Pregnancy and COVID-19: Case Reports and Literature Review

Nėštumas ir COVID-19: klinikiniai atvejai ir literatūros apžvalga

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Summary

The COVID-19 pandemic caused by the SARS-CoV-2 virus contributed to a global health crisis. Pregnant women are considered a vulnerable population that can develop severe SARS-CoV-2 infections due to physiological changes during pregnancy that affect a wide range of functions, causing cardiovascular instability, bleeding disorders, respiratory and immune dysfunction. These factors may adversely affect the course of COVID-19. In addition to pregnancy, a pregnant woman may have additional risk factors, including diabetes, obesity, advanced age (pregnancy >35 years), or chronic cardiovascular or respiratory disease. Early studies indicate that COVID-19 increases the risk of serious illness and death in pregnant women. In addition, COVID-19 was associated with adverse fetal outcomes as preterm birth. The mechanisms underlying the increased risk of adverse pregnancy outcomes in pregnant women with COVID-19 are not well-understood but may be related to the direct effects of SARS-CoV-2 on the placenta and the fetus, as well as the indirect effects of systemic inflammation and cytokine storm. During the pandemic, the SARS-CoV-2 delta variant in particular has been shown to be associated with severe disease. The new coronavirus variants pre-delta, as well as the omicron variant, seem to be generally associated with a milder course of disease.

Pregnant women should be encouraged to take preventive measures such as social distance, hand hygiene and wearing a mask. Pregnant women with suspected or confirmed COVID-19 should receive prompt and appropriate medical care to reduce the risk of adverse outcomes. The availability of vaccination against SARS-CoV-2 may protect vulnerable groups from a life-threatening course of disease. Vaccination against COVID-19 is also recommended during pregnancy and contributes to the protection of the expectant mother and the fetus.

Keywords: COVID-19, SARS-CoV-2, pregnancy, vaccination.

Santrauka

SARS-CoV-2 viruso sukelta COVID-19 pandemija prisidėjo prie pasaulinės sveikatos krizės. Nėščios moterys laikomos pažeidžiama populiacija, kuri gali susirgti sunkiomis SARS-CoV-2 formomis dėl nėštumo metu vykstančių fiziologinių pokyčių, turinčių įtakos įvairioms funkcijoms, sukeliančių širdies ir kraujagyslių sistemos nestabilumą, kraujavimo sutrikimus, kvėpavimo ir imuninės sistemos sutrikimus. Šie veiksniai gali neigiamai paveikti COVID-19 eigą. Be nėštumo, nėščia moteris gali turėti papildomų rizikos veiksnių, įskaitant diabetą, nutukimą, vyresnį amžių (nėštumas >35 metų) arba lėtines širdies ir kraujagyslių ar kvėpavimo takų ligas. Ankstyvieji tyrimai rodo, kad COVID-19 padidina nėščių moterų sunkių formų ir mirties riziką. Be to, COVID-19 buvo susijusi su nepalankiomis vaisiaus pasekmėmis, kaip priešlaikinis gimdymas. Mechanizmai, lemiantys padidėjusią nepageidaujamų nėštumo pasekmių riziką nėščioms moterims, sergančioms COVID-19, nėra gerai suprantami, tačiau gali būti susiję su tiesioginiu SARS-CoV-2 poveikiu placentai ir vaisiui, taip pat netiesioginiu sisteminiu uždegimu ir citokinų audra. Pandemijos metu įrodyta, kad SARS-CoV-2 delta variantas buvo susijęs su sunkia forma. Atrodo, kad nauji koronaviruso variantai prieš deltą, taip pat omikron variantas, paprastai yra susiję su švelnesne ligos eiga.

Nėščios moterys turėtų būti skatinamos imtis prevencinių priemonių, tokių kaip socialinis atstumas, rankų higiena ir kaukių dėvėjimas. Nėščioms moterims, kurioms įtariama arba patvirtinta COVID-19, turėtų būti suteikta greita ir tinkama medicininė pagalba, siekiant sumažinti nepageidaujamų pasekmių riziką. Galimybė skiepytis nuo SARS-CoV-2 infekcijos gali apsaugoti pažeidžiamas grupes nuo gyvybei pavojingos ligos eigos. Skiepijimas nuo COVID-19 taip pat rekomenduojamas nėštumo metu ir prisideda prie motinos ir vaisiaus apsaugos.

Raktažodžiai: COVID-19, SARS-CoV-2, nėštumas, vakcinacija.

Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus type 2) is a beta coronavirus that first caused respiratory distress in December 2019 and was identified as the causative agent of COVID-19 in early 2020 [1]. The inter-human transmission of this mRNA-virus occurs by aerosols and due to high virulence, the virus spreads rapidly.

