

# Effects of maternal SARS-CoV-2 infection on labor outcomes

Toni Jurić<sup>1</sup> , Helena Štrucelj<sup>2</sup> , Barbara Borovac<sup>1</sup> , Natalija Vuletić<sup>1</sup> , Marko Klarić<sup>1</sup> 

<sup>1</sup>Clinical Hospital, Center Rijeka, Department of Gynecology and Obstetrics, Rijeka, Croatia

<sup>2</sup>Faculty of Health Studies, University of Rijeka, Rijeka, Croatia

## Abstract

**Objective:** Aim was to compare labor outcomes between SARS-CoV-2 infected and control group.

**Methods:** This retrospective study included 104 women with acute SARS-CoV-2 infection at the time of labor and 101 randomly selected women without infection from March 2020 to January 2023.

**Results:** In SARS-CoV-2 infected group there are no differences in the severity of clinical presentation regarding the presence of obesity ( $U=622.00$ ,  $p=0.860$ ), age over 35 years ( $U=813.00$ ,  $p=0.081$ ) and pre-existing diseases ( $U=915.00$ ,  $p=0.757$ ). Severity of the clinical presentation is positively correlated with blood loss during labor ( $p=0.347$ ,  $p<0.001$ ), duration of hospitalization ( $p=0.403$ ,  $p<0.001$ ), and the day of the infection at time of labor ( $p=0.474$ ,  $p<0.001$ ).

There is no difference between the SARS-CoV-2 infected group and control group in the frequency of term births and preterm births ( $\chi^2=0.101$ ,  $p=0.750$ ), nor in the frequency of caesarean section compared to vaginal birth and instrumental delivery ( $\chi^2=1.555$ ,  $p=0.212$ ). Complications in the fourth stage of labor are similarly frequent in both groups ( $\chi^2=0.331$ ,  $p=0.565$ ), as well as blood loss during labor ( $U=5131.00$ ,  $p=0.717$ ). The duration of hospitalization was prolonged in the SARS-CoV-2 infected group compared to control group ( $\chi^2=10.877$ ,  $p=0.004$ ).

**Conclusion:** Results from this study proved that SARS-CoV-2 infection generally did not negatively affect obstetric outcomes. There was no statistically significant difference between type of childbirth initiation, gestational age at delivery, delivery route or anaesthesia placement between two groups. Complications during labor were more often in SARS-CoV-2 infected group, and the infection related to longer hospitalization.

**Keywords:** SARS-CoV-2, COVID, pregnancy, labor

## Introduction

Since the beginning of the COVID pandemic in late 2019, more than 1.2 million people in Croatia were infected with SARS-CoV-2 while more than 18 000 people died.<sup>[1]</sup> Worldwide, there were confirmed more than 760 million cases and more than 6.8 million deaths.<sup>[2]</sup> Pandemic remains as quite a challenge for clinicians. SARS-CoV-2 infection has been related with more frequent intrauterine fetal death, emergency caesarean section, premature labor, neonatal intensive care unit (NICU) admission and prolonged hospitalization with more frequent diseases associated with pregnancy, such as

preeclampsia and eclampsia.<sup>[3-5]</sup> Immunological changes during pregnancy put the pregnant women at a high-risk group and data regarding labor outcomes in this population is limited.

The aim of this study is to contribute to a better understanding of the impact of SARS-CoV-2 infection on labor complications. In this study we examined whether there were differences in the severity of the clinical presentation of the infection regarding the presence of obesity, age over 35 years and pre-existing diseases and its correlation with blood loss and duration of hospitalization. Also, we analysed differences in types of childbirth

**Correspondence:** Toni Jurić, Clinical Hospital, Center Rijeka, Department of Gynecology and Obstetrics, Rijeka, Croatia, **e-mail:** toni.juric0@gmail.com, **Received:** July 08, 2023, **Accepted:** February 27, 2024

**How to cite this article:** Jurić T, Štrucelj H, Borovac B, Vuletić N, Klarić M. Effects of maternal SARS-CoV-2 infection on labor outcomes. Perinatal Journal 2024;32(1):50-56 DOI: 10.59215/prn.24.0321008

**ORCID ID:** T Jurić 0000-0002-7175-6249; H Štrucelj 0000-0002-7739-2108; B Borovac 0009-0008-9158-9733; N Vuletić 0009-0004-1367-0238; M Klarić 0000-0002-4222-3232

initiation, gestational age at labor, frequency of caesarean section and postpartum complications between the SARS-CoV-2 infected group and control group.

