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The effect of COVID-19 disease diagnosed in the first trimester of pregnancy on obstetric outcomes

Gebeliğin ilk üç ayında teşhis edilen COVID-19 hastalığının obstetrik sonuçlara etkisi

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ÖZ

Amaç: Bu makalenin amacı, ilk trimesterde koronavirüs 2019 hastalığı tanısı alan gebeliklerin maternal, fetal ve obstetrik sonuçlarını analiz etmektir.

Gereç ve Yöntemler: Gebeliğin ilk üç ayında COVID-19 tanısı konan ve hastaneye yatırılan hastaların prospektif analizi yapıldı. Gebeliğin sonraki haftalarında obstetrik komplikasyonlar, doğum ve neonatal sonuçlar rapor edildi.

Bulgular: Yetmiş beş hastayı çalışmaya dahil ettik. Kovid-19 pozitif olan gebelerin ortalama yaşı 28.2 yıl, ortalama gebelik haftası 9.9 hafta idi. Ortalama doğum [illegible]tası 31,65±9,47 idi. Hastaların 27'si erken doğum yaptı. Hiçbir bebekte tü[illegible] arasında neonatal Sars Cov-2 pozitifliği yoktu. Şiddetli Covid-19 ha[illegible] hastanın 15'i erken doğumla sonuçlandı.

Sonuç: İlk trimesterinde ağır Covid-19 olan hamile kadınl[illegible] uterin fetal ölüm ve perinatal komplikasyon açısından d[illegible]

Anahtar Kelimeler: covid-19, sars cov-2 ve [illegible]onavirus-2019, erken doğum

ABSTRACT

Aim: The purp[illegible]e the maternal, fetal, and obstetric outcomes of pre[illegible]oronavirus 2019 disease in the first trimester.

Mate[illegible] [illegible]pective analysis of patients diagnosed with corona[illegible]imester of pregnancy and hospitalized was performed. [illegible], delivery, and neonatal outcomes were reported in the follow[illegible]egnancy.

[illegible] included seventy-five patients in the study. The mean age of pregnant women, coronavirus 2019 positive, was 28.2 years, and the mean gestational week was 9.9 weeks. The mean delivery week was 31.65±9.47. Twenty-seven of the patients had preterm delivery. There was no neonatal coronavirus 2019 positivity among all the cases in any babies. Fifteen of twenty-nine patients with severe Covid-19 resulted in preterm delivery.

Conclusion: Pregnant women with severe coronavirus 2019in their first trimester are at higher risk of premature birth, intrauterine fetal death, and perinatal complications.

Keywords: COVID-19, Sars Cov-2 and pregnancy, Coronavirus 2019 in the first trimester, Premature birth

INTRODUCTI[illegible]

The etiolo[illegible]navirus disease (COVID-19) was first re[illegible], Hubei Province, China, in December 20[illegible] infection has spread rapidly around the wo[illegible]ealth organization (WHO) declared this infection a[illegible]w type of Coronavirus Pandemic in March 2020, and the virus that causes COVID-19 was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (1).

Coronavirus (CoVs) are enveloped crown-like appearance under the electron microscope, positive-strand RNA viruses (2). To date, seven types of coronaviruses have been identified that can infect humans. Four of them cause a mild clinical presentation with cold symptoms. The other three types cause severe and sometimes fatal respiratory infections and epidemics in humans. COVID-19 is the same group as viruses that cause severe acute respiratory syndrome (SARS) and Middle East Respiratory Syndrome (MERS) (2,3). SARS-CoV-2 is 79% genetically similar to SARS-CoV and 50% to MERS-CoV (4). SARS was detected in February 2003, leading to 8000 cases and 770 deaths (5). MERS emerged in 2013, causing 860 deaths in 2500 infected cases (6). According to current data, mortality rates have been reported as 35-50% in MERS-CoV, 11% in SARS-CoV, and 3.4% in COVID-19 (7).

