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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

The Multi-Dimensional Effect of COVID-19 Infection on Pregnancy Process and Mode of Delivery Investigation

COVID-19 Enfeksiyonunun Gebelik Süreci ve Doğum Şekline Etkisinin Çok Yönlü İncelenmesi

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ABSTRACT

Aim: The aim of this study was to investigate the obstetric and neonatal outcomes of pregnant women with COVID-19 infection.

Material and Method: In this study, pregnant women with COVID-19 infection who applied to Lokman Hekim University Ankara Hospital between 01 July, 2021, and 31 December, 2021, in what week and how the pregnancy period ended, whether they received treatment for COVID-19 infection, which drugs they used, age, gravida, parity, hemogram, intrauterin-ex, abortion, premature birth, premature rupture of membranes, fetal weight, cesarean indications for those who had a cesarean section, and whether the babies stayed in the neonatal intensive care unit were examined.

Results: 82 pregnant patients with COVID-19 infection were included in the study. While the average age of the patients was 29.62±4.96 years, the gestational age at which they had COVID-19 was 21.41±9.54, hemoglobin (HGB) 10.62±1.49, hematocrit (HCT) 30.78±6.88, platelet (PLT) 195.32±76.90, birth week 35±8.70, and birth weight 3295.70±517.41. While the gravida of 65.9% is in the 1-2 group, 34.1% is in the 3-5 group. 52.4% have parity. The parity average of those who have parity is 1.47±0.59. 23.2% had abortion. The average abortion rate for those who had an abortion was 1.26±0.56. All of them do not have intaruterin-ex. The delivery method for 32.9% is vaginal birth, while 31.7% is cesarean section. 72% do not have early membrane rupture (EMR).

Conclusion: In this study, there was no maternal death due to COVID-19 infection, but the need for neonatal intensive care was observed to increase. In conclusion; considering all the data we obtained from the study, we think that COVID-19 infection during pregnancy adverse obstetric and neonatal outcomes.

Keywords: COVID-19, obstetric, pregnancy, neonatal

ÖZ

Amaç: Bu çalışmada, COVID-19 enfeksiyonu olan gebe kadınların obstetrik sonuçlarını ve neonatal sonuçlarını araştırmayı amaçladık.

Gereç ve Yöntem: Bu çalışmada 01 Temmuz 2021-31 Aralık 2021 tarihleri arasında Lokman Hekim Üniversitesi Ankara Hastanesi'ne başvuran COVID-19 enfeksiyonu geçiren gebelerin; gebelik sürecinin kaçıncı haftada ve nasıl sonuçlandığı, COVID-19 enfeksiyonu için tedavi alıp almadıkları, tedavi alanların hangi ilaçları kullandıkları, yaş, gravide, parite, hemogram, intaruterin-ex, abortus, erken doğum, erken membran rüptürü (EMR), fetal ağırlık, sezaryen olanların sezaryen endikasyonları, bebeklerin yeni doğan yoğun bakım ünitesinde kalıp kalmadıkları incelendi.

Bulgular: Çalışmaya 82 COVID-19 enfeksiyonu geçiren gebe hasta dahil edildi. Hastaların yaş ortalaması 29,62±4,96 yıl iken COVID-19 geçirdiği gebelik haftası 21,41±9,54, hemoglobin (HGB) 10,62±1,49, hematokrit (HCT) 30,78±6,88, trombosit (PLT) 195,32±76,90, doğum haftası 35±8,70 ve doğum kilosu 3295,70±517,41'dir. %65,9'unun gravidası 1-2 grubunda iken %34,1'inin 3-5 grubundadır. %52,4'ünde parite vardır. Parite olanların parite ortalaması 1,47±0,59'dur. %23,2'sinde abortus vardır. Abortus olanların abortus ortalaması 1,26±0,56'dır. Hiçbirinde intaruterin-ex yoktur. %32,9'unun doğum şekli vajinal doğum iken %31,7'sinin sezaryendir. %72'sinde EMR yoktur.

Sonuç: Bu çalışmada COVID-19 enfeksiyonuna bağlı anne ölümü yaşanmadı ancak yeni doğan yoğun bakım ihtiyacının arttığı görüldü. Sonuç olarak; bu çalışmadan elde ettiğimiz tüm veriler göz önüne alındığında gebelik sırasındaki COVID-19 enfeksiyonunun obstetrik ve neonatal sonuçları etkilediğini düşünmekteyiz.

