This is a provisional PDF only. Copyedited and fully formatted version will be made available soon.





ORGAN POLSKIEGO TOWARZYSTWA GINEKOLOGICZNEGO THE OFFICIAL JOURNAL OF THE POLISH GYNECOLOGICAL SOCIETY

ISSN: 0017-0011

e-ISSN: 2543-6767

SARS-CoV-2 infection during pregnancy — single-center retrospective study

Authors: Malgorzata Skalska-Swistek, Magdalena Kolak, Andrzej P. Jaworowski, Rafal Swistek, Agnieszka Micek, Hubert Huras

DOI: 10.5603/gpl.95565

Article type: Research paper

Submitted: 2023-05-13

Accepted: 2023-06-12

Published online: 2023-08-14

This article has been peer reviewed and published immediately upon acceptance. It is an open access article, which means that it can be downloaded, printed, and distributed freely, provided the work is properly cited. Articles in "Ginekologia Polska" are listed in PubMed.

ORIGINAL PAPER / GYNECOLOGY

SARS-CoV-2 infection during pregnancy — single-center retrospective study

Malgorzata Skalska-Swistek¹, Magdalena Kolak¹, Andrzej P. Jaworowski¹, Rafal Swistek², Agnieszka Micek³, Hubert Huras¹

¹Department of Obstetrics & Perinatology, Jagiellonian University Medical College, Cracow, Poland ²Department of Anaesthesiology and Intensive Therapy, University Hospital in Cracow, Poland ³Department of Nursing Management and Epidemiology Nursing, Institute of Nursing and Midwifery Faculty of Health Sciences, Cracow, Poland

Short title: SARS-CoV-2 infection during pregnancy

Corresponding author:

Malgorzata Skalska-Swistek Department of Obstetrics & Perinatology, Jagiellonian University Medical College, Cracow, Poland e-mail: malgorzata12.skalska@uj.edu.pl

ABSTRACT

Objectives: The SARS-CoV-2 virus infection has spread to almost all countries in the last two years. Pregnancy complicated with COVID-19 is a unique situation and challenge for doctors. The study aimed to evaluate obstetric results, and biochemical test results and to analyze the treatment used in pregnant patients complicated with COVID-19 infection.

Material and methods: A retrospective analysis of 146 pregnant patients hospitalized at the Department of Obstetrics and Perinatology Jagiellonian University Medical College (JUMC) in Krakow was conducted from July 2020 to August 2021.

Results: In the analyzed group respiratory failure occurred in 19.19% of cases and intravascular coagulation syndrome (DIC) in 1.37%. One patient died (0.68%). 16.6% of

cases were transferred to the Intensive Care Unit (ICU) and required intubation. The remaining cases were mild: 39.04% were asymptomatic, 41.78% reported cough, 30.82% dyspnoea and 23.97% myalgia. In the laboratory tests increased values of CRP and IL-6 were observed with normal levels of leukocytes. Additionally, a decreased level of total protein and an increased level of d-dimers were detected. 98.63% of patients received a prophylactic dose of low molecular weight heparin. 46.58% of cases needed additional antibiotic therapy. Cesarean sections were performed in 59.59% of cases. The children were born in good general condition. Vertical transmission of SARS-CoV-2 to the newborn has not been confirmed.

Conclusions: Data from the above study show a significant effect of COVID-19 on pregnant patients. Almost one in five pregnant women occurred respiratory failure and most of them had to be transferred to the ICU department and had to be intubated.

Key words: COVID-19, SARS-CoV-2, cesarean section, intensive care unit, ICU, pregnancy

INTRODUCTION

COVID-19 disease is caused by the SARS-CoV-2 virus infection. It was first recognized and described in the last months of 2019 in China (Wuhan, Hubei province). Over the next few months, the disease spread to almost all countries of the world. Due to the growing number of cases, on March 11, 2020, WHO declared a pandemic. As of 12/07/2022, the number of confirmed COVID-19 patients had exceeded 624 million, and the number of confirmed deaths from this disease had increased to over 6.56 million [1].

Incidence among pregnant women was relatively lower than in the general population. However, women whose pregnancy was complicated by diabetes, hypothyroidism, or hypertension and women in the third trimester of pregnancy, were at risk of a more severe disease course. This is mainly due to changes in the immune, respiratory and circulatory systems [2, 3].

It also has been noticed that SARS-CoV-2 infection enhances the prothrombotic potential. The accompanying "cytokine storm" leads to massive vasculitis, disseminated coagulation, shock, and hypotension, ultimately to multiple organ failure and death. The laboratory picture of hemostasis parameters in a patient suffering from COVID-19 resembles disseminated intravascular coagulation (DIC), sepsis-induced coagulopathy (SIC), thrombotic microangiopathy (TMA), and HELLP syndrome [4].

The study aimed to evaluate obstetric results, and biochemical test results and to analyse the treatment used in pregnant patients complicated with COVID-19 infection, who

were hospitalised at the Department of Obstetrics and Perinatology Jagiellonian University Medical College (JUMC) in Krakow from July 1, 2020, to August 31, 2021.

