



Treatment and outcome of pregnant women with COVID-19: a single-center descriptive study

Liječenje i ishod trudnoća kompliciranih infekcijom COVID-19: deskriptivna studija jednog centra

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Descriptors

COVID-19; PREGNANCY; DESCRIPTIVE STUDY; CT SCORE; ANESTHESIA

Deskriptori

COVID-19; TRUDNOĆA; DESKRIPTIVNA STUDIJA; CT REZULTAT; ANESTEZIJA

SUMMARY. This study aims to describe the clinical characteristics, radiological and laboratory results, therapy and outcome of pregnancies complicated by COVID-19 infection. *Methodology.* A retrospective descriptive study included all pregnant women with COVID-19 who gave birth in our hospital from April 2020 to January 2022. Exclusion criteria were: incomplete or unclear medical documentation, suspected COVID-19 infection without confirmation by PCR or rapid Ag test, previously diagnosed autoimmune diseases, positive history of malignant diseases, and started oxygen support in another institution before admission to our hospital. *Results.* Our study included 186 pregnant women who gave birth at KBC "Dr. Dragiša Mišović – Dedinje" in the mentioned period. Of these, 69 had no symptoms of COVID-19 infection, and 67 developed a milder clinical picture. In comparison, 41 pregnant women were diagnosed with bilateral pneumonia. A total of 38 pregnant women were admitted to the intensive care unit, of which 32 pregnant women needed oxygen support, 20 pregnant women were on an oxygen mask, 2 of them on a high-flow nasal canal, four pregnant women on non-invasive mechanical ventilation and six pregnant women on invasive mechanical ventilation. Of the total number of patients, 111 had a natural vaginal delivery, while 75 underwent cesarean section. Of 111 pregnant women who had a vaginal delivery, 92 (83%) received epidural analgesia, while 19 (17%) did not. Among pregnant women undergoing cesarean section, nine pregnant women (12%) received epidural anesthesia, 51 of them (68) received spinal anesthesia, while a cesarean section in 15 pregnant women (20%) was performed under general balanced anesthesia. Of 186 hospitalized and delivered pregnant women, 183 (98.4%) were discharged home in good general condition, while three (1.6%) had a fatal outcome. *Conclusion.* The clinical manifestations of pregnant women suffering from COVID-19 infection corresponded to the symptoms of the general population to the greatest extent. In contrast, the excessive use of antibiotics, even for asymptomatic patients, is very worrying.

SAŽETAK. Ovo istraživanje ima za cilj opisati kliničke karakteristike, radiološke i laboratorijske nalaze, terapiju i ishod trudnoća kompliciranih infekcijom COVID-19. *Metodologija.* Retrospektivna deskriptivna studija obuhvatila je sve trudnice s COVID-19 koje su rodile u našoj bolnici od travnja 2020. do siječnja 2022. Kriteriji za isključenje bili su: nepotpuna ili nejasna medicinska dokumentacija, sumnja na infekciju COVID-19 bez potvrde PCR-om ili brzim Ag testom, prethodno dijagnosticirane autoimune bolesti, pozitivna anamneza malignih bolesti, te započeta potpora kisikom u drugoj ustanovi prije prijema u našu bolnicu. *Rezultati.* Našim istraživanjem obuhvaćeno je 186 trudnica koje su se u navedenom periodu porodile u KBC "Dr. Dragiša Mišović – Dedinje". Od toga 69 nije imalo simptome infekcije COVID-19, a 67 je razvilo blažu kliničku sliku. Za usporedbu, kod 41 trudnice dijagnosticirana je obostrana upala pluća. Ukupno 38 trudnica primljeno je na jedinicu intenzivne njege, od čega su 32 trudnice trebale kisikovu potporu, 20 trudnica je bilo na kisikovoj maski, od toga 2 na visokoprotlačnoj nazalnoj njezi, četiri trudnice na neinvazivnoj, mehaničkoj ventilacijom i šest trudnica na invazivnoj mehaničkoj ventilaciji. Od ukupnog broja pacijentica, 111 je imalo prirodni vaginalni porod, a 75 je podvrgnuto carskom rezu. Od 111 trudnica koje su imale vaginalni porod, 92 (83%) dobile su epiduralnu analgeziju, a 19 (17%) nije. Od trudnica podvrgnutih carskom rezu, devet trudnica (12%) dobilo je epiduralnu anesteziju, njih 51 (68) spinalnu anesteziju, dok je carski rez u 15 trudnica (20%) obavljen u općoj uravnoteženoj anesteziji. Od 186 hospitaliziranih i porodilja, 183 (98,4%) otpuštene su kući u dobrom općem stanju, dok su tri (1,6%) imale smrtni ishod. *Zaključak.* Kliničke manifestacije trudnica oboljelih od infekcije COVID-19 u najvećoj su mjeri odgovarale simptomima opće populacije. Nasuprot tome, pretjerana uporaba antibiotika, čak i kod asimptomatskih pacijenata, vrlo je zabrinjavajuća.

