ORIGINAL RESEARCH

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Impact of Mode of Birth and Type of Anesthesia on Clinical Outcomes of Pregnant Women with COVID-19 in a Referral Pandemic Hospital: An Analytical Study

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ABSTRACT Objective: During the pandemic, pregnant women were more likely to develop severe illness, necessitating critical care, and require mechanical ventilation. Birth of the pregnant women can be necessary for the rapid decline in mother's clinical situation or for obstetric indication. This study aimed to investigate the clinical outcomes of pregnant women who gave birth during coronavirus disease-2019 (COVID-19) isolation period with regard to mode of birth and type of anesthesia in cesarean delivery. **Material and Methods:** The clinical outcomes of pregnant women who were admitted to the hospital, confirmed to be infected with severe acute respiratory syndrome-coronavirus-2, and gave birth during the hospitalization for COVID-19 treatment or isolation period between March, 2020 and November, 2021were analyzed according to mode of birth and type of anesthesia, retrospectively. **Results:** Among all pregnant women, 106 (%35.45) gave birth vaginally while 193 (64.55%) underwent cesarean section. Out of all cesarean births, 55 (28.5%) and out of all vaginal births, 2 (1.9%) had indication of birth as deterioration of maternal clinical status. Intensive care unit admission rate was 23.3%, maternal mortality rate was 11.9%, and preterm birth rate (<34 week) was 18.1% (odds ratio: 2.311, 95% confidence interval: 1.155-4.625) for cesarean births. There were 131 (67.88%) cesarean births with spinal anesthesia and 62 (32.12%) cesarean births with general anesthesia. **Conclusion:** The critical factor influencing the method and timing of birth as well as the negative outcomes for pregnant COVID-19 patients was the clinical severity and change in clinical status.

Keywords: Mode of birth; type of anesthesia; coronavirus disease-19

A substantial rise in severe maternal morbidity and mortality associated with coronavirus disease-2019 (COVID-19) was observed.[1,2] Pregnant women were more likely to develop severe illness, necessitate critical care, and require mechanical ventilation.[2-7] Pregnant women who have respiratory compromise caused by COVID-19 are prone to give birth for maternal reasons.[8] The cesarean delivery rate and preterm birth were observed to increase by COVID-19.[9] The mechanisms of the COVID-19 related adverse outcomes in pregnancy have been investigated. Women may be more likely to experience a more rapid clinical decline with COVID-19 during pregnancy due to lower lung volumes brought on by increases in uterus size, which could raise the chance of unfavorable pregnancy outcomes.[10] While oxygen consumption rises by 20% during pregnancy and the woman's functional residual capacity decreases, the gravid uterus has been proven to raise the diaphragm by up to 4 cm in the third trimester, making her intolerant to hypoxia.[10] Birth of the pregnant women could be necessary for the rapid decline in mother's

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clinical situation or for obstetric indication. The prompt delivery was not proven to improve the maternal clinical status but it may be beneficial to the fetus that is affected from maternal hypoxia.[11] Individual needs and obstetric indications should be taken into consideration when choosing the birth mode.[12] Ghosh et al. reported that there was clinical deterioration in pregnant women after cesarean birth and Debrabandere et al. reported the relation between maternal decompansation and cesarean birth but, no relation with vaginal birth.[13,14] From low and middle-income countries, maternal mortalities preceeding cesarean births under general anesthesia were reported.[15] Surgery related physiological stress has resulted in maternal postpartum problems.[16] With the rise of reported cesarean births, increased premature birth rates were also reported.[14,17]

This study aimed to investigate the clinical outcomes of pregnant women who gave birth during COVID-19 isolation period with regard to birth mode and type of anesthesia in cesarean section and preterm births.

MATERIAL AND METHODS

The present study was conducted with pregnant women retrospectively in a referral center for COVID-19 between March, 2020-November, 2021. The study center is a tertiary maternity ward in which just about 4,000 deliveries take place annually and the diagnosis, the management of the pregnant women with COVID-19 were applied in accordance with the recommendations of the World Health, Organization (WHO), the Turkish Ministry of Health and the local protocol of the maternity ward. This study was approved by the Ethics Committee of Şehit Prof. Dr. İlhan Varank Training and Research Hospital (date: February 16, 2022, no: E-4059653-020) and the Ministry of Health COVID-19 Scientific Research Evaluation Commission. The study was carried out in accordance with the principles of the Helsinki Declaration.