MATERIAL AND METHODS

Study population

It was a retrospective study including 146 patients hospitalised in the Department of Obstetrics and Perinatology Jagiellonian University Medical College (JUMC) in Krakow due to COVID-19 infection from 01/07/2020 to 31/08/2021. During the pandemic, this third-level reference centre had a separate department with an increased sanitary regime.

During this time 3,394 patients were hospitalised and there were 2,700 deliveries in total, including 1,654 cesarean sections and 1,046 vaginal deliveries. There was no COVID-19 vaccine available those days.

Data collection

A retrospective analysis of the patient's medical records was carried out, with particular emphasis on the data on the course of pregnancy, childbirth, general condition of the mother (the lowest values of blood saturation with atmospheric air, the need for oxygen therapy, antibiotics, anticoagulant prophylaxis), the severity of COVID-19 infection, laboratory test results (basic morphology, inflammatory markers, coagulation system parameters, renal and hepatic parameters). Laboratory tests were taken to the study on the day when the patients' atmospheric air saturation values were the lowest. Values are coded as lowered, normal, and elevated according to laboratory standards. The study also used data on the newborn after delivery [birth weight, Apgar score at 1 and 5 minutes, hospitalisation time, polymerase chain reaction (PCR) smear result for COVID-19 infection].

Inclusion and exclusion criteria

The inclusion criteria for the study were: confirmed COVID-19 infection (positive PCR or antigen test) and pregnancy over 16 weeks.

Statistical analysis

The results of the study were analysed by statistical methods using R software version 3.6.1 (Development Team, Vienna, Austria). Descriptive statistics were presented as means and standard deviations, or medians and interquartile ranges depending on the distribution.

The study is part of the obstetric project of the National Centre for Research and Development CRACoV-HHS — a model of multidisciplinary hospital and out-of-hospital care for patients with SARS-CoV-2 infection under the initiative, supporting multi-specialist hospitals in combating the spread of SARS-CoV-2 infection and treating COVID-19 [5]. The study has a positive opinion of the Bioethics Committee of the Jagiellonian University, number 1072.6120.202.2021 of September 29, 2021.

RESULTS

Characteristics of the research group

The mean age of the study group was 31.10 years (SD +/- 5.01). The mean body mass index (BMI) was 28.74 kg/m² (SD +/- 4.82). The most common comorbidities were hypothyroidism (34.93%), diabetes (11.64%), and hypertension (9.59%). One patient had gestational cholestasis (0.68%). Hospitalisation of 14 patients was associated with premature rupture of membranes (9.59%). In 36 pregnant patients (24.66%), steroid therapy with betamethasone was used in the antenatal period to accelerate the maturation of the foetal lungs. Detailed data are presented in Table 1.

The course of COVID-19 infection

Most of the patients admitted to the Department of Obstetrics and Perinatology had COVID-19 infection with flu-like symptoms. The most commonly reported symptoms were cough (41.78%), dyspnoea (30.82%), myalgia (23.97%), fever (18.49%), runny nose (17.81%), loss of smell and taste (16.44%). In 28 patients, the course of SARS-CoV-2 infection was acute (19.19%). Two patients developed disseminated intravascular coagulation syndrome (1.37%). One patient died of COVID-19 infection (0.68%). Only in 39.04% of hospitalised patients, the SARS-CoV-2 infection was asymptomatic. The data are presented in Table 2.

The course of pregnancy in patients with SARS-CoV-2 infection

87 patients (59.59%) gave birth by caesarean section. Another 45 patients (30.82%) continued the pregnancy, and 14 patients had a vaginal delivery (9.59%). The median gestational age of delivery was 37 weeks of pregnancy (Tab. 1).

Treatment

The median time for the patients to report symptoms of virus infection before admission to the hospital and for testing for COVID-19 infection was 2 days (0–4). The median hospitalisation time in the intensive care unit was 5 days. In most cases, the infection was mildly symptomatic — the patients were circulatory and respiratory efficient. 71.92% of patients did not require respiratory support, and the median value of peripheral blood saturation was 98%. In the case of patients whose saturation was < 95%, an oxygen cannula, a straight mask, a mask with a reservoir, or a high-flow nasal oxygen therapy (Optiflow) was used. Despite the oxygen therapy, 11 patients required intubation and admission to the Intensive Care Unit due to the increasing features of respiratory failure.

Patients with worsening symptoms of upper respiratory tract infection and significantly elevated parameters of inflammation received empirical antibiotic therapy (mainly third-generation cephalosporin). The treatment was applied to 68 women (46.58%). In addition, patients with a severe course of COVID-19 received glucocorticosteroids. Hydrocortisone was the most commonly administered. Low molecular weight heparins were used in all patients during hospitalisation (Tab. 2).

