Original Article

Comparison of Maternal, Perinatal, and Neonatal Outcomes of Asymptomatic and Symptomatic Pregnant Women with Coronavirus Disease-2019

Koronavirüs Hastalığı-2019 ile Enfekte Asemptomatik ve Semptomatik Gebe Kadınların Maternal, Perinatal ve Neonatal Sonuçlarının Karşılaştırılması

Tayfun VURAL[1], Burak BAYRAKTAR[1], Suna YILDIRIM KARACA[1], Ozan ODABAS[1], Nisel YILMAZ[2], Pınar SAMLIOGLU[2], Mehmet OZEREN[3]

[1]University of Health Sciences Turkey, Tepecik Training and Research Hospital, Clinic of Obstetrics and Gynecology, Izmir, Turkey
[2]University of Health Sciences Turkey, Tepecik Training and Research Hospital, Clinic of Clinical Microbiology, Izmir, Turkey
[3]University of Health Sciences Turkey, Tepecik Training and Research Hospital, Clinic of Perinatology, Izmir, Turkey

ABSTRACT

Objective: This study aimed to compare the postpartum outcomes of asymptomatic and symptomatic patients with coronavirus disease-2019 (COVID-19).

Methods: This retrospective cohort study included pregnant women with COVID-19. Pregnant women were categorized into two sets as asymptomatic and symptomatic according to their clinics at the time of application. COVID-19 was diagnosed using the real-time reverse transcriptase-polymerase chain reaction on the oropharyngeal and nasopharyngeal swabs. Asymptomatic and symptomatic patients were compared in terms of maternal and perinatal outcomes.

Results: Our study population consisted of 20 asymptomatic and 41 symptomatic patients with laboratory-confirmed COVID-19. The rate of primary cesarean section was more than twice in the symptomatic group (51.2%) than that of the asymptomatic group (20%) (p=0.019). Both groups are quite similar in terms of maternal [respiratory support, COVID-19-related treatment, and intensive care unit (ICU) admission], perinatal (preterm delivery, preterm premature rupture of membrane, preeclampsia, and mode of delivery), and neonatal outcomes [birth weight, Apgar scores, neonatal ICU (NICU) admission]. The rate of total cesarean section in the asymptomatic group (75%) was statistically similar to the symptomatic group (83%) (p=0.464). The NICU admission rate was found to be similar in the asymptomatic (54.2%) and symptomatic groups (50%) (p=0.858). However, NICU admissions were more frequent in the symptomatic group due to respiratory distress (p=0.032). The breastfeeding rate is higher in the asymptomatic pregnant group as expected (p=0.015). Additionally, the ferritin level was significantly lower in the asymptomatic group (p=0.006).

Conclusions: The rate of primary cesarean section is quite high in symptomatic patients with COVID-19. Additionally, the total cesarean section rate was extremely high in both groups. We expected more adverse outcomes in symptomatic patients; however, we found similar maternal, perinatal, and neonatal outcomes between both groups.

Keywords: SARS-CoV-2, asymptomatic infection, coronavirus, COVID-19, pregnancy, vertical transmission

ÖZ

Amaç: Bu çalışmada, koronavirüs hastalığı-2019 (COVID-19) ile enfekte asemptomatik ve semptomatik gebelerin maternal, perinatal ve neonatal sonuçlarının karşılaştırılması amaçlanmıştır.

Yöntemler: Çalışmamız COVID-19 ile enfekte gebelerin değerlendirildiği retrospektif kohort çalışmasıdır. Gebeler hastaneye başvurularında asemptomatik ve semptomatik olarak iki gruba kategorize edildi. COVID-19 tanısı, orofaringeal ve nazofaringeal sürüntülerde gerçek zamanlı revers transkriptaz polimeraz zincir reaksiyonu ile konuldu. Asemptomatik ve semptomatik hastalar maternal ve perinatal sonuçlar açısından karşılaştırıldı.