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COVID-19 infection is transmitted by close contact and respiratory droplets (8). Although the disease's incubation period is 3-7 days, it can spread up to 14 days. High fever, cough, and shortness of breath are the most common symptoms of the disease. In addition, myalgia, diarrhea, smell, and taste disorders are also quite joint (9). Approximately 80% of infections in COVID-19 are mild or asymptomatic; 15% are severe, requiring supplemental oxygen; and 5% are critical and require mechanical ventilation (10). Diagnosis of the disease is made by detecting viral RNA from swabs taken from the upper or lower respiratory tract (nasopharynx, oropharynx, bronchoalveolar lavage, tracheal aspiration) by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) method (11). Lymphopenia, leukopenia, thrombocytopenia, and abnormal liver function tests are expected laboratory results. Bilateral infiltration findings can be determined in COVID-19 pneumonia on x-ray imaging (12).

Due to pregnancy, physiological and immunological changes may cause systemic effects that increase the risk of complications from respiratory tract infections (e.g., diaphragm elevati increased oxygen consumption, and edema of the resp tract mucosa) (13). However, there is still limited d clinical consequences of COVID-19 in pregnar effects of SARS-CoV-2 infection on obstetri pathophysiology are not yet clear. Som gher effects due to easier transition. In a nd post-variant periods were compared the disease and obstetric outcomes in r the post-variant COVID-19 period show uble prognosis (14).

The course of the d) and obstetric outcomes may differ betw iesters. Even in pregnant women who d alth problems, a worse course of the dis (15). Previous studies have reported hig pregnancy outcomes such as preterm labo pture of membranes (PROM), and cesarean deliver egnant women with COVID-19 infection, especially in the last trimester (16,17). Therefore, pregnant women and their newborns should be considered potential risk groups in the current COVID-19 pandemic. Currently, we have limited information about the course of COVID-19 during the first trimester of pregnancy and obstetric outcomes.

This article analyzes the maternal, fetal, and obstetric outcomes of pregnancies diagnosed with COVID-19 in the first trimester.

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MATERIALS AND METHODS

Patients diagnosed with COVID-19 by Real-time PCR during the first trimester of pregnancy in a tertiary center between March 2020 and December 2020 and received treatment with hospitalization were prospectively evaluated. Maternal age, gestational week, laboratory tests, clinical symptom ulmonary CT results, and severity of infection of patie sis were recorded. Obstetric complications and al outcomes were recorded in the follow ancy. The results of 75 patients who con icy follow-ups in the exact center were e ethics committee approved this study w -KAEK-25 2020/11-03, and informed con or the study. Eligibility criteria include sed COVID-19, first trimester (0-14w) n ntation. Pregnant women whose pregn elivery data could not be reached were e udy.

n and clinical classification of the Covid-19 diguidelines of the World Health Organization and the of Health of the Republic of Turkey were taken as a rce (18,19).

Statistical analyses were performed using SPSS version 23 (IBM Corp, Armonk, NY, USA). Mean, or median values were used for descriptive variables according to data. Numbers and percentages were used for categorical data. The patients were grouped according to the severity of their diseases. Shapiro Wilk test was used to determine the distribution, and Mann Whitney U or chi-square tests were applied to determine the differences between the groups. P-value <0.05 was considered significant.

RESULTS

We included seventy-five patients who met our inclusion criteria at the time of the study. Demographic and clinical characteristics of women who were found to be positive for Covid-19 during the first trimester are given in Table 1.