Characteristic	Total n = 146
Age [years]#	31.10 (5.01)
Body mass index (BMI) [kg/m ²]#	28.74 (4.82)
Week of gestation [weeks]*	37.0 (31.25–39.00)
Comorbidities	n (%)
Hypertension	14 (9.59)
Intrahepatic cholestasis of pregnancy (ICP)	1 (0.68)
Hypothyroidism	51 (34.93)
Diabetes mellitus	17 (11.64)
Preterm Premature Rupture of Membranes (PPROM)	14 (9.59)
Treatment	
Antenatal corticosteroids for foetal lung maturity	36 (24.66)

Table 1. Patients baseline characteristic

Route of delivery	n (%)
Caesarean section	87 (59.59)
Caesarean section due to mother's respiratory distress **	21/87 (24.14%)
Natural birth	14 (9.59)
Continue a pregnancy	45 (30.82)
Preterm birth	24 (23.76%)

Data are presented as the number of cases and percentage: n (%). Data marked as (#) are presented as the mean and standard deviations (SD). Data marked as (*) are presented as the median and interquartile range; ** Respiratory distress defined as acute dyspnea (tachypnoea, shortness of breath) and persistently decreased blood saturation < 95% despite increasing oxygen therapy, the indication of CS was threatening fetal distress

General information	
Time from first symptoms to positive swab [days]*	2.0 (0.0–4.0)
Time from first symptoms to admission [days]*	2.0 (0.0–4.0)
Time of patient hospitalisation [days]*	5.0 (4.0–10.0)
Hospitalisation in ICU [days]*	n = 11
	7.0 (6.0–14.5)
Saturation [%] *	98.00 (96.00–98.00)
Symptoms	n (%)
Asymptomatic	57 (39.04)
Fever	27(18.49)
Dyspnea	45 (30.82)
Dysgeusia or dysosmia	24 (16.44)
Myalgia	35 (23.97)
Runny nose	26 (17.81)
Cough	61 (41.78)
Severe complication	n (%)

Table 2. The course of COVID-19 infection

Severe COVID infection with respiratory failure	28 (19.19)
Disseminated intravascular coagulation	2 (1.37)
Death	1 (0.68)
Treatment	n (%)
Antibiotics	68 (46.58)
Low molecular weight heparin	144 (98.63)
Corticosteroids: hydrocortisone	18 (12.33)
Corticosteroids: dexamethasone	9 (6.16)
Prone position	6 (4.11)
Oxygen Therapy	n (%)
Atmospheric air	105 (71.92)
Nasal cannula	20 (13.70)
Simple mask	5 (3.42)
Mask with reservoir bag	2 (1.37)
Optiflow	3 (2.05)
Intubation	11 (7.53)
Type of anaesthesia during caesarean section	n (%)
Spinal anaesthesia	75 (83.33)
General anaesthesia	15 (16.67)

Data are presented as the number of cases and percentage: n (%). Data marked as (*) are presented as the median and interquartile range; In oxygen therapy, the most advanced therapy was included in statistics; ICU — Intensive Care Unit

Laboratory test results

During hospitalisation all patients had blood morphology. In some patients, liver enzymes [aspartate aminotransferase (AST), alanine transaminase (ALT)], total protein, values of inflammatory parameters: C-reactive protein (CRP), procalcitonin, IL-6, coagulation parameters (fibrinogen, D-dimers) and the presence of protein in urine were additionally measured. In the performed tests, the leukocytosis of most of the patients remained within the normal range (71.92%). There was an increase in CRP in (53.42%) and IL-6 in (30.82%) of patients. Procalcitonin increased 9.59% of the cases. 27.4% had elevated liver test values. Total serum protein was below normal at 46.58%. Blood coagulation parameters indicated a decreased level of fibrinogen in 2.05% of patients and an increased concentration of d-dimers (50%). Detailed results of laboratory tests are presented in Table 3.

Parameter	Norm	Change type; n/total (%)
White blood count [×10^3 /mm ³]	4.00–10.00	increased; 41/146 (28.08)
C-reactive protein [mg/L]	< 5.00	increased; 78/96 (53.42)
Procalcitonin [ng/mL]	< 0.50	increased; 14/77 (9.59)
Interleukin-6 [pg/mL]	< 7	increased; 45/61 (30.82)
Fibrinogen [g/L]	1.8–3.5	decreased; 3/32 (2.05)
D-dimer on admission [mg/L]*	< 0.55	increased; 73/77 (50.0)
Liver enzymes (AST, ALT) [U/l]	10–35	increased; 27/92 (27.40)
Total protein [g/L]	66.0–87.0	decreased; 68/89 (46.58)
Proteinuria [g/L]	< 0.15	present; 34/ 71 (23.29)

Table 3. Laboratory test results on the day when the values of atmospheric air saturation were the lowest

Test values are presented in whole numbers (number of incorrect results/number of cases where a given parameter was tested and as a percentage; *D-dimers levels are presented from patient`s worst clinical condition day; AST — aspartate aminotransferase; ALT — alanine transaminase

Neonatological results

The median Apgar score at 1 and 5 minutes was 10 points. The average birth weight of newborns was 3045 grams. All newborns had nasopharyngeal swabs taken twice for COVID-19 infection and the PCR test was performed. The results of these tests revealed no infection in the newborns. Due to the severe course of COVID-19 in the mother, aspirate was obtained from the lower respiratory tract in one newborn. The test showed the presence of SARS-CoV-2, despite a negative nasopharyngeal test. The mean time of hospitalisation of the newborns was 9 days, and the time of their isolation lasted 2 days. The results are presented in Table 4.

