

## Pregnancy outcomes of COVID-19 positive pregnant women at the Cantonal Hospital Zenica, Bosnia and Herzegovina

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### ABSTRACT

**Aim** To investigate clinical presentation of COVID-19 infection in pregnancy, its course during pregnancy, effects on pregnancy outcomes for both mothers and newborns as well as the potential for vertical transmission.

**Methods** This retrospective observational study included all identified COVID-19-positive pregnant women admitted to the Cantonal Hospital in Zenica at any stage of pregnancy or labour from 30 April 2020 to April 30 2021. Maternity and newborns were followed until discharge from the hospital.

**Results** Twenty-four pregnant women were positive for COVID-19. There were 79.2% asymptomatic cases, 12.5% had mild symptoms, while 8.3% had more severe forms of the disease. The main follow-up morbidities were high BMI 33.3%, anaemia 16.7%, thrombocytopenia 12.5%, hypertensive disorders 4.2% and diabetes 4.2%. The rate of premature births was 33.3%, while 8.3% pregnant women had premature rupture of the amniotic sac. Caesarean section was done for 75% women while 25% delivered vaginally. Previous caesarean section (54.2%) was the most common indication for operative completion of labour. Twenty-three (92%) live babies were born, of which 8 (33.3%) were admitted to the neonatal intensive care unit. Two (8%) intrauterine foetal deaths were recorded that occurred before admission to our hospital. Two infants (8.7%) had a positive PCR test for COVID-19.

**Conclusion** COVID-19 viral disease in pregnancy is usually presented as an asymptomatic or mild disease. It is associated with high rates of preterm birth, admission of newborns to the intensive care unit and intrauterine foetal death. Vertical transmission is possible but the newborns were asymptomatic.

**Key words:** COVID-19, pregnancy, pregnancy outcome, SARS-CoV-2, vertical infection transmission

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## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) identified in December 2019 is the cause of COVID-19 disease (1,2). The first case of the disease that tested positive in Bosnia and Herzegovina was recorded on 5 March 2020 in Banja Luka after returning from a visit to Italy. By 22 April 2021, Bosnia and Herzegovina reached the fourth highest death rate per 1,000,000 inhabitants in the world, with 2,404 deaths per 1,000,000 1 million. In addition, access to testing in the country was less accessible as Bosnia and Herzegovina had had the 4th lowest testing rate in Europe since December 30. According to the World Health Organization in Bosnia and Herzegovina from 3 January 2020 to 18 May 2021 202,419 confirmed cases of COVID-19 were recorded with 9,026 deaths (3).

As this is a new disease, information on the effect of COVID-19 on the outcome of pregnancy for both mother and fetus is limited. Considering knowledge gained from previous human coronavirus epidemics such as Middle East Respiratory Syndrome (MERS) and severe acute coronavirus syndrome (SARS-CoV), it is hypothesized that COVID-19 disease may lead to a worse outcome in pregnant women compared to the healthy population (4,5). Earlier reports (6,7) did not show an increase of adverse effects of COVID-19 on pregnant women; however, there is evidence to show a higher risk of severe disease and increased admission to the intensive care unit of pregnant women with COVID-19 disease compared to non-pregnant women (8,9). There is no clear evidence of optimal delivery time, safety of vaginal delivery, and whether a caesarean section prevents the transmission of SARS-CoV-2 virus to the newborn at the time of delivery (10-12). Also, studies describing the prevalence of maternal and neonatal complications and brief narrative reviews suggest a possible increased risk of preterm birth in pregnant women with COVID-19 (13,14).

The aim of our study was to investigate clinical presentation of COVID-19 infection in pregnancy, pregnancy outcome, as well as the potential for vertical transmission.

## PATIENTS AND METHODS

This prospective observational study was conducted at the Cantonal Hospital, Zenica, Bosnia and Herzegovina (B&H) by collecting data from

24 identified COVID-19-positive pregnant women admitted to the Department of Gynaecology and Obstetrics at any stage of pregnancy or labour from 30 April 2020 to 30 April 2021. Data on maternal demographic characteristics, presenting symptoms, associated co-morbidities, pregnancy outcome, neonatal outcome and complications from medical histories were collected. Mothers and newborns were followed until discharged from the hospital.

