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Characteristics, Clinical Findings and Outcomes of 333 Pregnant Women with COVID-19 During Four Waves of Infection at a Tertiary Hospital in Turkey

Türkiye'deki Bir 3. Basamak Hastanede, Dört Enfeksiyon Dalgası Sırasında COVID-19 Olan 333 Gebe Kadının Özellikleri, Klinik Bulguları ve Sonuçları

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Abstract

Aim: Since the first case of SARS-CoV-2 in Turkey, it was confirmed in over 14 million people causing almost 95,000 of deaths. During the two years course of pandemic SARS-CoV-2 caused 4 waves of disease in Turkey. To enhance our knowledge on initial presentation, clinical course and severity, risk factors, and pregnancy outcomes of COVID-19 infection during the four different waves of pandemic.

Material and Method: Clinical records of 333 pregnant women with a verified positive PCR test was reviewed. The distribution of the patients during the two-year course of the pandemic was studied. Descriptive data regarding maternal age, gestational age, body mass index (BMI), education, employment status, ABO blood type, previous obstetric history, previous medical history, smoking status were collected. Maternal and immediate perinatal outcomes were examined. The primary endpoint of the study was comparison of four waves during the pandemic in terms of admission to ICU (Intensive Care Unit), use of mechanical ventilation or maternal and neonatal death.

Results: The distribution of number of the patients followed the same pattern as the general population in Turkey, except first wave, which did not seem to affect pregnant women. Most of the patients and all the maternal deaths were accumulated in the second and fourth waves. Those with more severe disease were older, at an earlier gestational age, and had a higher BMI.

Conclusion: The severity of the COVID-19 disease was strongly associated with the maternal age and gestational age. The worst maternal outcomes of the disease were detected during the second and fourth waves in Turkey.

Keywords: COVID-19, viral infection, pregnancy, risk factors, maternal outcomes

Öz

Amaç: Türkiye'de ilk SARS-CoV-2 vakası görülmesinden bu yana, 14 milyondan fazla insanda enfeksiyonun varlığı doğrulandı ve yaklaşık 95.000 ölüme neden oldu. SARS-CoV-2 pandemisi, iki yıllık seyri boyunca Türkiye'de 4 hastalık dalgasına neden oldu. Amacımız, dört farklı pandemi dalgası sırasında COVID-19 enfeksiyonunun ilk sunumu, klinik seyri ve şiddeti, risk faktörleri ve gebelik sonuçları hakkındaki bilgilerimizi geliştirmektir.

Gereç ve Yöntem: Doğrulanmış pozitif PCR testi olan 333 hamile kadının klinik kayıtları incelendi. Pandeminin iki yıllık seyri boyunca hastaların dağılımı incelendi. Anne yaşı, gebelik haftası, vücut kitle indeksi (VKİ), eğitim, çalışma durumu, ABO kan grubu, önceki obstetrik öyküsü, önceki tıbbi öyküsü, sigara içme durumu ile ilgili tanımlayıcı veriler toplandı. Maternal ve acil perinatal sonuçlar incelendi. Çalışmanın temel amacı, pandemi sırasındaki dört dalganın Yoğun Bakım Ünitesi'ne (YBÜ) kabul, mekanik ventilasyon kullanımı veya anne ve yenidoğan ölümü açısından karşılaştırılmasıydı.

Bulgular: Hasta sayısının dağılımı, hamileleri etkilemediği görülen birinci dalga dışında, Türkiye'deki genel popülasyonla aynı modeli izlemiştir. Hastaların çoğu ve anne ölümlerinin tamamı ikinci ve dördüncü dalgalarda toplanmıştır. Daha şiddetli hastalığı olanlar daha ileri yaşta kadınlar, gebeliğin daha erken aylarında ve daha yüksek vücut kitle indeksine sahipti.

Tartışma: COVID-19 hastalığının şiddeti, anne yaşı ve gebelik yaşı ile güçlü bir şekilde ilişkiliydi. Türkiye'de en kötü maternal sonuçlar, hastalığın ikinci ve dördüncü dalgalarında görüldü.