Neonatal outcomes	Total n = 101
Birth weight [grams]#	3045.88 (726.40)
Score in Apgar scale in 1st-minute life [point]*	10 (9.00–10.00)
Score in Apgar scale in 5th-minute life [point]*	10 (9.00–10.00)
Time of newborn hospitalisation [days]*	9.00 (6.00–16.00)
Time of newborn isolation [days] *	2.00 (1.00–2.00)
Negative nasopharyngeal swab for COVID-19	101 (100)
infection (PCR test)	

Table 4. Neonatal outcomes

Data are presented as the number of cases and percentage: n(%). Data marked as (#) are presented as the mean and standard deviations (SD). Data marked as (*) are presented as the median and interquartile range; PCR — polymerase chain reaction

DISCUSSION

Pregnant women are a special group of patients. During the diagnostic and therapeutic procedure, we must always remember two people - the woman and the foetus. The results of the study show the population of women in pregnancy complicated with COVID-19. In the period from July 2020 to August 2021 patients hospitalised in a third-level reference centre in the second and third trimesters of pregnancy, in whom the presence of SARS-CoV-2 was confirmed by microbiological tests were analysed.

In a retrospective work by Zhang et al. [6], it has been shown that the course of the disease was mild in 15 out of 16 pregnant patients complicated with COVID-19. In all the patients, the pregnancy was delivered by caesarean section at about 38 weeks of pregnancy. There was no difference in the results of newborns' birth weight and no difference in intraoperative blood loss compared to the control group. In a study by Elsadding et al. [7], it was found that the course of COVID-19 in pregnant patients was similar to that in non-pregnant women. However, pregnant women with SARS-CoV-2 infection required hospitalisation in the intensive care unit more often. In our study in 24.14% of patients,

despite the intensification of oxygen therapy, no improvement in blood oxygenation was achieved. Symptoms of respiratory failure were increasing. To avoid intrauterine asphyxia, it was necessary to finish the pregnancy. Caesarean section was the most common method of birth.

The results carried out by Stachura et al. [8] in the group hospitalised in the Pulmonology Department JUMC in Krakow due to COVID-19 infection in the period from March to July 2020, showed that 45% of patients developed respiratory failure, of which 17% required transferring to ICU. In the analysed period, 10% of patients died. The study group consisted of 100 men and women with an average age of 59 [8]. Our analysis, from the same hospital, a similar study period but another department, showed that in most cases the course of the disease was asymptomatic (39.04%). 19.19% of patients developed respiratory failure; 7.53% required hospitalisation in the intensive care unit. Moreover, two patients developed intravascular coagulation (1.37%) and one patient (0.68%) died [9].

Cavalcane et al. [10] found that the prone position facilitated lung ventilation during severe acute respiratory distress syndrome (ARDS). This position also reduces the pressure of the pregnant uterus on the maternal large vessels, while making it possible to monitor the well-being of the foetus [10]. Pourdowlat et al. [11] in their study described a case of a 24-year-old pregnant woman who was in a prone position due to increasing features of respiratory failure. The use of such a procedure improved the patient's results and had no negative impact on the foetus [11]. At our centre, 6/28 (4.11%) of patients with severe COVID-19 were treated in the prone position. This position facilitated the gas exchange, with the improvement of blood oxygenation and obtaining an improvement in the clinical condition of the patients.

According to research by Song et al. [12] concerning the innate and acquired immunity of newborns, it has been shown that transplacental transmission of IgG antibodies to the foetus occurs when a pregnant patient becomes infected with the virus. The level of IgG antibodies in infants is significantly higher when infection with the SARS-CoV-2 virus occurred 60-180 days before delivery. The level of antibodies in newborns was maintained up to 6 months of age [12]. In turn, in a systematic review by Kotlyar et al. [13] vertical transmission of the virus is possible, but it concerns a significant minority of newborns born in the third trimester of pregnancy. Serological tests performed on blood samples of newborns revealed the presence of IgM antibodies to SARS-CoV 2 virus in 3 out of 82 cases of newborns [13]. Our study showed no vertical transmission of the virus from nasopharyngeal swabs (PCR). However, one foetus had positive PCR results from aspirate from the lower respiratory tract despite negative nasopharyngeal swabs. The level of IgG and IgM antibodies to SARS-CoV-2 was not tested in newborns.

As the pandemic continues, studies have shown that the virus is not present in vaginal secretions in women with symptomatic COVID-19 infection, and vaginal delivery is safe for both mother and child [14]. Cai et al. [15] in a literature review concluded that there is insufficient evidence that caesarean section is superior to vaginal delivery in preventing vertical transmission of the virus. The way of birth should be individually adapted to the patient's clinical condition [15]. In the first months of the pandemic, it was unclear whether SARS-CoV-2 could be transmitted vertically with secretions from the genital tract, which would increase the risk of neonatal infection. Also, the time needed to perform a caesarean section was incomparably shorter than the vaginal delivery. The presence of an infected patient posed a risk to midwives and doctors. This was often caused by the limitation in the number of appropriate equipment to prevent infection. According to the recommendations of the Polish Society of Gynaecologists and Obstetricians in 2020, the increase in the incidence of COVID-19 among pregnant patients, the necessity to undergo quarantine, the pregnancies were planned to be delivered by caesarean section [16]. In our study, 59.59% of infected women were delivered by caesarean section. As the pandemic progressed, the vaginal route was recommended as the way of delivery. During the study period, 1.38% of patients had vaginal deliveries. Those patients had mild symptoms of infection.

