COVID-19 in the practice of maternity hospitals of various degrees in the Czech Republic

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ABSTRACT

Objective: Pregnancy is not considered a condition that increases the body's susceptibility to SARS-CoV-2 (severe-acute-respiratory-syndrome-related coronavirus-2) infection, but in the case of infection in pregnancy, there is an increased risk of a more severe course of COVID-19 (coronavirus disease-19). However, the course of infection in pregnancy is mild or asymptomatic in most cases. The main objective of the study in pregnant women with COVID-19 was to prove that the delivery method is not changed, and serious complications do not occur more frequently due to this disease.

Methods: In a retrospective, observational, multicentric study, the pregnant women positively tested to COVID-19 were admitted and subsequently gave birth in the period from 15 March 2020 to 15 March 2021. Data from the delivery departments of five centers in the Czech Republic during COVID-19 pandemic were analyzed in relation to the delivery method and time, COVID-19 symptoms and potential complications with respect to demographics and comorbidities of pregnant women. COVID-19 positivity was confirmed with PCR (polymerase-chain reaction). The Excel program was used during statistical analysis.

Results: During the observed study period, 236 pregnant women with COVID-19 were detected at study centers. Most of the patients were asymptomatic (59.7%). In symptomatic patients, most common symptoms were cough (52.6 %), cold (43.2%) and fever (37.9%), and COVID-19 pneumonia was diagnosed in 8 patients. The delivery was performed vaginally in 52.5% patients, the pregnancy was terminated by C-section (cesarean section) in 44.5%, per VEX (vacuum extractor) in 2.1% and per forcipem in 0.8% cases. The average week of pregnancy at the time of delivery was 38 (29–41) and preterm delivery was performed in 19.1% patients. The study results in pregnant women with COVID-19 demonstrated that the method of delivery was not changed and major delivery and neonatological complications did not develop in most cases. However, two presented serious courses of COVID-19 in pregnant women led to premature terminations of pregnancies. The only associated risk factor was the patient's obesity.

Conclusions: Although COVID-19 is a disease that is mostly asymptomatic in pregnant women or with only mild flu-like symptoms, it is associated with increased morbidity and mortality compared to pregnant women without COVID-19. The challenge for the future is the possibility of segregating patients into low- and high-risk groups based on proven risk factors, and consistent vaccination of pregnant women or women planning conception. In critical cases, the correct timing of premature termination of pregnancy and early indication of the beginning of fetal lung maturation is necessary.

KEYWORDS

COVID-19 – pregnancy – delivery

SOUHRN

Heřman H., Tefr Faridová A., Trojanová K., Jalůvková B., Šinská A., Pilka R., Šimetka O., Čečetková B., Janák J., Steyerová P.: Covid-19 v praxi porodnic různého stupně v České republice

Cíl: Těhotenství se nepovažuje za stav zvyšující náchylnost organismu k infekci SARS-CoV-2 (severe-acute-respiratory-syndrome-related coronavirus 2), avšak v případě nákazy v graviditě se zvyšuje riziko závažnějšího průběhu nemoci covid-19. Ve většině případů ovšem bývá průběh infekce v graviditě mírný nebo bezpříznakový. Hlavním cílem studie u těhotných žen s covidem-19 (coronavirové onemocnění) bylo dokázat, že způsob porodu se nemění a závažné komplikace jak porodnické, tak neonatologické se kvůli tomuto onemocnění nevyskytují častěji.

Metody: Do retrospektivní, observační, multicentrické studie byly zařazeny pacientky s pozitivním testem na covid-19, které byly přijaty a následně porodily v období od 15. března 2020 do 15. března 2021. Data z porodnických oddělení pěti center v České republice během pandemie covidu-19 byla analyzována ve vztahu k metodě a době porodu, symptomům covidu-19 a potenciálním komplikacím s ohledem na demografii a komorbidity těhotných žen. Infekce koronavirem byla u pacientek potvrzena pomocí PCR (polymerázové řetězové reakce). Statistická analýza byla hodnocena pomocí programu Excel.