## Methods

All pregnant women with suspected or previously confirmed COVID-19 infection were at first examined in the triage area and transferred to a negative, suspected, or positive (isolation) room according to their screening status for COVID-19. All health workers wore appropriate protective equipment and followed valid social distance protocols.

Pregnant women with suspected COVID-19 infection admitted to the hospital (including fever, dry cough, and tiredness, loss of taste or smell, aches and pains, headache, sore throat, nasal congestion, red eyes, diarrhoea, or a skin rash) were tested according to the diagnostic-therapeutic protocol for the treatment of COVID-19 positive patients at the Cantonal Hospital in Zenica. Tests for SARS-CoV-2 based on reverse transcriptase polymerase chain reaction (RT-PCR) (15) were done at the Department of Microbiology of the Cantonal Hospital in Zenica.

Asymptomatic women and those with mild symptoms of COVID-19 infection were discharged 24 hours after vaginal delivery and 48 hours after caesarean section with advice on home isolation and according to the current procedure. If the patient was discharged from hospital less than 14 days after the last positive PCR test, or three weeks after problems related to COVID-19, she was released with a recommendation on a 14-day home isolation.

All newborns were tested to COVID-19 infection within 24 hours of birth. Unfortunately, due to the specific organizational structure of the Intensive Care Unit (ICU) of the COVID Department, rooming in was not allowed.

## Statistical analysis

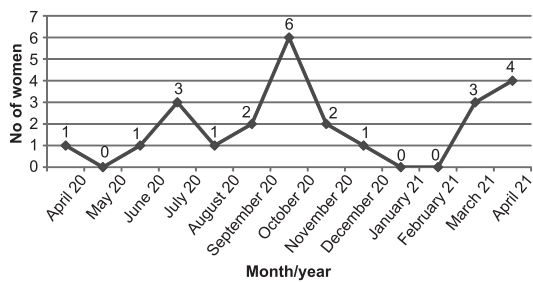
Data on 24 positive pregnant women for COVID-19 admitted to our hospital during the one-year study period (between 30 April 2020 and

30 April 2021) included the age, gestational age, symptoms, associated comorbidities, mode of delivery, and details of neonates. Continuous variables are expressed as mean +/- standard deviation (SD). All categorical variables are expressed as frequency and percentages.

**RESULTS**

In the period from April 2020 to April 2021, a total of 2,388 pregnant women were admitted to the Gynaecology and Obstetrics Department of the Cantonal Hospital Zenica. Out of those, 24 (1%) were confirmed to be COVID-19 positive. All 24 COVID-19 positive pregnant women gave birth within 48 hours of admission to our facility. Out of 24 positive women, 5 confirmed that they had had contacts with infected individuals and in 19 (20.83%) the source of infection could not be identified.

The first confirmed COVID-19 positive pregnant woman, and the first positive pregnant woman who gave birth by caesarean section, was admitted on 30 April 2020. Since then, there has been a slight increase in infected pregnant women in July and an exponential increase in the number of cases during October, reaching a peak from 2 to 10 October, followed by a decrease from December 2020 to February 2021. An exponential increase was again recorded during the months of March and April that followed the onset of the third wave of coronavirus in B&H (Figure 1).



**Figure 1. Temporal trend of coronavirus disease 2019 (COVID-19) cases in pregnant women during the period between April 2020 and April 2021**

The age of the patient ranged from 22 to 43 years with the maximum number of pregnant women in the age group of 25-34 years. The average age was 30.9 (+/- 5.18) years. The number of primigravidas was eight, and 16 multigravidas. Majority of pregnant women were in the third trimester of pregnancy, 23 (95.8%) (Table 1).