Anahtar Kelimeler: COVID-19, viral enfeksiyon, gebelik, risk faktörleri, maternal sonuçlar

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INTRODUCTION

The novel COVID-19 disease caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) was first defined in Wuhan, China in December 2019. Since then, it triggered a tremendous global health problem. According to World Health Organization, globally over 400 million people were infected, and more than 6 million deaths were reported.[1] In Turkey, the first case of COVID-19 was identified on March 11, 2020, and since then the virus was confirmed in over 14 million people causing almost 95,000 deaths.[2] While the virus had spread dramatically around the world clinical management had also aroused a serious challenge because there was limited information about the disease and even fewer data concerning the management of obstetrical patients.

Prevalence calculation of the disease among the pregnant raised a challenge as well. The spectrum of the disease varied from asymptomatic infection, mild upper respiratory syndrome to pneumonia, severe respiratory distress, and death.[1] One study reported that asymptomatic infection rate among obstetrical patients was 15-fold higher than that of surgical patients.[3] Recently, it had been concluded that the prevalence of SARS-CoV-2 infection among pregnant women range from 2-20%[4] that is yet to be confirmed.

Current data suggest that pregnant women are not necessarily more susceptible to SARS-CoV-2 infection than the ones that are not pregnant. However, respiratory failure might increase among the pregnant patients with the existence of comorbidities such as chronic lung disease, cardiovascular disease, hypertension, immunocompromised patients, body mass index above 40 kg/m², pregestational diabetes, chronic kidney, or liver disease.[5]

In Turkey, the first case of COVID-19 infection was identified on March 11, 2020, and afterwards the disease followed a pattern characterized with a series of infection waves.[1] The first wave of the disease was observed in April 2020. With strict infection prevention policies, the number of cases remained the lowest until August 2020. In August the number of cases started to accelerate with a spike in December 2020. A surge of new cases resulted with the third wave in April 2021. The arrival of vaccines helped to decrease new infection levels through the summer of 2021. Another surge, the fourth wave, started by the end of August 2021 and had two peaks. The first peak was in September 2021, due to contagious delta variant and the second peak occurred in February 2022 attributed to the circulation of Omicron variant. In March 2022, due to decreased number of hospitalization and death, the Turkish Ministry of Health decided to cease many of the restrictions.[1]

To our knowledge, no studies have investigated the characteristics and outcomes of pregnancies during the various stages of the COVID-19 infection. In this study, we identified and reviewed the medical records of 333 pregnant women in a single tertiary center with laboratory-confirmed SARS-CoV-2 infection to enhance our understanding on the initial presentation, clinical course and severity, risk factors, and pregnancy outcomes. In addition, we aimed to compare the characteristics of the disease during the four different waves of pandemic. We hypothesized that medical background, socioeconomic level, and gestational age would have a certain impact on the maternal and neonatal outcomes.

MATERIAL AND METHOD

This study was an observational cohort of pregnant women of all gestational ages with SARS-CoV-2 infection who were admitted at a single tertiary center **KKKKKKKKKKKKKKK** Hospital in Istanbul, Turkey. The study was primarily reviewed and approved by the Ministry of Health and then by the Medical Ethics Committee of **KKKKKKKKKKKKKK** Hospital (Decision number: 2022/514/222/43. Date: 30.03.2022).

From the beginning of the pandemic, universal testing with quantitative reverse transcriptase polymerase chain reaction (qRT-PCR) assay of maternal naso-pharyngeal swab specimens was required for all the hospital admissions. Pregnant patients with a positive PCR test were isolated in the COVID-19 section within the Obstetrics and Gynecology Department. During the study period, all the patients admitted to delivery were tested for SARS-CoV-2 regardless of symptoms or known exposures. We have screened the data between March 11, 2020, and March 3, 2022, which were the dates when the first case was confirmed in Turkey and many of the restrictions were ceased due to decrease in number of new cases, respectively.

