PERINATAL JOURNAL

Original Article

Perinatal Journal 2022;30(2):185–194

Maternal mortality cases due to COVID-19 pandemic in a tertiary referral hospital

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Abstract

Objective: This study aimed to report the clinical prognoses, laboratory findings, treatment procedures, and neonatal outcomes, from hospitalization to death, of Coronavirus Disease 2019 (COVID-19)-related cases of maternal mortality at our clinic.

Methods: Fifteen cases of COVID-19-related maternal mortality, between April 2020 and October 2021, in the Department of Obstetrics & Gynecology of a Training and Research Hospital were retrospectively analyzed for the purpose of the study.

Results: During the study period, a total of 501 symptomatic pregnant women received inpatient treatment for COVID-19. In our case group, 93.3% of maternal deaths due to COVID-19 occurred as a result of the worsening of the clinical condition of third-trimester pregnant women. In these patients whose clinical condition deteriorated, delivery was performed after the decision to give birth, and 86.6% of mortalities occurred in the postpartum period and 13.4% before delivery. There was at least one risk factor in 60% of the cases, with obesity being the most prevalent. In all mortality cases, there were pulmonary complaints (shortness of breath and cough) at admission, and bilateral lung involvement was observed during lung imaging; furthermore, there was a corresponding increase in the mean leukocytosis, AST, ALT, LDH, D-dimer, ferritin, procalcitonin, IL-6, and pro-BNP levels with the worsening of the clinical prognosis. The duration of hospitalization and intensive care unit stays were 6.87±3.18 and 5.33±3.27 days, respectively. The mean period of the delivery-to-mortality for mothers was 5.92±3.48 days and the mean period of the intubation-to-mortality for mothers was 3.33±3.15 days.

Conclusion: The risks of severe illness and death associated with COVID-19 increased in the third trimester compared to the first and second trimesters. All mortality cases involved unvaccinated pregnant women, of which most had at least one risk factor, obesity being the most prevalent. There was no COVID-19-related mortality in the newborns, and it was found that prematurity rates increased due to maternal disease.

Keywords: COVID-19, pregnancy, maternal death.

Introduction

The Coronavirus Disease 2019 (COVID-19) pandemic, which caused the most severe global health crisis since the 1918 influenza pandemic, continues to have a devastating effect throughout the world with more than 4 million deaths. Similar to the other RNA viruses, which undergo genetic mutations over time, variants of the severe acute respiratory syndrome coronavirus-2, i.e., SARS-CoV-2, with different characteristics have emerged. Several variants were evaluated during the last epidemiological update meeting of the World Health Organization (WHO), and it was stressed that the Delta variant featuring rapid transmission and a higher hospitalization rate had a higher incidence worldwide.[1–3]

The incidence of COVID-19 in pregnant women is similar to that in the non-pregnant population, and the disease is typically asymptomatic or manifests as a mild disease.[4,5] The hospitalization rate in pregnant women with COVID-19 was 31.5% according to the data by the Centers for Disease Control and Prevention, for the

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How to cite this article: Tunç Ş, Oğlak SC, Göklü MR, Gedik Özköse Z. Maternal mortality cases due to COVID-19 pandemic in a tertiary referral hospital. Perinat J 2022;30(2):185–194. doi:10.2399/prn.22.0302013

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months of January to June 2020, which was higher compared to the non-pregnant population (5.8%).[6] The rate of severe illness caused due to COVID-19 in pregnant or postpartum women was reported to be approximately 8%, whereas the rate of critical illness was approximately 1%.[7] The risk of severe disease was found to be increased in pregnant women who were COVID-19 positive compared to non-pregnant women. Further, elevations in intensive care admissions, invasive ventilation, extracorporeal membrane oxygenation requirement and mortality rates (10.5–3.9, 2.9–1.1, 0.7–0.3, and 1.5 vs. 1.1) were reported per 1000 patients.[8,9]