Bulgular: Toplamda, laboratuvar tarafından tanısı doğrulanmış 20 asemptomatik ve 41 semptomatik gebe vardı. Primer sezaryen oranı semptomatik grupta (%51,2) asemptomatik grubun (%20) iki katından fazlaydı (p=0,019). Her iki grup maternal [solunum desteği, COVID-19 ile ilgili tedavi, yoğun bakım ünitesine (YBÜ) yatış], perinatal (preterm doğum, preterm prematür erken membran rüptürü, preeklampsi, doğum şekli) ve yenidoğan sonuçları [doğum ağırlığı, Apgar skorları, yenidoğan YBÜ'ye (YYBÜ) yatış] açısından oldukça benzerdi. Asemptomatik grupta total sezaryen oranı (%75), semptomatik grupla (%83) istatistiksel olarak benzerdi (p=0,464). Asemptomatik grup (%54,2) ve semptomatik grup (%50) arasında YYBÜ'ye yatış oranları benzer izlendi (p=0,858). Ancak solunum sıkıntısı nedeniyle YYBÜ'ye yatış semptomatik grupta daha sık izlendi (p=0,032). Emzirme oranı asemptomatik gebelerde beklendiği gibi daha yüksek izlendi (p=0,015). Asemptomatik grupta ferritin düzeyi anlamlı olarak daha düşük izlendi (p=0,006).

Sonuçlar: Bu çalışmada COVID-19 ile enfekte semptomatik gebelerde primer sezaryen oranının oldukça yüksek olduğu bulunmuştur. Ayrıca toplam sezaryen oranı her iki grupta da son derece yüksekti. Çalışmada semptomatik hastalarda daha olumsuz sonuçlar beklememize rağmen, her iki grup arasında benzer maternal, perinatal ve neonatal sonuçlar izledik.

Anahtar kelimeler: SARS-CoV-2, asemptomatik enfeksiyon, koronavirüs, COVID-19, gebelik, vertikal geçiş

INTRODUCTION

Coronavirus disease-2019 (COVID-19) is an infectious disease that is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which can be transmitted to humans and cause a pandemic. The pandemic, which resulted in the death of many people globally, caused radical changes in health systems, socio-economic life, and the psychology of individuals and the environment. These changes may continue for a long time after the pandemic[1]. Despite the efforts to rapidly implement the COVID-19 vaccine in many countries worldwide, including Turkey, the third wave of the pandemic occurred[2-5].

New information about COVID-19 is being learned every day. COVID-19 is known as a respiratory tract infection with multi-organ involvement[6] and its severity ranges from asymptomatic to fatal[7]. COVID-19- related knowledge in pregnancy and its impact on perinatal outcomes is limited[8-10]. Initially, SARS-CoV-2 was thought to cause mostly mild to moderate symptoms or rarely severe symptoms. However, subsequent studies showed asymptomatic cases, which are equally important in the spread of the disease. To date, fetal and early neonatal outcomes of asymptomatic women with COVID-19 remain controversial[11-14].

Recently, seven different studies have shown a generally little or no difference in viral load between asymptomatic and symptomatic patients[15-21]. Additionally, asymptomatic groups tend to have a longer period of viral transmission than symptomatic groups[22]. Information about disease progression in pregnant women with asymptomatic COVID-19 is limited[11]. Thus, understanding the clinical importance of asymptomatic pregnant women with positive SARS-CoV-2 may lead to favorable outcomes in their follow-up.

Considering that asymptomatic patients with SARS-CoV-2 in Turkey may not seek medical care during their pregnancy, calculating the exact incidence of asymptomatic pregnant women would be difficult. Up to 14% of women who came for delivery were found to be positive for asymptomatic COVID-19[11-13]. Thus, this study aimed to investigate the postpartum outcomes of asymptomatic patients with SARS-CoV-2.

MATERIALS and METHODS

This retrospective cohort study evaluated pregnant women with COVID-19 diagnosis who were admitted to the University of Health Sciences Turkey, Tepecik Training and Research Hospital, Izmir, Turkey with obstetric complaints between March 30, 2020, and February 28, 2021.

The research was approved by the University of Health Sciences Turkey, Tepecik Training and Research Hospital Ethics Committee (decision no: 2021/03-39, date: 24.03.2021). Our study approval was obtained from the Turkish Ministry of Health (approval number: T19-04-31). The study complies with the 1964 Declaration of Helsinki. Written consent for data use was routinely obtained from all participants at admission.