Wang et al. [17] analysed the results of laboratory tests of pregnant women with SARS- CoV-2 infection to non-pregnant women with COVID-19 infection. The group consisted of 72 patients, 30 of which were pregnant. The results showed that the level of leukocytes, CRP protein, procalcitonin, and D-dimers was slightly higher in pregnant women [17]. In turn, Mo et al. [18] studied 155 patients with resistant pneumonia during COVID-19. They found that those with a severe course of infection were mainly elderly men with comorbidities. They showed higher levels of neutrophils, aspartate aminotransferase (AST), and C-reactive protein [18]. Our study showed in the vast majority of cases an increase in CRP level with a normal concentration of leukocytes and procalcitonin values. The increased concentration of D-dimers, which are markers of fibrinolysis, was of limited interpretation, as it physiologically increases during pregnancy. In 46.58% of the examined patients, a decrease in the level of total protein was found. The increase in the concentration of hepatic liver enzymes was demonstrated in 27.40% of the examined patients.

In case of deterioration in the general condition, the patient was treated with glucocorticosteroids (GCs). In our ward, patients mainly received hydrocortisone at a dose of

 3×50 mg. According to the recommendations of the Royal College of Obstetricians and Gynecologists (RCOG), the duration of therapy was approximately 10 days [19]. The RECOVERY study showed that the use of steroids in pregnant patients during moderate or severe COVID-19 significantly improved the condition of patients. The RECOVERY study also recommended the use of prednisolone 40 mg per day orally or hydrocortisone 80 mg intravenously twice a day for pregnant patients. The study showed that the use of steroids can reduce the risk of death and the time needed for mechanical ventilation in COVID-19 patients with developed ARDS. Corticosteroids cause immunosuppression, and their use has largely been controversial due to the potential increase in viral replication and hence the severity of the infection. However, no increased incidence of severe or critical pneumonia in the presence of COVID-19 was observed in patients taking long-term maintenance steroids [20]. Depending on the time of their action and concentration in the circulation, GCs show either a stimulating or an inhibitory effect on the immune response. Low to medium doses of GCs induce mild immunosuppression, reducing autoimmunity and cytokine toxicity. This action is aimed at reducing inflammation and the process of pulmonary fibrosis during an acute course of ARDS. Singh et al. [21] in a systematic review of the use of steroid therapy in patients with COVID-19 analysed the results of 4 retrospective studies and 1 quasi-prospective study. The results were heterogeneous, and it was difficult to conclude the final benefits of corticosteroid therapy during SARS-CoV-2 virus infection. Only the RECOVERY study showed significantly better treatment effects in patients with severe disease, associated with a 35% reduction in mortality in mechanically ventilated patients and 20% in patients using assisted ventilation [21]. In our study, steroid therapy was used in 36 patients (24.66%) to accelerate the maturation of the foetal lungs. In most cases, betamethasone was administered intramuscularly and the treatment lasted 48 hours. Betamethasone and dexamethasone are not metabolised by the placental steroid dehydrogenase 11-b-hydroxylase-type 2. Therefore, they have the highest transfer through the placenta [20]. Interchangeable administration of dexamethasone and betamethasone is possible. However, dexamethasone has not been used for a long time because it adversely affects the nervous system in the foetus — mainly the development of the hippocampus. Prenatal exposure to corticosteroids can affect the expression of various molecules such as the GR glucocorticoid receptors, corticoliberin (CRH), brain-derived neurotrophic factor (BDNF), and neuropeptide Y (NPY), found in the foetal hippocampus. In the future, this may determine the survival of neurons in the central nervous system in a child, and influence changes in behaviour, and the appearance of seizures [22]. This treatment step was followed by intravenous hydrocortisone therapy or oral

prednisolone therapy as they pass through the placenta to a lesser extent. Therefore, in the future, it will be important to assess the neurological development of children of mothers undergoing prolonged GCs therapy in the course of COVID-19 infection.

During the COVID-19 pandemic, the constant cooperation of obstetricians, neonatologists, and the anesthesiology team turned out to be very important. Often, the clinical condition of patients in our third-level reference centre required the establishment of a common consensus of action to improve the patient's general condition, the type of anaesthesia used during the caesarean section, as well as the management of the newborn immediately after birth. Due to COVID-19 infection, the risk of exposure of healthcare professionals to airborne virus particles during surgery had increased. This was an additional argument for limiting the use of general anaesthesia, if possible, in favour of regional anaesthesia [24]. The use of general anaesthesia for caesarean section was associated with the presence of contraindications to regional anaesthesia, such as low platelet count, confirmed coagulopathy, unknown coagulation status in patients at risk of coagulopathy or lack of sufficient time interval from the last dose of low molecular weight heparin, hypovolaemia, and respiratory failure. General anaesthesia was used in 16.67% of cases, and 83.33% of patients — spinal anaesthesia. In a retrospective analysis, Krawczyk et al. [25] showed that in the initial period of the COVID-19 pandemic, the use of general anaesthesia decreased in favour of regional anaesthesia.