## Methods

This is a retrospective study with data from March 2020 to January 2023 in a tertiary center, Clinical Hospital Center Rijeka. Participants were tested for SARS-CoV-2 using nasopharyngeal and oropharyngeal swab and RT-qPCR SARS-CoV-2 Biorad® and GeneXpert® testing upon admission into delivery room and divided into two groups: patients with infection at labor and those without the infection. In total, 104 parturients with acute SARS-CoV-2 infection at the time of labor and 101 randomly selected women without infection were included in this study. Both our groups were adjusted for age and parity to avoid systematic errors. When including SARS-CoV-2 negative parturients in the study, we took into consideration to include parturients from March 2020 until January 2023, as was the case with SARS-CoV-2 positive parturients. Parturients who were diagnosed with SARS-CoV-2 infection were transferred to an isolation room to prevent further spread of infection, they were monitored, and their vital parameters were regularly supervised. Upon discharge from the hospital, they were given detailed instructions about prevention of the spread of the infection.

Data was collected from medical documentation from hospital information system, with permission of Ethics Committee of Clinical Hospital Center Rijeka. Parameters that were examined in SARS-CoV-2 infected group include: 1) Severity of clinical picture of COVID infection: asymptomatic or mild (presenting with at least one of the following symptoms - sore throat, cough, temperature  $>37.8^{\circ}\text{C}$ , myalgia), moderate (viral pneumonia, without hypoxia), severe (advanced pneumonia, with  $\text{SpO}_2 < 90\%$ ), and critical (presenting with at least one of the following symptoms - acute respiratory distress syndrome, sepsis, septic shock, pulmonary embolism), 2) Presence of risk factors which could be associated with severe clinical picture: obesity expressed by body mass index (BMI) greater than  $30 \text{ kg/m}^2$ , age over 35 years at the time of labor, and pre-existing diseases (arterial hypertension, type 1 and type 2 diabetes, smoking), 3) Oxygen therapy during third trimester, labor, or postpartum period (nasal catheter/respiratory mask, high flow nasal cannula or respirator), 4) Medication ordained during third trimester, labor, and postpartum period, which include corticosteroids and low-molecular weight heparin, and 5) Presence of maternal or intrauterine fetal death.

Additionally, parameters that were examined in both

groups include: 1) Beginning of labor, which include premature rupture of membranes, contractions, and elective caesarean section, 2) Gestational age at labor, which include pre-term ( $<37$  weeks of gestation), term (37-42 weeks of gestation), and post-term ( $>42$  weeks of gestation), 3) Route of delivery, which include vaginal birth, instrumental delivery (vacuum assisted vaginal delivery), and caesarean section (both elective and emergency), 4) Postpartum complications, which include uterine atony diagnosed during labor or early postpartum period, delivery trauma (perineal lacerations of third- or fourth- degree), adherent or retained placenta diagnosed during third stage of labor, and coagulation disorders classified as prolonged or excessive bleeding during labor which cannot be associated with delivery trauma, adherent placenta or uterine atony, 5) Blood loss during labor, calculated from laboratory analysis both upon admission and after labor and divided into five categories:  $<500 \text{ mL}$ ,  $500\text{-}1000 \text{ mL}$ ,  $1001\text{-}1500 \text{ mL}$ ,  $1501\text{-}2000 \text{ mL}$ , and  $>2000 \text{ mL}$ , 6) Duration of hospitalization expressed in days, and 7) Use of anaesthesia during labor, both epidural/spinal, or endotracheal anaesthesia. Parameters that were examined are listed in Table 1.