This study is conducted in a tertiary pandemic hospital in Turkey. A separate delivery room, operating room, and service have been established for diagnosed or suspected cases of COVID-19. The personnel of these departments works in shifts with their personal protective equipment (PPE) only in their relevant departments. Some of the pregnant women with suspected COVID-19 were referred from surrounding hospitals, whereas others directly sought care at our hospital. Patients were quarantined in their isolated rooms. All participants were diagnosed with COVID-19 in our hospital, where all gave birth. No pregnant women were vaccinated during this study period.

COVID-19 was diagnosed using the real-time reverse transcriptase-polymerase chain reaction (rRT-PCR). The specimens were collected from the oropharyngeal and nasopharyngeal swabs. Swab samples were collected by trained personnel who wear appropriate PPE according to current guidelines. Swabs are transported to the microbiology laboratory in transfer tubes containing vNAT (viral nucleic acid buffer, Bio-speedy®, Bioexen LTD, Turkey) for processing within a few hours. All samples were run in biosafety level-2 facilities with full PPE. Viral RNA was detected using the Bio-speedy® COVID-19 qPCR kit (Bioexen LTD). One positive and one negative control were added to each run to ensure an accurate result. A cycle threshold value of <40 was considered as a positive result, with 99.4% sensitivity and 99.0% specificity. The rRT-PCR test was also performed in all asymptomatic cases with a history of suspected contact or travel.

Symptomatic patients present with one or more signs or symptoms (rhinorrhea, sore throat, myalgia or fatigue, cough, shortness of breath, fever, nausea/vomiting, headache, decreased taste, decreased odor, and diarrhea) at admission, whereas asymptomatic women have no signs or symptoms at presentation[23]. Follow-ups were conducted by phone for all pregnant women for 2 weeks postpartum to detect symptomatic infections. All neonates were tested for SARS-CoV-2 via rRT-PCR at 24 h of life. Neonatal events were recorded until 2 weeks postpartum. Comparisons were conducted on the two COVID-19 positive groups: one group with

COVID-19-related symptoms (n=41) and the other were asymptomatic (n=20). All symptomatic patients had clinically mild diseases (cough, fever, flu-like symptoms, minimal dyspnea, and O_2 saturation of >95% on room air) in the whole course.

All clinical and laboratory findings of patients were obtained from the hospital computer system. The patients' blood tests and PCR tests were simultaneously studied. Maternal age, gravity, parity, comorbidity, delivery mode and indications, COVID-19-related symptoms, complete blood count, and biochemical values were evaluated. Lymphopenia refers to decreased peripheral blood lymphocytes, which generally corresponds to <1,000 lymphocytes/microL in adults. Disease progression to severe COVID-19, respiratory support, COVID-19 treatment, and intensive care unit (ICU) admission were considered maternal outcomes. Nasal cannula, face mask, or mechanical ventilation was utilized as respiratory supports. Hydroxychloroquine, azithromycin, or other antiviral drugs (e.g., remdesivir) were used to treat COVID-19. Perinatal outcomes included gestational age at delivery, mode of delivery, preterm premature rupture of membrane (PPROM), preeclampsia (PE), and fetal growth retardation. Birth weight, Apgar score, and neonatal ICU (NICU) admission were evaluated as neonatal outcomes.

Definitions Used in This Study

PE was defined as proteinuria or end-organ dysfunction along with new-onset hypertension after 20 weeks of gestation in a formerly normotensive woman[24]. Gestational hypertension is the absence of proteinuria or coexistence of end-organ damage with new-onset hypertension at ≥20th week of pregnancy[24]. Gestational diabetes mellitus was diagnosed by comparing the two abnormal values on the 100 g oral glucose tolerance test in patients with abnormal results (≥140 mg/dL) on 50-g oral glucose load. Preterm delivery is birth at <37 weeks of gestation. PPROM is a rupture of membranes at <37 weeks of gestation. Low birth weight (LBW) is ≤2,500 g, whereas small for gestational age (SGA) is a birth weight below 10th percentile according to gestational age. Fetal or intrauterine growth restriction (FGR/IUGR) is defined as an estimated fetal weight at <10th percentile. An increased fever was defined as a body temperature of ≥38 °C.