Clinical records of pregnant women with a verified PCR test were reviewed. When the electronic medical records were not satisfying, researchers obtained additional data from paper files of each patient. Clinical data including epidemiological history, week of pregnancy, comorbidities, clinical and laboratory findings, treatment measures, maternal and immediate fetal outcomes were extracted. Two study investigators (EUS and MK) independently reviewed the data collection forms to verify data accuracy. All the disagreements between them were resolved by consultation with a third investigator (AK).

Distribution of pregnant patients and severity of the disease were demonstrated during the four waves of pandemic and for each spike of the disease, respectively. Descriptive data regarding maternal age, body mass index (BMI), education, employment status, ABO blood type, previous obstetric history, previous medical history, smoking status were calculated. BMI was categorized as healthy (BMI less than 25), overweight (BMI=25-30) and obese (BMI greater than 30). Education and employment status were also enumerated. Initial laboratory findings which were previously studied as possible signs of prognosis including complete blood count, neutrophil, platelet, and lymphocytes counts, and their ratio (neutrophil/lymphocytes or platelet/lymphocytes), D-dimer levels, c-reactive protein levels were collected.

Gestational age of the patients was calculated based on self-reported last day of menstruation and confirmed with previous ultrasound imaging when possible. The gestational age at the time of positive SARS-CoV-2 test was presented in the study. Patients were classified as first trimester (0-13 weeks), second

trimester (14-26 weeks) and third trimester (>27 weeks). The third trimester were further categorized into three groups: preterm (27-36 weeks), term (37-40 weeks) and post term (>40 weeks).

Based on self-reported symptoms and clinical status patients were classified as asymptomatic, mild, moderate/severe, and critical defining severity of the disease. Guidelines specified by the National Institutes of Health (NIH) was modified for this purpose.[6] Patients with non-COVID-19 relevant symptoms or no symptoms were classified as the 'asymptomatic' group. Patients mainly with upper respiratory tract symptoms formed the 'mild' group. Self-reported dyspnea without tachypnea, SpO_2 above 95%, and normal findings on chest scanning were also included in the mild group. 'Moderate-Severe' cases were defined as dyspnea with requirement of oxygen therapy, oxygen saturation below 95% and COVID-19 related findings on chest scanning (X-Ray or computerized tomography). Finally, patients admitted to critical care formed the 'critical' disease group (**Table 1**).

Table 1. SARS-CoV-2 classification based on severity of clinical presentation. Patients were divided into four groups concerning clinical course of the disease. Modified from National Institutes of Health guidance.

Asymptomatic (n=97, 29%)	Mild (n=123, 37%)	Moderate-Severe (n=98, 29%)	Critical (n=15, 4,5%)
	• Fever, cough, sore throat, fatigue, muscle pain, chills, back pain, nausea, vomiting, joint pain, nasal stuffiness, loss of smell or taste, gastrointestinal symptoms • Self-reported dyspnea with normal chest scanning and SpO_2 above 95%	• Dyspnea with requirement of oxygen therapy • Oxygen saturation below 95% • COVID-19 related findings on chest scanning	• Admission to critical care

Obstetric outcomes included maternal death, preterm birth, primary cesarean birth, placenta previa, secondary infections, chorioamnionitis, detachment of placenta, hypertensive disorders of pregnancy, existence of meconium in the amniotic fluid, venous thromboembolism, and postpartum hemorrhage. Primary cesarean birth was defined as no prior cesarean birth that included patients without prior pregnancy ahead of 20th week of gestation or history of only vaginal births. Secondary infections and chorioamnionitis were defined as infections confirmed with positive culture tests of blood, urine, and amniotic fluids, respectively. Hypertensive disorders of pregnancy were defined as preeclampsia, gestational hypertension, and chronic hypertension with superimposed preeclampsia. Venous thromboembolism was defined as deep venous thrombosis. Postpartum hemorrhages were defined as cumulative blood loss greater than 1000 mL or signs and symptoms of hypovolemia within 24 hours of birth.[7] All the pregnant patients with a positive PCR test received therapeutic doses of anti-coagulant therapy. Additional therapies included antibiotics, steroids, anti-viral therapy, and anti-fungal therapy.