No definitive therapeutic drug protocol for COVID-19 has been established yet. In addition to drugs that can be used for the treatment of COVID-19, with low or negligible risks during pregnancy, such as lopinavir-ritonavir, chloroquine, interferon beta, corticosteroids, and ivermectin, there have been studies on remdesivir as well. However, the data on its use in pregnant women is insufficient.[10] Studies on vaccines for COVID-19 have rapidly progressed, and the UK was the first country to issue an immediate approval for the widespread use of the COVID-19 vaccine, on December 2, 2020. The fact that pregnant women cannot directly participate in clinical studies increases hesitations about the vaccine.[11] However, the American Society of Obstetrics and Gynecology (ACOG) recommended the administration of the COVID-19 vaccine in pregnant women through its public statement on July 30, 2021. Pregnancy comprises a unique immunological situation that is modulated since the immune system is affected by signals generated from the placenta.[12–18] Moreover, it was reported that pregnant women are predisposed to serious complications and death due to seasonal influenza epidemics compared to the general population.[19] This study aimed to report the experiences of our clinic on maternal deaths due to COVID-19. Our clinic maintains an average rate of more than 20 thousand births annually and operates within the scope of a tertiary pandemic hospital.

Methods

Fifteen cases of COVID-19-related maternal mortality were retrospectively analyzed for the purposes of the study between April 2020 and October 2021 in the Obstetrics and Gynecology Clinic of Diyarbakır Gazi Yaşargil Training and Research Hospital. The approval of the Ethics Committee of our hospital was obtained before the commencement of the study. We performed this study consistent with the Declaration of Helsinki Ethical Principles.

The information of the patients included in the study was retrieved from the hospital's archive system and patient files. The pregnant women included in the study were classified under the categories asymptomatic, mild, moderate, severe, and critical, in compliance with the guidelines of the National Institutes of Health as per the diagnosis based on physical examinations and vital findings, PCR tests from nasopharyngeal swab samples, chest X-rays, and, if necessary, a thorax computerized tomography (CT).[20,21] Cases that were asymptomatic or classified in the mild disease group (who presented with flu-like symptoms) and the moderate disease group (who had pneumonia, $SpO_2 \geq 94\%$ in room air, and did not need oxygen therapy) were followed up as outpatients, whereas those in the moderate disease group who required oxygen therapy and those in the severe and critical disease groups were treated as inpatients. During the study period, a total of 501 pregnant women who were COVID-19 positive were hospitalized due to COVID-19 symptoms, obstetric reasons, or both. Maternal mortality was seen in 15 out of 501 pregnant inpatients who were COVID-19 positive.

This study investigated the following parameters of maternal mortality cases: maternal age, obstetric history, week of gestation, body mass index, smoking and comorbidities (diabetes, hypertension, chronic renal disease, asthma, chronic obstructive pulmonary disease [COPD]), symptoms, and examination findings, vaccination and contact history, PCR test and lung imaging results, blood tests (reported for the first admission, prenatal, and pre-death), drug treatments, hospitalization time, duration of intensive care stay, delivery type and timing, intubation timing, and time of death. Postpartum hemorrhage (PPH) was defined as blood loss more than 1000 mL following cesarean section delivery.[22] Furthermore, the parameters pertaining to the newborns of the mortality cases, including weight, Apgar score, umbilical cord blood gas tests, as well as intensive care admission and mortality, were also included in the investigation.

Statistical analysis

Two independent groups were compared using Student's t and/or Mann-Whitney U tests in accordance with the results of the Shapiro-Wilk and

Kolmogorov-Smirnov tests that analyzed the normality hypothesis. The mean ± standard deviation and median (minimum–maximum) expressions were used for continuous variables, whereas frequency distributions and percentages were used for categorical variables with an aim to summarize the variables related to our case series. IBM SPSS Statistics for Windows, Version 25.0 software package (IBM; Armonk, New York, USA) was used to perform statistical tests and compute descriptive statistics. A p-value of less than 0.05 was considered statistically significant for the purposes of this study.

Results

During the study period, a total of 501 pregnant women who were COVID-19 positive were treated as inpatients due to COVID-19 symptoms, obstetric reasons, or both. Of these, 22% were infected with variants (n=108; 78 patients with the Delta variant, five with the Alpha variant, and 25 with other variants). All COVID-19 patients described cough and shortness of breath at admission. During the follow-up period, 18 patients experienced missed abortion, and two patients experienced intrauterine fetal demise. During the hospitalization period, 37.9% (n=190) of all COVID-19 cases (n=501) gave birth and 57% (n=108) of deliveries were performed by cesarean section. Among the pregnant inpatients, the rates of admission to the maternal intensive care unit and mortality were 11.6% (n=58) and 2.9% (n=15), respectively.