Anahtar Kelimeler: COVID-19, doğum, gebelik, yeni doğan

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INTRODUCTION

The Coronavirüs disease 2019 (COVID-19) is causing the severe acute respiratory syndrome coronavirüs pandemic and caused morbiditiy and mortality among countries all over the world. On December 31, 2019, by WHO China Country Office; after reporting that there are many unknown cases of pneumonia in Wuhan city of Hubei province of China, WHO first announced that the cause of these complaints is a new type of coronavirus (2019-nCoV). The WHO Director-General declared this outbreak as the "COVID-19 Pandemic" on March 11, 2020, and "in the past two weeks, the number of cases outside China has increased by thirteen times, and the number of affected countries has tripled (1,2).

Initial evidence demostrated that having COVID-19 during pregnancy causes increased likelihood of adverse maternal, obstetric and neonatal outcomes (3). Hypersensitivity reaction, increased coagulation and hypoxia are observed of severe COVID-19 infection and might be the reasons for the serious side effects during pregnancy and newborn babies (4,5). Moreover, Hariyanto et al. (2020) undertook a meta-analysis which reported that maternal anemi were significantly associated with severe illness COVID-19 infection (6).

Recent study reported that pregnant women with COVID-19 causes increased risk of abortion, preterm birth, intrauterine growth retardation (IUGR), need for endotrachealin tubation, need for intensive care unit (ICU), still birth, coagulation (DIC) (7,8).

In the present study, we aimed to investigate the obstetric outcomes and neonatal outcomes of pregnant women with COVID-19 infection.

MATERIAL AND METHOD

This study is a retrospective cohort study conducted with patients who had pregnant women-COVID-19 symptoms. All patients who applied to Lokman Hekim University, Ankara Hospital with suspected COVID-19 disease between July 01, 2021, and December 31, 2021, and were infected with laboratory-confirmed SARS-CoV-2 were included in the study. How did laboratory–corfirmed SARS-CoV-2 case idenditfy should be explained for example SARS-CoV-2 real-time reverse-transcription-polymerase chain reaction (rRT-PCR) test positive cases identified as laboratory-confirmed cases. This study was approved by the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee (No: 2021/079). The data of 82 patients confirmed with pregnant women-COVID-19 were studied. The COVID-19 patients participating in the study did not have any additional diseases defined. Demographic, clinical characteristics, and laboratory findings of the patients were obtained from hospital information system records. All data were checked by physicians who are experts in gynecologist, internal medicine, infectious diseases, and clinical microbiology. Those who were diagnosed with COVID-19 in the first 12 weeks of pregnancy were included in the first trimester, those who were diagnosed with COVID-19 in the 12-24 weeks of pregnancy were included in the second trimester, and those who were diagnosed with COVID-19 in the 24-40 weeks of pregnancy were included in the group of those who had the disease in the third trimester. All patients participating in this study were laboratory-confirmed COVID-19 patients, and the diagnostic criteria for COVID-19 were based on the positive rRT-PCR tests results. Fetal growth restriction, multifetal pregnancy, gestational diabetes mellitus, epilepsy, and systemic disease were accepted as exclusion criteria.

It is also stated whether pregnant women received medication for COVID-19 and whether they were treated as inpatients. Age, gravity, parity, hemogram, liver and kidney function tests, and fasting blood sugar levels were recorded. Pregnant women were followed until birth. Data of patients who continued their pregnancy follow-up in a different health institution were accessed by phone. Those whose pregnancies ended in abortion, those who presented with premature rupture of membranes, and those who had intrauterine exitus were recorded. Birth types, birth weeks, birth weight of newborns, gender, and whether they need incubators were included in the analysis.

Statistical Analysis

All statistical analyses were performed by using the statistical package SPSS for Windows, version 26.0 (SPSS, Chicago, Illinois, USA). While evaluating the study data, frequencies (number, percentage) for categorical variables and descriptive statistics (mean, standard deviation (SD)) are given for numerical variables.

The normality assumptions of the numerical variables were examined with the Kolmogorov Smirnov test of normality and it was seen that the variables were normally distributed. For this reason, parametric statistical methods were used in the study.

Differences between two independent groups were examined with the Independent Sample t-Test. The relationships between the two independent numerical variables were checked with the Pearson correlation coefficient and the relationships between the two independent categorical variables were checked with Chi-square analysis. Statistical significance was interpreted at the 0.05 level in analyzes.