Summary statistics were calculated for baseline and clinical characteristics. The mean and standard deviation (SD) for maternal age; median, first and third quartiles for BMI were calculated. Missing BMI values were not imputed. All the other variables were presented as median and percentages. Cross-tabulation was used to quantitatively analyze the relationship between severity of the disease and the baseline and clinical characteristics of the patients. Previous cesarean birth, previous preterm birth and previous hypertensive disorder of pregnancy were also included among the baseline and clinical variables.

Neonatal outcomes included miscarriage, perinatal death, preterm birth before the 37th week of gestation, birth weight, Apgar scores of 1- and 5-minute. Since the newborns were followed through the delivery hospitalization only immediate outcomes were presented in the study. Birth weight, 1-minute and 5-minute Apgar scores were presented as median, first and third quartile, miscarriage and perinatal death were expressed as number of cases and percentages.

For ordinal and nominal variables, the chi-square test and for continuous variables Kruskal-Wallis test was used to assess trends in baseline and clinical characteristics of the groups based on severity of the disease. All analyses were performed with IBM SPSS, version 20.0 and Microsoft Excel.

RESULTS

Throughout the four waves of pandemic, between March 11, 2020, and March 3, 2022, pregnant patients of all gestational ages with a positive SARS-CoV-2 test admitted to the hospital were included in the analysis. The distribution of the disease followed the general pattern in Turkey except the first wave which did not seem to affect the pregnant patients (**Figure 1**). Of 333 patients with a positive test, 97 (29%) were asymptomatic, 123 (37%) had mild illness, 98 (29%) had moderate-severe illness, and 15 (5%) had critical illness. 5 maternal deaths (1,5%) were attributed to COVID-19 infection. Distribution of the disease in terms of severity during the four waves showed that the majority of the critical group was hospitalized during the second and fourth waves (**Figure 2**) which is consistent with the distribution of the disease in the general population. Of 5 maternal deaths, one occurred during the second and the rest occurred during the fourth wave of the disease. All the maternal deaths were attributed to COVID-19 infection.

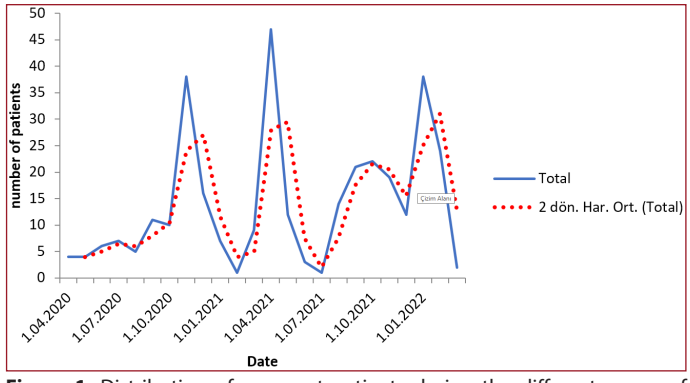

Figure 1. Distribution of pregnant patients during the different waves of infection. Continuous line describes the monthly data of COVID-19 disease among the pregnants. Dashed line shows the trend of distribution. (2 per. Mov.Avg: 2 period moving average)

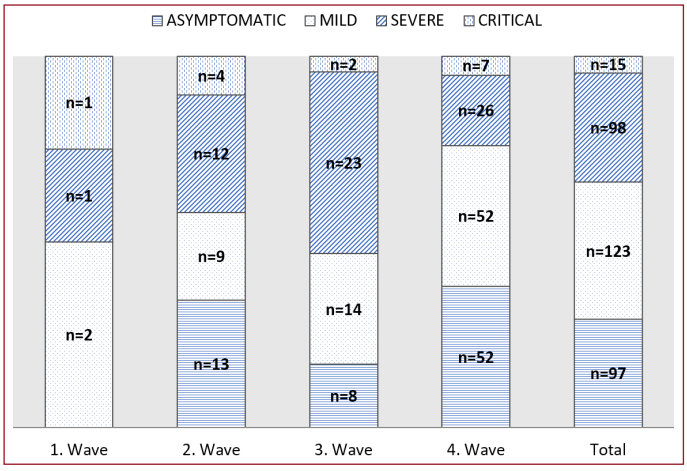

Figure 2. Grouping of the pregnants according to disease severity, during four waves of disease.