PATIENTS

The data of the pregnant women who were admitted to the hospital, confirmed to be infected with severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) by nasopharyngeal swab reverse transcription polymerase chain reaction (PCR) test, and gave birth during the hospitalization for COVID-19 treatment or isolation period (14 days after diagnosis) were analyzed retrospectively using hospital electronic health records. Pregnant women who gave birth after the 24th week of pregnancy or with a fetal weight of more than 500 grams were included. The data of demographic characteristics, obstetric results, and clinical characteristics of mothers infected with SARS-CoV-2 were collected from electronic health records.

The effect of Delta wave was accepted after August 1, 2021 with the declarations of the Ministry of Health.[18]

HOSPITALIZATION

Hospitalization was provided for pregnant women who had COVID-19 diagnoses according to WHO clinical progression scale.[19] Pregnant women who were infected with SARS-CoV-2 and hospitalized were classified as mild, moderate, and severe disease as well as they were scored according to the WHO clinical progression scale at their first admission to the hospital and during hospital follow-up.[19,20] Hospitalization was provided for pregnant women who had COVID-19 diagnoses of moderate, severe, or critical. In accordance with the standard local protocol, the patients' lung involvement was scored 0 to 3 with lung ultrasound at the time of hospital admission.[21] Pregnant women with a lung ultrasound (LUS) score of 2 or 3, difficulties obtaining follow-up care at home, or both were hospitalized. Asymptomatic pregnant women and pregnant women with mild disease were also hospitalized owing to the beginning of labor.

BIRTH

The beginning of labor were either due to COVID-19 or obstetric indications. Pregnant women who had a clinical deterioration [increased need of oxygen, requirement of mechanical ventilation or intensive care unit (ICU) admission] have been induced for vaginal birth or underwent cesarean section.

All babies were controlled for infection with SARS-CoV-2 by nasopharyngeal swab reverse transcription PCR in 12 hours after birth and followed-up

for symptoms of COVID-19 during their hospitalized period.

The primary outcome of the study was to investigate the clinical outcomes of pregnant women who gave birth during COVID-19 isolation period with regard to birth mode. The secondary outcomes were to investigate the effect of anesthesia on clinical outcomes in patients with cesarean section and neonatal outcomes related to birth mode.

The data of this study were analyzed with IBM SPSS Statistics version 22.0 (IBM Corporation, Armonk, NY). The assumption of normality of the variables was checked using the Shapiro-Wilk test and skewness, kurtosis values. Continuous variables were expressed as mean, standard deviation, median, interquartile range according to the assumption of normality. Categorical variables were expressed as number and frequency. Chi-square test and Fisher's exact test were used to compare categorical variables. Independent samples t-test, paired samples t-test or Wilcoxon signed-rank test and Mann-Whitney U test were used to compare continuous variables according to the assumption of normality. Statistical significance was defined as 2-sided p values less than 0.05.

RESULTS

Overall 299 pregnant women gave birth in their isolation period of COVID-19.

All of pregnant women were diagnosed with real-time PCR. Out of all, 216 (72.24%) pregnant women had a history of contact with COVID-19.

There were no vaccinated pregnant women in this study cohort.

The age of pregnant women range between 18-43 years and the gestational week at the time of diagnosis range between 24-41 weeks. The singleton pregnancies were 99.3% (n=297) of all pregnancies, there were one twin pregnancy 0.3% (n=1), and one triplet 0.3% (n=1). Among all pregnant women, 106 (%35.45) gave birth vaginally while 193 (64.55%) underwent cesarean section.

TABLE 1A: Demographic and obstetric characteristics of pregnant women, according to birth mode.

	Vaginal birth (n=106)	Cesarean section (n=193)	Odds ratio (95% confidence interval)	p value
Age (year)	27.59±4.97	29.56±5.29		**0.002**
BMI (kg/m^2)	25.96±3.05	26.58±3.68		0.144
Gestational age at birth (week)	37.86±3.05	36.46±3.4		**<0.0001**
Parity	1 (2)	1 (2)		0.9
Fetal birth weight	3087.38±615.79	2833.35±766.61		**0.003**
Multiple gestation	-	1 (0.5%) twin	NA	0.575
	-	1 (0.5%) triplet		
Preterm				
<34 week	7 (6.6%)	35 (18.1%)	2.311 (1.155-4.625)	**0.006**
34-37 week	10 (9.4%)	28 (14.5%)	1.398 (0.802-2.435)	0.208
Apgar 5. minute < 7	-	10 (5.1%)	NA	**0.017**
Stillbirth	6 (5.7%)	2 (1%)	0.458 (0.298-0.705)	**0.018**
NICU admission	21 (20.6%)	65 (34%)	1.602 (1.065-2.412)	**0.016**
Indications of NICU admissions				
Prematurity	7 (6.6%)	46 (23.83%)	3.609 (1.574-8.275)	**0.002**
Transient tachypnea of the newborn	8 (9%)	15 (8.4%)	1.03 (0.423-2.508)	0.949
Hypocalcemia	-	2 (1%)	NA	
Suspected sepsis	1 (0.9%)	1 (0.5%)	NA	
Hyperbilirubinemia	1 (0.9%)	1 (0.5%)	NA	
Inability to establish feeding	3 (2.8%)	-	NA	
Congenital anomaly	1 (0.9%)	-	NA	