The mean age in the mortality cases was 32.2±5.55 years, whereas the mean week of gestation was 31.5±5 weeks. There were pulmonary manifestations (shortness of breath, cough) and bilateral involvement during lung imaging in all the pregnant women. Further, variant positivity was detected in 47% of the women (**Table 1**).

Eight of the fatalities developed renal failure, and four of them underwent hemodialysis. One patient had spontaneous pneumothorax, whereas one patient underwent a tracheostomy due to subcutaneous emphysema.

In our case group, 93.3% of maternal deaths due to COVID-19 occurred as a result of the worsening of the clinical condition of third trimester pregnant women due to COVID-19. In these cases whose clinical condition deteriorated, delivery was performed after the decision to give birth, and 86.6% of mortalities occurred in the postpartum period and 13.4% before delivery. There was at least one concomitant disease in

Table 1. Maternal and fetal findings.

	Age/year	Week of gestation	Variant	Birth week	Birth weight/g	Neonatal death
Case 1	37	35w4d	None	35w4d	3000	None
Case 2	34	34w	None	35w	2500	None
Case 3	41	34w	None	34w2d	2250	None
Case 4	29	31w	Delta	No delivery	-	IUMF
Case 5	34	31w	Alpha	31w	1750	None
Case 6	32	38w5d	None	38w5d	2900	None
Case 7	35	34w	None	34w	2250	None
Case 8	28	17w	Delta	No delivery	-	IUMF
Case 9	27	34w	None	34w	2400	Yes
Case 10	26	36w3d	Delta	36w5d	2750	None
Case 11	29	30w	None	30w2d	1500	None
Case 12	26	33w	Delta	33w4d	1900	None
Case 13	25	29w	None	29w2d	1500	None
Case 14	40	29w	Delta	29w5d	1550	None
Case 15	40	30w	Delta	30w	2200	None
Mean±SD	32.2±5.55	31w5d±5w		33w1d±3w6d	2188.46±521.28	
Median (min–max)	32 (25–41)	33w (17w–38w5d)		34w (29w2d–38w5d)		

60% of the cases, the most prevalent being obesity. Cases 1, 2, 6, 7, 12, and 13 were obese, cases 2 and 15 had hypertension, case 10 had gestational diabetes, case 14 had hypothyroidism, and case 13 had a history of smoking. All of the fatalities were unvaccinated, and 80% did not have a history of contact. The mean duration of hospitalization was 6.87±3.18 days, whereas the mean duration of admission to the intensive care unit was 5.33±3.27 days. All the cases underwent a cesarean section, except for one patient who refused to give birth because of the fear of worsening her disease and a pregnant woman (17 weeks of gestation) who was not operated on to avoid extremely preterm delivery. Of the cesarean section deliveries, 53.3% of them were emergency cesarean sections due to maternal acute respiratory failure. No cases experienced excessive PPH following cesarean section delivery. All the intubations were performed during the postpartum period and within 3.6±2.06 days after hospitalization. The mean period of the delivery-to-mortality for mothers was 5.92±3.48 days and the mean period of the intubation-to-mortality for mothers was 3.33±3.15 days. All the maternal deaths occurred during the postpartum period, except for two cases where deliveries could not be performed (**Table 2**).

The mean birth week of the newborns was 33.1±3.6 weeks, the mean birth weight was 2188.46±521.28 grams, and the mean 1-minute and 5-minute Apgar scores were 6.15±1.52 and 7.92±0.76, respectively (**Table 1**). The mean duration of neonatal intensive care stay in 12 cases was 11.78±7.43 days: one was due to isolation, the other was due to the presence of a major cardiac anomaly, and all the remaining hospitalizations were due to prematurity. The blood test results indicated a mean pH-value of 7.24±0.1, a mean base deficit of -7.34±6.35, and a mean lactate level of 2.72±2.83. A PCR test was done for all the infants, and no clinical manifestation of COVID-19 was observed in the only infant with a PCR-positive result. A total of three fetal deaths occurred, two in the intrauterine period and one in the postpartum period, due to severe cardiac anomalies (**Table 1**).

Blood tests indicated an increase in the mean levels of leukocytosis, aminotransferases (AST, ALT), lactate dehydrogenase (LDH), D-dimer, ferritin, procalcitonin, interleukin-6 (IL-6), and brain natriuretic peptide (Pro-BNP) parallel to the worsening of the clinical prognosis (**Table 3**).