It is also worth paying attention to the topic of prematurity among newborns. Prematurity is still a complicated pathophysiological condition associated with an increased risk of long-term morbidity and mortality in newborns. It is the main cause of death of children in Poland. The birth rate before 37 weeks of gestation remains at the level of 6.7% of live births [26]. Wood et al. investigated whether the number of preterm births in the United States increased or decreased during the 2020 pandemic compared to the pre-pandemic in 2019 during the same periods — from April to July. There was no difference in the number of premature deliveries [27]. In turn, in a study conducted in Denmark by Hedermann et al. [28] and in Ireland by Philip and al. [29], a reduction in the number of preterm deliveries among newborns was found. However, Akhtar et al. [30] in their systematic review, found that pregnancy complicated by COVID-19 infection increases the risk of preterm labour and the risk of premature rupture of membranes. Among the group of patients we studied, 24 cases (23.76%) of preterm labour before 37 weeks of gestation occurred, which is more than in the general population in Poland in 2021 [26]. At the same time, 30.82% of patients were discharged home with a sustained pregnancy.

An additional, readily available, and non-invasive method of detecting and diagnosing pneumonia developing during COVID-19 may be lung ultrasound (LUS). The most common symptoms visible in ultrasound were focal B lines and the image of a light beam [31]. In a study conducted on a group of patients in the first stage of labour and just after delivery at the Obstetrics and Perinatology JUMC in Krakow in the period before the COVID-19 pandemic, it was found that most patients had at least one positive region (\geq 3 B lines) in the LUS study before and after childbirth. Thus, women during uncomplicated labour may present incorrect LUS results, which may affect the interpretation of the results in a pregnancy complicated with SARS-CoV-2 infection [32]. A popular tool is the BRIXIA scale, in which a chest X-ray is used to assess the severity of inflammatory changes in the lungs on the day of admission to hospital (A), discharge (E), the mildest (L) and most severe condition of the patient during hospitalisation (H). The scale is 18 points. The greater the number of points, the greater the damage to the lungs. Agrawal et al. [33] conducted a study of 130 patients (men and women), with an average age of 57 years, assessed using the BRIXIA scale. They found that the score above 12 points increased with the increased mortality in COVID-19 patients [33]. On the other hand, Covali et al. [34] in their work did not show a significant correlation between the results of the mother, the foetus and the BRIXIA score. In our centre we did not perform routine LUS or X-ray examinations on pregnant patients.

The advantages of the study were a large group of analysed patients compared to other single-centre studies. In addition, an undoubted advantage is a comprehensive assessment of the condition of patients and newborns.

Our research also had several limitations. It is a retrospective study with typical features of such work, including a lower strength of evidence. It was not always possible to obtain the results of screening tests, *e.g.*, morphology with a smear, level of CRP protein, procalcitonin, liver tests, and D-dimers. The research group of COVID-19 patients hospitalised between July 2020 and August 2021 contains a relatively high proportion of mild cases compared to the later period of the pandemic. A comparative analysis of patients from the later period of the COVID-19 pandemic is planned. The study was conducted in a third-level reference centre, so the presented study group consisted of patients at high risk of pregnancy compared to other maternity wards.

CONCLUSIONS

The data show a significant effect of COVID-19 on pregnant patients. Although most cases from July 2020 to August 2021 were mild, as much as 19% of cases were transferred to

the ICU and intubated. Also, other severe complications occurred (DIC and death). Almost half of the patients need additional antibiotics therapy and ¹/₅ glucocorticosteroids therapy.

In the laboratory tests, normal levels of leukocytes were performed. But decrease the level of total protein and increase in the value of C-reactive protein, IL-6, d-dimers were observed.

Caesarean section was the most common way of delivery. The children were born in good general condition. Analysing the results of PCR tests from the nasopharynx of newborns, it can be concluded that there is no vertical transmission of the SARS-CoV-2 virus.

Article informations and declarations

Author contributions

Conceptualization, M.S.-Ś., H.H. and M.K.; methodology, M.S.-Ś. and M.K.; validation M.S.-Ś., H.H., A.P.J. and M.K.; formal analysis, M.K. and A.P.J.; investigation, M.S.-Ś., H.H., A.P.J. and M.K.; resources, M.S.-Ś.; writing — original draft preparation, M.S.-Ś.; writing — review and editing, M.S.-Ś., R.Ś., A.P.J. and M.K.; visualization, M.S.-Ś. and R.Ś.; supervision, H.H. and M.K. All authors have read and agreed to the published version of the manuscript.

Funding

This publication was supported by the National Center for Research and Development CRACoV-HHS project (model of multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection) through the initiative "Support for specialist hospitals in fighting the spread of SARS-CoV-2 infection and in treating COVID-19" (contract number — SZPITALE-JEDNOIMIENNE/18/2020). The described research was implemented by consortium of the University Hospital in Cracow and the Jagiellonian University Medical College.

Conflict of interest

The authors declare no conflict of interest.

REFERENCES

- 1. https://www.worldometers.info/coronavirus/ (12.07.2022).
- 2. Hanna N, Hanna M, Sharma S. Is pregnancy an immunological contributor to severe or

controlled COVID-19 disease? Am J Reprod Immunol. 2020; 84(5): e13317, doi: <u>10.1111/aji.13317</u>, indexed in Pubmed: <u>32757366</u>.