✉ Adresa za dopisivanje:

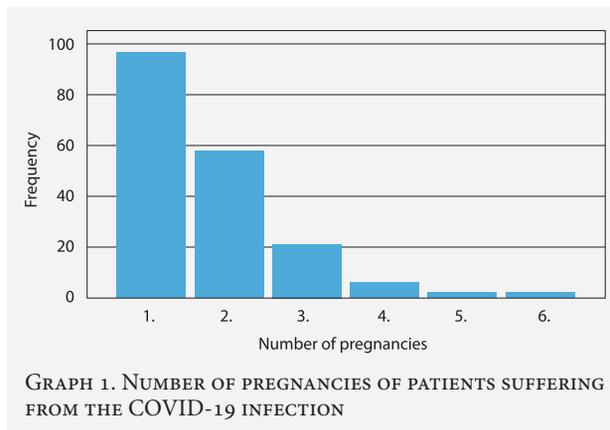
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TABLE 1. BASIC DEMOGRAPHIC DATA

Variable	Age
Min	17
Max	42
Average	31,4
Pregnancy	
Singleton	173 (93%)
Twin	13 (7%)
Previous births	
Primipara	97 (52%)
Multipara	89 (48%)
Comorbidities	
Hypertension	31 (16,7%)
Gestational diabetes	31 (16,7%)
Insulin resistance	22 (11,8%)
Obesity	12 (6,5%)
HELLP Sy	1 (0,53%)
Others (cholestasis, asthma, COPD, GERD, heart rhythm disorders)	41 (22%)

In December 2019, there was an outbreak of the new coronavirus disease 2019 – COVID-19, caused by severe acute respiratory syndrome virus corona 2 – SARS COV 2. The disease was initially reported in Wuhan, China, but quickly spread to over 150 countries worldwide. On March 13, 2020, the World Health Organization (WHO) declared a pandemic and reported over 94 million confirmed cases of COVID-19 and more than 2 million deaths. (1) A new respiratory disease was established, highly contagious, with possible damage to multiple organs and a fatal outcome. (2)

It is known that pregnancy is a state of suppressed immune response due to numerous physiological changes that occur in the “other state,” which makes pregnant women susceptible to a less favorable outcome in viral infections. (3,4) The risk of vertical virus transmission from the pregnant woman to the newborn also resulted in modified prenatal care. For example, childbirth preparation classes were suspended, and the number of medical visits to the gynecologist and anesthesiologist before childbirth was reduced in favor of online education. All this significantly increased the risk of adverse birth outcomes. (5) A 2020 systematic review showed that pregnant women did not have an increased risk of SARS-CoV-2 infection or symptomatic COVID-19 but were at greater risk of developing severe COVID-19 compared to women of similar age who were not pregnant. (6) COVID-19 is associated with increased obstetric complications such as fetal distress, cesarean deliv-



ery, and iatrogenic and spontaneous preterm birth. (7) Despite the large number of cases of COVID-19, there are still limited data on the clinical characteristics of pregnant women suffering from this disease. (8) Therefore, there is a need for more information and evidence on the outcomes and clinical characteristics of COVID-19 infection in pregnancy to form protocols for managing pregnancy and delivering to pregnant women affected by this disease. This descriptive study describes the clinical characteristics, radiological and laboratory results, applied therapy and outcome of pregnancies complicated by COVID-19 infection.