BMI: Body mass index; NICU: Neonatal intensive care unit.

TABLE 1B: Detailed presentation of comorbidities according to birth mode.

	Vaginal birth (n=106)	Cesarean section (n=193)
Hypothyroidism	6 (5.7%)	17 (8.8%)
Gestational diabetes	4 (3.8%)	9 (4.7%)
Asthma	4 (3.8%)	7 (3.6%)
Preeclampsia	3 (2.8%)	9 (4.7%)
Hyperthyroidism	2 (1.9%)	2 (1%)
Gestational cholestasis	1 (0.9%)	
Pregestational diabetes	1 (0.9%)	
Chronic hypertension		4 (2.1%)
Rheumatoid arthritis		3 (1.6%)
Epilepsy		1 (0.5%)

A woman can have more than one comorbidity.

Demographic and obstetric characteristics of pregnant women according to birth mode are presented in Table 1A and Table 1B. In the first 12 hours after birth, nasopharyngeal PCR and at least 24 hours follow-up of babies for symptoms revealed no evidence of vertical transmission to infants.

In relation to the mode of birth, Table 2 summarizes the clinical characteristics of the pregnant women associated to COVID-19.

The cesarean section indications were previous cesarean section 90 (46.63%), deterioration of maternal clinical status 55 (28.5%), fetal distress 33 (17.1%), oligohydramnios 7 (3.63%), and preeclampsia 6 (3.11%).

TABLE 2: COVID-19 related clinical characteristics of the pregnant women with regard to birth mode.

	Vaginal birth (n=106)	Cesarean section (n=193)	Odds ratio (95% confidence interval)	p value
Gestational age at COVID-19 diagnosis (week)	37.56±3.09	36.01±3.61		**<0.0001**
Duration of hospitalization (day)	5 (4)	5 (7)		**0.001**
Score of the clinical progression scale before birth[a]	4 (0)	4 (1)		**<0.0001**
Score of the clinical progression scale after birth[a]	1 (0)	1 (3.5)		**<0.0001**
Clinical severity of COVID-19				
Asymptomatic/mild/moderate	49 (83.1%)	53 (27.5%)	0.594 (0.377-0.936)	**0.025**
Severe	10 (9.4%)	60 (31.1%)	3.295 (1.62-6.704)	**0.001**
Delta wave	43 (40.6%)	59 (30.6%)	0.759 (0.559-1.029)	0.081
Primary symptom for hospital admission				
Asymptomatic	47 (44.3%)	57 (29.5%)	0.666 (0.423-1.048)	0.079
Cough	17 (16%)	38 (19.7%)	1.228 (0.661-2.280)	0.516
Shortness of breath	12 (11.3%)	49 (25.4%)	2.243 (1.143-4.402)	**0.019**
Malaise	11 (10.4%)	24 (12.4%)	1.198 (0.565-2.542)	0.637
Fever	4 (3.8%)	10 (5.2%)	1.373 (0.420-4.484)	0.6
Myalgia	4 (3.8%)	3 (1.6%)	0.412 (0.091-1.875)	0.251
Sore throat	3 (2.8%)	6 (3.1%)	1.098 (0.269-4.481)	0.896
Anosmia	3 (2.8%)	1 (0.5%)	0.183 (0.019-1.782)	0.144
Headache	2 (1.9%)	3 (1.6%)	0.824 (0.136-5.008)	0.833
Diarrhea-nausea	2 (1.9%)	2 (1%)	0.549 (0.076-3.955)	0.552
Nasal discharge	1 (0.9%)	-	NA	
Contact history	74 (69.81%)	142 (73.58%)	1.125 (0.810-1.563)	0.487
Comorbidity*	19 (17.92%)	52 (26.94%)	1.426 (0.938-2.168)	0.080
Chest computerized tomography finding (pneumonia)	61 (57.5%)	116 (60.1%)	1.044 (0.707-1.543)	0.827
Lung ultrasound score				
0-1	55 (51.9%)	83 (43%)	0.829 (0.547-1.255)	0.375
2	43 (40.6%)	60 (31.1%)	0.766 (0.485-1.211)	0.255
3	8 (7.5%)	50 (25.9%)	3.433 (1.569-7.511)	**0.002**
ICU admission	4 (3.8%)	45 (23.3%)	4.998 (1.931-12.935)	**<0.0001**
Supplemental oxygen need with nasal cannula during follow-up	15 (14.2%)	59 (30.6%)	1.995 (1.236-3.221)	**0.002**
Non-invasive mechanical ventilation during follow-up	6 (5.7%)	53 (27.5%)	4.097 (1.891-8.876)	**<0.0001**
Invasive mechanical ventilation during follow-up	1 (0.9%)	27 (14%)	10.849 (1.574-74.777)	**<0.0001**
Extracorporeal membrane oxygenation during follow-up	-	13 (6.7%)	NA	**0.006**
Maternal death	2 (1.9%)	23 (11.9%)	4.745 (1.245-18.082)	**0.003**