3. Gęca T, Wojtowicz K, Guzik P, et al. Increased Risk of COVID-19 in Patients with Diabetes Mellitus-Current Challenges in Pathophysiology, Treatment and Prevention. Int J Environ Res Public Health. 2022; 19(11), doi: <u>10.3390/ijerph19116555</u>, indexed in Pubmed: <u>35682137</u>.

4. Hadid T, Kafri Z, Al-Katib A. Coagulation and anticoagulation in COVID-19. Blood Rev. 2021; 47: 100761, doi: <u>10.1016/j.blre.2020.100761</u>, indexed in Pubmed: <u>33067035</u>.

 Sydor W, Wizner B, Strach M, et al. CRACoV-HHS Investigators and Collaborators listed in supplementary material — link available in Acknowledgment. CRACoV-HHS: an interdisciplinary project for multi-specialist hospital and non-hospital care for patients with SARS-CoV-2 infection as well hospital staff assessment for infection exposure. Folia Med Cracov. 2021; 61(4): 5–44, doi: <u>10.24425/fmc.2021.140002</u>, indexed in Pubmed: <u>35180200</u>.
 Zhang L, Jiang Y, Wei M, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. Zhonghua Fu Chan Ke Za Zhi. 2020; 55(3): 166–171, doi: <u>10.3760/cma.j.cn112141-20200218-00111</u>, indexed in Pubmed: <u>32145714</u>.

7. Elsaddig M, Khalil A. Effects of the COVID pandemic on pregnancy outcomes. Best Pract Res Clin Obstet Gynaecol. 2021; 73: 125–136, doi: <u>10.1016/j.bpobgyn.2021.03.004</u>, indexed in Pubmed: <u>33832868</u>.

8. Stachura T, Celejewska-Wójcik N, Polok K, et al. A clinical profile and factors associated with severity of the disease among Polish patients hospitalized due to COVID-19 - an observational study. Adv Respir Med. 2021; 89(2): 124–134, doi: <u>10.5603/ARM.a2021.0035</u>, indexed in Pubmed: <u>33966260</u>.

 9. Skalska-Świstek M, Huras H, Jaworowski AP, et al. COVID-19 Infection Complicated by Disseminated Intravascular Coagulation during Pregnancy-Two Cases Report. Diagnostics (Basel). 2022; 12(3), doi: <u>10.3390/diagnostics12030655</u>, indexed in Pubmed: <u>35328208</u>.
 10. Cavalcante FM, Fernandes Cd, Rocha LD, et al. Use of the prone position in pregnant women with COVID-19 or other health conditions. Rev Lat Am Enfermagem. 2021; 29: e3494, doi: <u>10.1590/1518-8345.5181.3494</u>, indexed in Pubmed: <u>34755775</u>.

 Pourdowlat G, Mikaeilvand A, Eftekhariyazdi M, et al. Prone-Position Ventilation in a Pregnant Woman with Severe COVID-19 Infection Associated with Acute Respiratory Distress Syndrome. Tanaffos. 2020; 19(2): 152–155, indexed in Pubmed: <u>33262803</u>.
 Song D, Prahl M, Gaw SL, et al. Passive and active immunity in infants born to mothers with SARS-CoV-2 infection during pregnancy: Prospective cohort study. medRxiv. 2021, doi: <u>10.1101/2021.05.01.21255871</u>, indexed in Pubmed: <u>33972953</u>.

13. Kotlyar AM, Grechukhina O, Chen A, et al. Vertical transmission of coronavirus disease 2019: a systematic review and meta-analysis. Am J Obstet Gynecol. 2021; 224(1): 35–53.e3, doi: <u>10.1016/j.ajog.2020.07.049</u>, indexed in Pubmed: <u>32739398</u>.

14. Uslu Yuvacı H, Aslan MM, Köse O, et al. Evaluation of the presence of SARS-COV-2 in the vaginal fluid of reproductive-aged women. Ginekol Pol. 2021 [Epub ahead of print], doi: <u>10.5603/GP.a2021.0018</u>, indexed in Pubmed: <u>33751509</u>.

15. Cai J, Tang Mi, Gao Yu, et al. Cesarean Section or Vaginal Delivery to Prevent Possible Vertical Transmission From a Pregnant Mother Confirmed With COVID-19 to a Neonate: A Systematic Review. Front Med (Lausanne). 2021; 8: 634949,

doi: <u>10.3389/fmed.2021.634949</u>, indexed in Pubmed: <u>33681259</u>.

16. Najnowsze wytyczne i stanowisko ekspertów w sprawie zakażenia wirusem COVID-19 | Polskie Towarzystwo Medycyny Perinatalnej. <u>http://ptmp.edu.pl/</u> (25.07.2022).

17. Wang Z, Wang Z, Xiong G. Clinical characteristics and laboratory results of pregnant women with COVID-19 in Wuhan, China. Int J Gynaecol Obstet. 2020; 150(3): 312–317, doi: <u>10.1002/ijgo.13265</u>, indexed in Pubmed: <u>32510581</u>.

18. Mo P, Xing Y, Xiao Yu, et al. Clinical Characteristics of Refractory Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis. 2021; 73(11): e4208–e4213,

doi: <u>10.1093/cid/ciaa270</u>, indexed in Pubmed: <u>32173725</u>.

