Comparison of perinatal and neonatal outcomes of symptomatic pregnancy infected with SARS-CoV-2

Oğuz Arslan[1], Burak Giray[2], Niyazi Tuğ[1]

[1]Department of Obstetrics and Gynecology, University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, İstanbul, Turkey

[2]Department of Obstetrics and Gynecology, Koç University Faculty of Medicine, İstanbul, Turkey

Abstract

Objective: In this study, maternal and neonatal outcomes of pregnant women with positive severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) RNA tests were evaluated according to their symptomatic status. The clinical progression of SARS-CoV-2-positive pregnant women and the effect of coronavirus disease-2019 (COVID-19) on newborns was investigated.

Material and Methods: This retrospective cohort study was conducted at a tertiary pandemic hospital specializing in caring for pregnant women infected with SARS-CoV-2. We included patients with a positive SARS-CoV-2 polymerase chain reaction test at delivery, subdividing them into symptomatic and asymptomatic groups.

Results: Two hundred and forty-nine patients were included in the study. The mean age of the pregnant women in the symptomatic group was higher than those in the asymptomatic group ($p=0.001$). The iatrogenic preterm birth rates in the symptomatic and asymptomatic groups were 43.37% and 8.43%, respectively ($p<0.001$). Cesarean section rate was higher in symptomatic group ($p=0.01$). Maternal death was significantly higher in symptomatic pregnant women ($p<0.001$). The neonatal intensive care unit admission rate was higher in symptomatic pregnant women ($p<0.001$).

Conclusion: The maternal and fetal outcomes for mothers with symptomatic infections tend to be worse, highlighting the importance of careful management, good follow-up and the advisability of closer monitoring. (J Turk Ger Gynecol Assoc 2024; 25: 81-9)

Keywords: COVID-19, maternal outcomes, pregnancy, preterm birth

Received: 05 July, 2023 **Accepted:** 22 March, 2024

Introduction

In December 2019, pneumonia cases of unknown origin were reported in the city of Wuhan, China (1). The virus isolated from respiratory tract samples taken from these cases was named severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) (2). The virus resulted in the coronavirus disease-2019 (COVID-19) global pandemic (3). Due to the physiological adaptation mechanisms induced by pregnancy, it was predicted that COVID-19 may progress more severely in pregnant women. Many researchers have attempted to define the clinical course of COVID-19 in pregnant women, how the disease affects pregnancy and delivery results, which factors affect the severity of the disease and how much it worsens these results (4). In this study, maternal and neonatal outcomes of pregnant women with positive SARS-CoV-2 RNA tests at delivery were evaluated according to their symptomatic status. Anticipating the complications that may occur in the management of symptomatic COVID-19-positive pregnant women, it was planned to implement necessary medical interventions earlier in the study population. Whether there was a difference between the postpartum clinical course of symptomatic COVID-19-infected pregnant women and the clinical course of their newborns and asymptomatic COVID-19 pregnant women was investigated.

Address for Correspondence: *Oğuz Arslan*
e.mail: oguzarslan29@hotmail.com ORCID: orcid.org/0000-0003-4014-4511
DOI: 10.4274/jtgga.galenos.2024.2023-6-4

Material and Methods

This retrospective cohort study was conducted at a tertiary pandemic hospital specializing in caring for pregnant women infected with SARS-CoV-2. The data of patients who were confirmed to have COVID-19 by reverse transcription polymerase chain reaction (PCR) test from the nasopharyngeal swab and who gave birth between March 1, 2020, and December 31, 2022, were analysed retrospectively from electronic health records. The collected data were anonymized. The procedures followed were approved by the ethical standards of the responsible committee on human experimentation and in keeping with the Helsinki Declaration of 1975, revised in 2013. COVID-19-positive patients with other reasons for elevated serum liver transaminases, C-reactive protein (CRP), leukocytes, and chronic illness were excluded from the study. Lung ultrasonography (LUS) before delivery and thorax computed tomography (CT) after delivery were performed in all pregnant women. Patients with a positive SARS-CoV-2 PCR test at delivery were included, subdivided into symptomatic and asymptomatic groups. Demographic characteristics, obstetric outcomes, newborn outcomes, maternal laboratory results, maternal intensive care unit (ICU) admission, maternal mortality, and clinical features were compared between the two groups. The University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Institutional Ethics Committee approval was granted (approval number: 165, date: 14.12.2022).