Continuous variables are given as mean±standard deviation and median (interquartile range) according to distribution characteristics, categorical variables are given as n (percentage); [a]Clinical progression scales of pregnant women after and before birth were compared for vaginal birth and cesarean section and p values were <0.0001 (-9.206), <0.0001 (z=-6.319) respectively (Wilcoxon Signed Ranks Test); *Comorbidities are presented in detail in the Supplemental Table 1; COVID-19: Coronavirus disease-2019; ICU: Intensive care unit.

TABLE 3: Obstetric and clinical characteristics of the pregnant women with or without indication of deterioration of clinical status for birth with regard to birth mode.

	Births with obstetric indications			Births due to deterioration of clinical status		
	Vaginal birth (n=104)	Cesarean section (n=138)	p value	Vaginal birth (n=2)	Cesarean section (n=55)	p value
Age (year)	27.54±5	29.34±5.34	0.008	30.5±0.71	30.17±5.19	0.914
BMI (kg/m^2)	25.97±3.07	26.39±3.75	0.341	25.47±2.25	27.09±3.53	0.406
Gestational age at COVID-19 diagnosis (week)	37.57±3.11	37.31±2.51	0.480	37±1.41	32.66±3.91	0.125
Gestational age at birth (week)	37.87±3.08	37.74±2.25	0.713	37.5±0.71	33.24±3.67	0.102
Fetal birth weight	3093.38±619.87	3088.3±548.18	0.947	2790±289.91	2198.38±864.02	0.345
Parity	1 (2)	1 (2)	0.968	1	1 (2)	0.947
Multiple gestation	-	1 (0.7%) twin	1	-	1 (1.8%) triplet	1
Preterm						
<34 week	7 (6.7%)	8 (5.8%)	0.766	-	27 (49.1%)	0.492
34-37 week	10 (9.6%)	17 (12.3%)	0.508	-	11 (20%)	1
Apgar 5. minute < 7	-	4 (3.1%)	0.079	-	6 (11.5%)	1
Stillbirth	6 (5.8%)	2 (1.4%)	0.078	-	-	
NICU admission	-	4 (3.1%)	0.136	1 (50%)	36 (65.5%)	1
Duration of hospitalization (day)	5 (4)	4 (4)	0.443	12	14 (11)	0.692
Score of the clinical progression scale before birth[a,b]	4 (0)	4 (0)	0.444	5.5	5 (1)	0.847
Score of the clinical progression scale after birth[a,b]	1 (0)	1 (0)	0.741	5.5	7 (9)	0.880
Clinical severity of COVID-19			0.898			1
Asymptomatic/mild/moderate	96 (92.31%)	126 (91.3%)		-	7 (12.7%)	
Severe	8 (7.69%)	12 (8.7%)		2 (100%)	48 (87.3%)	
Delta wave	40.4 (40.6%)	29.7 (30.6%)	0.083	1 (50%)	18 (32.7%)	1
Primary symptom for hospital admission			0.489			0.999
Asymptomatic	47 (45.2%)	57 (41.3%)		-	-	
Cough	16 (16%)	22 (15.9%)		1	16	
Shortness of breath	11 (10.6%)	17 (12.3%)		1	32	
Malaise	11 (10.6%)	22 (15.9%)		-	2	
Fever	4 (3.8%)	8 (5.8%)		-	2	
Myalgia	4 (3.8%)	2 (1.4%)		-	1	
Sore throat	3 (2.9%)	6 (4.3%)		-	-	
Anosmia	3 (2.9%)	-		-	1	
Headache	2 (1.9%)	3 (2.2%)		-	-	
Diarrhea-nausea	2 (1.9%)	1 (0.7%)		-	1	
Nasal discharge	1 (0.9%)	-		-	-	
Contact history	73 (70.2%)	99 (71.7%)	0.793	1 (50%)	43 (78.2%)	0.407
Comorbidity	19 (18.3%)	35 (25.4%)	0.190	-	17 (30.9%)	1
Chest computerized tomography finding (pneumonia)	60 (57.5%)	79 (57.2%)	0.957	1 (50%)	37 (67.3%)	0.714
Lung ultrasound score			0.570			0.122
0-1	55 (51.9%)	79 (57.3%)		-	4 (7.3%)	
2	41 (39.4%)	47 (34.1%)		2 (23.6%)	13 (100%)	
3	8 (7.7%)	12 (8.7%)		-	38 (69.1%)	
ICU admission	4 (3.8%)	45 (23.3%)	1	1 (50%)	40 (72.7%)	0.486
Supplemental oxygen need with nasal cannula during follow-up	13 (12.5%)	12 (8.7%)	0.336	2 (100%)	47 (85.5%)	1
Non-invasive mechanical ventilation during follow-up	4 (3.8%)	7 (5.1%)	0.762	2 (100%)	46 (83.6%)	1
Invasive mechanical ventilation during follow-up	-	2 (1.4%)	0.508	1 (50%)	25 (45.5%)	1
Extracorporeal membrane oxygenation during follow-up	-	1 (0.7%)	1	-	12 (21.8%)	1
Maternal death	1 (1.0%)	1 (0.7%)	1	1 (50%)	22 (40%)	1