The median (interquartile range) gestational age at the time of admission to the hospital with a positive SARS-CoV-2 test result was 36 weeks of gestation (30–38). Statistical tests showed a significant difference between the groups in terms of severity according to gestational age (p<0.001) (**Table 2**). During the first trimester none of the patients had critical disease. Of 15 patients in the critical group, 8 patients were at the preterm period and 6 patients at the second trimester. There was only one patient at the term group transferred to the ICU. The majority of the severe group consisted of second trimester and preterm patients as well. Of 98 patients in the moderate-severe group, 67% of them were either at the second trimester (n=20) or preterm patients (n=46).

Table 2. Baseline Demographic and Clinical Characteristics

Characteristic	Disease Severity				p-value	Total (n=333)
	Critical (n=15)	Moderate-Severe (n=98)	Mild (n=123)	Asymptomatic (n=97)		
Gestational age					< 0,001	
1. Trimester	0	4 (4%)	7 (7 %)	3 (3%)		
2. Trimester	6 (40%)	20 (20%)	13 (10%)	2 (2%)		
Preterm	8 (53%)	46 (47%)	56 (45%)	10 (10%)		
Term	1 (7%)	25 (26%)	46 (37%)	71 (73%)		
Postterm	0	3 (3%)	1 (1%)	11 (12%)		
Age (y)	32±3,1	31±5,9	29,9±5,9	28,4±5,4	0,006	29,9±5,74
BMI (kg/m²)	28 (25,9 - 30,3)	29,8 (25,9 - 34,7)	27,8 (24,9 - 31,1)	28,9 (26,4 - 31,6)	0,02	28,70 (25,75-31,80)
Healty (BMI<25)	2 (13%)	14 (14%)	26 (21%)	10 (10%)		52
Overweight (30<BMI<25)	7 (47%)	33 (33,7%)	45 (36,5%)	35 (36%)		120
Obesity (BMI>30)	3 (20%)	44 (45%)	32 (26%)	30 (31%)		109
Previous cesarean birth	7 (47%)	34 (35%)	43 (35%)	35 (36%)	0,468	119
Previous preterm birth	0	1 (1%)	3 (2%)	1 (1%)		5
Previous hypertensive disorder of pregnancy	0	1 (1%)	4 (3%)	2 (2%)		7
Education					0,006	
İlliterate	0	8 (8%)	6 (5%)	13 (13%)		27
High School	3 (20%)	60 (61%)	77 (63%)	61 (63%)		201
University	7 (47%)	24 (24%)	23 (19%)	10 (10%)		64
Employment Status	6 (40%)	21 (21%)	24 (20%)	8 (8%)	< 0,001	61
Smoking habit	0	3 (3%)	6 (5%)	6 (6%)	0,471	15
Blood type					0,139	
0	6 (40%)	30 (31%)	37 (30%)	41 (42%)		114
A	8 (53%)	40 (41%)	52 (42%)	36 (37%)		136
B	1 (7%)	15 (15%)	27 (22%)	15 (15%)		58
AB	0	13 (13%)	7 (7%)	5 (5%)		25
Rh-positive	14 (93%)	84 (86%)	108 (88%)	82 (85%)	0,765	288
Asthma or chronic obstructive pulmonary disease	2 (13%)	7 (7%)	11 (9%)	2 (2%)	0,14	22
Chronic cardiovascular disease	0	3 (3%)	11 (9%)	3 (3%)	0,102	17
Thyroid disease	3 (20%)	13 (13%)	18 (15%)	17 (18%)	0,806	51
Pregestational diabetes	2 (13%)	8 (8%)	11 (9%)	8 (8%)	0,924	29
Chronic hematological	0	2 (2%)	2 (2%)	2 (2%)	0,947	6
Chronic neurological	0	0	3 (2%)	2 (2%)	0,447	5
Chronic other diseases	0	2 (2%)	5 (4%)	0	0,194	7