19. 2022-03-07-coronavirus-covid-19-infection-in-pregnancy-

v15.pdf. <u>https://rcog.org.uk/</u> (30.06.2022).

20. Isidori AM, Arnaldi G, Boscaro M, et al. COVID-19 infection and glucocorticoids: update from the Italian Society of Endocrinology Expert Opinion on steroid replacement in adrenal insufficiency. J Endocrinol Invest. 2020; 43(8): 1141–1147, doi: <u>10.1007/s40618-020-01266-</u><u>w</u>, indexed in Pubmed: <u>32335855</u>.

21. Singh AK, Majumdar S, Singh R, et al. Role of corticosteroid in the management of COVID-19: A systemic review and a Clinician's perspective. Diabetes Metab Syndr. 2020;
14(5): 971–978, doi: <u>10.1016/j.dsx.2020.06.054</u>, indexed in Pubmed: <u>32610262</u>.

22. Corp A, Lawton T, Young A, et al. Steroid use in Pregnancy with Severe COVID-19. Authorea. 2021, doi: <u>10.22541/au.163880761.13878113/v2</u>.

23. Velísek L. Prenatal corticosteroid impact on hippocampus: implications for postnatal outcomes. Epilepsy Behav. 2005; 7(1): 57–67, doi: <u>10.1016/j.yebeh.2005.04.008</u>, indexed in Pubmed: <u>15975854</u>.

24. Raising the Standard: A compendium of Audit Recipes for Continuous Quality

Improvement in Anaesthesia. The Royal College of

Anaesthetists. <u>https://www.rcoa.ac.uk/sites/default/files/documents/2019-09/CSQ-ARB-2012_0.pdf</u>.

25. Krawczyk P, Jaśkiewicz R, Huras H, et al. Obstetric Anesthesia Practice in the Tertiary Care Center: A 7-Year Retrospective Study and the Impact of the COVID-19 Pandemic on Obstetric Anesthesia Practice. J Clin Med. 2022; 11(11), doi: <u>10.3390/jcm11113183</u>, indexed in Pubmed: <u>35683567</u>.

26. Mikulak I, Borszewska-Kornacka M, Puskarz-Gasowska J, et al. Polish growth charts for preterm infants - comparison with reference Fenton charts. Ginekol Pol. 2021; 92(12): 865–871, doi: <u>10.5603/GP.a2021.0090</u>, indexed in Pubmed: <u>33914307</u>.

27. Wood R, Sinnott C, Goldfarb I, et al. Preterm Birth During the Coronavirus Disease 2019 (COVID-19) Pandemic in a Large Hospital System in the United States. Obstet Gynecol.
2021; 137(3): 403–404, doi: <u>10.1097/AOG.00000000004237</u>, indexed in Pubmed: <u>33595244</u>.

28. Hedermann G, Hedley PL, Bækvad-Hansen M, et al. Danish premature birth rates during the COVID-19 lockdown. Arch Dis Child Fetal Neonatal Ed. 2021; 106(1): 93–95, doi: <u>10.1136/archdischild-2020-319990</u>, indexed in Pubmed: <u>32788391</u>.

29. Philip RK, Purtill H, Reidy E, et al. Unprecedented reduction in births of very low birthweight (VLBW) and extremely low birthweight (ELBW) infants during the COVID-19 lockdown in Ireland: a 'natural experiment' allowing analysis of data from the prior two decades. BMJ Glob Health. 2020; 5(9), doi: <u>10.1136/bmjgh-2020-003075</u>, indexed in Pubmed: <u>32999054</u>.

30. Akhtar H, Patel C, Abuelgasim E, et al. COVID-19 (SARS-CoV-2) Infection in Pregnancy: A Systematic Review. Gynecol Obstet Invest. 2020; 85(4): 295–306, doi: <u>10.1159/000509290</u>, indexed in Pubmed: <u>32728006</u>.

31. Vetrugno L, Sala A, Orso D, et al. PINK-CO study investigators. Lung Ultrasound Signs and Their Correlation With Clinical Symptoms in COVID-19 Pregnant Women: The "PINK-CO" Observational Study. Front Med (Lausanne). 2021; 8: 768261,

doi: <u>10.3389/fmed.2021.768261</u>, indexed in Pubmed: <u>35127744</u>.

32. Krawczyk P, Jastrzębska A, Sałapa K, et al. Abnormal lung ultrasound pattern during labor: A prospective cohort pilot study. J Clin Ultrasound. 2019; 47(5): 261–266, doi: <u>10.1002/jcu.22692</u>, indexed in Pubmed: <u>30729529</u>.

33. Agrawal N, Chougale S, Jedge P, et al. Brixia Chest X-ray Scoring System in Critically Ill Patients with COVID-19 Pneumonia for Determining Outcomes. J Clin of Diagn Res. 2021,

doi: <u>10.7860/jcdr/2021/48844.15197</u>.

34. Covali R, Socolov D, Pavaleanu I, et al. Brixia Score in Outcomes of Alpha versus Delta Variant of Infection in Pregnant Critical COVID-19 Patients. International Journal of Translational Medicine. 2022; 2(1): 66–77, doi: <u>10.3390/ijtm2010007</u>.