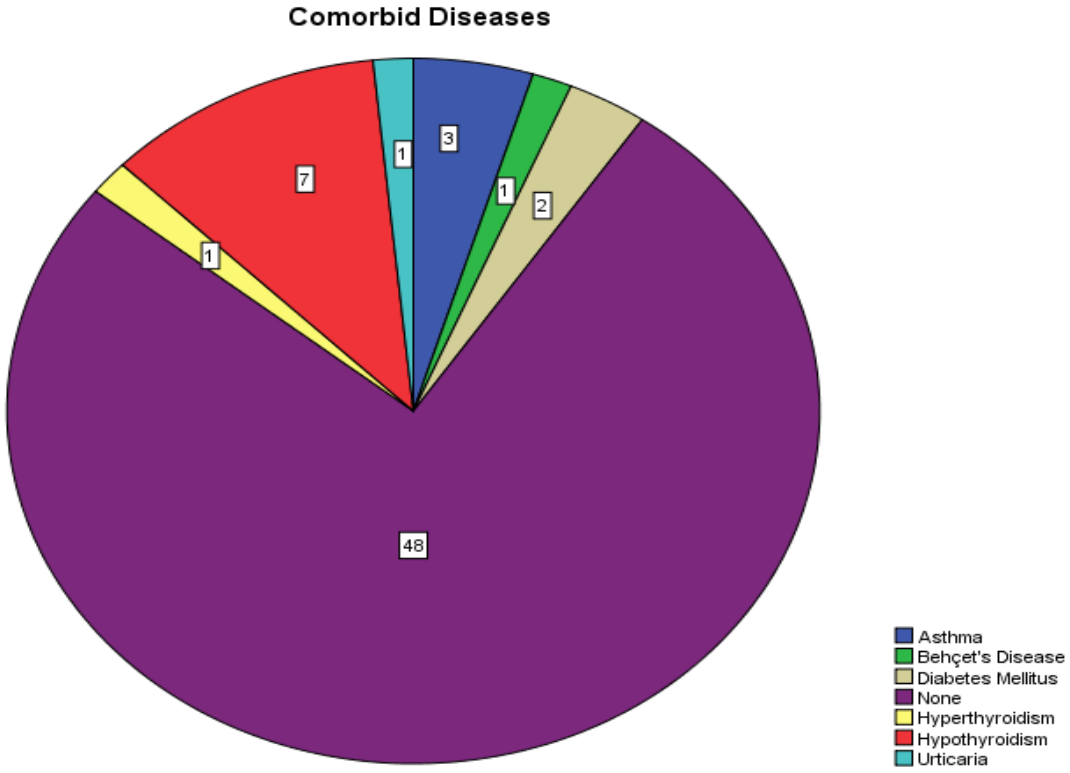
The Statistical Package for the Social Sciences (SPSS), version 15.0 was used for statistical analysis. The conformity of the independent variables to the normal distribution was examined using analytical methods (Kolmogorov-Smirnov test). Since the data were distributed normally, mean±SD was used to describe the variables.

3. Results

In the study involving 63 COVID-19 positive pregnant women followed up in the inpatient ward, fever (41.2%) was the most common complaint at admission. The second most common complaint following the fever complaint was dry cough (36.5%). Asymptomatic COVID-19 positivity was present in 2 patients (Graph 1).



Graph 1. Symptoms



Graph 2. Comorbid Diseases

Of the patients, 76.1% did not have a systemic disease accompanying pregnancy. The most common chronic disease was hypothyroidism (11%) (Graph 2).

The mean age of 63 pregnant patients hospitalized due to COVID-19 positivity was 30.3 (±6.02) years, the mean BMI was 29.4 (±4.9), the mean gestational week was 29.5 (±8.3) weeks. The mean number of days between the onset of symptoms and PCR positivity was found to be 2.7 (±2.8) days (Table 1). The earliest gestational week when COVID-19 positivity was detected was 7 weeks, and the latest week was 41 weeks. 66.7% of patients received lopinavir/ ritonavir antiviral therapy. (Table 1).