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Výsledky: Během sledovaného období bylo ve studijních centrech detekováno 236 těhotných žen s covidem-19. Většina pacientek byla asymptomatická (59,7 %). U symptomatických pacientek byly nejčastějšími příznaky kašel (52,6 %), nachlazení (43,2 %) a horečka (37,9 %) a covidová pneumonie byla diagnostikována u 8 pacientek. Porod byl proveden vaginálně u 52,5 % pacientek, těhotenství bylo ukončeno císařským řezem v 44,5 %, per VEX (vakuumextrakce) v 2,1 % a per forcipem v 0,8 % případů. Průměrný týden gravidity v době porodu byl 38 a předčasný porod byl proveden u 19,1 % pacientek. Výsledky tyto studie u těhotných žen s covidem-19 prokázaly, že způsob porodu se nezměnil a výskyt větších komplikací jak porodnických, tak neonatologických nebyl ve většině případů zaznamenán. Dva prezentované závažné průběhy covidu-19 u těhotných žen však vedly k předčasnému ukončení těhotenství. Jediným přidruženým rizikovým faktorem byla obezita pacientky.
Závěry: Ačkoli je covid-19 onemocnění, které je u těhotných žen většinou asymptomatické nebo má pouze mírné příznaky podobné chřipce, je spojeno se zvýšenou nemocností a úmrtností ve srovnání s těhotnými ženami bez covidu-19. Výzvou do budoucna je možnost segregace pacientek do nízko a vysoce rizikových skupin na základě prokázaných rizikových faktorů a důsledné očkování těhotných žen nebo žen plánujících početí. V kritických případech je nutné správné načasování předčasného ukončení těhotenství a včasná indikace počátku zrání plic plodu.

KLÍČOVÁ SLOVA
covid-19 – těhotenství – porod

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INTRODUCTION

The worldwide spread of a new type of coronavirus SARS-CoV-2 caused extensive damage to health and lives and has exposed the population, including pregnant women, to a new challenge and threat, either directly through the coronavirus disease 2019 (COVID-19) or indirectly by postponing scheduled or screening examinations due to fears of infection. The first cases COVID-19 were described in December 2019 in Wuhan, China [1]. COVID-19 was declared a global pandemic by the World Health Organization on 11 March 2020 [2]. COVID-19 is a highly infectious viral disease, it is a droplet infection with the most common symptoms as fever, cough and dyspnoea, other symptoms such as muscle aches, sore throat, fatigue, diarrhea or anosmia are less common [3]. In total, 5% of infected individuals are very serious to critical, threatening the patient and, in the case of a pregnant woman, the fetus, immediately in life. Among clinical units, this includes acute respiratory distress syndrome (ARDS), thromboembolism, sepsis, septic shock, and multiorgan failure [3]. According to current knowledge, pregnant women do not have a greater affinity for COVID-19 but in case of SARS-CoV-2 infection in pregnancy, they have a higher risk of more severe course, including the need for hospitalization in the intensive care unit (ICU), development of ARDS and need of invasive lung ventilation [4]. In 75–90% of cases, however, the course of infection in pregnancy is mild or asymptomatic [5]. In infected pregnant women, risk factors are described that exacerbate the course of the infection and increase the likelihood of hospitalization, the development of severe respiratory distress, and the need for respiratory support and ventilation compared to a group of low-risk pregnant women with the same infection. These risk factors are very similar to the risk factors for a more severe course of COVID-19 in the non-pregnant population. These include pre-existing chronic diseases (gestational diabetes mellitus, chronic hypertension, autoimmune diseases, obesity) or conditions complicating pregnancy (preeclampsia, gestational hypertension, gestational diabetes mellitus) [6]. COVID-19 positive pregnant women have a higher risk of preterm birth with consequent need of admitting the preterm fetus in the ICU than COVID-19 negative women [7]. Vertical transmission of the infection to the fetus via the placenta is possible but probably very rare and it has not been reported [8, 9].

In collaboration with the Institute for the Care of Mother and Child in Podolí (UPMD), the University Hospital Ostrava, the University Hospital Olomouc, the Hospital of the Merciful Brothers in Brno, the Hospital of Rudolf and Stefanie Benešov, the presented study aimed to analyze data from pregnant women with COVID-19 from these delivery departments during COVID-19 pandemic.