Table-1. Demographic and clinical characteristics of patients

VALUES	VARIABLES
Maternal Age (years) (min-max)*	28,22±6,46 (17-40)
BMI (kg/m2)*	26,27±3,78
Gravida, median (min-max)	2(0-8)
Parity, median (min-max)	1(0-7)
Gestational week at diagnosis (weeks) (min-max)	9,97±2,86 (4-14)
Length of hospitalization (days)*	Length of hospitalization (days)*
COVID-19 severity	
Mild	42 (56)
Moderate	21 (28)
Severe	12 (16)
Computed tomography (pulmonary)	
Normal	21 (28)
Pneumonia	8 (
Ground glass opacities	
COVID treatment	
Antibiotics + LMWH	((62,7)
Antiviral + Antibiotics + LM	20(26,7)
Antiviral + Antibiotic roid	7(9,3)
Antiviral + Ar H +steroid +plas-mapheresis	1(1,3)

Values are c ecified. */values are given as mean ±SD

T iese pregnant women was 28.2 years, and the mean gestational week was 9.9 weeks. They stayed in the hosp verage of 7 days, and twelve of them had severe illnesses. While giving only antibiotics and low molecular weight heparin t orty-seven patients (62.7%) upon the recommendation of the infectious diseases specialist; We also applied antiviral therapy to 20 (26.7%) patients. We performed plasmapheresis in only one patient, and seven of the patients (9.3%) needed steroids.

We performed computed tomography on forty-six patients. Twenty-one of them had normal imaging findings, while seventeen patients (22.7%) had ground-glass opacity (Table-1).

Table-2 shows the laboratory parameters we evaluated during the first hospitalization. Mean hemoglobin values of pregnant women were 12.1 (g/dl), neutrophil values were 5.90 (103/ml), and lymphocyte values were 1.38 (103/ml). We looked at a standardized infection panel for Covid-19 patients. Accordingly, the mean C-reactive protein values were 18.6 mg/dl, ferritin 147.8 ng/ml, fibrinogen 477.4 mg/dl, and D-dimer (µg/mL) 0.76 in the first trimester covid-19 positive pregnant women. While aminotrans-

ferase and creatinine values of these pregnant women were within normal limits, mean troponin-T values were 3.48±1.85 (Table-2).

Table-2. Laboratory characteristics of patients

VALUES	VARIABLES
Blood type	
A+	24 (32)
A-	3 (4)
B+	9 (12)
B-	2 (2,7)
AB+	4(5,3)
AB-	4(5,3)
0 +	27 (36)
0 -	2 (2,7)
Laboratory parameters*	
Hemoglobin (g/dL)	12,14
WBC (mcL)	8
Lymphocyte (10^3/mL)	
Neutrophil (10^3/mL)	,2
Platelets (mcL)	,88±58,51
C-reactive protein (mg/L)	18,67±28,11
Ferritin	147,84±98,00
Fibrinogen (mg/dL	477,48±122,99
Prothrombin T	12,17±1,20
aPTT (s	25,58±2,74
D-d	0,76±0,94
g/mL)	3,48±1,85
nase (ng/mL)	67,36±60,91
H (mg/dL)	104,92±46,33
AST(IU/L)	23,64±23,38
ALT(IU/L)	21,87±19,79
LDH (IU/L)	234,54±84,07
BUN (mg/dL)	7,48±2,57
Creatinine (mg/dL)	0,48±0,10

Values are given as n (%) unless specified. */values are given as mean ±SD

In the third table, we see the final obstetric results of the pregnant women. The mean week of delivery was 31.65±9.47. Twenty-one patients had a vaginal delivery, while 41 (54.7%) had a cesarean section. Twelve (29.2%) of the pregnant women who had cesarean section had a cesarean section before, and 16 of them (39%) were taken to cesarean section due to fetal distress indications. Only 1 case resulted in an emergency cesarean section due to decompensation of the mother's vital signs. The progressing 27 (36%) of the pregnant mothers hospitalized with the first trimester Covid-19 positivity resulted in preterm delivery. While the first trimester missed abortion developed in 12 (16%) cases, intrauterine ex fetus occurred in only two instances in older weeks. We did not find any neonatal Sars Cov-2 positivity among all the cases in any babies. Seventeen of the babies remained in the neonatal intensive care unit for various other reasons. Only one maternal death occurred in the seventy-five patients we [illegible] (Table-3).