BMI= body mass index. Data are mean±SD, median (interquartile range), or n (%) unless otherwise specified. Number of missing values: BMI (n=52), Education (n=41), Employment status (n=36), Smoking habit (n=26)

The distribution of the blood type among the patients showed the same pattern with the general population of Turkey 8. Interestingly, we did not find any relation between the severity of the disease and medical comorbidities including asthma or chronic obstructive pulmonary disease, chronic cardiovascular disease, thyroid disease, pregestational diabetes, hematological, neurological or other chronic diseases (**Table 2**). Within the groups there was a difference in terms of education and employment status. However, regression analysis did not allow us to draw a conclusion about a relation between education or employment status and severity of the disease.

The most common patient-reported symptoms were cough (26%), dyspnea (23%), fever (11%), fatigue (%), and myalgia or body aches (6%) (**Table 3**). 46 patients had COVID-19 related findings on chest imaging (chest X-ray or computed tomography scan) that were in either critical or severe-moderate group.

Vital sign and laboratory findings by COVID-19 severity are described in **Table 4**. On admission, critical group had a higher heart rate, higher body temperature, lower hematocrit levels, lower white blood cells count, higher rates of neutrophil/lymphocyte and platelet/lymphocyte, and higher C-reactive protein (CRP) levels.

34 of the patients refused to use any medication other than anticoagulants and anti-inflammatories. Therapeutic doses of anticoagulant therapy were used for 306 patients which consists of 92% of the patients. Antibiotics, steroids and immunomodulators were used for 17% (n=56), 16% (n=54) and 1% (n=3) of the patients, respectively. Only 2 of the patients admitted to the ICU received anti-fungal therapy.

Table 3. Coronavirus Disease 2019 (COVID-19) Disease Severity Classification for Study Cohort

Data Through Delivery Hospitalization	Critical (n=15)	Moderate-Severe (n=98)	Mild (n=123)	Asymptomatic (n=97)	Total (n=333)
Death due to COVID-19	5 (33%)				5 (1.5%)
SpO_2 less than 94%	11 (73%)	53 (54%)			64 (19%)
Abnormal chest imaging results	10 (66%)	36 (37%)			46 (13.8%)
Documentation of self-reported dyspnea	9 (60%)	39 (40%)	28 (23%)		76 (22.8%)
Any other self-reported symptoms (excluding dyspnea)					
Cough	6 (40%)	38 (39%)	43 (35%)		87 (26%)
Myalgia or body aches	1 (7%)	8 (8%)	10 (8%)		19 (5.7%)
Fever	4 (27%)	15 (15%)	20 (16%)		39 (11.7%)
Nasal stuffiness or rhinorrhea	0	2 (2%)	2 (1.6%)		4 (1.2%)
Headache	0	5 (5%)	4 (3.2%)		9 (2.7%)
Anosmia or loss of smell/Ageusia or loss of taste	0	1 (1%)	0		1 (0.3%)
Fatigue	2 (1%)	8 (8%)	13(10%)		23 (69%)
Sore throat	0	2 (2%)	3 (2.4%)		5 (1.5%)
Nausea or vomiting	2 (1%)	4 (4%)	3 (2.4%)		9 (2.7%)
Back or joint pain	0	0	3 (2.4%)		3 (1%)
Diarrhea	0	1 (1%)	0		1 (0.3%)
Other symptoms	3 (20%)	22 (22%)	64 (52%)		89 (26.7%)
No symptoms				97 (100%)	97 (29%)

Data was presented as number and percentage within the group.