RESULTS

A total of 82 patients participated in this study. While the mean age and standard deviation of the participants in the study was 29.62±4.96, the gestational week at which they had COVID-19 was 21.41±9.54, hemoglobin (HGB) 10.62±1.49, hematocrit (HCT) 30.78±6.88, platelet (PLT) 195.32±76.90, birth week is 35±8.70, and birth weight is 3295.70±517.41. While 65.9% of them have gravida in the 1-2 group, 34.1% have it in the 3-5 group. The abortus mean and standard deviation of those with parity is 1.47±0.59. 23.2% had abortion. The mean and standard deviation of those who had an abortion were 1.26±0.56. All of them do not have intaruterin-ex. The delivery method for 32.9% is vaginal birth, while 31.7% is cesarean section. 72% do not have early membrane rupture (EMR). 62.2% do not need an incubator (**Table 1**).

As a result of the correlation analysis applied, there is a statistically significant, moderately positive relationship between the week of pregnancy during which COVID-19 was experienced and the week of birth (r=0.499). There is a statistically significant, moderately positive relationship between birth week and birth weight (r=0.560) (**Table 2**).

As a result of the Independent Sample t Test, there is a statistically significant difference in age between people with gravida 1-2 and gravida 3-5 (p<0.05). Accordingly, the age level of people with gravida 3-5 is significantly higher than people with gravida 1-2 (p<0.05). As a result of the applied Chi-square analysis, there is a statistically significant relationship between gravida and parity, abortion, type of birth and EMR (p<0.05). The rate of people with gravida 1-2 having vaginal delivery is significantly higher than those with vaginal birth in gravida 3-5 (p<0.05) (**Table 3**).

As a result of the Independent Sample t Test applied, there is a statistically significant difference in age between people with and without parity (p<0.05). Accordingly, the age level of people with parity is significantly higher than people without parity (p<0.05) (**Table 4**).

Table 1. Descriptive statistics

	Mean	SD
Age (years)	29.62	4.96
COVID-19 pregnancy week	21.41	9.54
HGB	10.62	1.49
HCT	30.78	6.88
PLT	195.32	76.90
Birth week	35.00	8.70
Birth weight	3295.70	517.41
	n	**%**
Gravidity (mean±SD (2.06±1.08))		
1-2	54	65.9
3-5	28	34.1
Parity		
Existent (mean±SD (1.47±0.59))	43	52.4
Absent	39	47.6
Abortus		
Existent (mean±SD (1.26±0.56))	19	23.2
Absent	63	76.8
İntaruterin-ex		
Existent	0	00
Absent	82	100
Type of birth		
Abortus	13	15.9
Vaginal birth	27	32.9
Cesarean section	26	31.7
Past surgery	15	18.3
Still birth	1	1.2
EMR		
Existent	23	28.0
Absent	59	72.0
Gender		
Girl	33	47.1
Man	37	52.9
Incubator need		
Existent	31	37.8
Absent	51	62.2

HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet, EMR: Early membrane rupture

Table 2. Examining the relationships between variables

		Age	COVID-19 passed through pregnancy week	HGB	HCT	PLT	Birth week	Birth weight
Age (years)	r	1.000	0.063	-0.018	-0.11	-0.11	0.075	-0.122
	p		0.572	0.871	0.324	0.324	0.509	0.314
Pregnancy week with COVID-19	r		1.000	0.053	0.103	0.174	.499**	0.044
	p			0.635	0.358	0.119	0.000	0.719
HGB	r			1.000	.739**	-0.1	0.052	-0.065
	p				0.000	0.37	0.649	0.593
HCT	r				1.000	-0.1	0.033	-0.035
	p					0.372	0.773	0.775
PLT	r					1.000	0.177	0.069
	p						0.116	0.572
Birth week	r						1.000	.560**
	p							0.000
Birth weight	r							1.000
	P							

r: Correlation coefficient *p<0.05, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet

Table 3. Examination of differences and relationships according to gravida

	Gravidity				t
	1-2		3-5		
	Mean	SS	Mean	SS	
Age (years)	28.57	4.83	31.64	4.64	-2.763
Pregnancy week with COVID-19	21.74	9.48	20.79	9.78	0.428
HGB	10.64	1.57	10.57	1.33	0.194
HCT	31.65	5.95	29.11	8.25	1.602
PLT	191.26	81.62	203.14	67.59	-0.661
Birth week	35.15	8.63	34.69	9.00	0.218
Birth weighy	3272.60	547.89	3346.09	451.56	-0.549
	n	%	n	%	Chi-square
Parity					27.850
(+)	17	31.5	26	92.9	
(-)	37	68.5	2	7.1	
Abortus					22.074
(+)	4	7.4	15	53.6	
(-)	50	92.6	13	46.4	
Type of birth					14.211
Abortus	6	11.1	7	25.0	
Vaginal delivery	23	42.6	4	14.3	
Cessarian	19	35.2	7	25.0	
Previous surgery	6	11.1	9	32.1	
Still birth	0	0.0	1	3.6	
EMR					3.991
(+)	35	64.8	24	85.7	
(-)	19	35.2	4	14.3	
Gender					0.706
Female	21	43.8	12	54.5	
Male	27	56.3	10	45.5	
Need of neonatal intensive care					0.040
(-)	34	63.0	17	60.7	
(+)	20	37.0	11	39.3	