**Table 1.** Examined parameters

In SARS-CoV-2 infected group	
1	Severity of clinical picture of infection (mild, moderate, severe, critical)
2	Presence of risk factors for more severe clinical picture (obesity, age over 35 years, and pre-existing diseases)
3	Medications ordained during third trimester, labor, and postpartum period (did not require additional therapy, corticosteroids, low-molecular-weight heparin, or both)
4	Oxygen therapy during third trimester, labor, and postpartum period (did not require additional oxygen therapy, nasal catheter/respiratory mask, high flow nasal cannula, respirator)
5	Maternal death and intrauterine fetal death (yes/no)
In both groups:	
1	Beginning of labor (premature rupture of membranes, contractions, or elective caesarean section)
2	Gestational age at labor (pre-term, term, postterm). Duration of hospitalization (days)
3	Route of delivery (vaginal birth, instrumental delivery, caesarean section)
4	Postpartum complications (no complications, uterine atony, delivery trauma, adherent or retained placenta, coagulation disorder)
5	Blood loss during labor ( $<500 \text{ mL}$ , $500\text{-}1000 \text{ mL}$ , $1000\text{-}1500 \text{ mL}$ , $1500\text{-}2000 \text{ mL}$ , $> 2000 \text{ mL}$ )
6	Duration of hospitalization (days)
7	Use of anesthesia during labor (without anesthesia, epidural, spinal, endotracheal anesthesia)

Primary aim of this study was to compare the labor outcomes (type of childbirth initiation, gestational age at the time of labor, route of delivery, complications during labor, duration of hospitalization, blood loss, and anaesthesia placement) between SARS-CoV-2 infected group and control group.

Secondary aims were to examine the correlation between the presence of risk factors (obesity, age over 35 years, and pre-existing diseases) with the severity of clinical picture in the SARS-CoV-2 infected parturients, as well as to examine the correlation between the severity of clinical picture in the SARS-CoV-2 infected parturients with the duration of hospitalization, blood loss and day of the infection at the time of labor.

Data were analysed using t-test, Chi-square test, Mann-Whitney U test and Spearman correlation in Statistica 14.0.0.15 (TIBCO Software Inc.), and power estimation for the statistical tests used for the primary aim was calculated using Psychometrica and G\*Power 3.<sup>[6,7]</sup> CONSORT guideline was used for this research report.

## Results

Firstly, we analysed the effect of SARS-CoV-2 infection on positive parturients. Among the SARS-CoV-2 infected group, we divided the severity of clinical symptoms into four categories: asymptomatic or mild, moderate, and critical. Most of parturients, 98 of them, presented with mild clinical symptoms or as asymptomatic (94.2%), while two parturients presented with moderate symptoms (1.9%), three presented with severe symptoms (2.9%) and one presented with critical symptoms (1%). Furthermore, two parturients continued their treatment in Intensive Care Unit after labor, and both reached full recovery.

We examined the relationship between risk factors (obesity, age over 35 years, and pre-existing diseases, e.g. arterial hypertension, diabetes mellitus and smoking) and severity of SARS-CoV-2 infection. Out of 104 parturients, six of them were obese (6%), eleven parturients were over 35 years and the time of labor (11%), twelve had pre-existing diseases (12 %), and fifteen had some combination of risk factors (14%).

We used Mann-Whitney U test and did not find statistically significant differences in the severity of clinical presentation in subgroups regarding presence of obesity ( $U=622.00$ ,  $p=0.860$ ), age over 35 years ( $U=813.00$ ,  $p=0.081$ ) and pre-existing diseases ( $U=915.00$ ,  $p=0.757$ ). However, severity of the clinical presentation was positively correlated with blood loss during labor (Spearman  $\rho=0.347$ ,  $p<0.001$ ), duration of hospitalization (Spearman  $\rho=0.403$ ,  $p<0.001$ ) and the day of infection at the time of labor (Spearman  $\rho=0.474$ ,  $p<0.001$ ), meaning that longer lasting infections were connected with more severe pre-

sensation of infection.

Furthermore, most of infected parturients, 93 of them, did not require additional medication for COVID symptoms (89.4%). Six of them (5.8%) were treated with combination of corticosteroid therapy and low molecular weight heparin (LMWH), two of them (1.9%) with corticosteroid therapy alone and three of them (2.9%) required therapy with LMWH alone. Similarly, most of the parturients did not require additional oxygen therapy ( $N=99$ , 95.2%). Four parturients required nasal catheter or respiratory mask (3.8%) and one required high flow nasal cannula (1%). There were no maternal deaths nor intrauterine fetal deaths among the SARS-CoV-2 infected group.