Continuous variables are given as mean±standard deviation and median (interquartile range) according to distribution characteristics, categorical variables are given as n (percentage); [a]Clinical progression scales of pregnant women who gave birth due to obstetric indications after and before birth were compared for vaginal birth and cesarean section and p (z) values were <0.0001 (-9.543), <0.0001 (-10.649) respectively (Wilcoxon Signed Ranks Test); [b]Clinical progression scales of pregnant women who gave birth due to deterioration of clinical status after and before birth were compared for vaginal birth and cesarean section and p (z, ranks) values were 1 (0, 1 positive , 1 negative ranks), 0.010 (-2.574, 36 positive, 14 negative ranks) respectively (Wilcoxon Signed Ranks Test); NICU: Neonatal intensive care unit; ICU: Intensive care unit, BMI: Body mass index; COVID-19: Coronavirus disease-2019.

Out of all vaginal births, 91 (85.85%) were spontaneous and the remaining were induced due to 6 (5.7%) intrauterine fetal death, 3 (2.8%) oligohydramnios, 3 (2.8%) preeclampsia, 2 (1.9%) deterioration of maternal clinical status, and 1 (0.9%) postterm pregnancy.

Obstetric and clinical characteristics of the pregnant women with or without indication of deterioration of clinical status for birth with regard to mode of birth are presented in Table 3.

There were 131 (67.88%) cesarean sections with spinal anesthesia and 62 (32.12%) cesarean sections with general anesthesia. Obstetric and clinical characteristics of the pregnant women who underwent cesarean section under spinal and general anesthesia are presented in Table 4.

The graphic of the clinical progression scales of pregnant women after and before birth were compared for vaginal birth and cesarean section, and p values were <0.0001 (-9.206), <0.0001 (z=-6.319) respectively (Wilcoxon Signed Ranks Test) (Figure 1a).

The graphic of the clinical progression scales of pregnant women who gave birth due to deterioration of clinical status after and before birth were compared for vaginal birth and cesarean section, and p (z, ranks) values were 1 (0, 1 positive , 1 negative ranks), 0.010 (-2.574, 36 positive,14 negative ranks), respectively (Wilcoxon Signed Ranks Test) (Figure 1b).

The graphic of clinical progression scales after birth and before birth were compared and p (z) values were 0.056 (-1.910) and <0.0001 (-6.407) for general anesthesia and spinal anesthesia, respectively (Figure 1c).