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) v26.0 (IBM® SPSS® Statistics, New York, US) package program was used for the analysis and arrangement of tables[25]. Descriptive data were given as a number (n), percentage mean and stand deviation [mean ± standard deviation (SD)], and median [minimum (min) and maximum (max)]. The normality of the distributions was evaluated with the Shapiro-Wilk test and histogram graphs. The Student's t-test was used for the variables in which the parametric test conditions were met and data were presented as mean ± SD. The Mann-Whitney U test was used when the parametric test conditions were not met and the data were presented as median (min, max). Categorical variables were compared using the chi-square test. P-values of <0.05 were accepted as statistical significance.

RESULTS

This study compared 20 asymptomatic SARS-CoV-2-positive pregnant women with 41 symptomatic SARS-CoV-2-positive pregnant women. All participants were diagnosed with COVID-19 and were in the third trimester. Asymptomatic and symptomatic groups were mainly nulliparous (65% and 73.2%, respectively; p=0.511). The asymptomatic group was older than the symptomatic group (p=0.042). The median gestational weeks at diagnosis was 34.4±6.9 in asymptomatic pregnant women and 33.4±7.1 in symptomatic women, with no statistical difference between them. No differences were found in maternal comorbidity or obstetric history between asymptomatic and symptomatic women. The time between COVID-19 diagnosis of and delivery was similar for both groups, as was the hospital stay duration (Table 1).

The most common symptoms in symptomatic pregnant women were fatigue (78%), myalgia (76%), sore throat (56%), cough (54%), and fever (41%) (Table 2).

Asymptomatic and symptomatic pregnant women were compared in terms of maternal, perinatal, and neonatal outcomes. This study revealed a statistically similar total rate of cesarean section in the asymptomatic (75%) and symptomatic group (83%) (p=0.464). However, the rate of primary cesarean section in symptomatic women (51.2%) was more than twice the rate of the asymptomatic group (20%) (p=0.019). The rate of preterm birth was higher in asymptomatic women (15%) than in symptomatic women (7.3%); however, these differences were not statistically significant (p=0.344). Similarly, the rate of LBW was higher in the asymptomatic pregnant participants (14.3%) than those symptomatic (2.4%) but differences were not statistically significant (p=0.067).

Table 1. Baseline characteristics of the study population with SARS-CoV-2 infection.			
	Asymptomatic group n=20	Symptomatic group (mild diseases) n=41	p-value
Maternal age (year) (mean ± SD)	31±5.1	27±4.7	0.042
Gravity median (min, max)	3 (1-10)	1 (1-7)	0.053
Parity (n, %)	-	-	0.511
Nulliparous	13 (65%)	30 (73.2%)	-
Multiparous	7 (35%)	11 (26.8%)	-
Multiple gestation prevalence (n, %)	1 (5%)	1 (2.4%)	0.598
PCR positive week of pregnancy (week) (mean ± SD)	34.4±6.9	33.4±7.1	0.614
Travel history (n, %)	0	0	N/A
Maternal comorbidity (n, %)			
Obesity (BMI of ≥30.0 kg/m²)	2 (10%)	1 (2.4%)	0.199
Asthma	0	1 (2.4%)	0.481
Other chronic lung diseases	0	0	N/A
Chronic cardiac diseases	0	1 (2.4%)	0.481
Pregestational diabetes mellitus	0	1 (2.4%)	0.481
Pregestational hypertension	0	0	N/A
Thrombophilia	0	0	N/A
Hypothyroidism	1 (5%)	3 (7.32%)	0.731
Other thyroid diseases	0	0	N/A
Smoking (n, %)	0	0	N/A
Assisted reproductive techniques (n, %)	0	0	N/A
Obstetric history (n, %)			
Previous gestational diabetes mellitus	2 (10%)	1 (2.4%)	0.199
Previous gestational hypertension	0	0	N/A
Previous preeclampsia	0	0	N/A
Previous fetal growth retardation	1 (5%)	0	0.148
Interval between COVID-19 positivity and birth (day) (mean ± SD)	28.6±46.1	39.1±49	0.425
Hospitalization duration (day) (mean ± SD)	2.8±1.1	3.2±2	0.385
Oxygen saturation (mean ± SD)	97.7±0.51	97.2±0.53	0.820
Systolic blood pressure (mmHg) (mean ± SD)	121±12	118±15	0.670
Diastolic blood pressure (mmHg) (mean ± SD)	82±11	84±12	0.630
Fever (°C) (mean ± SD)	36.4±0.26	36.5±0.26	0.960
Respiratory rate median (min-max)	19 (18-20)	19 (17-22)	0.770