Statistical analysis

Data were statistically analysed using the SPSS, v.21.0 (IBM Inc., Armonk, NY, USA). The Shapiro-Wilk test was used to check whether data were normally distributed. Continuous variables are expressed as mean and standard deviation or median and range, as appropriate. Categorical variables were expressed as frequency and percentage. The Independent t-test was used to compare continuous variables, as appropriate. The Pearson's chi-squared test or Fisher's exact test were used to compare qualitative data. A logistic regression analysis was performed. A p-value <0.05 was considered statistically significant.

Results

The study included 249 pregnant women, of whom 166 (66.66%) were asymptomatic and 83 (33.34%) were symptomatic. Of the symptomatic patients, 57 (68.7%) had shortness of breath, 22 (26.5%) had cough, and 4 (4.8%) had fever.

The mean ages of the pregnant women in the symptomatic group were higher than those in the asymptomatic group (p=0.001) (Table 1). The nationalities of the pregnant women were evaluated and 155 (93.37%) in the asymptomatic group

Table 1. Comparison of maternal demographics with symptomatic status

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Maternal age (years)	28.91±5.50	31.10±4.73	**0.001**
Nationality			0.333
Turkish	155 (93.37)	80 (96.38)	
Arabic	11 (6.63)	3 (3.62)	
COVID-19-year			
2020	39 (23.5)	15 (18.1)	0.328
2021	98 (59)	62 (74.7)	**0.015**
2022	29 (17.5)	6 (7.2)	**0.028**
BMI (kg/m^2)	26.65±3.62	27.50±3.72	0.085
Blood type			0.403
A	74 (44.57)	39 (46.98)	
B	22 (13.25)	9 (10.84)	
AB	13 (7.83)	10 (12.04)	
0	57 (34.33)	25 (30.12)	
Rhesus			0.894
Positive	145 (87.34)	72 (86.74)	
Negative	21 (12.65)	11 (13.25)	
Gravida	2 (1-8)	2 (1-7)	0.091
Parity	1 (0-6)	1 (0-6)	0.133
Abortion history	0 (0-4)	0 (0-3)	0.196

Table 1. Continued

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Chronic disease	26 (15.6)	14 (16.8)	0.880
Hypothyroidism	13 (7.8)	7 (8.4)	
Hyperthyroidism	1 (0.6)	0 (0)	
Diabetes mellitus	3 (1.8)	2 (2.4)	
Asthma	5 (3.0)	3 (3.6)	
Cardiac arrhythmia	1 (0.6)	0 (0)	
Celiac disease	1 (0.6)	1 (1.2)	
Epilepsy	1 (0.6)	0 (0)	
FMF disease	0 (0)	1 (1.2)	
Behçet's disease	1 (0.6)	0 (0)	

Values are presented mean ± standard deviation, median (range), and n (%). BMI: Body mass index, COVID-19: Coronavirus disease-2019, FMF: Familial Mediterranean fever

were Turkish and 11 (6.63%) were ethnically Arabic, while in the symptomatic group 80 (96.38%) were Turkish and 3 (3.62%) were Arabic. There was no significant difference between the nationalities of the pregnant women in the two groups (p=0.333). There was no significant difference between blood groups (p=0.403) or rhesus (Rh) factor status (p=0.894) between the groups. The two groups did not differ for gravida (p=0.091), parity (p=0.133) or history of abortion (p=0.196).

Gestational weeks of pregnancies in the symptomatic group were lower than in the asymptomatic group (p<0.001) (Table 2). The preterm birth rate in the symptomatic group was 48.2% (n=40), significantly higher than the asymptomatic group where it was 14.5% (n=24) (p<0.001). Premature rupture of membranes (PROM) developed more frequently in asymptomatic pregnant women (p<0.001). The vaginal delivery rate was higher in asymptomatic pregnant women, while the cesarean section rate was higher in symptomatic pregnant women (p=0.01). Both maternal ICU admission and maternal death were significantly higher in symptomatic pregnant women (p<0.001). All of the pregnant women in the symptomatic group were diagnosed with COVID-19 pneumonia by thorax CT and 78 (94%) by LUS (p<0.001).