METHODS

In March 2020, a clearly defined hygienic-epidemiological regime was set up for positively tested patients in the Czech Republic, thanks to which it was possible to isolate every pregnant woman and mother and thus prevent community transmission. This retrospective, observational, multicentric study was focused on pregnant women with COVID-19 who were admitted and subsequently gave birth in five maternity centers in the Czech Republic in the period from 15 March 2020 to 15 March 2021. Data were analyzed in relation to the

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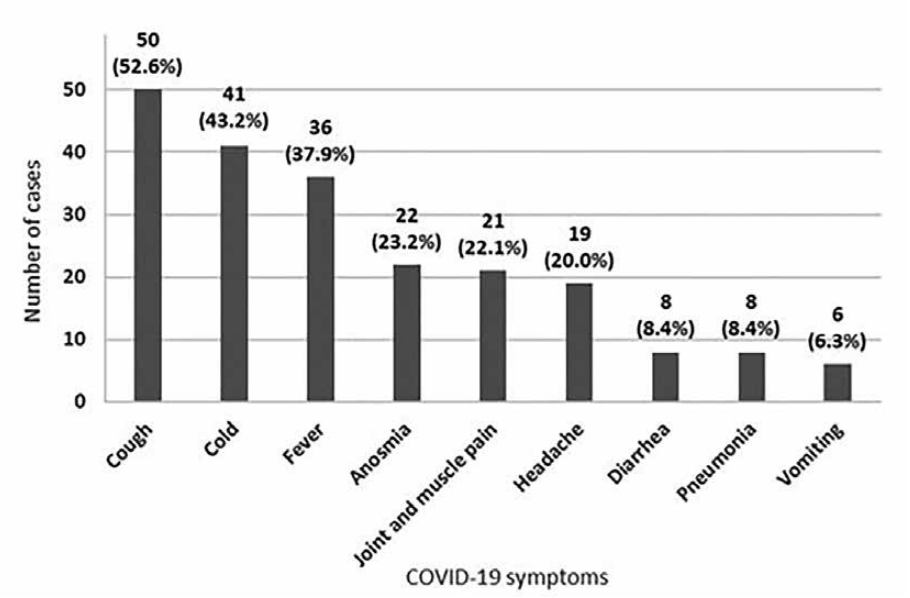

Figure 1. Proportion of COVID-19 symptoms in symptomatic pregnant women

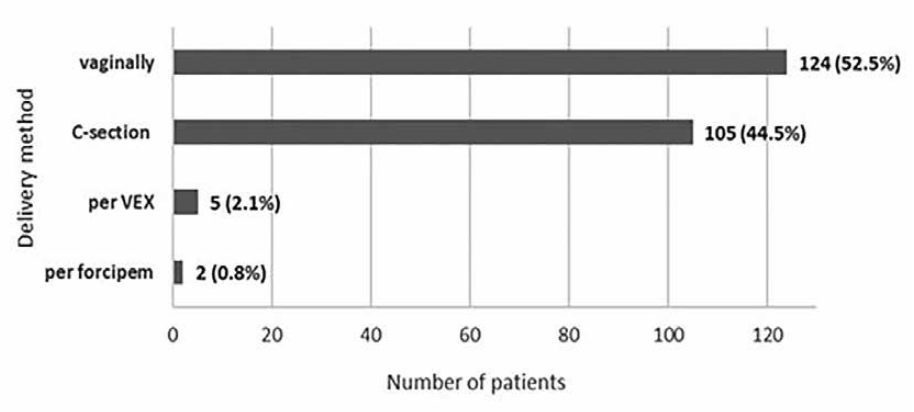

Figure 2. Delivery methods in COVID-19 positive women

delivery method and time, COVID-19 symptoms and potential complications with respect to demographics and comorbidities of pregnant women. The statistical data was evaluated in Excel.

RESULTS

During the observed study period, 236 pregnant women positively tested to COVID-19 were detected at study centers (with PCR), 0,18% positively detected pregnant women out of the total number of women delivered in 5 maternity centers (12 737 deliveries). 81 positively tested pregnant women from UPMD, 9 women from Benešov, 40 women from Ostrava, 28 from Brno, 78 from Olomouc. 141 patients with confirmed COVID-19 of total number positively tested pregnancy women (59.7%) were asymptomatic, 95 (40.3%) patients were symptomatic. 50 of symptomatic patients (52.6%) were diagnosed with cough, 41 (43.2%) cold, 36 (37.9%) fever, 22 (23.2%) anosmia, 21 (22.1%) joint and muscle pain, 19 (20.0%) headache, 8 (8.4%) diarrhea, and 6 patients (6.3%) experienced vomiting; COVID-19 pneumonia was diagnosed in 8 patients (8.4%) (Figure 1). The diagnosis of pneumonia was established by clinical examination.