PCR: Polymerase chain reaction, SD: Standard deviation, COVID-19: Coronavirus disease-2019, SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2, min: Minimum, max: Maximum, BMI: Body mass index

Table 2. Distribution of symptoms.		
Symptomatic group (mild diseases) n=41	**n**	**%**
Fever of ≥38 °C	17	41%
Cough	22	54%
Shortness of breath	5	12%
Fatigue	32	78%
Muscle or body aches	31	76%
New loss of smell	9	22%
New loss of taste	8	20%
Sore throat	23	56%
Chest pain	1	2%
Nausea and/or vomiting	2	5%
Diarrhea	4	10%

Respiratory support was not required in either group except for one symptomatic patient. In this patient, only a nasal cannula was used as respiratory support. Intubation was not required in any of the patients in either the asymptomatic or symptomatic group (Table 3).

Perinatal and neonatal outcomes did not differ between the two groups. Both groups were statistically similar in terms of pregnancy complications, stillbirth, birth weight, Apgar score, and NICU admission. NICU admission rates were determined as 54.2% in the asymptomatic group and 50% in the symptomatic group (Table 3).

Table 3. Maternal, perinatal, and neonatal outcomes of the study population.			
	Asymptomatic group n=20	Symptomatic group (mild diseases) n=41	p-value
Gestational age at delivery (week) (mean ± SD)	38.4±1.4	38.5±1.5	0.724
Preterm delivery prevalence (<37 weeks) (n, %)	3 (15%)	3 (7.3%)	0.344
Threatened abortion (n, %)	3 (15%)	4 (9.8%)	0.546
PPROM (n, %)	0	0	N/A
Stillbirth* (n, %)	0[a]	0[b]	N/A
Fetal growth retardation* (n, %)	0[a]	0[b]	N/A
Fetal congenital anomaly* (n, %)	0[a]	0[b]	N/A
Pregnancy complications (n, %)			
Gestational hypertension	1 (5%)	2 (4.9%)	0.983
Preeclampsia	0	1 (2.4%)	0.481
Gestational diabetes	2 (10%)	3 (7.3%)	0.719
Intrahepatic cholestasis of pregnancy	1 (5%)	2 (4.9%)	0.983
Onset of labor (n, %)			
Elective cesarean section	14 (70%)	29 (70.7%)	0.953
Spontaneous	3 (15%)	5 (12.2%)	0.760
Induced	3 (15%)	7 (17.1%)	0.837
Delivery type (n, %)			0.464
Vaginal delivery	5 (25%)	7 (17.1%)	
Cesarean section	15 (75%)	34 (82.9%)	
Primary C-section prevalence	4 (20%)	21 (51.2%)	0.019
Gender* (n, %)	[a]	[b]	0.592
Male prevalence	12 (57.1%)	21 (50%)	
Female prevalence	9 (42.9%)	21 (50%)	
Birth weight* (g) (mean ± SD)	3150.3±518	3268.5±470.4	0.398
LBW* (<2,500 g) (n, %)	3[a] (14.3%)	1[b] (2.4%)	0.067
Apgar score* (n, %)	[a]	[b]	
<7 at 1st minute	2 (9.5%)	7 (16.7%)	0.445
<7 at 5th minute	1 (4.8%)	1 (2.4%)	0.611
NICU hospitalization* (n, %)	11[a] (52.4%)	21[b] (50%)	0.858
Cause of NICU admission*,c (n, %)	[a]	[b]	
Prematurity	1 (4.8%)	1 (2.4%)	0.611
Respiratory distress	6 (28.6%)	14 (33.3%)	0.032
COVID-19 protocol	10 (47.7%)	13 (31%)	0.250
Other	0	1 (2.4%)	0.476
Days in NICU* (mean ± SD)	2.4±1.4	2.8±1.5	0.424
Perinatal mortality* (n, %)	0[a]	0[b]	N/A
Maternal mortality (n, %)	0	0	N/A
Maternal breastfeeding (n, %)	20 (100%)	31 (75.6%)	0.015
Neonatal PCR positivity* (n, %)	1[a] (4.8%)	0[b]	0.154
Maternal intensive care unit admission (n, %)	0	0	N/A