All patients received broad-spectrum antibiotics and low molecular weight heparin as well as antiviral and cor-

Table 2. Maternal clinical prognosis and survival.

	Duration of hospitalization/day	Duration of intensive care admission/day	Intubation day	Postnatal survival/day	Post-intubation survival/day	Intubation time
Case 1	9	7	5	9	4	Postnatal
Case 2	11	4	8	7	3	Postnatal
Case 3	9	9	1	8	8	Postnatal
Case 4	3	3	3	No delivery	0	No delivery
Case 5	2	2	0	2	2	Postnatal
Case 6	7	3	7	11	0	Postnatal
Case 7	7	7	2	5	5	Postnatal
Case 8	3	3	3	No delivery	0	No delivery
Case 9	11	11	2	11	9	Postnatal
Case 10	3	2	2	1	1	Postnatal
Case 11	7	5	5	4	2	Postnatal
Case 12	5	4	4	3	1	Postnatal
Case 13	12	12	3	9	9	Postnatal
Case 14	7	2	5	2	2	Postnatal
Case 15	7	6	3	5	4	Postnatal
Mean±SD or Median (min–max)	6.87±3.18	5.33±3.27	3 (1–8)	5.92±3.48	3.33±3.15	

Table 3. Maternal blood parameters.

Parameters	Cases 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	Mean±SD
Leukocytes (4–10)×10³																
At admission	5.8	6.7	7.8	8.2	13	4.3	6.8	5.6	15	6.7	6.6	5.9	7.1	4.9	8.4	7.5±2.9
Prenatal	5.5	8.2	17	-	18	-	6.2	-	-	-	15.6	8.5	9.3	6.8	12	10.8±4.7
Before death	7.3	22	5.9	9.4	26	32	9.6	15	17	9.2	15.5	14	52	12.7	18	17.8±12
Lymphocyte (0.8–40)×10³																
At admission	0.7	1.5	0.3	0.9	0.8	1.3	0.7	0.7	1	0.6	0.5	0.6	1.3	1.1	0.7	0.8±0.3
Prenatal	0.8	1.6	0.7	-	0.8	-	0.7	-	-	-	0.6	0.9	1.2	0.7	0.7	0.9±0.3
Before death	1.3	2.5	2.5	0.6	0.4	4.1	1.2	0.9	0.9	0.6	0.9	0.8	1.0	2.6	1.9	1.5±1
Biochemistry urea 16.6–48 (mg/dL)																
At admission	10	8	16	6	27	8	7	10	8	8	9	10	7	7	13	10.3±5.3
Prenatal	10	12	21	-	28	-	5	-	-	-	12	7	6	28	13	14.2±8.6
Before death	35	122	110	5	47	74	86	24	27	7	196	34	42	50	54	60.9±50.6
Creatinine 0.5–0.9 (mg/dL)																
At admission	0.6	0.6	0.6	0.5	0.4	0.6	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.4	0.4	0.5±0.1
Prenatal	0.5	0.6	0.6	-	0.5	-	0.5	-	-	-	0.3	0.5	0.4	0.4	0.4	0.5±0.1
Before death	20	2.7	3.8	0.4	0.6	2.7	2.7	0.5	0.4	0.5	4.8	0.6	0.6	1.6	0.5	2.8±5
Aspartate aminotransferase (AST) 0–32 (U/L)																
At admission	14	58	21	63	18	97	41	23	42	51	34	17	9	73	57	41.2±25.2
Prenatal	32	78	19	-	22	-	47	-	-	-	38	14	14	50	44	35.8±20
Before death	20	825	69	28	34	4202	808	26	84	29	414	24	22	192	42	454.6±107
Alanine aminotransferase (ALT) 0–33 (U/L)																
At admission	13	31	38	62	15	49	49	12	35	40	20	12	15	102	36	35.3±24.2
Prenatal	14	31	29	-	17	-	51	-	-	-	19	21	12	34	26	25.4±11.6
Before death	8	165	151	28	18	1959	173	13	49	23	89	14	10	47	23	184.7±494
Lactate dehydrogenase (LDH) 135–255 (U/L)																
At admission	280	309.0	393	389	299	440	297	300	365	457	300	200	224	456	297	333.7±79
Prenatal	363	408.0	400	-	496	-	353	-	-	-	468	251	199	272	401	361±95