Table 4. Vital Signs and Laboratory Values by COVID-19 Severity Classification

	Disease Severity				p-value
	Critical (n=15)	Moderate-Severe (n=98)	Mild (n=123)	Asymptomatic (n=97)	
Highest heart rate (beats/minute)	88 (80 -94)	86 (80-97)	84 (80-88)	80 (80-86)	0,016
Lowest SpO_2 (%)	88 (79-91)	93 (90-95)	96 (95-97)	97 (96-98)	< 0,001
Highest temperature (Celsius)	37,1 (36,7-37,5)	36,9 (36,7-39,5)	36,8 (36,6-37,2)	36,8 (36,6-36,9)	0,005
Lowest platelet count ($\times 10^3$/mm3)	194 (173-249)	192 (164-234)	203 (168-241)	214 (169-257)	0,28
Diastolic BP	60 (60-70)	70 (60-70)	70 (60-70)	70 (60-70)	0,386
Systolic BP	105 (100-110)	110 (100-110)	110 (100-110)	110 (100-110)	0,095
Lowest hematocrit (%)	32,1 (30,9-34,5)	34,9 (31,8-37)	34,2 (31,5-37)	35 (33,1-37,4)	0,033
Lowest hemoglobin (g/dL)	10,8 (9,5-11,5)	11,55 (10,7-12,6)	11,5 (10,2-12,4)	11,6 (10,9-12,5)	0,141
Lowest WBC ($\times 10^3$/mm3)	8,8 (6,22-11,76)	7,57 (5,9-9,28)	8,15 (6,44-10,33)	9,8 (8,11-11,81)	< 0,001
Neutrophil/Lymphocytes	9,42 (8-11,77)	4,88 (3,9-7,03)	4,44 (3,43-6,42)	3,62 (2,88-5,36)	0,016
Platelet/Lymphocytes	227,63 (217,98-415,91)	169,78 (125-227,5)	155,06 (117,8-219,33)	122,38 (90,36-169,6)	< 0,001
Highest D-dimer (ng/mL)	2110 (1120-4040)	1635 (1020-3220)	1790 (1090-2845)	2170 (1370-4400)	0,046
CRP	86 (40-121)	41 (19-71)	14,5 (6-35)	9,5 (5-24,5)	< 0,001

Data are median (interquartile range). Number of missing values: hearth rate (n=32), SpO_2 (n=30), temperature (n=28), D-dimer (n=9), CRP (=11).

Maternal and immediate perinatal outcomes are presented in **Table 5**. Among 333 patients, 6 of them had abortion and 108 patients had no record of delivery. In the critical group, 1 patient died before delivery, and 3 of them were at the earlier stages of second trimester and had no records of delivery. Therefore, maternal-perinatal outcomes in the critical group were calculated for 11 patients only. Only one patient revealed thromboembolic event, subacute deep vein thrombosis (DVT).

DISCUSSION

Principal Findings

We described the effect of COVID-19 disease on pregnancy throughout the different stages of pandemic in 333 hospitalized patients from March 2020 to March 2022, in a tertiary center. Among these patients, 15 of them were transferred to the ICU and 5 of them died because of systemic effects of the virus. The highest number of patients and maternal deaths were detected during the second (n=1) and fourth waves (n=4) of the COVID-19 infection in Turkey. These results are also consistent with the distribution of total patients in the general population.

We found that gestational age is an essential risk factor that influences the severity of the COVID-19 disease. In the critical group, 14 out of 15 patients (%93) were at the second trimester or preterm stages of the pregnancy. Maternal death was also detected within this group of pregnants.

Clinical and Research Implications

US center for Disease Control and Prevention (CDC) data showed that the pregnants are at an increased risk of death (1.5 per 1000) and ICU admission (10.5 per 1000).[4] Metz et al.[9] reported 4.8 % ICU admission rate and 0.3 % maternal death. Our maternal death rate was 1.5% (5/333 patients with COVID-19), and the ICU admission rate was 4.5 % (15/333). Both rates in our study were higher. This might be partially attributed to the admission of critical patients from other health care facilities to the tertiary care center. In addition, different from the previous study,[9] we included all the hospital admissions of all gestational ages. Moreover, inclusion of the data from the fourth wave, a subsequent period, did also have a certain impact on difference of our results as 4 of the maternal deaths occurred during the fourth wave.