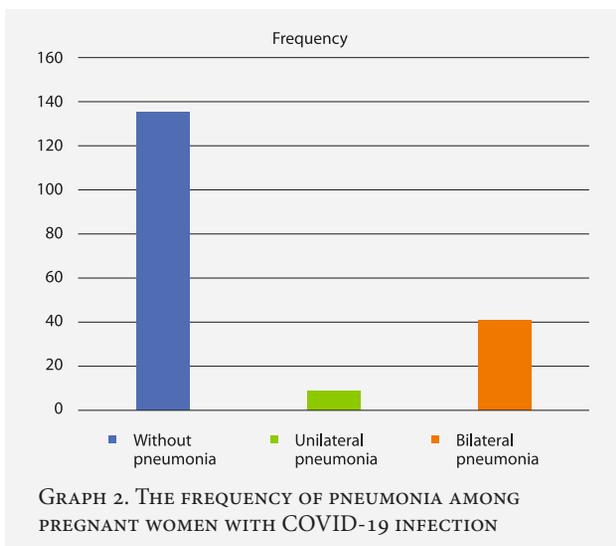
During the first three months of the pandemic, the University Clinical Hospital Center “Dr. Dragiša Mišović – Dedinje,” Belgrade, Serbia, was the only maternity hospital for pregnant women suffering from the COVID-19 infection in the territory of Belgrade, where over 2 million people live. As part of this center, there is a hospital for gynecology and obstetrics, where about 4300 women give birth annually. As the pandemic progressed, the hospital was organized to function with split capacity for pregnant women who had and did not have a COVID-19 infection.

Materials and method

After receiving the approval of the ethics committee of KBC “Dr. Dragiša Mišović – Dedinje,” a retrospective descriptive study was conducted, which included all pregnant women suffering from COVID-19 who gave birth in the hospital from April 2020 to January 2022. The study included pregnant women in whom, in nasopharyngeal swab samples, the presence of COVID-19 infection was laboratory confirmed, with a positive reverse transcription chain amplification reaction test – RT-PCR for SARS-Cov-2 or with a positive rapid antigen (Ag) test for SARS-Cov-2.

The exclusion criteria were:

- incomplete or unclear medical documentation,
- suspected COVID-19 infection without confirmation by PCR or rapid Ag test,



GRAPH 2. THE FREQUENCY OF PNEUMONIA AMONG PREGNANT WOMEN WITH COVID-19 INFECTION

- previously diagnosed autoimmune diseases (inflammatory bowel diseases, neurological autoimmune diseases, hematological autoimmune diseases, infectious liver diseases),
- positive history of malignant diseases,
- started oxygen support in another institution before admission to our hospital.

By reviewing the medical documentation, we obtained data on demographic characteristics, comorbidities, symptoms, laboratory and radiographic results, drug therapy and treatment outcomes. The obtained data were then statistically processed using the SPSS version 24 program for statistical analysis.

The results

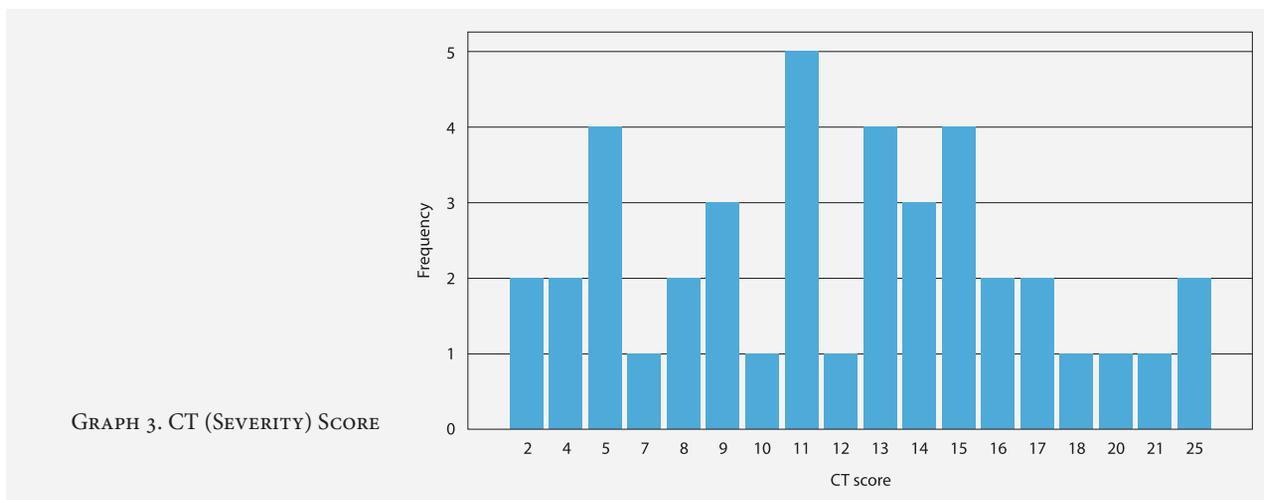
During the monitoring period, 481 pregnant women with COVID-19 infection in different stages of gestational age were hospitalized in our center. Out of the total number of hospitalized pregnant women suffer-