Symptomatic women had a higher rate of leukocytosis (p<0.001) and lymphopenia (p<0.001) than asymptomatic patients. Other laboratory parameters, such as CRP (p<0.001), alanine aminotransferase (ALT) levels (p=0.018), aspartate aminotransferase (AST) levels (p=0.01), blood urea nitrogen (BUN) (p<0.001), creatinine (CR) levels (p=0.029), and

Table 2. Comparison of maternal obstetric characteristics with symptomatic status

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Gestational hypertension	2 (1.2)	0 (0)	0.554
Gestational diabetes mellitus	7 (4.2)	4 (4.8)	0.829
Gestational age (week)	38.10±1.87	35.61±3.47	**<0.001**
Preterm birth (<37 week)	24 (14.5)	40 (48.2)	**<0.001**
Spontaneous	10 (6.02)	4 (4.83)	0.689
Iatrogenic	14 (8.43)	36 (43.37)	**<0.001**
Premature rupture of membranes	24 (14.5)	2 (2.4)	**<0.001**
Mode of delivery			**0.01**
Vaginal	73 (43.97)	23 (27.72)	
Cesarean section	93 (56.03)	60 (72.28)	
Maternal ICU	1 (0.6)	40 (48.2)	**<0.001**
Maternal death	0 (0)	18 (21.7)	**<0.001**
Maternal transfusion	5 (3)	10 (12)	**0.002**
Thoracic CT - COVID-19 pneumonia	51 (30.7)	83 (100)	**<0.001**
LUS - COVID-19 pneumonia	62 (37.3)	78 (94)	**<0.001**

Values are presented mean ± standard deviation and n (%). ICU: Intensive care unit, COVID-19: Coronavirus disease-2019, CT: Computed tomography, LUS: Lung ultrasonography

international normalized ratio values (p=0.013) were also significantly higher in symptomatic pregnant women (Table 3). When the results of newborn parameters were evaluated, birth weight (p<0.001), newborn length (p=0.001), newborn head circumference (HC) (p<0.001), 1 minute Activity pulse grimace appearance respiration (APGAR) score (p=0.016), and 5 minute APGAR score (p=0.012) was lower in symptomatic women. The neonatal intensive care unit (NICU) admission rate was higher in symptomatic pregnant women (p<0.001). The rates of indications for NICU admission, including respiratory distress (p=0.009) and prematurity (p=0.012), were higher in the symptomatic group (Table 4).

The delivery rate due to the indication of maternal general condition disorder was higher in the symptomatic group (p<0.001). The birth rate due to PROM (p=0.002), elective cesarean section (p=0.007), and pregnant in term action (p=0.002) was higher in the asymptomatic group (Table 5).

A logistic regression model was developed to assess risk factors in women within the symptomatic group. This showed that symptomatic infection was associated with an increased risk of iatrogenic preterm birth [odds ratio (OR): 8.31, 95% confidence interval (CI): 4.13-16.72; p<0.001] cesarean section (OR: 2.04, 95% CI: 1.15-3.62; p=0.013), maternal death (OR: 1.27, 95% CI: 1.14-1.43; p<0.001), and NICU admission (OR: 4.81, 95% CI: 2.26-8.69; p<0.001) (Table 6).

Discussion

The first COVID-19 case was seen in Turkey on March 11, 2020. On the same date, the World Health Organization declared the coronavirus a pandemic (5). During the course of the pandemic, 102,174 (0.12%) people died due to COVID-19 in Turkey in three years (6). In the present study, the clinical progression of SARS-CoV-2 positive pregnant women according to their symptomatic status was investigated. We found a relatively high rate of asymptomatic pregnant women (n=166, 66.6%). In the study of Vousden et al. (7), the rate of asymptomatic women was 66% and in the systematic review by Allotey et al. (4), the rate of asymptomatic pregnant women was 54-77%. The high rate of asymptomatic patients has been associated to the vaccines developed against COVID-19. The severity of the disease decreased with increasing use of the vaccine. We found the mean age of symptomatic women to be significantly higher than asymptomatic women, a finding also reported by Minisha et al. (8). In the present study, it was also shown that the risk of severe diseases rises with advancing age. The escalation in disease severity correlates with the rise in age-related comorbidities, heightened susceptibility to diseases, and the age-associated diminishing of immunocompetence (9). This heightened risk of severe diseases contributes to symptomatic manifestations in patients.