Table 1. Sociodemographic and Clinical Features

Age (Mean ± SD)	30.3651 ± 6.02763
Parity (Mean ± SD)	1.4921 ± 1.34252
Weight (Mean ± SD)	76.0000 ± 12.77977
Height (Mean ± SD)	160.6825 ± 6.20308
BMI (Mean ± SD)	29.4501± 4.90463
Gestational week (Mean ± SD)	29.5556 ± 8.33527
5th-min Apgar (Mean ± SD) N:12	9.0000 ± 2.56348
Antiviral therapy **Yes (%)** **No (%)**	 66.7% 33.3%

All of the pregnant women had single fetus except for one twin pregnancy. There was no known fetal anomaly in the fetuses. Except for the diagnosis of placenta previa in one of the pregnant women, no placental anomaly was detected in the others. Upon examining amniotic fluid volumes (AFVs), oligohydramnios was detected in three pregnant women. The AFI of the other pregnant women was sufficient. None of them had an antenatal invasive genetic diagnostic test. When pregnancy-related diseases and comorbidities were examined, gestational diabetes (GDM) was detected in 6 patients, and gestational hypertension (GHT) was revealed in 3 patients. One fetus had intrauterine growth retardation (IUGR). Fifteen of the pregnant women we followed up in the inpatient ward with the diagnosis of COVID-19 infection gave birth. 2 patients gave birth by normal spontaneous vaginal delivery, while 13 patients gave birth by cesarean section due to both obstetric and COVID-19-related indications. Four of the 15 newborn infants were followed up in the NICU. One of them was followed up due to jaundice and 3 of them due to respiratory distress. A COVID-PCR test was taken from 3 of the newborn infants on the first day of birth. No COVID-19 positivity was detected in any of them. Of the 15 newborn infants, 2 were born preterm, and 13 were born at term. Antenatal corticosteroid therapy was administered to mothers of preterm infants. No maternal and fetal loss was observed in any of the 63 pregnant women during the follow-up period in the hospital.

Radiological imaging with chest x-ray was performed in 6 of the pregnant women with a preliminary diagnosis of COVID-19 pneumonia. The preliminary diagnosis of pneumonia was confirmed by imaging in four (6.3%) of them as visualizing ground glass densities. All COVID-19 PCR tests were performed with a nasopharyngeal swab sample. Except for two patients, the first PCR test results of all patients were positive. The PCR test results of the remaining two patients became positive in the third repetition. Both of these patients, one of whom was in the ICU, were followed up and treated with the diagnosis of COVID-19-related pneumonia. There was no need for antiviral therapy in 21 (33.3%) of the 63 pregnant women. Patients receiving antiviral therapy were administered lopinavir/ritonavir therapy. Fifty-five of the patients were followed up in room air without the need for oxygen support. The remaining 8 patients received oxygen support by nasal cannula. There was no need for mechanical ventilation in any of the patients.

4. Discussion

COVID-19 is transmitted by droplets and by contact with contaminated surfaces. The incubation period is 5 days on average, and the most common symptoms are fever and cough. The mortality of the disease in the general population has been reported to be 2.3% (Wu & McGoogan, 2020). There is no specific treatment developed against the COVID-19 virus yet. There are not sufficient data showing that pregnant women are at a higher risk than the normal population, and the clinical picture of the disease is similar to the general population. In the present study, we identified fever (41.2%) as the most common reason for admission to the hospital. There was no maternal mortality in any of the 63 pregnant women followed up in our clinic.

COVID-19 disease usually has a mild course during pregnancy but can quickly progress to severe disease. Severe disease is more frequently observed, especially in the presence of comorbidities accompanying pregnancy, such as advanced maternal age, obesity, asthma, hypertension, and diabetes (Allotey et al., 2020; Şahin, Tanaçan, Webster, & Moraloğlu

Tekin, 2021). In accordance with this information, the patients followed up in our clinic had a mild infection during pregnancy. One of our patients, followed up in the ICU, was at gestational week 37 and was diagnosed with asthma. During pregnancy, COVID-19 causes not only lung and multiorgan damage but also placental damage due to hypercoagulation and hyperinflammation secondary to thrombosis. It includes a wide spectrum of pathological mechanisms, including placenta-related disorders such as immuno-thrombosis, preterm birth, IUGR, preeclampsia, and recurrent pregnancy loss (Ferrer-Oliveras et al., 2021). Pregnancy is a physiological hypercoagulation condition with increased coagulation factors, such as fibrinogen and FVIII, and decreased fibrinolytic proteins, such as protein S. These special conditions of pregnancy can be aggravated by infectious diseases (Abbassi-Ghanavati, Greer, & Cunningham, 2009).