Table 3 continued			
	Asymptomatic group n=20	Symptomatic group (mild diseases) n=41	p-value
Respiratory support (n, %)			
Nasal cannula	0	1 (2.4%)	0.481
Breathing mask	0	0	N/A
Intubation	0	0	N/A
COVID-19 treatment (n, %)			
Hydroxychloroquine	0	1 (2.4%)	0.481
Azithromycin	0	0	N/A
Remdesivir/other antivirals	1 (5%)	1 (2.4%)	0.598
Low molecular weight heparin	4 (20%)	10 (24.4%)	0.701
Bronchodilator	0	1 (2.4%)	0.481

*63 fetuses, [a]21 fetuses, [b]42 fetuses, [c]Each fetus may receive more than one diagnosis, CPD: Cephalopelvic disproportion, PPROM: Preterm premature rupture of membrane, LBW: Low birth weight, NICU: Neonatal intensive care unit, PCR: Polymerase chain reaction, COVID-19: Coronavirus disease-2019

No difference was detected in the COVID-19 treatment between the two groups. Hydroxychloroquine, azithromycin, or antiviral agents were not used by either group except for one symptomatic case, in which hydroxychloroquine was administered. Low molecular weight heparin was used in up to a quarter of cases in both groups. No ICU admissions were recorded from either group, as well as maternal deaths. The breastfeeding rate was higher in asymptomatic pregnant women as expected (p=0.015). Additionally, NICU admissions were more frequent in the symptomatic group due to respiratory distress (p=0.032). Within the first 24 h of life, 63 infants were tested with a nasopharyngeal swab, which revealed a positive COVID-19 test in only 1 newborn (from the asymptomatic group). All others were negative for COVID-19 (Table 3).

The laboratory findings for both the asymptomatic and symptomatic groups are compared in Table 4. Ferritin was significantly lower in the asymptomatic group (p=0.006). No significant differences were found between the groups in point of C-reactive protein (CRP) levels, lymphocyte counts, lymphopenia rates, platelet counts, D-dimer levels, and aspartate transaminase (AST)/alanine aminotransferase (ALT) ratios.

DISCUSSION

The principal study results revealed that the rate of primary cesarean section in the symptomatic group is twice more than that of the asymptomatic group. A second finding was that both groups were quite similar in terms of maternal, perinatal, and neonatal outcomes. Third, the total rates of cesarean section and preterm delivery were not statistically different in both groups.

Fourth, the symptoms of asymptomatic patients did not progress, and they remained asymptomatic. Fifth, the clinical course and laboratory values of the asymptomatic and symptomatic groups were quite similar. And finally, the third trimester seemed to be the most vulnerable period to infection.

This study revealed that cesarean section rates were similar between the asymptomatic and symptomatic women. Similarly, London et al.[11] revealed that cesarean section rates were not statistically different in both groups, although its rate in symptomatic patients (45.8%) was higher than that of asymptomatic patients (27.3%). Jenabi et al.[26] revealed that the rate of cesarean section in symptomatic patients was more than four times higher than in asymptomatic patients. However, the present study revealed that the rate of primary cesarean section was more than two times higher in symptomatic women (51.2%) than in asymptomatic women (20%). A systematic review by Turan et al.[27] reported that the total cesarean rate was 84.1% and the vaginal delivery rate was 15.9% in patients with COVID-19. Other articles revealed that the cesarean section rate in patients with SARS-CoV-2 was 58.5%, 65%, 66.4%, 71.2%, and 92%, respectively[28-32]. Consistent with the literature, the rate of cesarean section in the present study was 80.3% with a 19.7% rate of vaginal delivery. Extremely high cesarean rates in patients with COVID-19 may be mainly due to concerns about perinatal transmission or contagion to healthcare workers as well as obstetric indications. Additionally, Turan et al.[27] reported that this high cesarean section rate may be iatrogenic.