Interestingly, it was observed that pregnant women who contracted COVID-19 exhibited a higher rate of symptomatic cases in 2021 and, conversely, a higher rate of asymptomatic cases in 2022 (p=0.015 and p=0.028, respectively). We attribute this reduction in symptomatic infections among pregnant women in 2022 to the widespread adoption of vaccines. Citizen vaccination programmes against the coronavirus commenced in Turkey in January 2021, with a firm recommendation for pregnant women to receive the vaccine published in June 2021 (10). Despite this recommendation, vaccine hesitancy

Table 3. Comparison of maternal laboratory results with symptomatic status

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Lymphocyte (103/µL)	1.89±0.63	0.70±0.29	**<0.001**
Leukocyte (10^3/µL)	8.32±2.02	16.40±8.92	**<0.001**
Prenatal Hb (g/dL)	11.73±1.43	11.16±1.45	**0.003**
Postnatal Hb (g/dL)	10.37±1.67	10.09±1.59	0.208
Decrease in Hb (g/dL)	1.34±0.99	1.07±0.83	**0.037**
Prenatal hematocrit (%)	35.58±3.80	33.96±3.97	**0.002**
Postnatal hematocrit (%)	31.65±4.12	30.74±4.41	0.110
Decrease in hematocrit (%)	3.94±2.95	3.21±2.54	0.055
C-reactive protein (mg/dL)	1.84±2.53	13.82±12.09	**<0.001**
Alanine aminotransferase (u/L)	17.46±30.01	177.64±605.08	**0.018**
Aspartate aminotransferase (u/L)	25.15±31.82	376.80±1745.38	**0.01**
Blood urea nitrogen (mg/dL)	13.07±5.77	19.86±15.92	**<0.001**
Creatinine (mg/dL)	0.54±0.10	0.69±0.63	**0.029**
Uric acid (mg/dL)	4.46±1.25	4.97±2.16	0.052
INR	0.94±0.08	1.45±1.82	**0.013**

Values are presented mean ± standard deviation. Hb: Hemoglobin, INR: International normalized ratio

Table 4. Comparison of neonatal characteristics with symptomatic status

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Birth weight (g)	3137.74±515.02	2711.73±777.47	**<0.001**
Newborn length (cm)	49.60±2.52	47.64±4.85	**<0.001**
Newborn head circumference (cm)	34.40±1.48	33.18±2.75	**<0.001**
APGAR 1 minute	8 (4-8)	8 (2-8)	**0.016**
APGAR 5 minute	9 (6-9)	9 (5-9)	**0.012**
Fetal gender			0.656
Male	89 (53.61)	42 (50.60)	
Female	77 (46.39)	41 (49.40)	
NICU admission	28 (22.9)	41 (49.4)	**<0.001**
Congenital anomaly	2 (1.2)	0 (0)	0.343
Down syndrome	1 (0.6)	0 (0)	
AVSD	1 (0.6)	0 (0)	
Neonatal COVID-19 test positive	2 (1.2)	0 (0)	0.158
NICU indications			
Respiratory distress	28 (16.9)	27 (32.5)	**0.009**
Sepsis	4 (2.4)	6 (7.2)	0.123
Prematurity	4 (2.4)	10 (12)	**0.012**
Hypoglycemia	2 (1.2)	-	0.158
Hypocalcemia	1 (0.6)	-	0.481
Pyloric stenosis	1 (0.6)	-	0.481

Values are presented mean ± standard deviation, median (range), and n (%). COVID-19: Coronavirus disease-2019, NICU: Neonatal intensive care unit, APGAR: Activity pulse grimace appearance respiration, AVSD: Atrioventricular septal defect

Table 5. Comparison of delivery indications with symptomatic status

	Asymptomatic (n=166)	Symptomatic (n=83)	p
Preeclampsia	4 (2.4)	2 (2.4)	0.988
Oligohydramnios	4 (2.4)	1 (1.2)	0.525
Pregnant in term action	50 (30.1)	11 (13.3)	**0.002**
Premature rupture of membranes	21 (12.7)	2 (2.4)	**0.001**
Preterm delivery	3 (1.8)	4 (4.8)	0.383
Cholestasis	4 (2.4)	2 (2.4)	0.988
Maternal general condition disorder	1 (0.6)	35 (42.2)	**<0.001**
Elective cesarean section	40 (34.1)	8 (9.6)	**0.007**
Labour arrest	5 (3)	1 (1.2)	0.383
Breech presentation	4 (2.4)	4 (4.8)	0.365
Fetal distress	19 (12.6)	13 (15.6)	0.767
Placental abruption	2 (1.2)	-	0.158
Eclampsia	1 (0.6)	-	0.481
Macrosomia	3 (1.8)	-	0.083
Transverse presentation	1 (0.6)	-	0.481
Gestational diabetes mellitus	2 (1.2)	-	0.158

Values are presented n (%)

Table 6. Elevated risk factors among women in the symptomatic group (asymptomatic groups shown for reference)