Before death	905	2306	850	426	1019	1213	2995	521	1052	460	1984	587	1416	1272	658	1177±739
C-reactive protein (CRP) 0–5 (mg/L)																
At admission	96	108	90	103	65	50	54	84	106	93	83	17	117	94	122	85.5±28.2
Prenatal	116	106	45	-	52	-	84	-	-	-	58	74	92	113	99	83.9±25.8
Before death	38	224	18	100	308	34	128	29	11	99	10	105	6.9	229	54	93.1±93.3
D-dimer 0–243 (ng/mL)																
At admission	661	444	394	0.2	1.2	0.8	-	0.2	0.5	2.7	0.4	0.2	0.4	0.4	6.9	108±219
Prenatal	-	605	117	-	5.7	-	0.4		-	-	-	0.1	-	0.1	10	105±224
Before death	2792	4336	2134	0.9	20	9.6	3.1	0.1	5.7	3.3	18	-	11	13	10	719±1426
Procalcitonin <0.05 (ng/mL)																
At admission	0.3	0.2	0.3	0.4	0.02	0.1	0.7	0.1	4.2	0.3	0.2	0.1	0.1	0.3	1.2	0.6±1.1
Prenatal	0.3	0.2	0.2	-	-	-	0.7	-	-	-	0.1	0.3	0.1	0.8	2.9	0.6±0.9
Before death	0.1	0.1	-	-	0.4	1.4	69.9	0.0	0.1	0.2	6.7	2.2	0.2	59.0	0.5	10.8±24
(IL-6) 0–5.9 (pg/ mL)																
At admission	-	-	-	-	-	-	23	29	20	-	7	10	37	-	27	22.4±10.4
25-OH vitamin D 20–50 (ng/mL)																
At admission	-	22	-	-	-	-	19	-	7	-	11	12	21	25	-	17.3±6.8
Pro-BNP <96 (pg/mL)																
At admission	-	-	-	-	-	-	59	407	905	78	113	70	37	458	1786	434.8±582
Blood gas pH (7.35–7.45)																
At admission	7.5	7.4	7.4	7.5	7.5	7.4	7.5	7.5	7.4	7.5	7.4	7.4	7.2	7.4	7.4	7.4±0.1
Prenatal	7.3	7.2	7.4	-	7.4	-	7.4	-	-	-	7.3	7.5	7.4	7.5	7.3	7.4±0.1
Before death	7.0	6.7	6.7	7.4	6.7	7.2	7.1	7.3	7.2	7.5	7.1	7.5	7.0	7.0	7.2	7.1±0.3
O_2 saturation (%)																
At admission	42	98	83	88	82	34	82	90	90	72	64	49	84	93	89	76.1±19.8
Prenatal	82	57	75	-	56	-	85	-	-	-	61	94	87	95	81	77.5±14.6
Before death	53	40	24	43	43	34	84	79	27	79	89.6	85	36	55	52	55.1±22.4
PO_2 80–108 (mmHg)																
At admission										34	32	23	53	65	62	51.6±20.2
Prenatal	50	37	44	-	23	-	57	-	-	-	39	70	52	73	25	47.4±17
Before death	54	39	30	27	44	30	74	48	19	39	77	53	33	42	33	43.2±16.3
PCO_2 15–125 (mmHg)																
At admission	30	21	26	28	32	36	27	31	32	23	30	31	39	30	30	30.3±4.4
Prenatal	46	47	31	-	47	-	28	-	-	-	46	26	27	26	41	37±9.6
Before death	104	198	136	35	84	57	45	36	136	21	46	34	73	38	69	74.5±49.6

Table 4. IL6-R blocker (tocilizumab) – survival relationship.

	Survival day (Mean±SD)	Survival day Median (min–max.)	p-value
IL6-R blockers used (n=8)	4.75±2.55	3.5 (2.0–9.0)	0.683
IL6-R blockers not used (n=7)	6.00±4.04	5.0 (2.0–12.0)	
Total	5.33±3.27	4.0 (2.0–12.0)	

IL6-R: Interleukin 6 receptor.

ticosteroid therapies. There was no significant difference between the patients included in the tocilizumab-treatment group (53.3%, n=8) and the tocilizumab-naive group, who were not administered tocilizumab based on the duration of intensive care unit stay (**Table 4** and **Fig. 1**).