Table 4. Laboratory findings.

	Asymptomatic group n=20	Symptomatic group n=41	p-value
Lymphocyte (*10^3/mm^3) (mean ± SD) (min-max)	1,524±689 (500-2,600)	1,508±699 (500-3,400)	0.938
Lymphopenia <1000 (*10^3/mm^3) (n, %)	4 (20%)	7 (17.1%)	0.780
AST (U/L) (mean ± SD) (min-max)	18.93±9.56 (9-46)	19.36±8.91 (10-48)	0.713
ALT (U/L) (mean ± SD) (min-max)	16.94±10.66 (5-60)	17.17±11.43 (7-49)	0.680
AST/ALT ratio (mean ± SD)	1.28±0.49	1.32±0.61	0.813
Platelet (*10^3/mm^3) (mean ± SD) (min-max)	217,000±98,944 (99,000-370,000)	216,000±64,677 (114,000-380,000)	0.965
CRP (mg/L) (mean ± SD) (min-max)	7.46±4.89 (1-60)	13.25±17.12 (1-100)	0.299
Ferritin (ng/mL) (mean ± SD) (min-max)	17.53±10.26 (1-85)	34.94±26.22 (6-115)	0.006
D-dimer (ug/L) (mean ± SD) (min-max)	2862.7±2510.2 (454-10,670)	2484.4±2470.7 (220-12,790)	0.620

AST: Aspartate transaminase, ALT: Alanine transaminase, CRP: C-reactive protein, SD: Standard deviation, min: Minimum, max: Maximum

Follow-ups were conducted for all patients in the study by phone for 2 weeks postpartum to detect symptomatic infections. None of the asymptomatic patients developed symptoms. Similarly, the literature reported that most asymptomatic patients remain asymptomatic[11,12,14,28]. This result is likely related to the ages of the pregnant women in our cohort. However, another study showed that 89% of asymptomatic elderly people with COVID-19 living in nursing homes developed symptoms[15]. Turan et al.[27] reported that approximately 3% of all mild diseases progress to severe or critical infections. The present study revealed that none of the asymptomatic patients became clinically severe.

Data from population-based studies and case series suggest that COVID-19 infection in pregnancy is mostly asymptomatic or mild, as in non-pregnant women[12-14, 29-34]. Similarly, in our study group, all symptomatic patients had clinically mild diseases (cough, fever, flu-like symptoms, minimal dyspnea, and O$_2$ saturation of >95% on room air) in the whole course.

The rate of preterm delivery was higher in asymptomatic women than those symptomatic (15% vs. 7.3%); however, this variation was statistically insignificant (p>0.05). Similarly, Berry et al.[28] reported no statistical difference between the asymptomatic and symptomatic groups in terms of preterm delivery (11.9% vs. 20%). The rate of preterm birth (12.6%) in hospital admissions of patients with SARS-CoV-2 was higher than the United States average (10%) in 2018[35]. Delahoy et al.[23] revealed that preterm birth occurred nearly three times more often in symptomatic patients than in those asymptomatic (23.1% vs. 8%). Additionally, London et al.[11] found that the rate

of preterm delivery was higher in symptomatic patients than in those asymptomatic (27.3% vs. 0%).

To the best of our knowledge, only one research has compared symptomatic and asymptomatic groups in terms of LBW. Jenabi et al.[26] reported that the rate of LBW was significantly higher in the symptomatic group. Contrarily, the present study revealed that the rates of LBW were higher in asymptomatic women than those symptomatic (14.3% vs. 2.4%) but were not statistically significant.