	Asymptomatic (n=166)	Symptomatic (n=83)	Univariate		
			OR	95% CI	p
Iatrogenic preterm birth					
No	152 (91.57)	47 (56.63)	8.31	4.13-16.72	**<0.001**
Yes	14 (8.43)	36 (43.37)			
Cesarean section					
No	73 (43.97)	23 (27.72)	2.04	1.15-3.62	**0.013**
Yes	93 (56.03)	60 (72.28)			
Maternal death					
No	166 (100)	65 (78.3)	1.27	1.14-1.43	**<0.001**
Yes	0 (0)	18 (21.7)			
NICU admission					
No	138 (77.1)	42 (50.6)	4.81	2.26-8.69	**<0.001**
Yes	28 (22.9)	41 (49.4)			

Values are presented n (%). OR: Odds ratio, CI: Confidence interval, NICU: Neonatal intensive care unit

persisted among pregnant women, resulting in an increase in coronavirus vaccination rates among this demographic in the last half of 2021.

In the present study gestational age at birth was significantly lower and the number of iatrogenic preterm births was significantly higher amongst symptomatic patients compared to asymptomatic women. In a systematic review by Khan et al. (11), the rate of preterm birth was also reported to be higher in symptomatic patients. We distinguished between iatrogenic and spontaneous preterm births. We found that symptomatic COVID-19 infection did not affect the spontaneous preterm birth rate (p=0.689), but significantly increased the iatrogenic preterm birth rate (p<0.001). For women in the symptomatic group, the prominence of vital sign deterioration was attributed to the severity of the disease. To avert fatal consequences in fetuses of mothers with compromised vital functions and to alleviate the physiological burden of pregnancy on the mother, the decision to induce labor was made following the administration of necessary agents for fetal lung maturity. The risk of iatrogenic preterm birth was 8.31 times higher in the symptomatic group in the present study and we believe that the higher rates of iatrogenic preterm birth in the symptomatic group stem from the impairment of the maternal general condition. Many studies in the literature have not distinguished between spontaneous and iatrogenic preterm births.

We found higher cesarean rates in symptomatic women (p=0.01). In the study conducted by Şahin et al. (12), the cesarean delivery rate in pregnant women with COVID-19 was reported to be 66.4%. Metz et al. (13) found that cesarean section rates were higher in severe COVID-19 patients than in asymptomatic patients. During pregnancy, changes in the immune system, diaphragmatic elevation, edema in the respiratory tract and increased oxygen consumption occur. These physiological adaptation mechanisms increase the susceptibility of pregnant women to respiratory tract infections (14). Attempting normal birth in mothers with compromised vital functions is somewhat risky, so in cases where the decision for emergency delivery was taken, a cesarean section was performed. This decision was influenced by an increeased oxygen requirement, worsening respiratory failure, worsening clinical condition, and loss of consciousness. The risk of caesarean section was 2.04 times higher in the symptomatic group in the present study and we attribute this higher cesarean delivery rate in women in the symptomatic group to the development of potentially fatal complications arising from COVID-19 infection.

We found high rates of maternal ICU admission (48.2%) and maternal mortality (21.7%) in the symptomatic group. Similarly, Metz et al. (13), reported maternal ICU admission at 35.5% but lower maternal mortality (4.3%) rates in women with severe COVID-19 infection (10). Hantoushzadeh et al. (15) reported that 77.77% of pregnant women with critical COVID-19 died. Tunç et al. (16), demonstrated that all maternal deaths from COVID-19 infection involved reported symptoms of shortness of breath and cough upon initial hospital admission. The risk of maternal death was 1.27 times higher in the symptomatic group in our cohort. Pregnancy adversely affects COVID-19 progression, maternal ICU requirement and maternal mortality rates increase compared to non-pregnant women (17).

In symptomatic women, COVID-19 pneumonia findings detected by radiological methods were more prevalent than in the asymptomatic group (p<0.001) and were present in 78

(94%) of the pregnant women in the symptomatic group with LUS examination before delivery. The finding of COVID-19 pneumonia was confirmed in all women in the symptomatic group with thorax CT after delivery. The diagnostic efficacy of LUS in detecting radiological manifestations of COVID-19 pneumonia appears to be comparable to that of thoracic CT. Lu et al. (18) reported that the sensitivity of LUS was higher in severe disease. In the study by Karacaer et al. (19), the detection rates for confirmed COVID-19 cases were similar at 74% for thoracic CT and 70% for LUS. We performed LUS on admission in all patients because LUS is easy to apply, does not contain radiation, and allows us to obtain radiological findings at the beginning of the hospitalization. The LUS findings were evaluated without the need for a radiologist. Moreover, the treatment of patients with suspicious LUS findings was started at an early stage of admission.