Furthermore, we compared both SARS-CoV-2 infected group and control group. Both groups were adjusted for age and parity (Table 2). When comparing two groups (Table 3), there was no statistically significant difference in the frequency of the three examined types of childbirth initiation (prelabor rupture of membranes, contractions, and induction of labor),  $\chi^2=0.98$ ,  $p>0.05$ . When comparing gestational age at the time of labor (preterm, term and postterm births), we found similar results in both groups,  $\chi^2=0.101$ ,  $p>0.05$ . In both groups, four parturients had labor in <37 weeks of pregnancy, with no postterm pregnancies >42 weeks. We compared different types of delivery route (vaginal birth and instrumental delivery vs caesarean section). Total of 35 births in SARS-CoV-2 group and 25 births in control group were delivered via caesarean section,  $\chi^2=1.555$ ,  $p>0.05$ .

Additionally, we compared complications during labor in both groups. Complications included uterine atony, third- and fourth-degree perineal injuries, adherent or retained placenta and coagulation disorders. Frequency of complications was higher in SARS-CoV-2 group ( $N=17$  in SARS-CoV-2 positive group,  $N=10$  in negative group), without statistically significant difference,  $\chi^2=0.331$ ,  $p>0.05$ . In both groups coagulation disorders were the most common complication in labor. Blood loss was similar in both groups ( $U=5131.00$ ,  $p>0.05$ ), as most of parturients in both groups had blood loss under 500 mL.

The duration of hospitalization was prolonged in the SARS-CoV-2 infected group ( $\chi^2=10.877$ ,  $p=0.004$ ). Minimal duration of hospitalization was two days in both groups, while maximal duration was 22 days in SARS-CoV-2 group, and 5 days in control group.

We did not find statistically significant difference between groups related to use of anesthesia during labor,  $\chi^2=0.01$ ,  $p>0.05$  (Table 4). Less than half of parturients in SARS-CoV-2 infected group had birth with anesthesia ( $N=44$ , 42.3%), most of which with epidural and spinal anesthesia ( $N=13$  or 12.5% and 29 or 27.9%, respecti-

vely) and two parturients (1.9%) were under endotracheal anesthesia during caesarean section. Similarly, less than half of parturients in control group had birth with anesthesia (N=42, 41.6%), most of which with epidural and spinal anesthesia (N=18, 17.8% and 18, 17.8%, res-

**Table 2.** Age and parity in SARS-CoV-2 infected group and control group

Group	Descriptives	Group difference
<b>Age</b>		
SARS-CoV-2 infected group	M = 30.808, SD = 5.022 CI95% 4.420-5.816 Range 17-43 years	t = -0.197 p = 0.483
Control group	M=30.941, SD=4.602, CI 95% 4.043-5.432 Range 18-41 years	
<b>Parity</b>		
SARS-CoV-2 infected group	First birth N = 44 (42.3%) Second birth N = 43 (41.4%) Third birth and more = 17 (16.3%)	$\chi^2 = 0.093$ df = 2 p = 0.955
Control group	First birth N = 43 (42.6%) Second birth N = 43 (42.6%) Third birth and more = 15 (14.8%)	

pectively), five parturients (5%) were under endotracheal anesthesia during caesarean section, and one was under endotracheal anesthesia after previously having epidural. (Table 4).