**Table 1. Demographic characteristics of 24 COVID-19 positive pregnant women**

Parameter	Number (%) of women
<b>Age group (years)</b>	
20-24	3 (12.5)
25-29	7 (29.2)
30-34	7 (29.2)
35-39	6 (25)
40-44	1 (4.1)
<b>Parity</b>	
Primigravida	8 (33.3)
Multigravida	16 (66.7)
<b>Period of gestation (weeks)</b>	
12-28	1 (4.1)
>28	23 (95.9)

Of the 24 COVID-19 positive pregnant women, 19 (79.2%) were asymptomatic, three (12.5%) had mild symptoms (cough, fever, rhinitis, myalgia or fatigue); two (8.3%) had COVID-19 pneumonia and a more severe clinical presentation, and they were admitted to the Intensive Care Unit (ICU) of the COVID Department due to the need for non-invasive ventilation support. Due to obstetric indications (pelvic presentation in multigravida and premature birth and premature rupture of foetal membranes in primigravida), they were delivered by caesarean section within 24 hours from the moment of admission to the ICU COVID Department; they were retested after 14 days and with the results of the COVID-19 negative test they were discharged in a stable condition for further home treatment. The main comorbidities recorded were high BMI (body mass index) in eight (33.3%), anaemia in four (16.7%), and thrombocytopenia in three (12.5%) pregnant women. Hypertensive disorder was reported in pregnant women with COVID-19 pneumonia and severe clinical presentation (Table 2).

**Table 2. Maternal presenting symptoms and associated comorbidities of 24 COVID-19 positive pregnant women**

Parameter	Number (%) of women patients
<b>Symptoms at admission</b>	
Asymptomatic	19 (79.2)
Mild (diarrhoea/vomiting, fever or shortness of breath)	3 (12.5)
COVID-19 pneumonia	2 (8.3)
<b>Maternal co-morbidities</b>	
HTN/PE/GHTN	1 (4.2)
DM/GDM	1 (4.2)
Anaemia	4 (16.7)
Thrombocytopenia	3 (12.5)
BMI >30	8 (33.3)

HTN/PE/GHTN, hypertension, preeclampsia, gestational hypertension; DM/GDM, diabetes mellitus, gestational diabetes mellitus;

All SARS-CoV-2-positive women gave birth within 48 hours of admission to our facility. A high rate of preterm births was observed, eight (33.3%),

who gave birth before 37 weeks of gestation. In 18 (75%) women the delivery was completed by caesarean section, while six (25%) gave birth vaginally. The most common indication for caesarean section was a previous caesarean section, 13 (54.2%), followed by foetal distress, six (25%), prolonged vaginal delivery, three (12.5%), and breech presentation in three (12.5%) women. Premature rupture of the membranes was observed in two (8.3%) women (Table 3).

**Table 3. Pregnancy outcome**

Parameter	Number (%) of women
<b>Time of delivery</b>	
<34 weeks	5 (20.8)
34-37 weeks	3 (12.5)
>37 weeks	16 (66.7)
<b>Mode of delivery</b>	
Vaginal delivery	6 (25)
Lower section caesarean section	18 (75)
<b>Indication for lower section caesarean section</b>	
Previous caesarean section	13 (54.2)
Foetal distress	6 (25)
Non-progress of labour	3 (12.5)
Cephalopelvic disproportion	1 (4.2)
Breech presentation	3 (12.5)
Placenta previa	1 (4.2)
Situs transversus	1 (4.2)
Prelabor rupture of membranes	2 (8.3)

A total number of babies born in the observed group of pregnant women was 25 with one twin pregnancy. Two (8%) women were diagnosed with intrauterine foetal death on admission to our hospital (none of them prenatally controlled at our hospital). A total of 23 (92%) live children were born (Table 4).