The delivery in COVID-19 positive women was performed vaginally in 124 (52.5%) patients, the pregnancy was terminated by C-section in 105 (44.5%), per VEX in 5 (2.1%) and per forcipem in 2 (0.8%) cases (Figure 2). Average age of analyzed women was 32,3 (16-46 years old). The average week of pregnancy at the time of delivery was 38 (29–41 weeks of pregnancy). Preterm delivery was performed in 45 (19.1%) patients. Preterm birth is defined when it occurs before the completion of the 37th week of pregnancy.

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Within the observed group, patients were also treated with gestational illnesses, such as 20 with gestational diabetes, 16 with gestational hypertension, 10 had HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome and 8 patients experienced preeclampsia. The average birth weight of newborns was 3116 grams (930–4180 grams), 14 newborns belonged to the FGR (fetal growth restriction) group and 13 to the LGA (large for gestational age) group. 114 boys and 125 girls were born (including 3 geminis). The average Apgar score was 9-9-10.

In conclusion, the study results demonstrate that in pregnant women with COVID-19, the delivery method was not changed and major delivery and neonatological complications did not occur in most cases (diagnosis of severe cases excludes COVID-19 in neonates). To illustrate that the serious course of COVID-19 in pregnant women may lead to a premature termination of pregnancy, two serious cases are presented (with patient's informed consent). The only associated risk factor was the patient´s obesity and symptomatic COVID-19.

A 31-year-old woman at 29+5 weeks of pregnancy was admitted to the internal ward of the Hospital of Merciful Brothers in Brno for a week of febrile illness, weakness, productive cough and progression of dyspnea. The patient was confirmed to be COVID-19 positive. This was the patient´s third pregnancy, the previous two births were conducted vaginally. Of the risk factors, the patient suffered from obesity (BMI – body mass index – 36.42 kg/m^2). The measured oxygen saturation at admission in the blood was 88% during movement. After connecting to the oxygen support by oxygen goggles, the patient was with normal saturation and the dyspnea subsides. The diagnosis of bilateral infiltrative pneumonia typical for COVID-19-type pneumonia was confirmed by a chest X-ray. The patient was transferred to the Anesthesiology and Resuscitation Department of the hospital, where non-invasive ventilation (NIV) with a face mask was initiated. Due to further alteration of the patient's condition and the inability to achieve satisfactory saturation values with non-invasive ventilatory support, the patient was intubated and connected to the pulmonary ventilator 72 hours after admission to the hospital and on day 8 after proven COVID-19 infection. Left ventricular dysfunction also occurred due to severe COVID-19 pneumonia. The patient's dependence on a high inspiratory oxygen fraction (which reaches 100% FiO2 – fraction of inspired oxygen) persisted, with a breathing rate of 30 breaths per minute. At these values, the patient reached blood oxygen saturation values below 90%. Based on this and further deterioration of the patient's clinical condition after clinical check-up, the patient's connection to extracorporeal membrane oxygenation (ECMO) was indicated (Horowitz index < 100). This connection of the patient was not possible due to the unavailability of the gynecology and obstetrics department at the nearest workplace, which had the opportunity to provide ECMO to the patient.

The pregnancy was terminated from the vital indication of the mother by an acute C-section at 30+1 week of pregnancy, 74 hours after admission to the hospital. This radical multidisciplinary decision was made in an effort to improve maternal ventilation conditions. With regard to the high risk of transporting a critically ill patient, it was decided to perform a C-section at a workplace with first-degree accreditation, followed by the transport of the immature newborn to the perinatology center. C-section was performed without complication, a living boy was delivered in a longitudinal position with his head, who was intubated after a short scream for apnea and bradycardia. According to a previous agreement, the newborn was transported by a newborn transport team to the neonatal ICU with adequate postpartum recovery. Vertical transmission of SARS-CoV-2 was not detected.