DISCUSSION

In the study population of pregnant women with COVID-19, cesarean births were twice as common as vaginal births, and one-third of them were caused by the deterioration of clinical status of the pregnant women. For births due to deterioration of clinical status, cesarean birth was the commonly preferred mode of delivery. Overall, COVID-19 adverse outcomes were more likely to occur in pregnant women who underwent cesarean section; however, when pregnant women who experienced clinical deterioration as a result of COVID-19 were excluded, the relationship between adverse outcomes and mode of delivery remained unchanged. Invasive mechanical ventilation and maternal deaths were found to be 2 times more common in general anesthesia than in spinal anesthesia. Furthermore, when the clinical severity of COVID-19 has increased and deterioration of maternal status was indication of birth, the preterm birth and neonatal intensive care unit admission were observed to rise.

The cesarean section rate was high in the study cohort, but almost half of the pregnant women had an indication of previous cesarean section since, there is no attempt of trial of labor after cesarean in our center. The deterioration of clinical status of pregnant women with COVID-19 has lead to 28.5 percent of cesarean sections. At the outset of the pandemic, deterioration was accepted to be the increase of supplemental oxygen need and during the progress of the COVID-19 pandemic, deterioration has been defined as mechanical ventilation requirement in our center. Debrabandere et al. reported 22.6% worsening of maternal status due to COVID-19 as an indication of cesarean section and stated that contrary to women who gave birth vaginally, cesarean birth was strongly related with maternal clinical worsening.[14] Masud et al. reported a 71.4% cesarean section rate for COVID-19 pregnant women and this high rate was attributed to maternal respiratory problems and fetal distress in their study. Recently, Vimercati et al. reported that the mode of birth and timing of birth were significantly associated with the clinical severity of COVID-19 in pregnant women and in case of respiratory distress of mother and fetal hypoxia, the emergent cesarean sections were increased.[17,22] The mother's clinical state associated with COVID-19, particularly respiratory distress, guided the obstetricians' decision to have a cesarean section. According to our data, pregnancies with clinical deterioration were associated with higher rates of cesarean section, poor outcomes including ICU admission, requirement for mechanical ventilation, need for extracorporeal membrane oxygenation during patient follow-up, and maternal mortality rate. Cesarean or

TABLE 4: Obstetric and clinical characteristics of the pregnant women who underwent cesarean section under spinal and general anesthesia.

	Spinal anesthesia (n= 131)	General anesthesia (n= 62)	Odds ratio (95% Confidence interval)	p value
Age (year)	29.66±4.8	29.37±6.26		0.751
BMI (kg/m^2)	26.32±3.61	27.13±3.8		0.153
Gestational age at birth (week)	36.59±3.24	36.09±3.75		0.435
Parity	1 (2)	1 (2)		0.452
Fetal birth weight	2868.43±773.73	2748.24±749.30		0.334
Cesarean section due to obstetric indication	96 (73.28%)	42 (67.74%)	0.924 (0.577-1.482)	0.744
Cesarean section due to deterioration of clinical status	35 (26.72%)	20 (32.26%)	1.207 (0.645-2.260)	0.556
Multiple gestation	1 (0.8%) twin	1 (1.6%) triplet	NA	0.274
Preterm birth				
<34 week	22 (16.8%)	13 (21%)	1.098 (0.833-1.445)	0.482
34-37 week	17 (13%)	11 (17.7%)	1.138 (0.831-1.559)	0.380
Apgar 5. minute < 7	5 (3.8%)	5 (9.4%)	1.445 (0.772-2.704)	0.131
Stillbirth	1 (0.8%)	1 (1.6%)	1.361 (0.339-5.461)	0.586
NICU admission	31 (51.7%)	34 (26%)	1.472 (1.145-1.892)	**<0.0001**
Delta wave	43 (32.8%)	16 (25.8%)	0.901 (0.739-1.098)	0.323
Gestational age at COVID-19 diagnosis (week)	36.21±3.36	35.6±4.09		0.310
Duration of hospitalization (day)	5 (7)	6 (7)		0.343
Score of the clinical progression scale before birth[a]	4 (1)	4 (1)		0.550
Score of the clinical progression scale after birth[a]	1 (0)	1 (7)		0.170
Clinical severity of COVID-19				
Asymptomatic/mild/moderate	93 (70.09%)	40 (64.52%)	0.909 (0.563-1.466)	0.7
Severe	38 (29.01%)	22 (35.48%)	1.223 (0.668-2.242)	0.514
Primary symptom for hospital admission				
Asymptomatic	40 (30.5%)	17 (27.4%)	0.898 (0.472-1.708)	0.743
Shortness of breath	30 (22.9%)	19 (30.6%)	1.338 (0.699-2.561)	0.379
Cough	25 (21%)	13 (19.1%)	1.098 (0.527-2.292)	0.802
Malaise	18 (13.7%)	6 (9.7%)	0.704 (0.266-1.862)	0.48
Fever	7 (5.3%)	3 (4.8%)	0.906 (0.227-3.621)	0.888
Sore throat	4 (3.1%)	2 (3.2%)	1.057 (0.188-5.924)	0.95
Headache	1 (0.8%)	2 (3.2%)	4.226 (0.376-47.496)	0.243
Myalgia	3 (2.3%)	-	NA	
Diarrhea-nausea	2 (1.5%)	-	NA	
Anosmia	1 (0.8%)	-	NA	
Contact history	96 (73.3%)	46 (74.2%)	1.015 (0.817-1.262)	0.893
Comorbidity	39 (29.8)	13 (21%)	0.870 (0.714-1.060)	0.198
Chest computerized tomography finding (pneumonia)	70 (53.4%)	46 (74.2%)	1.388 (0.860-2.242)	0.180
Lung ultrasound score				
0-1	61 (46.4%)	22 (35.4%)	0.762 (0.429-1.352)	0.353
2	40 (30.5%)	20 (32.3%)	1.057 (0.571-1.956)	0.861
3	30 (22.9%)	20 (32.3%)	1.409 (0.742-2.675)	0.295
ICU admission	28 (21.4%)	17 (27.4%)	1.118 (0.870-1.438)	0.354
Supplemental oxygen need with nasal cannula during follow-up	39 (29.8%)	20 (32.3%)	1.039 (0.837-1.289)	0.726
Non-invasive mechanical ventilation during follow-up	35 (26.7%)	18 (29%)	1.038 (0.831-1.298)	0.737
Invasive mechanical ventilation during follow-up	13 (9.9%)	14 (22.6%)	1.476 (0.986-2.210)	0.018
Extracorporeal membrane oxygenation during follow-up	9 (6.9%)	4 (6.5%)	0.979 (0.672-1.426)	0.914
Maternal death	11 (8.4%)	12 (19.4%)	1.476 (0.953-2.287)	0.028