Table-3. Obstetric and neonatal outcomes of patients.

FINDINGS	VARIABLES
Gestational age at end of the pregnancy (weeks)*	31,65±9,47
End of pregnancy	
Vaginal delivery	21(28)
C-section	41(54,7)
Abortus	12 (16)
Termination-intrauterine exitus	2 (2,7)
Cesarean indications	
Previous cesarean delivery	[illegible]
Fetal distress	
Cephalopelvic disproportion	
Placenta previa	[illegible],4)
Malpresentation	5(12,1)
Maternal health conditions	1(2,4)
Pregnancy complicatio[illegible]	
Missed abortus	12 (16)
Intrauterin[illegible]	2 (2,7)
Prete[illegible]	27 (36)
[illegible] membranes	6 (8)
[illegible] ption	3 (4)
Birth w[illegible] (g)*	2882, 06±798,35
APGAR score**	
1st Minute	8(0-9)
5th minute	10 (0-10)
Neonatal Sars COV-2 positivity	0 (0)
Admission to NICU	17 (22,6)
Maternal mortality	1 (1,3)
Length of hospitalization (days)*	7,21±4,24

Values are given as n (%) unless specified. */values are given as mean ±SD **values are given as median (min-max)

We divided the disease into three groups according to its pneumonia and clinical findings as mild, moderate, and severe. Accordingly, we compared the mild and moderate/severe groups according to pregnancy outcomes. The mean age of mothers in the mild disease group was 27.9; the moderate/severe disease group's mean age was 26.7. While the mean birth week of the mild course Covid-19 group was 36.9, the moderate/severe group gave birth at 31.8 weeks. In the moderate/severe disease group, none of the pregnant women delivered vaginally, and we performed cesarean section in 19 of 29 cases in this group. Other cases resulted in abortion. While 22 of 46 pregnant women with the mild disease had a cesarean section, 20 had a vaginal delivery. In addition, 15 of 29 cases with severe course resulted in preterm delivery, but this number was only 12 (27.9%) in the group with the mild course (Table-4-5).

Table-4. Evaluation of pregnancy outcomes according to COVID infection severity

	Mild disease	**Moderate/severe disease**	
Maternal age*	27,93±6,48	26,70±5,47	
Gestational age at end of the pregnancy (weeks)*	36,95±2,97	31,80±4,86	,001*
Birth weight (g)*	3142,32±641,54	2322,50±828,9[illegible]	<0,001*
End of pregnancy			<0,001
Vaginal delivery	20 (43,5)	0(0)	
C-section	22 (47,8)		
Abortus	3 (6,5)		
Termination-intrauterine exitus	1 (2,2)	(3,4)	
Pregnancy complications			<0,001
Absent		4(13,8)	
Present	,8)	25 (86,2)	
Preterm delivery	(27,9)	15 (78,9)	<0,001

Values are given as [illegible] and the chi-square test was used.

*Values are gi[illegible] Mann Whitney U test was used.

Table-5: Binary Logistic Regression Analysis in terms of the prediction of labor outcomes of pregnant women who had covid-19 in the 1st trimester

Risk Factors	Wald	O.R.	%95 C.I.	p
Gestational age at end of the pregnancy (weeks)	10.894	0.684	0.546-0.857	<0.001
End of pregnancy	6.910	0.605	0.415-0.880	0.018

OR: odds ratio; CI: confidence interval; Wald: test statistic value. Since the dependent variable consists of 2 groups ...sion was used. Backward LR method used in the analysis. Hosmer and Lemeshow test p values: 0.914, and the models had good

DISCUSSION

This study described the obstetric outcomes, labor outcomes, and pregnancy complications in the following weeks of hospitalized pregnant women due to SARS CoV-2 positivity in the first trimester of pregnancy. We also attempted to correlate severity of the disease with these outcomes. Our results

- Except for primary cesarean indications very can occur unless there is maternal or fe
- Covid-19 may trigger the probability ...th. Mothers with severe disease give birth ...national weeks, and the possibility of pr ...er in these groups.
- No evidence of ...ion of SARS-COV-2 was found on postn ...erology.
- The r ...rs with severe disease may increase th ...ountering abortion, cesarean delivery, ...