The patient's oxygenation parameters improved within a few hours after the surgery (FiO_2 80%, PEEP – positive end-expiratory pressure – 15, SpO_2 93%). Remdesivir was discontinued, for which the patient did not meet the indication criteria when using artificial lung ventilation. A great positive effect on the state of ventilation was the positioning in the pronation position which was well feasible due to the absence of pregnancy. For persistent febrile conditions, intravenous antibiotic therapy with cefuroxime was empirically escalated to piperacillin/tazobactam administered for a total of 8 days with a positive effect on febrile states, laboratory signs of inflammation and the overall health of the patient. During postpartum hospitalization, hypertension was decompensated with the need for continuous intravenous antihypertensive therapy and the development of paralytic ileus with gradual adjustment without the need for revision of the abdominal cavity. The need for analgesia and ventilation support was gradually reduced and the patient was extubated on the 12th day after admission. The following week, mild oxygen dependence on oxygen glasses persisted, persistent hypertension was successfully corrected with peroral medication, and respiratory rehabilitation with the use of mucolytics and bronchodilators was started. Bilateral infiltrates persisted on the control chest X-ray, breathing was clear when listening. Oxygen saturation in the blood was repeatedly more than 96%. After setting up antihypertensive medication, the patient was dismissed home after 20 days of hospitalization in generally good clinical condition.

As part of outpatient care, echocardiographic examination 4 months after dismissal was normal, only a slight thickening of lung interstitium was described on the control HRCT (high-resolution computed tomography) (Figure 3). Spirometric examination performed 5 months after dismissal was normal.

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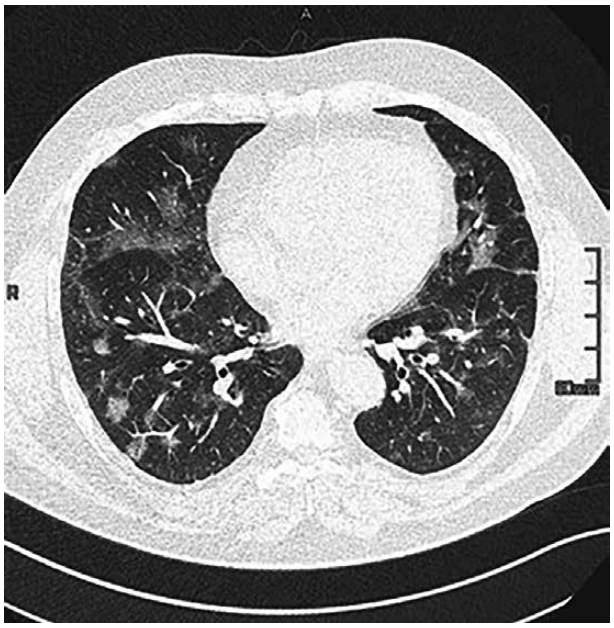

Figure 3. HRCT: Map-like ground-glass areas with predominance of peripheral involvement, nonhomogeneous consolidation and infiltrates in the parenchyma in later stages

The 28-year-old woman at 32+5 weeks of pregnancy was admitted to the gynecology and obstetrics department of the Rudolf and Stefanie Hospital in Benešov for cough, dyspnoea, chest pain and lower abdominal pain. BMI was 33,4 kg/m^2. No other comorbidities were detected. The PCR test for COVID-19 was positive. Saturation without oxygen support was 87–90%, on oxygen support 97%. Tachypnoea of 25–40 breaths per minute is present. Due to the severity of the condition and the positivity of the PCR test for COVID-19, a transport to the perinatology center of the General University Hospital in Prague was arranged. Induction of pulmonary maturity of the fetus, intravenous dexamethasone 8 mg per 24 hours was indicated. 24 hours after admission, an intravenous administration of remdesivir was indicated, followed by anaphylactic reaction in the patient, development of bronchospasm, desaturation to 30% and unconsciousness. Intravenous propofol, adrenaline, methylprednisolone and hydrocortisone and inhalation ipratropium/fenoterol were administered. Intubation was impossible, therefore a laryngeal mask was used. Full recovery of consciousness in a matter of minutes. A gynecologist indicated termination of pregnancy by an acute C-section. The intubation in the operation theater was no longer difficult, the surgery was without complications. In the ICU, the patient was without further need for circulatory support. The patient was extubated the next day. The clinical condition was dominated by somnolence with significantly reduced muscle strength. There was still a need for oxygen therapy on a half mask. Diffuse involvement on RTG of the lung parenchyma was described bilaterally. Diuretic therapy was used to achieve a negative fluid balance. The day after, there was significant improvement of chest X-ray findings, gradual improvement of clinical condition and state of consciousness, only the tendency to hypertension on urapidil therapy and thrombocythemia on acetylsalicylic acid therapy persisted. Due to the good clinical condition, the patient was dismissed to homecare on the 10th day of hospitalization. After dismissal, the patient continued with antihypertensive and antiplatelet therapy. The neonate was immediately after C-section transferred to the intensive care unit on CPAP (continuous positive airway pressure), adequate postpartum adaptation was observed for this week of pregnancy. Vertical transmission of SARS-CoV-2 was not detected.