**Table 4. Neonatal outcomes and complications**

Parameter	Number (%) of women
<b>Neonatal outcome</b>	
Intrauterine foetal deaths	2 (8)
Live births	23 (92)
<b>Birth weight (grams)</b>	
<2000	4 (16)
2000- 2500	2 (8)
>2500	19 (76)
Small for gestational age (<10th centile)*	3 (12)
<b>Neonatal complication</b>	
NICU admission	8 (34.7)
Transport to tertiary care hospital	3 (13)
<b>Neonatal deaths</b>	
COVID-19 positive	2 (8.7)
Total live births	23 (92)

\*Against the international INTERGROWTH-21st Newborn Size Standards; NICU, neonatal intensive care unit;

Three (16%) babies of birth weights below 2000 g, two (8%) between 2000-2500 g and 19 (76%) above 2500 g were born. The weight of newborn babies ranged from 1000 to 4450 grams with an

average birth weight of 3118 g. Eight (34.7%) babies were admitted to the Neonatal Intensive Care Unit (NICU). Twenty babies (87%) were discharged from the hospital after recovery, while three (3%) were transported to another higher-level health care centre (all three were of low birth weight of <2500 g with developed respiratory distress syndrome). Unfortunately, during the hospitalization, the newborns did not stay in the same room with their mothers due to specific organizational structure of the ICU of the COVID department. All five previously admitted babies were discharged from the NICU, as well as three babies who were transported to the tertiary care centre.

Samples of nasal swabs for screening for SARS-CoV-2 were done in all 23 babies within 24 hours after birth. Two (8.7%) babies had a positive test but they were asymptomatic. Both positively tested babies were born by caesarean section. Their mothers had mild symptoms of COVID-19 disease.

## DISCUSSION

The aim of this study was to examine the clinical presentation of COVID-19 infection in pregnancy, its course during pregnancy, the effects on pregnancy outcomes for both mother and newborn as well as the potential for vertical transmission.

Our study included 24 pregnant women positive for COVID-19, most of whom (98.8%) were in the third trimester of pregnancy. Nineteen pregnant women (79.2%) were asymptomatic, three (12.5%) had a mild form of the disease, while only two (8.3%) pregnant women had a serious illness that required intensive care. Global data indicate that a large number of pregnant women carrying the virus have a mild clinical presentation of the disease (16), with complete recovery (16-18). Similar to our results were reported in a study of 141 patients in Mumbai where most of the women (97%) were asymptomatic or had mild symptoms (8). One possible reason for higher prevalence of asymptomatic presentation in our and other studies could be the fact that testing was mostly done in late pregnancy (third trimester), close to delivery, when the symptoms which are more pronounced at early gestational age, disappeared (19). Fortunately, in our study group of pregnant women, only two women had

a serious presentation of the disease and required intensive care, and there were no death cases. However, some research has shown that pregnant women have a higher risk of severe illness and increased admission to the ICU compared to non-pregnant women (6,18,20,21).

The main recorded comorbidities in our study were high BMI (33.3%), anaemia (16.7%) and thrombocytopenia (12.5%). In the US cohort study obesity was shown to be a key concomitant morbidity (22), as well as in an Italian study (median BMI was 30 kg/m<sup>2</sup> in 14 women with severe disease) (23). Obesity is known to alter the physiology of the immune response (24). Hypertensive disorder has been reported in pregnant women with COVID-19 pneumonia and a more severe clinical presentation (25).

In our study, of 24 COVID-19 positive pregnant women, 18 completed the delivery by caesarean section reflecting a higher rate of pregnancy complications in this group. The most common indications for caesarean section were previous caesarean section, foetal distress, prolonged vaginal delivery and presentation of the buttocks. We must note that due to the specific organizational structure of the ICU of the COVID Department, we did not decide on an induction of labour in pregnant women with a previous caesarean section. Our position is that the manner of childbirth should not be affected by the presence of COVID-19, unless the mother's respiratory condition requires urgent childbirth. Most previous studies done on COVID-19 positive pregnant women reported very high caesarean section rates, where most caesarean sections were done in maternal interest and due to concern for respiratory function (10,13,26). The main reason for the large number of caesarean sections could be attributed to local protocols aimed at helping to improve maternal lung ventilation. Experts' opinion is that acute COVID-19 infection should not be an indication for surgical completion of preterm labour unless maternal or foetal decompensation occurs during labour itself (27). The second most common indication for caesarean section of our examined pregnant women was foetal distress. Shanes et al. showed that the placenta of pregnant women infected with COVID-19, who gave birth in the third trimester of pregnancy, showed signs of fetoplacental insufficiency (vascular malper-

fusion and intervillous thrombi) (28). Although no pathohistological changes of the placenta have been identified, these findings suggest abnormal maternal circulation associated with adverse perinatal outcomes (28). These changes may reflect a systemic inflammatory or hypercoagulable condition that affects placental physiology.