In ... with 55 pregnant women who were diagnos... -19 before the 26th gestational week, it was reporte... there were no adverse fetal, obstetric, or neonatal outcomes attributable to this disease in early pregnancy. There was no evidence of vertical transmission of SARS CoV-2 infection or causing neonatal infection in this study (20). On the contrary, in a study conducted with a more significant number of pregnant women, a preterm birth rate of around 26% was reported after Covid-19 infection, as in our results. This study was carried out with 388 pregnant women and included third-trimester pregnant women. Differently, we evaluated the pregnant women diagnosed in the first trimester. Again in this study, while ... natal intensive care hospitalization rate ... .5%, SARS-CoV-2 was found positive ... RT-PCR (21). In their study, Cosma S. ... at Covid-19 is not an independent predictor ... ncy loss (22).

... nowledge about the result of maternal SARS CoV-2 ...on at early gestation on fetal and pregnancy outcomes is ...ited. Pregnancy resulted in missed abortion in 16% of our study population. Of these, 75% (9/12) consisted of women with severe disease. Freiesleben N la C. et al. published an article that studied the first trimester SARS-CoV-2 positive pregnant women. In this cohort study, there was no significant increased risk of pregnancy loss in women with positive antibodies. None of the women had been hospitalized for SARS-CoV-2 infection (23).

Although studies show that vertical transmission is low, its relationship with poor obstetric outcomes such as miscarriage, premature birth, intrauterine fetal death, and abruptio placentae has not been demonstrated yet. Zeng L. et al. analyzed the birth results of 33 positive pregnant women and showed Covid-19 positivity in 3 newborns. None of these three infants died, and they attributed the symptoms to prematurity and asphyxia rather than covid (24). Issues such as vaccination and pre-/post-exposure prophylaxis in disease prevention are still discussed and written. Sahin D. et al. stated that the preliminary results for the administration of SARS-CoV-2 vaccines in the pregnant population are promising (25).

In a multicenter study with Covid-19 positive pregnant women, the overall perinatal mortality rate was 4.2% (n=11/265). A secondary analysis of this study revealed that the incidence

of combined adverse fetal outcomes was significantly higher when infection occurred in the first trimester. All neonatal deaths were considered adverse events related to prematurity. Only one of 250 live-born newborns was positive in postnatal RT-PCR pharyngeal swabs. This study revealed that the main determinants of adverse perinatal outcomes in fetuses with maternal COVID-19 infection are early gestational age at infection, maternal ventilatory supports, and low birth weight (26).

With the findings in our study, we think that first-trimester maternal covid positivity may increase the rate and probability of preterm birth. In addition, supporting the above research, we consider that the possibility of premature birth, low birth weight, labor complications, and intrauterine fetal death may increase in mothers with severe disease. The most significant limitation of our study is that we researched only hospitalized patients, and we followed similar populations. Results need to be replicated in more extensive cohort studies as the pandemic impacts early pregnancies worldwide.

This study is essential in eliminating some uncertainties in the future outcomes of pregnant women diagnosed with covi in the literature. It provides crucial information for ongo prospective pregnancies during this pandemic. ger-scale studies will support the preliminary d

CONCLUSION

In conclusion, pregnant women -19 in their first trimester are at higher r th, intrauterine fetal death, and perinata erefore, it is essential to screen pregn erform severe infection control measure cted mothers, and closely monitor the OVID-19.

Disclo

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Bu makale sorumlu yazarın isteği üzerine geri çekilmiştir.