t: Independet Sample t Test *p<0.05, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet, EMR: Early membrane rupture

Table 4. Examination of differences and relationships according to parity

	Parity				t
	(+)		(-)		
	Mean	SS	Mean	SS	
Age (years)	31.00	4.51	28.10	5.04	2.746
Pregnancy week with COVID-19	19.98	9.51	23.00	9.43	-1.443
HGB	10.53	1.47	10.71	1.51	-0.516
HCT	29.95	7.44	31.69	6.17	-1.146
PLT	187.60	72.58	203.82	81.49	-0.953
Birth week	34.41	9.43	35.62	7.93	-0.615
Birth weight	3239.40	434.87	3352.00	589.63	-0.909
	n	%	n	%	Chi-square
Abortus					2.533
(+)	13	30.2	6	15.4	
(-)	30	69.8	33	84.6	
Type of birth					29.742
Abortus	9	20.9	4	10.3	
Vaginal delivery	10	23.3	17	43.6	
Cessarian	8	18.6	18	46.2	
Previous surgery	15	34.9	0	0.0	
Still birth	1	2.3	0	0.0	
EMR					3.996
(-)	35	81.4	24	61.5	
(+)	8	18.6	15	38.5	
Gender					1.433
Female	19	54.3	14	40.0	
Male	16	45.7	21	60.0	
Need of neonatal intensive care					0.328
(-)	28	65.1	23	59.0	
(+)	15	34.9	16	41.0	

t: Independet Sample t Test *p<0.05, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet, EMR: Early membrane rupture

As a result of the applied Chi-square analysis, there is a statistically significant relationship between parity, mode of birth and EMR (p<0.05). Accordingly, the rate of birth by cesarean in people without parity is significantly higher than the rate of cesarean by birth in people with parity (p<0.05). The rate of people with parity who have undergone surgery is significantly higher than the rate of people with non-parity who have had surgery (p<0.05). The rate of those without EMR in those with parity is significantly higher than the rate of those without EMR in those without parity (p<0.05) (**Table 5**).

As a result of the Independent Sample t Test applied, there is a statistically significant difference in birth weight between those who need incubators and those who do not (p<0.05). Accordingly, the birth weight of those who need incubators is significantly higher than the birth weight of those who do not need incubators (p<0.05) (**Table 6**).

Table 5. Examining differences and relationships according to EMR

	EMR				t
	(-)		(+)		
	Mean	SS	Mean	SS	
Age (years)	29.73	4.70	29.35	5.69	0.311
Pregnancy week with COVID-19	20.75	9.00	23.13	10.81	-1.018
HGB	10.64	1.45	10.54	1.60	0.274
HCT	31.24	6.26	29.61	8.30	0.963
PLT	201.97	77.87	178.26	73.22	1.259
Birth week	35.51	8.18	33.74	9.95	0.822
Birth weight	3328.90	442.68	3206.58	685.85	0.878
	n	%	n	%	Chi-square
Abortus					0.037
(+)	14	23.7	5	21.7	
(-)	45	76.3	18	78.3	
Type of birth					1.879
Abortus	8	13.6	5	21.7	
Vaginal delivery	19	32.2	8	34.8	
Cessarian	19	32.2	7	30.4	
Previous surgery	12	20.3	3	13.0	
Still birth	1	1.7	0	0.0	
Gender					0.001
Female	24	47.1	9	47.4	
Male	27	52.9	10	52.6	
Need of neonatal intensive care					2.807
(-)	40	67.8	11	47.8	
(+)	19	32.2	12	52.2	

t: Independet Sample t Test *p<0.05, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet, EMR: Early membrane rupture

Table 6. Examination of differences and relationships according to incubator need