**Table 3.** Comparison between SARS-CoV-2 infected group and control group

Parameter	Categories	SARS-CoV-2 infected group (N = 104)	Control group = 101	(N)	Difference (Chi-square test or Mann Whitney U test)	Power estimation
Type of childbirth initiation	Prelabor rupture of membranes	27 (26%)	24 (24%)	$\chi^2$ =0.133 df = 2 p = 0.936	0.065	
	Contractions	47 (45%)	47 (47%)			
	Induction of labor	30 (29%)	30 (29%)			
Gestational age at the time of labor	Pre-term birth	100 (96%)	97 (96%)	$\chi^2$ =0.101 df = 1 p = 0.750	0.061	
	Term birth	4 (4%)	4 (4%)			
Route of delivery	Caesarean section	35 (34%)	25 (25%)	$\chi^2$ = 1.555 df = 1 p = 0.212	0.251	
	Vaginal birth and instrumental delivery	69 (66%)	76 (75%)			
Complications during labor	Occurred	14 (13%)	10 (10%)	$\chi^2$ = 0.331 df = 1 p = 0.565	0.088	
	Did not occur	90 (87%)	91 (90%)			
Duration of hospitalization	≤48 h	N = 51 (49%)	N = 46 (45.5%)	$\chi^2$ = 10.877 df = 2 p = 0.004	0.919	
	3-4 days	N = 33 (31.7%)	N = 49 (48.5%)			
	≥5 days	N = 20 (19.2%)	N = 6 (5.9%)			
Blood loss during labor		Average rank = 104.16	Average rank = 101.8	U = 5131.00 p = 0.717	0.234	

**Table 4.** Comparison of anesthesia placement between SARS-CoV-2 infected group and control group

Parameter		SARS-CoV-2 infected group (N=104)	Control group (N=101)	
<b>Anesthesia (all N = 205)</b>	Yes	44 (42.3%)	42 (41.6%)	$\chi^2 = 0.01$ df = 1 p = 0.916
	No	60 (57.7%)	59 (58.4%)	
<b>Anesthesia – vaginal birth (N = 144)</b>	Yes	9 (13.2%)	17 (22.4%)	$\chi^2 = 1.45$ df = 1 p = 0.228
	No	59 (86.8%)	59 (77.6%)	
<b>Type of anesthesia – caesarean section (N = 60)</b>	Epidural	5 (14.3%)	3 (12%)	$\chi^2 = 3.30$ df = 2 p = 0.192
	Spinal	29 (82.9%)	18 (72%)	
	Endotracheal	1 (2.9%)	4 (16%)	



## Discussion

Study was performed in Clinical Hospital Center Rijeka, maternity hospital with around 2300 births per year. This was a single-center study and all parturients were treated with the same protocol and by the same obstetric team. Parturients were tested upon admission into hospital, and SARS-CoV-2 positive patients were put under intensive supervision. Vital parameters were regularly monitored, and patients who showed deterioration of clinical symptoms were transferred into Clinical Care Unit. We used data from extended period, from 2020 until 2023 and included patients with various variants of SARS-CoV-2 virus. Most of parturients who developed more severe clinical picture of the infection or continued treatment in Intensive Care Unit were hospitalized in the earlier stage of the pandemic, during 2020 and 2021. Patients who were infected with Omicron variant generally presented with milder clinical picture, which corresponds with published data.<sup>[8]</sup>

Although comorbidities, such as obesity, pre-existing diseases and older age at delivery are believed to relate to more severe clinical picture of the infection<sup>[9-14]</sup>, our results did not confirm this hypothesis. As regarded above, most of parturients in our research did not require additional therapy regarding COVID symptoms (89.4%). Total of eleven parturients were treated with corticosteroids, e.g. dexamethasone (N=2), low-molecular-weight heparin (N=3), or combination of both (N=6). Dexamethasone has proven to lower the risk of death in pregnant women and has low risk of adverse effects on the fetus, which is why we justified its use in parturients with more severe clinical picture.<sup>[15]</sup> COVID-19 is associated with coagulopathies, and low-molecular-weight heparin (e.g. enoxaparin) was used for prevention of thromboembolic incidents because of its safety and easy administration.<sup>[15]</sup>

Most of patients in our SARS-CoV-2 infected group had satisfying saturation without oxygen therapy (4.8% required additional therapy). These results contradict earlier data where 38.8% participants required additional therapy.<sup>[16]</sup> Per recommendations published by Eid et al, saturation  $\geq 95\%$  is satisfying in patients with COVID-19, and saturation between 92 and 96% is satisfying in patients with acute respiratory distress.<sup>[17]</sup> Considering most of parturients included in our study presented as asymptomatic or with mild symptoms, oxygen therapy was in most cases not needed.