DISCUSSION

Pregnancy is not considered a condition that increases the body's susceptibility to COVID-19 but in the case of infection in pregnancy, there is an increased risk of a more severe course of this disease. Briefly, risk factors for a more severe course of COVID-19 in pregnancy include maternal age over 35, obesity, pregestational diabetes mellitus, pre-existing hypertension, bronchial asthma, and cardiac disease. COVID-19 is associated with more frequent hospitalization in inpatient facilities, hospitalization in the ICU with various respiratory support, from oxygen support to the need for intubation and artificial lung ventilation, or respiratory support via extracorporeal membrane oxygenation (ECMO) [1]. ARDS has been observed in pregnant women in the past due to viral respiratory infections. It has been shown to be more severe in pregnant women than in non-pregnant women of the same age [11, 12]. These were mainly a H1N1 pandemic known as swine flu and coronavirus diseases (SARS, MERS) [12]. The Australian Gynecology and Obstetrics Society recommends early intubation in patients with ARDS and respiratory failure to maintain optimal oxygenation of the patient and thus prevent fetal hypoxia. There are several risk factors that exacerbate the course of COVID-19, especially chronic diseases of mothers and diseases associated with pregnancy in the foreground with preeclampsia [6, 14]. The results of this prospective longitudinal study published in June 2021 showed a clear association of the above-mentioned diseases with increased maternal morbidity and mortality and an increased risk of preterm birth [14]. Obesity is a factor exacerbating the course of COVID-19 in pregnant women [6, 15].

The Australian Recommendations of the Gynecology and Obstetrics Society state that antenatal induction of lung corticoid maturity in women at risk of preterm birth before the 34th week of pregnancy is part of standard prenatal care and is independent of the presence

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of COVID-19 [13]. The Swedish Federation of Gynecologists and Obstetricians directly recommends the use of antenatal corticosteroids before the end of the 34th week of pregnancy in case of ongoing COVID-19 infection with risk of preterm birth [16]. In the case of the presented patient with serious COVID-19, the induction of pulmonary maturity of the fetus was not finished due to the acute deterioration of the mother's health. Corticosteroids reduce mortality in adult patients with severe or critical COVID-19 [17, 18]. Pregnant women have not been included in studies assessing the effect of corticotherapy. The use of corticoids in the medication of COVID-19 positive pregnant women is indicated in the case of mechanical ventilation and oxygen dependence [13]. If induction of pulmonary maturity is indicated, intramuscular dexamethasone 6 mg 12 hours to the 4th dose [19], followed by dexamethasone 6 mg intramuscularly daily for a maximum of 10 days. Intramuscular methylprednisolone (32 mg/day, in one or more doses), which crosses the placental barrier less and does not lead to repeated dose adverse reactions in the fetus (neurological developmental disorders, fetal growth restriction, small head circumference, increased risk of neonatal hypoglycaemia), appears to be better after completion of fetal pulmonary maturity [20]. There is no evidence of use of remdesivir in pregnant or lactating women. Several studies of remdesivir have been performed in non-pregnant populations. This medicine should shorten the time of healing. The effect on mortality is uncertain [15]. The benefit of remdesivir treatment is greatest at the beginning of the infection and is questionable after the seventh day of the infection. There are strict rules for the administration of remdesivir in the Czech Republic. A five-day protocol is commonly used; if the patient's clinical condition does not improve, further treatment is not indicated. International studies have discussed the administration of the drug in a five- or ten-day regimen with unclear results. The use of remdesivir in pregnant and lactating women should not be routinely indicated [13]. No data are available on the remdesivir crossing across the placental barrier [21]. COVID-19 increases the risk of thromboembolic disease (TEN), which is already physiologically increased in pregnancy and postpartum. It is recommended that low molecular weight heparin (LMWH) should be administered to all pregnant women admitted to hospital with confirmed COVID-19 [13]. The LMWH treatment was also administered to the presented pregnant patient with serious COVID-19 in all 5 documented centers, in postpartum therapy it was gradually increased to 100 mg subcutaneous enoxaparin every 12 hours, which is in line with the general international recommendations for the use of LMWH in COVID-19 positive patients [22, 23].