[a]Clinical progression scales after birth and before birth were compared and p (z) values were 0.056 (-1.910) and <0.0001 (-6.407) for general anesthesia and spinal anesthesia, respectively; BMI: Body mass index; NICU: Neonatal intensive care unit; ICU: Intensive unit; COVID-19: Coronavirus disease-2019.

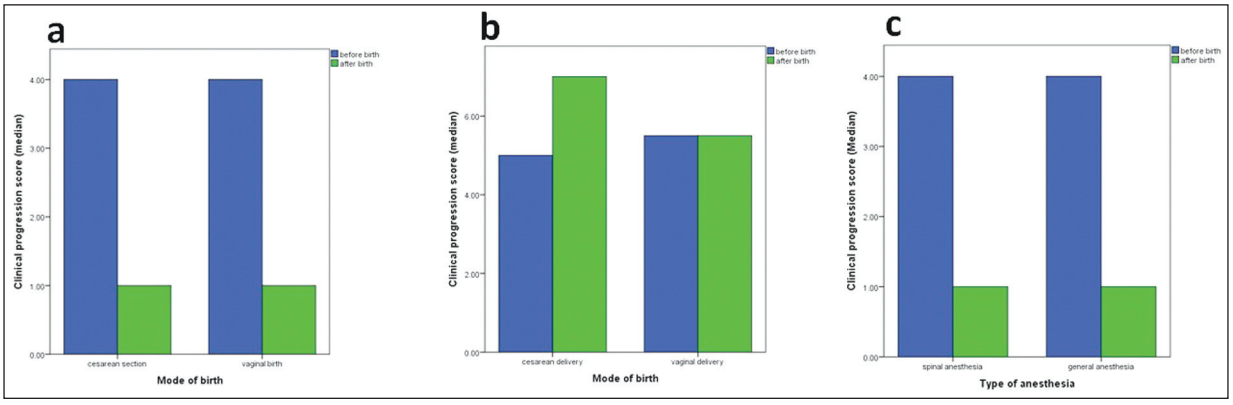

FIGURE 1: The graphics of clinical progression scale scores after and before birth **(a)** according to mode of birth, **(b)** in pregnant women with indication of clinical deterioration according to mode of birth, **(c)** in pregnant women with cesarean section according to type of anesthesia.

vaginal births may not have an impact on these women's clinical state. Due to the small number of pregnant women gave birth vaginally, the predictions for vaginal births were limited particularly for pregnant women with clinical deterioration. However, one of the 2 vaginal births that were suffering from COVID-19, a severe disease, tragically resulted in death.