ing from COVID-19 infection, 199 pregnant women gave birth, of which 186 pregnant women met the criteria for entering the study. Basic demographic data are presented in Table 1 and Graph 1.

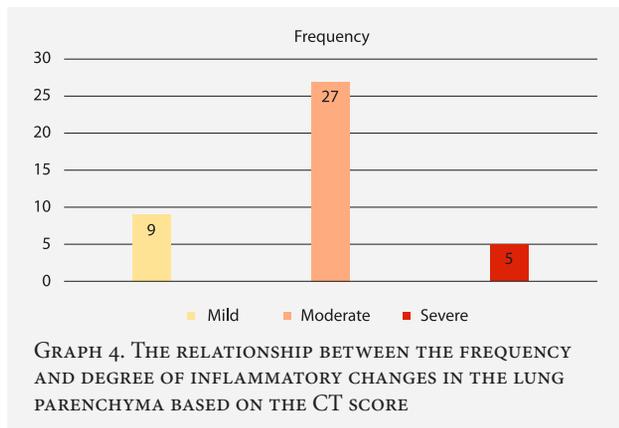
Of the 186 women, 69 had no symptoms of COVID-19 infection. Of the remaining 117 women, 67 developed a milder clinical picture with elevated tempera-

TABLE 2. CT (SEVERITY) SCORE

	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	2	1.1	4.9	4.9
	4	1.1	4.9	9.8
	5	2.2	9.8	19.5
	7	.5	2.4	22.0
	8	1.1	4.9	26.8
	9	1.6	7.3	34.1
	10	.5	2.4	36.6
	11	2.7	12.2	48.8
	12	.5	2.4	51.2
	13	2.2	9.8	61.0
	14	3	13.6	74.6
	15	4	18.0	92.6
	16	2	9.0	101.6
	17	2	9.0	110.6
	18	1	4.5	115.1
	20	1	4.5	119.6
	21	1	4.5	124.1
	25	2	9.0	133.1
Total	41	22.0	100.0	
Missing System	145	78.0		
Total	186	100.0		



GRAPH 3. CT (SEVERITY) SCORE



GRAPH 4. THE RELATIONSHIP BETWEEN THE FREQUENCY AND DEGREE OF INFLAMMATORY CHANGES IN THE LUNG PARENCHYMA BASED ON THE CT SCORE

ture as the dominant symptom; nine pregnant women had unilateral pneumonia, while 41 were diagnosed with bilateral pneumonia and underwent radiological diagnosis with computed tomography (CT). (Graph 2) Cough was present in about 50% of symptomatic pregnant women. The severity of pneumonia was determined based on the percentage involvement of the lung parenchyma with inflammatory changes, shown through the CT “severity score,” whose values are divided into three categories: 0–7 (mild degree of inflammatory changes of the lung parenchyma), 8–17 (moderate degree of inflammatory changes of lung parenchyma) 18–25 (severe degree of inflammatory changes of lung parenchyma). A mild degree of inflammatory changes in the lung parenchyma (CT “severity score” 0–7) was recorded in 9 patients (4.8%), a moderate degree (CT “severity score” 8–17) in 27 patients (14.5%) and a severe degree of inflammatory changes lung parenchyma (CT “severity score” 18–25) in 5 patients (2.7%). (Table 2, Graph 3, Graph 4)