In our study, we observed a high rate of preterm birth (before 37 weeks of gestation) (33.3%). In the same period in 2019, the rate of premature births in our institution was 5.8%. Premature rupture of membranes (PROM) was observed in 2 (8.3%) pregnant women. Previous research has shown that viral pneumonia in pregnant women is associated with an increased risk of preterm birth, foetal growth retardation (FGR), and perinatal mortality (29). A Spanish group of obstetricians in their recent study using multivariate models found that COVID-19 positive pregnant women had more preterm births, premature rupture of membranes at term, and admission of newborns to NICU compared to uninfected pregnant women (30). Currently there is insufficient evidence to establish any association between spontaneous preterm birth and COVID-19 infections in pregnancy.

Along with a large number of premature births, we also found high prevalence (24%) of babies of both low birth weight and admissions of newborns to the NICU (34.7%). In the same period in 2019, the prevalence of babies of low birth weight was 4.2%. A total of 8% of pregnant women on admission to our hospital were diagnosed with intrauterine foetal death, while neonatal death fortunately was not recorded. Nayak et al. also reported low birth weight in 29.77% of neonates and an intrauterine death rate of 2.23% of pregnant women positive for COVID-19 (8). Allotey et al. concluded that although COVID-19 is more likely to cause preterm birth, low birth weight infants, and higher neonatal admissions, the overall rate of intrauterine and neonatal death is not higher than the rest of the pregnant population (18). In our examined group, the rate of intrauterine death was higher in relation to the healthy population of pregnant women, but our sample was also relatively small and it was about pregnant women who were not controlled in our institution before hospitalization.

Samples of nasal swabs for screening for SARS-CoV-2 were done in all 23 babies within 24 hours



after birth. Two babies had a positive test but were asymptomatic. Both positively tested babies were born by caesarean section. Initial reports from China documented the presence of immunoglobulin M (IgM) antibodies in neonates born to mothers who tested positive for COVID-19, raising concerns about the possibility of vertical transmission of the virus due to the fact that IgM cannot cross the fetoplacental barrier (31,32). Moreover, several recent studies have shown that COVID-19 can infect the placenta, as evidenced by the presence of viral RNA and SARS-CoV-2 protein in the placenta and evidence of the presence of virions found in the syncytiotrophoblast (33). In a large systemic review that included 666 infants born to mothers with confirmed COVID-19 infection, 4.2% were postnatally confirmed to have COVID-19 infection (34).

In light of existing evidence (35), we advise that the benefits of breastfeeding outweigh any potential risks of transmitting the virus through breast milk.

Although our study was limited to a small number of pregnant women, it can provide useful information for our population, improve our existing knowledge of COVID-19 infection in pregnancy,

and help develop antenatal counselling and management protocols to achieve safe and beneficial outcomes for both mothers and newborns. There is currently no evidence that a pregnant woman with COVID-19 infection is more prone to developing severe pneumonia than a non-pregnant patient. The high rate of preterm birth, low birth weight, and increased admission of newborns to the intensive care unit suggest that COVID-19 infection in pregnant women may affect pregnancy outcomes. Neonatal COVID-19 infection is possible but rare, mostly asymptomatic, and the rate of infection does not differ regardless of whether the child was born vaginally or by caesarean section. There is an urgent need for a long-term follow-up of pregnant women who have recovered from COVID-19 infection for possible long-term health effects, to examine residual or delayed effects in the neonate, including long-term COVID-19.

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#### TRANSPARENCY DECLARATION

Competing interests: None to declare.

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