Discussion

There is limited data on pregnant women hospitalized for critical illness due to COVID-19. Relevant studies in the literature reported that the risk of COVID-19-related maternal mortality was higher in low- and middle-income countries, surpassing the number of deaths due to obstetric hemorrhage and preeclampsia.[23–26]

According to a study with the largest study sample in the literature on COVID-19-related maternal mortality by Torres-Torres et al., 2.46% (n=322) of the patients were admitted to the intensive care unit, 1.42% (n= 185) were intubated, and 1.35% died (n=176).[26] In a study by Blitz et al., 15% (n=70) of pregnant women who were COVID-19 positive were classified as having a severe or critical illness, and 19% (n=13) of them required intensive care unit admission. Also, 15% of those hospitalized in the intensive care unit and 25% of those who were connected to a mechanical ventilator have died.[24]

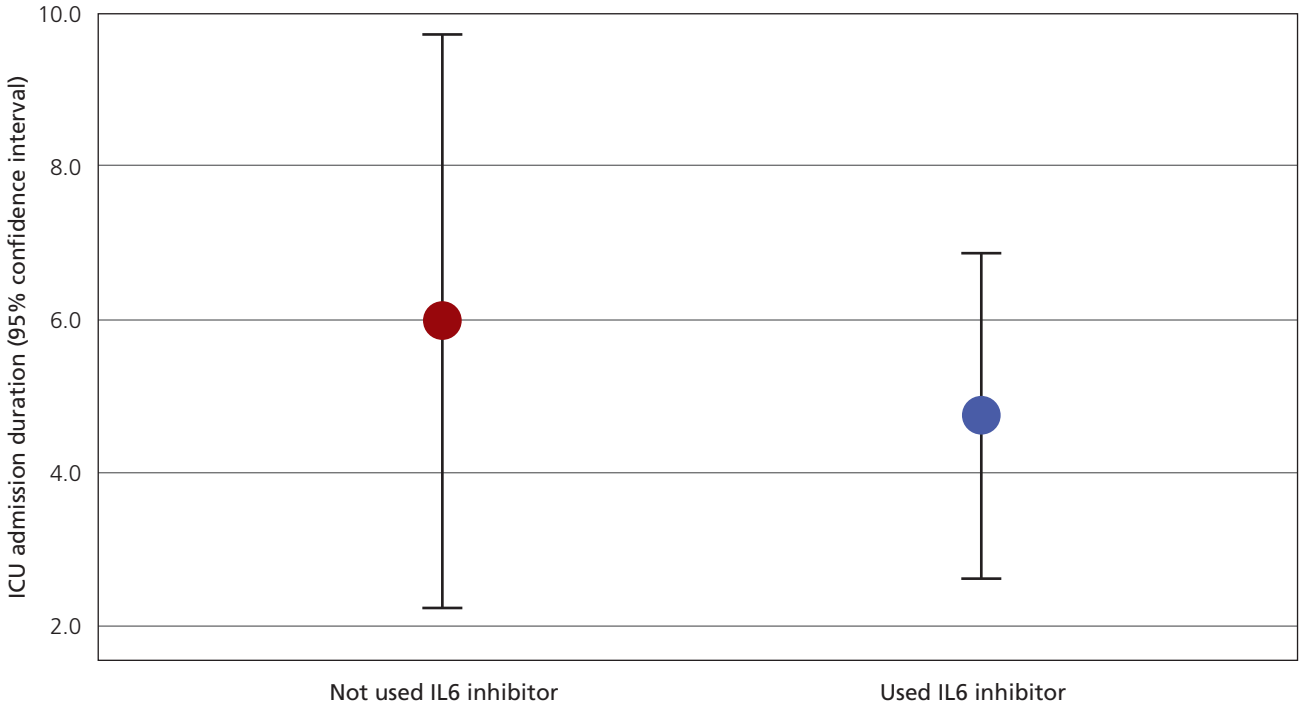

Fig. 1. The distribution of cases using and not using an interleukin-6 receptor blocker (Tocilizumab).