Older maternal age, increased body mass index and pre-existing comorbidities were defined as risk factors for severe COVID-19 infection.[9,10] Consistent with previous studies, in our study risk factors for severity of the disease also included older age and increased BMI. Interestingly, we did not find any association between comorbidities and the severity of the disease.

Initial clinical and laboratory findings were worse in the critical group. However, we were unable to evaluate the effect of treatments on outcomes of the disease except anticoagulant therapy. We used therapeutic doses of anticoagulant therapy for each patient. Whether this treatment had an additional prevention on previously reported complications of pregnancy such as hypertensive disorder of pregnancy or postpartum hemorrhage,[4,11] is yet to be confirmed.

Strengths and limitations

The strength of this study includes the standardized care of patients and the wide range of time including four different

Table 5. Perinatal Outcomes by Coronavirus Disease 2019 (COVID-19) Severity

Outcome	Critical (n=11)	Moderate-Severe (n=49)	Mild (n=71)	Asymptomatic (n=88)	p-value	Total (n=219)
Maternal death*	4 (36%)					4 (1.8%)
Cesarean birth	11 (100%)	31 (63%)	44 (62%)	49 (56%)	0,042	135 (61.6%)
Primary Cesarean birth	6 (55%)	13 (27%)	21 (30%)	15 (17%)		55 (25.1%)
Postpartum hemorrhage	1 (9%)	1 (2%)		1 (1%)		3 (1.4%)
Hypertensive disorders of pregnancy		1 (2%)	2 (3%)			3 (1.4%)
Preterm birth	8 (73%)	12 (24%)	17 (24%)	6 (7%)		43 (19.6%)
Live birth	11 (100%)	46 (94%)	70 (98.6%)	88 (100%)		216 (98.6%)
Fetal death		3 (6%)	1 (1.4%)		0,199	11 (5%)
Birth weight (g)	2031,8±839,7	2894,4±835	3050,5±702,1	3521,2±497,7	< 0,001	
Plasenta previa		2 (4%)	1 (1.4%)			3 (1.4%)
Secondary infection		3 (6%)				3 (1.4%)
IUGR				1 (1%)		1 (0.5%)
Meconium		2 (4%)	1 (1.4%)	5 (6%)		8 (3.7%)
Kolestase		1 (2%)	3 (4%)			4 (1.8%)
Detachment of placenta			3 (4%)			3 (1.4%)
Polyhidramniosis			3 (4%)			3 (1.4%)
APGAR-1	5±3	7±2	7±2	8±1	0,001	
APGAR-5	7±3	8±2	8±2	9±1	< 0,001	
Koryoamniosis			1 (1.4%)			

* Of 5 maternal deaths, one did not give birth Data are n (%) or mean±SD.

waves of pandemic. We were able to conclude that severity of the disease was strongly associated with the gestational age and different waves of the disease. As one of the biggest healthcare units in Istanbul, a city with the highest population in Turkey, our results might also reflect the general population in this country.

Limitations of this study include the fact that we only had information of inpatient settings, which prevents to draw a conclusion about the prevalence of the disease among pregnants in Turkish society. Moreover, due to descriptive nature of data, analyses were not adjusted for multiple comparisons.

CONCLUSION

These results suggest that the severity of COVID-19 infection is related to the gestational age, maternal age and BMI levels of the individuals. Given the universality and severity of the COVID-19 crisis, an important focus should be placed on planning for additional measures to reduce the number of severe cases and deaths in the more vulnerable populations. Collection of tremendous amounts of information still did not seem to prevent the destructive effect of the disease during the last wave, in Turkey. Consequently, it is of vital importance to keep collecting information to develop a road map for immediate global actions against possible new infection threats.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission Kartal Dr. Lütfi Kirdar City Hospital Clinical Researches Ethics Committee (Date: 30.03.2022, Decision No: 2022/514/222/43) .

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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