When we examined the laboratory parameters of the pregnant women, leukocytosis, lymphopenia, and elevated CRP were prevalent in the symptomatic group ($p<0.001$). In the study of Grgić et al. (20), lymphocyte levels were lower and leukocyte and CRP values were higher in symptomatic women. London et al. (21) found lower lymphocyte levels in the symptomatic group. In the study of Grechukhina et al. (22), CRP values were found to be useful parameters in predicting the severity of the disease at the time of admission to the hospital. The coronavirus viral genome and antigenic determinants damage the lymphocyte cell skeleton, leading to disintegration. Infection-induced factors, such as soluble Fas Ligand and vascular cell adhesion molecule-1 and the occurrence of cytokine storm exacerbate lymphopenia by inducing programmed death in lymphocytes. In cases of severe pneumonia, lymphocyte counts decrease even further (23). CRP, an acute-phase reactant, serves as a reliable and well-known biomarker of inflammation. It is typically unmeasureable in healthy individuals, with levels rising in response to viral or bacterial infections, concurrently with leukocytes, as part of the reaction of the immune system to inflammatory stimuli (24).

In the present study, prenatal hemoglobin values were significantly lower in the symptomatic group. A meta-analysis conducted by Taneri et al. (25) also found that hemoglobin levels were lower in patients with severe COVID-19 compared to those with moderate severity. Moreover, it has been observed that clinical conditions necessitating intensive care admission due to COVID-19 are associated with even lower hemoglobin levels (25). The mechanism explaining the association between low hemoglobin and COVID-19 infection focuses on iron metabolism and compromised iron utilization in the body. The increased viral load in COVID-19 prevents iron use in erythrocyte biochemical pathways. In addition, iron is crucial for viral particle biogenesis and virus replication. While the host's natural immunity attempts to restrict the virus from using iron, it can exacerbate the anemia (26). Consequently, hemoglobin levels tend to decrease during viral infections.

There were elevated levels of ALT, AST, BUN, and CR in symptomatic women. Severe COVID-19 is known to increase liver and kidney function biomarkers due to multiple organ involvement. The involvement of these organs is linked to the expression of the angiotensin-converting enzyme 2 (ACE2) receptor. The ACE2 receptor facilitates the entry of SARS-CoV-2 into cells, and its presence in the liver and kidneys leads to viral uptake and organ damage (27). Enzymes surge due to organ damage, and their elevation correlates with the severity of COVID-19. A study, excluding chronic liver patients, demonstrated that liver damage intensifies with the severity of COVID-19 and the emergence of the need for intensive care (28).

In the present study, newborns born to the symptomatic group of women had lower birth weight, length and HC. Jenabi et al. (29) also showed the number of low birth weight newborns to be higher in the symptomatic group. The higher rates of preterm birth in the symptomatic group resulted in lower neonatal anthropometric measurements. Furthermore, NICU requirement was higher in the symptomatic group. In the study conducted by Çelik et al. (30), it was reported that the risk of low birth weight, NICU admission, and prematurity increased in babies of mothers with severe COVID-19. In the present study the risk of NICU admission was 4.81 times higher in the symptomatic group. We also believe that the adverse in-utero environment in symptomatic pregnant women with COVID-19 and iatrogenic preterm births contribute to increased NICU rates (31).

COVID-19 was detected in two (1.2%) newborns in the asymptomatic group of our cohort. No infected newborns were detected in the symptomatic group. Two tests were performed to detect SARS-CoV-2 transmission to newborns in the hospital. The first test was done in the first hour after birth, and the second test was performed 24 hours after birth using the nasopharyngeal swab RT-PCR method. The overall congenital infection rate was 0.81% (n=2). In a systematic review by Allotey et al. (32), the rate of congenital infection was <2%. Vertical transmission was detected at a rate of 1.8% (33). In addition, we think that SARS-CoV-2 is transmitted to the newborn by the fecal-oral route during delivery, droplets during breastfeeding, and may be of nosocomial origin too.

Study limitations

We did not follow up involved women after discharge to monitor possible long-term adverse outcomes. We did not obtain data on the coronavirus variant types and vaccination status of all women. However, we did distinguished between iatrogenic and spontaneous preterm births and found that

symptomatic COVID-19 infection did not affect the spontaneous preterm birth rate, but increased the iatrogenic preterm birth rate.