When pregnant women with COVID-19 were investigated, the clinical improvement was measured in the current study using the WHO's previously reported clinical progression scale scores before and after birth. Clinical progression scale ratings of the women with delivery indications of clinical deterioration did not significantly improve after birth. However, there was a noticeable improvement in the clinical progression scale scores for pregnant women with obstetric indications of birth, whether they gave birth vaginally or via cesarean section. There were studies which investigated the respiratory status of mothers before and after birth. Pineles et al. found the arterial partial pressure of oxygen to the fraction of inspired oxygen ratio's (pO_2/FiO_2) trajectory was improved in pregnant women (n=17) who delivered after developing COVID-19-related acute respiratory distress syndrome.[8] Lapinsky et al. conducted a study of 10 pregnant women who gave birth while receiving mechanical ventilation and the results showed that the maternal respiratory advantage is limited and that not all patients will have an improvement as well as there were no definite indicators of which pregnant women would benefit found.[23] Ghosh et al. found a higher rate of clinical worsening in mothers following cesarean section.[13] The decision of birth for the critical state of pregnant women is challenging, both the state of mother and the fetus should be considered for both mode of births. Weighting the pregnant women' gestational age, severity of respiratory distress and intrauterine death risk, the decision of birth or expectant management should be given.[24]

For cesarean deliveries, gestational age at birth, fetal birth weight, and preterm delivery rate, and neonatal intensive care unit admission rate were high in this study. We analyzed births subtracting the pregnant women with an indication of clinical deterioration for births and after that, the rate of preterm birth and gestational age of women were similar both for cesarean and vaginal births. According to our study results, the main reason for the increase of preterm birth was the respiratory distress of mothers due to COVID-19 during the pandemic. In a multicenter study that covered United States academic centers concluded as, compared to women without COVID-19, women with COVID-19 had a higher likelihood of giving birth earlier than 37 weeks.[6] Another international study recently reported that, in comparison to no COVID-19, the probability of preterm birth increased significantly with severe COVID-19 late in pregnancy.[25] Bezhenar et al. found that preterm labor was common in severe COVID-19, and the proportion of cesarean sections was more than twice as com-

mon as vaginal births.[26] The present study focused on the births of COVID-19 pregnant women in either active infection or in isolation period and for these women the preterm birth rate was related to COVID-19 severity.

In the current study, two third of the cesarean sections were performed under spinal anesthesia. Since neuraxial anesthesia cannot be used for cesarean sections due to a variety of factors, such as the need for an urgent cesarean section, low platelets, confirmed coagulopathy, or a lack of sufficient time since the last dose of low-molecular-weight heparin, maternal respiratory failure, general anesthesia is preferred.[27,28] There have been recorded cases of maternal deaths linked to general anesthesia during cesarean sections in low- and middle-income nations.[15] In our cohort, preference of general anesthesia was lower than spinal anesthesia and as an adverse outcome, maternal mortality rate was higher for pregnant women who underwent cesarean section under general anesthesia. When we evaluated computed tomography findings, pneumonia was relatively higher in pregnant women whose cesarean section were performed under general anesthesia, also the need of invasive mechanical ventilation was higher for pregnant women with general anesthesia. Therefore, general anesthesia might not be directly related to maternal mortality, it seems to be the necessity for these pregnant women with COVID-19. Furthermore, when clinical progression scores were evaluated before and after birth, scores after birth were generally lower, even with general anesthesia, birth might improve respiratory function of pregnant women with COVID-19.

The decision of birth is challenging and should be given considering both the mother and the baby. Particularly obstetric indications should lead to the choice of birth mode. COVID-19 clinical severity and change in clinical status was the important determinant of birth mode and time as well as adverse outcomes of the pregnant women with COVID-19. The decision of vaginal birth may be hard due to the clinical situation and the unfavorable obstetric situation of pregnant women with COVID-19, however, cesarean section was not related with the improvement of clinical status of these women. The adverse outcomes regarding the mother and the baby might be mainly due to effects of COVID-19 on pregnancy and expectant management may be considered rather than birth for appropriate patients with severe COVID-19.

CONCLUSION

The critical factor influencing the method and timing of birth as well as the negative outcomes for pregnant COVID-19 patients was the clinical severity and change in clinical status. The decision of vaginal birth may be hard, however, cesarean birth was not related with the improvement of clinical status of these women.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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