The literature has been reported that the clinical course of COVID-19 infection is more severe and maternal and perinatal outcomes are more adverse in symptomatic pregnant women. Delahoy et al.[23] reported that the disease progressed more seriously in symptomatic pregnant women with 16.2% being admitted to the ICU, 8.5% needing mechanical ventilation, and 1% dying due to the disease. Additionally, among the asymptomatic patients, only 1 was admitted to the ICU, none required mechanical ventilation, and death was not observed. London et al.[11] reported that pregnant women with COVID-19 symptoms on admission had a higher rate of severe illness than those asymptomatic. The present study revealed no statistical difference between the symptomatic and asymptomatic groups in terms of the clinical course of COVID-19 (ICU admission, need for intubation, and maternal death). No severe diseases were observed in any of the symptomatic pregnant women on admission and the whole course.

Additionally, ferritin levels were significantly higher in the symptomatic group but no significant differences

between the groups in terms of CRP levels, lymphocyte counts, lymphopenia rates, platelet counts, D-dimer levels, and AST/ALT ratios. Some studies suggested that ferritin, CRP, and lymphocyte levels may be markers for COVID-19 severity[36-38]. However, similar to our study, other research suggests that lymphopenia rates, platelet counts, D-dimer levels, and AST/ALT ratios were similar between the symptomatic and asymptomatic groups[39-42]. The differences between these studies may be due to many factors such as genetics, comorbid diseases, and environmental factors. Additionally, our cohort was pregnant, and during pregnancy, many physiological changes occur in the respiratory, circulatory, and immunological systems.

The literature reported that approximately 14% of women who are admitted to the delivery room are asymptomatic with COVID-19, without difference in viral burden between asymptomatic and symptomatic patients, and with longer viral transmission period of asymptomatic. COVID-19 screening in all women hospitalization for delivery is essential for detecting asymptomatic patients and the protection of healthcare personnel[11-13, 15,21,22].

The mother-to-child intrauterine transmission of SARS-CoV-2 has not yet been demonstrated[39]. Recent studies reported that SARS-CoV-2 was not detected in throat swab, breast milk samples, cord blood, and amniotic fluid, and no evidence was found for mother-to-infant transmission[32,43,44]. Studies of 38 Chinese patients infected with SARS-CoV-2 did not show mother-to-infant transmission[43-46]. Additionally, some studies demonstrated the vertical SARS-CoV-2 transmission[47-50]. This study tested 63 newborns for nasopharyngeal swabs in the first 24 hours of life. A positive PCR test was detected in only 1 newborn (from the asymptomatic group) out of the 63 newborns. More research is needed to fully uncover the mother-to-child intrauterine transmission of SARS-CoV-2.

Study Limitations

This study has two main limitations. The sample size of this study was small. Further research with larger sample sizes is needed as not all confounders can be controlled. Additionally, COVID-19 prevalence in asymptomatic pregnant women admitted to the hospital was impossible as universal screening is not performed in the delivery room. However, in the literature, nearly 14% of patients were asymptomatic with COVID-19 when hospitalized for delivery[11-13]. This study is one of the few studies in the literature that investigated the postpartum outcomes of asymptomatic COVID-19 infection.

CONCLUSIONS

The rate of primary cesarean section was quite high in symptomatic pregnant women with COVID-19. Additionally, the total cesarean section rate was extremely high in both groups. Obstetricians can reduce the iatrogenic cesarean sections with obstetric interventions in the management of pregnant women with COVID-19. More adverse outcomes were expected in symptomatic patients, and similar maternal, perinatal, and neonatal outcomes were seen in both groups. Pregnant women who presented without symptoms tended to remain asymptomatic. Insufficient universal COVID-19 testing means that most cases go undetected. SARS-CoV-2 screening is required from all pregnant women who apply for delivery to protect the healthcare workers and identify asymptomatic patients.

Ethics

Author Contributions

Concept: T.V., B.B., Design: T.V., B.B., Data Collection and/or Processing: T.V., B.B., S.Y.K., O.O., N.Y., P.S., M.O., Analysis and/or Interpretation: T.V., B.B., S.Y.K., O.O., N.Y., P.S., M.O., Critical Revision: T.V., B.B., S.Y.K., O.O., N.Y., P.S., M.O., Writing: T.V., B.B., S.Y.K., O.O., N.Y., P.S., M.O.

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