A recent study found the rate of preterm delivery as 7.2% in pregnant women with COVID-19, while this rate was 5.8% in pregnant women without COVID-19 (Jering et al., 2021). Fifteen of the pregnancies followed up in our clinic resulted in birth, 2 of them (13.3%) were preterm births, which is a high rate compared to the literature. Antenatal corticosteroid therapy was administered to mothers of preterm infants. During pregnancy, COVID-19 disease has been associated with increased obstetric complications such as preterm birth, fetal distress, cesarean delivery, fetal loss, preeclampsia, and prolonged hospital stay (Şahin et al., 2021). As the disease severity increases, the incidence of complications also increases. Of the 63 pregnant women followed up in our clinic, 2 gave preterm birth, and 13 gave birth at term. 13 of the 15 patients gave birth by cesarean section. The cesarean section rate also increased in the COVID-19 patient group, as predicted by the literature (Chen et al., 2020).

Although a study documented intrauterine vertical transmission from the mother to the infant in a few cases (Vivanti et al., 2020), there are more studies stating that there is not sufficient evidence showing the vertical transmission of COVID-19 from the mother to the infant (Chen et al., 2020; Joma, Fovet, Seddiki, Gressens, & Laforge, 2021; Zhu et al., 2020). No positivity was detected in the PCR results obtained from 3 of 15 infants born in our clinic. Since the use of favipiravir is contraindicated during pregnancy, lopinavir/ritonavir therapy was administered to 42 of our 63 patients hospitalized in our clinic in light of the recommendations of the Ministry of Health's COVID-19 guideline. It is known that the frequency of fetal anomaly does not increase in the antiretroviral use of the lopinavir/ritonavir combination (Martínez-Sánchez, De la Calle Fernández-Miranda, & Bartha, 2021).

The World Health Organization (WHO) suggests that cesarean section should be performed only for medical and obstetric indications. As contact precautions, patients should be followed up in single rooms, and medical masks, protective glasses, gloves, and gowns should be used when entering the room. Hands should be washed before and after the procedure. If possible, the tools to be used should be disposable, and the materials to be used again should be properly disinfected. Patient follow-ups in our hospital were performed according to this algorithm. N95 and above protective masks, waterproof gowns, eye protection, surgical hair caps, and double-layer gloves were used during births.

5. Conclusion and Suggestions

More attention should be paid to pregnant women infected with COVID-19. COVID-19 infection during pregnancy has been associated with poor obstetric outcomes. As the disease severity increases, the worsening in obstetric outcomes becomes evident. There are not sufficient data on vertical transmission from the mother to the infant. Although vaginal birth is not contraindicated as a mode of delivery, we see that a significant part of deliveries are performed by cesarean section. It is necessary to manage the COVID-19 infection during pregnancy with a multidisciplinary approach in which knowledge, experience, and responsibilities are shared. We would like to draw attention to the importance of personal hygiene, isolation, and vaccination since a specific treatment has not been developed yet.

Declarations

All of the authors declare that the article is original and they have approved the final version submitted. Additionally, there are no conflicts of interest in connection with this article, and the study described has not been published previously or currently under consideration for publication elsewhere. The article has been prepared according to the submission rules explained under "Author Guidelines" and "Review Process" pages. All directives of the Helsinki Declaration have been followed and informed consent was obtained from the participants. This study was approved by the clinical research ethics committee of Gümüşhane University (date: 23.03.2022 decision no: E-95674917-108.99-86712). Author contributions Idea: BT, BLK, HT Design: HT Inspection:HT, BLK Resources: BT Materials: BT, HT Data Collection or Processing: BT, HT Analysis and Interpretation: BT, BLK, HT Literature search: BT, BLK, HT. Writing: BT, BLK, HT Critical review: BT, BLK, HT.