	Need of neonatal intensive care				t
	(-)		(+)		
	Mean	SS	Men	SS	
Age (years)	29.71	4.52	29.48	5.69	0.195
Pregnancy week with COVID-19	21.80	9.46	20.77	9.78	0.472
HGB	10.55	1.51	10.73	1.45	-0.520
HCT	30.33	7.22	31.52	6.32	-0.753
PLT	198.31	72.18	190.39	85.10	0.450
Birth week	35.22	9.16	34.63	8.01	0.290
Birth weight	3409.33	387.80	3114.74	642.01	2.397
	n	%	n	%	Chi-square
Abortus					0.962
(+)	10	19.6	9	29.0	
(-)	41	80.4	22	71.0	
Type of pregnancy					1.195
Abortus	8	15.7	5	16.1	
Vaginal delivery	16	31.4	11	35.5	
Cessarian	17	33.3	9	29.0	
Previous surgery	9	17.6	6	19.4	
Still birth	1	2.0	0	0.0	

t: Independet Sample t Test *p<0.05, HGB: Hemoglobin, HCT: Hematocrit, PLT: Platelet

DISCUSSION

In the present study, we found moderately positive relationship between the week of pregnancy during which COVID-19 was experienced and the week of birth (r=0.499). Furthermore, that neonatal incubator need rate of %37.8, EMR ratio %28.

Increasing evidence shows that it leads to excessive inflammatory state, maternal fever, hypoxia, which can worsen maternal health, perinatal outcomes (9). Recent study reported that pregnant women with COVID-19 infection had increase risk caserean section, preterm labor and admission to the neonatal intensive care unit (NICU) (10).

Smith et al. meta-analysis reported that COVID-19 infection during pregnancy increased risk of maternal death, admission to intensive care unite. Moreover, increase preterm labor, low birth weight and increase admitted to neonatal care unit after birth (11). Wei et al. systematic review and meta-analysis demonstrated that preeclampsia, preterm labor, and still birth significant increase risk of with COVID-19 infection during pregnancy compared with those without COVID-19 diagnosis. In addition to demonstrated that pregnant women risk factor severe COVID-19 infection was associated with preterm labor, cesarean delivery, admission to the NICU compared with mild COVID-19 infection (3).

Jering et al. reported that the rate of preterm birth in those who had COVID-19 infection during pregnancy was 7.2% (12). Similarly, Simbar et al. meta-analysis including 74 cohort and case-control studies demonstrated that COVID-19 infection during pregnancy increased risk of preterm delivery (13). In this study, we found that the average birth week of pregnant women was 35 weeks.

Current data from Turkey neonatal intensive care unit (NICU) admission rate was %9.9 (14). Our study reported that NICU admission rate was %37.8. The results of our study were found to be higher than the literature. We think that this may be due to the fact that our hospital is a tertiary center and follow-up high-risk patients. We found that increased neonatal birth weight was associated with decreased admission to NICU. However, there is no relationship with the gender factor of newborns admitted to NICU. We demonstrated that no statistically significant relationship between gestational age when COVID-19 infection and the newborns were admitted to NCIU.

Chinn et al. reported that COVID-19 infection not associated with an increased cesarean delivery however preterm labor significant associated with during COVID-19 infection pregnancy (10). However, Smith et al. reported that symptomatic COVID-19 infection were more increased cesarean delivery compared the vaginal labor (11). In our cohort, we demonstrated that the cesarean section rate was found to be statistically significantly higher in primigravida pregnant women than in multiparous pregnant women.

Furthermore, our study reported that premature rupture of membranes was statistically significantly higher in primigravida pregnant women than in multiparous pregnant women

Recent studies reported that COVID-19 infection likehold increases likelihood abortion ratio (15-17). Several authors suggest that the reason for COVID-19 abortion is that the virus causes inflammation on the placenta and can cause placental insufficiency (18,19). However, Rotshenker-Olshinka et al. reported that there was no statistical difference in the rate of spontaneous abortion between the COVID and pre-COVID periods (20). Our study finding that spontan abortus ratio %15.9.

Our study has limitations, which include the following aspects. The absence of severe infection category patients in pregnancy, lack of information about the COVID vaccine, absence of medical history regarding COVID-19 treatment.

CONCLUSION

COVID-19 infection during pregnancy affects obstetric and neonatal outcomes. We reveal the obstetric and neonatal outcomes of patients with COVID-19 during pregnancy. There was no maternal death due to COVID-19 infection, but we detected an increased need for neonatal intensive care.

ETHICAL DECLARATIONS

Ethics Committee Approval: This study was approved by the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee (No: 2021/079).

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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