Anesthesiological outcomes were assessed based on the pregnant women’s need for oxygen support. A total of 38 pregnant women were admitted to the intensive care unit, of which 32 pregnant women needed oxygen support, and 20 pregnant women were on an oxygen mask, 2 of them on a high flow nasal cannula – HFNC, 4 pregnant women on non-invasive mechanical ventilation and six pregnant women on invasive mechanical ventilation. (Table 3) Sixty pregnant women had associated comorbidities, most often hypertension (16.7%), gestational diabetes (16.7%) and insulin resistance (11.7%), among others were obesity, obstetric cholestasis, HELLP syndrome, etc. (Table 1)

When we talk about the laboratory parameters, at the time of admission to the hospital, most pregnant women (81%) had an average leukocyte count (4–10x 10⁹/L), 1.6% had a low leukocyte count, and 17.4% had an elevated leukocyte count. Lymphocytes were decreased (<20%) in 134 pregnant women and the normal range (20–40%) in 151 pregnant women. A

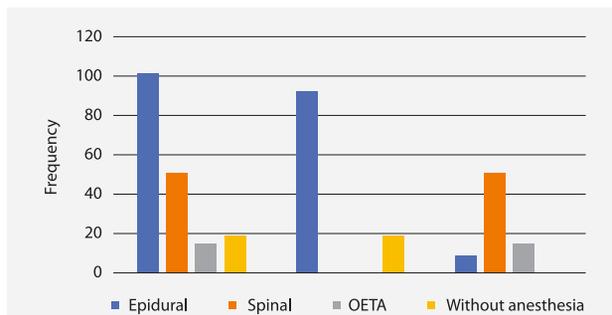
TABLE 3. OXYGEN SUPPORT (HFNC – HIGH-FLOW NASAL CANNULA, NIV – NON-INVASIVE MECHANICAL VENTILATION, IMV – INVASIVE MECHANICAL VENTILATION)

	Frequency	Percent	Cumulative percentage
Without oxygen support	154	82,8	82,8
Oxygen mask	20	10,8	93,5
HFNC	2	1,1	94,6
NIV	4	2,2	96,8
IMV	6	3,2	100
Total	186	100	

significant increase in neutrophil granulocytes (>70%) was noted in 75.2% of cases, i.e., 140 pregnant women. As for biochemical parameters, during hospitalization, elevated values of C-reactive protein (153 pregnant women – 82.2%), ferritin (122 pregnant women – 65.6%) and procalcitonin (115 pregnant women – 61.8%) were observed in a large percentage of pregnant women.

Studying the medical documentation of our pregnant women, we concluded that during hospitalization, 38 pregnant women (20.4%) received corticosteroid therapy, six pregnant women (3.2%) received antiviral therapy, 158 pregnant women (84.9%) received prophylactic anticoagulant therapy. In contrast, as many as 169 (90.9%) pregnant women received antibiotic therapy.

The delivery method was determined based on obstetric indications, and of the total number of patients, 111 had a natural vaginal delivery, while 75 patients underwent cesarean section. Of 111 pregnant women who had a vaginal delivery, 92 (83%) received epidural analgesia, while 19 (17%) did not. Among pregnant women undergoing cesarean section, nine pregnant women (12%) received epidural anesthesia, 51 of them (68) received spinal anesthesia, while a cesarean section in 15 pregnant women (20%) was performed under general balanced anesthesia. (Graph 5)



GRAPH 5. TYPE OF ANESTHESIA/ANALGESIA IN VAGINAL DELIVERY AND CAESAREAN SECTION

The mean gestational age at diagnosis of COVID-19 was 38.41±2.24 weeks (minimum 29 weeks gestation; maximum 42 weeks gestation). Thirty-eight pre-term infants, 145 term and 16 post-term infants were born. Of the total number of babies born, five were stillborn, five babies had an Apgar score of less than 7 in the first minute, while all other babies (176 babies) had an Apgar score of 7 to 10 in the first and greater than 8 in the fifth minute. Of 186 hospitalized and delivered pregnant women, 183 (98.4%) were discharged home in good general condition, while three (1.6%) had a fatal outcome.