There were no reported maternal deaths nor intrauterine fetal deaths in the SARS-CoV-2 infected group, which is contradictory with some of the earlier published research.<sup>[9-10, 18-20]</sup> We believe that because of relatively small number of infected patients, we were able to monitor and

enhance care of infected patients. Cooperation with other specialists, mostly anaesthesiologists, was successful throughout the pandemic. We tested all parturients among admission into delivery room and regularly monitored vital parameters, which helped us triage patients who required more enhanced monitoring.

Even though there were no published data regarding the difference of childbirth initiation between infected and control group, we report that most of parturients in both groups in our study started their labor with contractions (47% in control group and 45% in infected group).

We did not find statistically significant difference in the rate of preterm birth when we compared two groups (there were four births before 37 weeks in both SARS-CoV-2 infected and control group), which contradicts earlier published research<sup>[13,20]</sup>, as well as meta-analysis on 293 152 pregnant and recently pregnant women with COVID-19.<sup>[12]</sup> Similarly, there was data that proved connection between severe COVID-19 infection and preterm labor.<sup>[9,10]</sup> Since most of our parturients with the infection presented with mild clinical symptoms of the infection, it is reasonable to assume that this might be the reason for the discrepancy with earlier data.

In the SARS-CoV-2 infected group caesarean section as route of delivery was more prominent than in control group (33 vs 24%, respectively), as was instrumental delivery (one case vs zero, respectively). However, there was no statistically significant difference between two groups, which contradicts some of the earlier data.<sup>[3-5]</sup> The reason for this might be because most of our COVID infected parturients presented with mild symptoms or as asymptomatic and there were no obstacles for vaginal delivery. Rate of deliveries with caesarean section in the infected group was similar with our maternity hospital's average.

Like in the published data, SARS-CoV-2 infected patients were at bigger risk for postpartum haemorrhage and required blood transfusion more often.<sup>[21]</sup> COVID-19 is also associated with coagulopathies characterized by mild thrombocytopenia, slight prolongation of the prothrombin time, high levels of D-dimer, and elevated levels of fibrinogen, factor VIII, and von Willebrand factor, as well as with sepsis-induced disseminated intravascular coagulopathy (DIC).<sup>[22]</sup> As expected, severity of clinical picture of the infection was related to more severe blood loss. Although blood loss during labor should be closely monitored in all cases, emphasis should be put on parturients with more severe COVID infection.

Like in published data<sup>[18]</sup> COVID infection is related to longer hospitalisation. Although most of parturients included in the study presented with mild symptoms, en-

hanced monitoring before and after labor was ordained, especially in the early stages of the pandemic when there was sparse knowledge regarding the virus.

Regarding anesthesia during labor, recommendations have emphasized the importance of early neuraxial labor anesthesia with a well-functioning epidural catheter to reduce the risk of general anesthesia should emergency caesarean section occur.<sup>[23]</sup> There are many reasons why neuraxial analgesia is a preferred option, mainly because of lower risk of contamination for operation room staff, combined with greater complications during general anesthesia, superior perioperative analgesia, earlier skin to skin contact, and decreased blood loss and duration of hospitalization.<sup>[24]</sup> Similarly to our results, rates of endotracheal anesthesia during caesarean section declined in the pandemic.<sup>[24]</sup>

We found that identifying COVID positive parturients was very important in order not only to enhance prenatal and postnatal care, but also to protect obstetric team and other parturients in the delivery ward. However, the rate of false negative COVID tests remained a concern during the pandemic.<sup>[25]</sup> Vaccination status of participants was mostly unknown, although it would be useful to determine the connection between immunization and both severity of clinical picture and obstetric outcomes.

The question of vertical transmission of SARS-CoV-2 from mother to the fetus was beyond the scope of this research, but we believe that future studies could include the effect of infection on the neonate. Furthermore, it is of utmost importance to evaluate the effect of immunisation on severity of clinical symptoms and on labour complications.

## Conclusion

Although SARS-CoV-2 infection generally did not have negative impact on obstetric outcomes, enhanced monitoring is advised. Severity of the infection is positively correlated with blood loss during labor and prolonged hospitalization, and intensive supervision is required. We believe that further studies regarding outcome of neonates and puerperas would be useful to better understand infection's effect on labor and post labor period.

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