Positioning patients with ARDS in the pronation position usually leads to a significant improvement in oxygenation and reduced mortality [24, 25]. Positioning a pregnant patient in a pronation position is possible, although supporting of the pregnant uterus, prevention of aorto-caval compression and regular monitoring of the fetus are necessary. In pregnant women, there is no study describing a clear benefit of pronation position on the general condition [26].

COVID-19 positive pregnant women have a higher risk of C-section. Several studies have made this finding [27]. There is an increased risk in patients with severe symptoms and especially in patients with comorbidities and other risk factors that increase the likelihood of a serious infection. In the presented patient with a serious course of COVID-19, the only associated risk factor was obesity. The risk of prematurity is twice as high in women with COVID-19 after adjustment for factors usually associated with prematurity [32]. This summary of a number of studies shows that 55.9% of the indications for C-section were COVID-19 pneumonia [28]. The increased percentage of C-sections in COVID-19 positive pregnant women is in most cases due to the worsening of the mother's symptoms, which are directly related to COVID-19 [27, 28, 29]. Findings of this study with 236 patients are in correlation with above mentioned studies [27, 28], as 44.5% of pregnancies were terminated by C-section and 52.5% by vaginal delivery. The rate of preterm birth was 19.1%, which corresponds with findings of Borges Charepe et al. [30]. In a small percentage of cases, SARS-CoV-2 infection can lead to the development of ARDS with subsequent respiratory failure and worsen other maternity complications [31], as we presented in our analysis.

In our retrospective analysis, 236 pregnant women were positive for COVID-19 via PCR detection. The total number of pregnant women recruited for our analysis from 5 maternity centers was 12 737. Most of COVID-19 positive women were asymptomatic (59.7%). In symptomatic patients, most common symptoms were cough (52.6%), cold (43.2%), fever (37.9%), and 8 patients (8.4%) were treated with COVID-19 pneumonia. Admission for ICU after delivery was presented in 20,7% patients. Interpretation is limited due to standard care after surgical approach for delivery. C-section was performed in 44,50% cases, this number is higher than the national percentage. In 2020 24,8% of C-section was performed in the Czech republic, although the number of C-section in perinatal center are higher (around 40%), the lowest percentage of C-sections was in Benešov (22%) and Ostrava (24%).

COVID-19 positive pregnant women have a higher risk of preterm birth with the need for subsequent hospitalization of the newborn in the ICU. 2 newborns died during first day (0,08% of COVID-19 infected pregnant women), this number is compared to very low perinatal mortality in the Czech republic (0,017%). This result is a limited sample size of data and different levels of maternity centers.

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CONCLUSIONS

COVID-19 is a disease which is mostly asymptomatic in pregnant women or with only mild „flu" symptoms, yet it is connected with increased morbidity and mortality compared to non-infectious pregnant women. Limitations of this study include its own data measure used to collect the data, self-reported data from different hospital information systems. Severe cases are demonstrated only in two patients, this could be considered as limited sample size.

The challenge for the future is the possibility of dividing patients into low-risk and high-risk groups based on proven risk factors associated with a more severe course of the disease and also consistent vaccination of pregnant women or women planning conception. In the case of a critical condition of a pregnant patient, the correct timing of premature termination of pregnancy and early indication of the beginning of fetal lung maturation is necessary. Although our data are imperative to emphasize the importance of an individualized, multidisciplinary approach, and good healthcare infrastructure for optimal management of this group of patients.

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