Different studies reported the intensive care admission rates, in pregnant women who were COVID-19 positive, between 3% and 28%, intubation rates between 1.4% and 12%, and mortality rates between 0% and 2%.[5,19,27,28] It was reported that the mean duration of hospitalization in pregnant women due to COVID-19 was 13 days, and the duration of admission to the intensive care unit was 8 days. During the postpartum period, 75% of the cases underwent intubation, whereas 25% of them during pregnancy; 85% of the mortalities were seen in the second or third trimesters, and 80–84% of the mortalities occurred in the postpartum period.[24,25,29] In this study, the mean duration of hospitalization and intensive care admissions were 6.87±3.18 days and 5.33±3.27 days, respectively, whereas the intensive care admission rate was 11.6%, and the maternal mortality rate was 2.9%. The fact that outpatient pregnant women were excluded from this study because of asymptomatic or mild disease and that pregnant women with severe/critical illness were referred to our center might have accounted for the high mortality rates and lower durations of hospitalization. In our case group, consistent with the results reported by the relevant literature, 93.3% of maternal deaths due to COVID-19 happened as a consequence of the worsening of the clinical condition of third-trimester pregnant women due to COVID-19. In these cases, delivery was performed after the decision to give birth, and 86.6% of mortalities occurred in the postpartum period and 13.4% before delivery.[24,29] Physiological changes that become evident with progressing pregnancy may aggravate disease manifestation and thus explain the increased mortality rate in the third trimester.[11,12]

Pneumonia was detected in 89% to 98% of the symptomatic pregnant women with concomitant conditions such as tachycardia, tachypnea, and hypoxia. High fever was reported in 32% to 69%, cough in 33% to 41%, shortness of breath in 11% to 64%, and fatigue in 30% of the cases.[5,19,24,27,28] In this study, there was at least one pulmonary symptom (cough, shortness of breath, or tachypnea) in all of the cases at the time of admission, whereas SpO_2 in room air was ≤94% in 60% of the cases.

The most common laboratory findings in pregnant women with COVID-19 have been reported as lymphocytopenia, increase in inflammatory markers (C-reactive protein (CRP), procalcitonin, and ferritin), D-dimer, and transaminases, which were similar to that of the non-pregnant population.[5,19,24,27,28,30] The rate of involvement of the lungs, as revealed by the CT, varied between 30.4% and 98.7%; ground-glass opacities were reported to be the most prevalent radiological pattern.[27] In this study, repeated blood tests on different days were included to reflect the clinical course of the disease. Consistent with the results reported in the relevant literature, the worsening of clinical prognosis and eventual death were accompanied by elevations in the mean levels of leukocytes, AST, ALT, LDH, CRP, ferritin, D-dimer, procalcitonin, and IL-6, an important component of the inflammatory response, as well as pro-BNP, an important marker in sepsis. Lymphocytopenia was not observed.[5,19,24,27,28,31,32]

Risk factors for severe disease and mortality included pregnancies in advanced ages,[24–26,28,29,33] diabetes,[26,29,34] hypertension,[26,34] obesity,[24,26,29,34] chronic renal disease,[26] and asthma–COPD (24,29). Interestingly, Torres-Torres et al. reported that smoking and asthma–COPD did not reveal a significant association with mortality.[26] There was at least one risk factor in 60% of the cases of maternal mortality, obesity being the most prevalent.

In a study by Blitz et al., all the patients admitted to the intensive care unit were administered anticoagulants; 85%, hydroxychloroquine; and 92%, antibiotics for community-acquired pneumonia. Within the scope of clinical studies, 23% of the patients received remdesivir; 38%, IL-6 receptor blockers; and 5%, plasma therapy.[24] Zaigham et al. reported that approximately 90% of the patients received antiviral treatment; all patients received antibiotics for potentially superimposed bacterial pneumonia or cesarean section prophylaxis, and approximately 15% received corticosteroids.[28] Similar to relevant literature, antiviral therapy, low molecular weight heparin, broad-spectrum antibiotics as prophylaxis against bacterial pneumonia, and corticosteroid therapy, to restrain pulmonary inflammation due to cytokine storm, were administered in this study to all of the cases. Tocilizumab treatment was tried in 53.3% of the cases; however, it was not successful.