Discussion

From the results obtained in this study, first of all, it can be noted that of the total number of pregnant women, as many as 63% had symptoms of infection, while 37% were asymptomatic. Common symptoms were fever, cough, malaise, sore throat, loss of taste and sense of smell. The results obtained in this study coincide with the results of the study by London V et al. (9) in which 68 pregnant women with confirmed COVID-19 were examined, of whom 67.6% had symptoms of infection, the most common of which were fever and cough, while 32.4% were asymptomatic. An approximately similar percentage of pregnant women in the same study required some oxygen support, 21.8% to be exact, while in our study, that percentage was 17.2%. The most significant number of pregnant women, 20, were on oxygen support with a mask, and two were on HFNC.

In comparison, intubation and mechanical ventilation were necessary for six pregnant women, i.e., in 3.2% of the total number of pregnant women included in the study. Similar results were shown by the research of Keita H et al. (10) conducted in France included 126 pregnant women with confirmed COVID-19 who were admitted to the hospital for delivery. Namely, in this study, out of 126 pregnant women, 28 were on an oxygen mask or HFNC, and four patients, i.e., 3.1%, were intubated and connected to mechanical ventilation.

A large body of research has found that laboratory findings in pregnant women with COVID-19 are atypical compared to the general population. A study by Liu H et al. (11) proved that leukocytosis and an increased number of neutrophil granulocytes are more common in pregnant women with COVID-19 compared to the general population, which supports the results of our study, where 75.2% of patients had an elevated number of neutrophil granulocytes, while the number of leukocytes was within the reference values for the majority of the examined patients. In addition, elevated values of C-reactive protein and D-dimer were observed, which is also following the results of our research.

When discussing gestational age at the time of delivery, some studies have shown an increased rate of pre-term births in pregnant women with COVID-19 (12). In our study, most pregnant women had a term delivery; more precisely, the number of premature babies was 38, representing 19% of the total number of babies born. Similar results were obtained in a study conducted in Nepal (13), where out of 48 infants born to mothers with COVID-19, only 8 (17%) were born before term. Unlike the study done in Nepal, where the outcome of all newborns was positive, in this study, there were a total of 5 stillbirths. However, such an outcome cannot be attributed with certainty to the COVID-19 infection, considering that the mothers of the stillborn babies had different degrees of severity in the clinical picture. Regarding the delivery method, numerous studies have shown an increased cesarean section rate in pregnant women with COVID-19 (13,14), which was not the case in this study. This can be attributed to the selection of respondents in the research, more precisely to a more significant number of patients with high-risk pregnancies and many associated comorbidities. In our study, 75 pregnant women were delivered by cesarean section, 40.32%, while 59.68% were delivered vaginally. The most significant number of pregnant women (101 patients – 60.5%) received epidural anesthesia or analgesia. Epidural analgesia is recommended early in labor to reduce the exhaustion of the respiratory system and the risk of spreading infection during induction of general anesthesia in case of an emergency cesarean section. (15). In second place is spinal anesthesia, which was received by 51 patients (30.5%), while the lowest percentage of births, more precisely 9%, was performed under general balanced anesthesia. The data collected in our study match the data of the study by Keita H et al. (10) conducted in France, in which also the most significant number of pregnant women (55%) received epidural anesthesia during childbirth, 32% spinal anesthesia, and 17% of deliveries were performed under general anesthesia.

Conclusion

The clinical manifestations of pregnant women suffering from COVID-19 infection corresponded to the greatest extent to the symptoms of the general population. Most pregnant women with this disease had an asymptomatic or mild clinical picture. Excessive use of antibiotics despite the abovementioned asymptomatic or mild clinical picture is very worrying. However, more detailed epidemiological and experimental research is needed to understand better the effects of socioeconomic and demographic factors and the impact of SARS-Cov-2 on birth outcomes to develop effective preventive strategies.

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