References

Abbassi-Ghanavati, M., Greer, L. G. and Cunningham, F. G. (2009). Pregnancy and laboratory studies: a reference table for clinicians. *Obstet Gynecol, 114*(6), 1326-1331. https://doi.org/10.1097/AOG.0b013e3181c2bde8

Allotey, J., Stallings, E., Bonet, M., Yap, M., Chatterjee, S., Kew, T. et al. Thangaratinam, S. (2020). Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *Bmj, 370*, m3320. https://doi.org/10.1136/bmj.m3320

Chen, H., Guo, J., Wang, C., Luo, F., Yu, X., Zhang, W. et al. (2020). Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet, 395*(10226), 809-815. https://doi.org/10.1016/ s0140-6736(20)30360-3

Ferrer-Oliveras, R., Mendoza, M., Capote, S., Pratcorona, L., Esteve-Valverde, E., Cabero-Roura, L. et al. (2021). Immunological and physiopathological approach of COVID-19 in pregnancy. *Arch Gynecol Obstet, 304*(1), 39-57. https://doi.org/10.1007/s00404-021-06061-3

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y. et al. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet, 395*(10223), 497-506. https://doi.org/10.1016/s0140-6736(20)30183-5

Jering, K. S., Claggett, B. L., Cunningham, J. W., Rosenthal, N., Vardeny, O., Greene, M. F. et al. (2021). Clinical Characteristics and Outcomes of Hospitalized Women Giving Birth With and Without COVID-19. *JAMA Intern Med, 181*(5), 714-717. https://doi.org/10.1001/jamainternmed.2020.9241

Joma, M., Fovet, C. M., Seddiki, N., Gressens, P. and Laforge, M. (2021). COVID-19 and Pregnancy: Vertical Transmission and Inflammation Impact on Newborns. *Vaccines (Basel), 9*(4). https://doi.org/10.3390/vaccines9040391

Martínez-Sánchez, N., De la Calle Fernández-Miranda, M. and Bartha, J. L. (2021). Safety profile of treatments administered in COVID 19 infection in pregnant women. *Clin Invest Ginecol Obstet, 48*(3), 100663. https://doi.org/10.1016/j.gine.2021.01.004

Mor, G., Aldo, P. and Alvero, A. B. (2017). The unique immunological and microbial aspects of pregnancy. *Nat Rev Immunol, 17*(8), 469-482. https://doi.org/10.1038/nri.2017.64

Şahin, D., Tanaçan, A., Webster, S. N. and Moraloğlu Tekin, Ö. (2021). Pregnancy and COVID-19: prevention, vaccination, therapy, and beyond. *Turk J Med Sci, 51*(Si-1), 3312-3326. https://doi.org/10.3906/sag-2106-134

Vivanti, A. J., Vauloup-Fellous, C., Prevot, S., Zupan, V., Suffee, C., Do Cao, J. et al. (2020). Transplacental transmission of SARS-CoV-2 infection. *Nat Commun, 11*(1), 3572. https://doi.org/10.1038/s41467-020-17436-6

Wu, Z. and McGoogan, J. M. (2020). Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *Jama, 323*(13), 1239-1242. https://doi.org/10.1001/jama.2020.2648

Yilmaz, N., Buyuk, G. N., Ersak, D. T., Ersak, B., Kahyaoglu, I., Tas, D. Ö. et al. (2021). The Impact of COVID 19 Pandemic on Pregnancy Outcomes of ART Cycles. *Journal of Infertility and Reproductive Biology, 9*(4), 155-159.

Zambrano, L. D., Ellington, S., Strid, P., Galang, R. R., Oduyebo, T., Tong, V. T. et al. (2020). Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep, 69*(44), 1641-1647. https://doi.org/10.15585/mmwr.mm6944e3

Zhu, H., Wang, L., Fang, C., Peng, S., Zhang, L., Chang, G. et al. (2020). Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr, 9*(1), 51-60. https://doi.org/10.21037/tp.2020.02.06