Di Toro et al. reported that 25% of the deliveries were performed by emergency cesarean section due to the development of acute maternal respiratory failure, whereas Blitz reported that 85% of the pregnant women admitted to the intensive care unit underwent cesarean section.[19,24] While the rates reported for cesarean section range from 52% to 96% in the population of pregnant women who are COVID-19 positive, preventing disease transmission from the mother to the fetus or deteriora-

tion in maternal health due to COVID-19 were shown to be primary reasons for high rates of cesarean section.[5,27,28,35] The cesarean section rate for the healthy pregnant population was 36% at our clinic previously, whereas the same rate was 57% for the pregnant women who were COVID-19 positive. In the cases of maternal mortality, all the deliveries were performed by cesarean section, including 53.3% of cases due to maternal emergencies. It is evident that COVID-19 led to an increase in the rates of primary cesarean sections.

The preterm birth rate in COVID-19 positive pregnancies was higher compared to that in the general obstetric population (5% in European countries, 18% in African countries) due to both the deterioration of the well-being of the fetus as a result of the mother's worsened clinical prognosis and the increase in the spontaneous rupture of membranes during labor, which was considered to have been induced by viral infection.[19,34] Di Toro et al., as part of a meta-analysis on newborns in COVID-19 positive pregnancies, reported that the mean week of birth was 37.97, the mean birth weight was 3144.71 grams, the rate of preterm (<37 weeks) was 23%, and the mean week of preterm babies was 35.74.[19] To the best of our knowledge, no study has reported neonatal morbidity and mortality results for solely maternal mortality cases due to COVID-19. In this study, the rate of preterm birth was 92%, the mean delivery week was 33.1±3.6 weeks, and the mean birth weight was 2188.46±521.28 grams. This is a natural consequence of severe disease during which intrauterine follow-up was not possible and maternal mortality occurred as a result.

In a study with 225 newborns born to mothers who were COVID19 positive, it was suggested that maternal infection did not have a significant effect on fetal well-being, on the grounds that only one infant had a 1-minute Apgar score and only three had a 5-minute Apgar score of <7; only one out of 54 newborns with respiratory symptoms required nasal continuous positive airway pressure therapy, and no infant required intubation.[19] Most of the relevant studies reported that admissions to the neonatal unit aimed to isolate the infants from their mothers, the COVID-19-related neonatal mortality rate was very low, and there was no direct connection between the six deaths (three intrauterine deaths and three neonatal deaths) and COVID-19.[19,27,36] Di Toro et al. found positive nasopharyngeal swabs in 19 newborns, but it was considered to have been due to contamination rather than an intrauterine infection, since the swabs were not taken immediately after birth, and viral RNA could not be detected in the cord or neonatal blood samples.[19] In this study, the mean 1-minute and 5-minute Apgar scores were 6.15±1.52 and 7.92±0.76, respectively. We consider lower Apgar scores to be associated with prematurity. Twelve perinatal deaths were reported, seven of which were intrauterine, in a study by Hessami et al., which investigated mortality in pregnant women, who were COVID-19 positive, and newborns. Six out of seven intrauterine mortality cases were associated with severe illness (acute respiratory distress syndrome, septic shock, and multi-organ failure) in mothers due to COVID-19. In the only remaining intrauterine mortality case, there was a history of preterm premature rupture of membranes (36 weeks) and decreased fetal movements in the follow-up; there was no clear association with COVID-19. There was no vertical transmission or direct infection in the five neonatal deaths, and it was reported that they were caused by prematurity.[29] There were three perinatal deaths in this study, two of which were intrauterine due to severe maternal disease and the other was postpartum due to severe cardiac anomalies; only one fetus was PCR positive and the infant was discharged with no signs of COVID-19.

The fact that the targeted parameters could not be retrieved completely due to the retrospective design is a limitation of the study. However, the findings from this study are crucial since the interventions related to an improvement in one outcome may be related to improvement in another outcome. Ensuring that more professionals are aware of and utilize the COVID-19 maternal mortality cases will end in more efficient management of these cases.

Conclusion

In our study, maternal deaths due to COVID-19 increased especially in the third trimester. All the maternal mortality cases had at least one risk factor; the most prevalent being obesity. The severe disease was associated with high cesarean section rates and iatrogenic prematurity. The main reason for neonatal intensive care admissions was prematurity, and there was no vertical transmission. We would like to emphasize the increased mortality due to COVID-19, especially in the later weeks of pregnancy.

Funding: This work did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics, the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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