Conclusion

The severity of COVID-19 increased with age. Iatrogenic preterm births and cesarean sections were more common in symptomatic COVID-19 patients because maternal general condition disorder was more prevalent. NICU admission, maternal ICU admission, and maternal mortality rates were higher amongst women with symptomatic COVID-19 infection. We recommend that clinical follow-up is important and closer follow-up is necessary in these women.

Ethics Committee Approval: *The University of Health Sciences Turkey, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Institutional Ethics Committee approval was granted (approval number: 165, date: 14.12.2022).*

Informed Consent: *Retrospective study.*

Author Contributions: *Surgical and Medical Practices: O.A., B.G., N.T.; Concept: O.A.; Design: O.A., B.G., N.T.; Data Collection or Processing: O.A.; Analysis or Interpretation: O.A., B.G., N.T.; Literature Search: O.A.; Writing: O.A.*

Conflict of Interest: *No conflict of interest is declared by the authors.*

Financial Disclosure: *The authors declared that this study received no financial support.*

References

1. Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol 2021; 19: 141-54.
2. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol 2020; 5: 536-44.
3. Ortiz-Prado E, Simbaña-Rivera K, Gómez-Barreno L, Rubio-Neira M, Guaman LP, Kyriakidis NC, et al. Clinical, molecular, and epidemiological characterization of the SARS-CoV-2 virus and the Coronavirus Disease 2019 (COVID-19), a comprehensive literature review. Diagn Microbiol Infect Dis 2020; 98: 115094.
4. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al.; for PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020; 370: m3320.
5. Ministry of Health of the Republic of Türkiye (2023). COVID 19 information platform [online]. [accessed 20 April 2023]. 2023. Available from: https://covid19.saglik.gov.tr/TR-66494/pandemi.html/
6. Ministry of Health of the Republic of Türkiye (2023). COVID 19 information platform [online]. [accessed 20 April 2023]. 2023. Available from: https://covid19.saglik.gov.tr/
7. Vousden N, Bunch K, Morris E, Simpson N, Gale C, O'Brien P, et al. The incidence, characteristics and outcomes of pregnant women hospitalized with symptomatic and asymptomatic SARS-CoV-2 infection in the UK from march to September 2020: a national cohort study using the UK obstetric surveillance system (UKOSS). PLoS One 2021; 16: e0251123.
8. Minisha F, Farrell T, Abuyaqoub S, Abdel Rahim A, Ahmed H, Omer M, et al. Maternal risk factors of COVID-19-affected pregnancies: A comparative analysis of symptomatic and asymptomatic COVID-19 from the Q-PRECIOUS registry. Qatar Med J 2022; 2022: 52.
9. Davies NG, Klepac P, Liu Y, Prem K, Jit M; CMMID COVID-19 working group; Eggo RM. Age-dependent effects in the transmission and control of COVID-19 epidemics. Nat Med 2020; 26: 1205-11.
10. Maternal - Fetal Medicine and Perinatology Association Türkiye (2021). Opinion of the turkish maternal fetal medicine and perinatology association on covid-19 vaccines in pregnant and breastfeeding mothers [online]. [accessed 29 January 2024]. 2024. Available from: https://www.tmftp.org/files/uzman-gorusleri/gebelerde_covid19_asisi.pdf
11. Khan DSA, Hamid LR, Ali A, Salam RA, Zuberi N, Lassi ZS, et al. Differences in pregnancy and perinatal outcomes among symptomatic versus asymptomatic COVID-19-infected pregnant women: a systematic review and meta-analysis. BMC Pregnancy Childbirth 2021; 21: 801.
12. Sahin D, Tanacan A, Erol SA, Anuk AT, Yetiskin FDY, Keskin HL, et al. Updated experience of a tertiary pandemic center on 533 pregnant women with COVID-19 infection: A prospective cohort study from Turkey. Int J Gynaecol Obstet 2021; 152: 328-34.
13. Metz TD, Clifton RG, Hughes BL, Sandoval G, Saade GR, Grobman WA, et al.; for the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) Maternal-Fetal Medicine Units (MFMU) Network. Disease Severity and Perinatal Outcomes of Pregnant Patients with Coronavirus Disease 2019 (COVID-19). Obstet Gynecol 2021; 137: 571-80.
14. Liu D, Li L, Wu X, Zheng D, Wang J, Yang L, et al. Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: a preliminary analysis. AJR Am J Roentgenol 2020; 215: 127-32.
15. Hantoushzadeh S, Shamshirsaz AA, Aleyasin A, Seferovic MD, Aski SK, Arian SE, et al. Maternal death due to COVID-19. Am J Obstet Gynecol 2020; 223: 109.e1-16.
16. Tunç Ş, Oğlak SC, Göklü MR, Özköse ZG. Maternal mortality cases due to COVID-19 pandemic in a tertiary referral hospital. Perinatal Journal, 2022; 30: 185-94.
17. Zambrano LD, Ellington S, Strid P, Galang RR, Oduyebo T, Tong VT, et al.; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status - United States, January 22-October 3, 2020. MMWR Morb Mortal Wkly Rep 2020; 69: 1641-7.
18. Lu W, Zhang S, Chen B, Chen J, Xian J, Lin Y, et al. A clinical study of noninvasive assessment of lung lesions in patients with coronavirus disease-19 (COVID-19) by bedside ultrasound. Ultraschall Med 2020; 41: 300-7.
19. Karacaer C, Karabay O, Gunduz Y, Yaylacı S, Guclu E. Correlation of Lung Ultrasound and Computed Tomography Findings in COVID-19 Pneumonia. J Coll Physicians Surg Pak 2020; 30: 147-52.
20. Grgić G, Cerovac A, Hudić I, Laganà AS, Favilli A, Garzon S, et al. Clinical Manifestation and Obstetric Outcomes in Pregnant Women

with SARS-CoV-2 Infection at Delivery: A Retrospective Cohort Analysis. J Pers Med 2022; 12: 1480.

21. London V, McLaren R Jr, Atallah F, Cepeda C, McCalla S, Fisher N, et al. The Relationship between Status at Presentation and Outcomes among Pregnant Women with COVID-19. Am J Perinatol 2020; 37: 991-4.
22. Grechukhina O, Greenberg V, Lundsberg LS, Deshmukh U, Cate J, Lipkind HS, et al. Coronavirus disease 2019 pregnancy outcomes in a racially and ethnically diverse population. Am J Obstet Gynecol MFM 2020; 2: 100246.
23. Chan PK, Chen GG. Mechanisms of lymphocyte loss in SARS coronavirus infection. Hong Kong Med J 2008; (14 Suppl 4): 21-6.
24. Chang HL, Chen KT, Lai SK, Kuo HW, Su IJ, Lin RS, et al. Hematological and biochemical factors predicting SARS fatality in Taiwan. J Formos Med Assoc 2006; 105: 439-50.
25. Taneri PE, Gómez-Ochoa SA, Llanaj E, Raguindin PF, Rojas LZ, Roa-Díaz ZM, et al. Anemia and iron metabolism in COVID-19: a systematic review and meta-analysis. Eur J Epidemiol 2020; 35: 763-73.
26. Wessling-Resnick M. Crossing the Iron Gate: Why and How Transferrin Receptors Mediate Viral Entry. Annu Rev Nutr 2018; 38: 431-58.
27. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020; 579: 270-3.
28. Medetalibeyoglu A, Catma Y, Senkal N, Ormeci A, Cavus B, Kose M, et al. The effect of liver test abnormalities on the prognosis of COVID-19. Ann Hepatol 2020; 19: 614-21.
29. Jenabi E, Bashirian S, Khazaei S, Masoumi SZ, Ghelichkhani S, Goodarzi F, et al. Pregnancy outcomes among symptomatic and asymptomatic women infected with COVID-19 in the west of Iran: a case-control study. J Matern Neonatal Med 2022; 35: 4695-7.
30. Celik IH, Tanacan A, Canpolat FE. Neonatal outcomes of maternal prenatal coronavirus infection. Pediatr Res 2024; 95: 445-55.
31. Flaherman VJ, Afshar Y, Boscardin WJ, Keller RL, H Mardy A, Prahl MK, et al. Infant Outcomes Following Maternal Infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2): First Report from the Pregnancy Coronavirus Outcomes Registry (PRIORITY) Study. Clin Infect Dis 2021; 73: e2810-3.
32. Allotey J, Chatterjee S, Kew T, Gaetano A, Stallings E, Fernández-García S, et al.; PregCOV-19 Living Systematic Review Consortium. SARS-CoV-2 positivity in offspring and timing of mother-to-child transmission: living systematic review and meta-analysis. BMJ 2022; 376: e067696.
33. Jeganathan K, Paul AB. Vertical transmission of SARS-CoV-2: A systematic review. Obstet Med 2022; 15: 91-8.