The whole world has been confronted by the COVID-19 pandemic up to now, precipitating the need for medical advancements and measures in public health. Although the infection by the current variant (Omicron) may be asymptomatic or cause mild colds in the majority, it can also lead to severe pneumonia and result in life-threatening conditions. Risk factors that significantly impact the severity of infection include elderly age (50–60+), male sex, obesity, trisomy 21, chronic disease (cardiovascular disease, chronic lung disease, chronic liver/kidney disease, neurological/psychiatric disease, diabetes mellitus, immunosuppression), and pregnancy [2].

The course of COVID-19 in pregnant women can vary widely. While many pregnant patients experience asymptomatic SARS-CoV-2 infection, those with symptomatic disease are at increased risk for severe disease. Several studies have reported a higher risk of severe illness and death in pregnant women with COVID-19 compared to non-pregnant women of reproductive age [3]. A systematic review and meta-analysis of 77 studies including 11,432 pregnant women with COVID-19 showed that pregnant women with COVID-19 are at increased risk of severe maternal morbidity, intensive care unit (ICU) admission and death, compared to non-pregnant women of reproductive age [3]. There is also evidence that SARS-CoV-2 infection during pregnancy may increase the risk of adverse pregnancy outcomes such as preterm birth, stillbirth, and fetal distress. Another systematic review and meta-analysis of 77 studies including 438,548 pregnant women showed that pregnant women with COVID-19 had an increased risk of preterm birth, stillbirth and neonatal death compared to pregnant women without COVID-19 [4]. The mechanisms underlying the increased risk of adverse pregnancy outcomes in pregnant women with COVID-19 are not well-understood but may be related to the direct effects of SARS-CoV-2 on the placenta and fetus, as well as the indirect effects of systemic inflammation and cytokine storm.

Due to the novelty of the COVID-19, recent studies and data are inconsistent or rapidly changing. Different virus variants influence the results of studies, and new treatment options and/or preventive measures and evidence lead to different recommendations.

However, in the face of many changes, the evidence for the COVID-19 vaccine recommendations is clear: vaccination prevents severe courses and vulnerable groups benefit from vaccination success. Nevertheless, with different vaccines, vaccination schedules and preferences for the vaccine of choice varied.

Methods

The medical cases of a total of four pregnant patients with COVID-19 from the Infectious Diseases Department of the Vilnius University Hospital Santaros klinikos (VUH SK) were reviewed and the most relevant findings were summarized and discussed. The cases are presented anonymously with the consent of the patients, the approval of the department of the Infectious Disease Clinic, and the VUH SK administration.

The literature search was performed in PubMed using the following search terms: „SARS-CoV- 2; COVID-19; Pregnancy.“ This search yielded 4,928 results. When restricting to reviews, the search yielded in total 767 results, including 234 in 2020, 345 in 2021, 243 in 2022, and 33 in 2023 (as of March 3, 2023). When restricted to a systematic review, 218 results were still found. In 2020, there were 67 hits, in 2021, there were 90 hits, in 2022, there were 80 hits, and in 2023, there were 9 hits (as of March 3, 2023).

In addition, the COVID-19 prefilter provided by PubMed for the items: SARS-CoV-2; COVID-19; Pregnancy was used. This was used to prefilter the most recent COVID-19 publications [5]. The reviews published in the most relevant journals were used as well as high-impact studies to gain specific information within the studied population. In order to understand the cellular mechanisms leading to a SARS-CoV-2 infection of the placenta reviews were used which were identified via PubMed and the search item: “placenta histopathology infection SARS-CoV-2”. In addition – standard medical educational material was used such as UpToDate [6] as well as the COVID-19 info pages of the Robert Koch Institute [2] and CDC [7].

Case reports of pregnant women infected with SARS-CoV-2

Patient 1, 40-year-old woman

1) Current reason for presentation with symptoms

40-year-old woman at 30 weeks’ gestation presented with symptoms of generalized weakness, sore throat, and fever episodes in mid/late March 2021. Six days after the onset of symptoms, she was hospitalized with a positive SARS-CoV-2 PCR test (CT number unknown). Hospitalization was justified because of her COVID-19 disease during pregnancy with a complicated gynecological history.

2) Anamnesis

There were no known chronic illnesses, and she was not taking any long-term medications. However, her medical history was marked by her a complicated gynecologic past. Her current pregnancy was her fifth (G5, P2, A2; one living child). The complicated gynecological history and her current age at pregnancy were conspicuous and considered as a risk.

3) Physical examination findings

The patient was awake and responsive. She had no fever. Pulse, and blood pressure were within normal range. Mild tachypnoea (18/min) with oxygen saturation of 96% on room air. With a National Early Warning Score (NEWs score) of 1-point, a low risk was expected. Further gynecologic ultrasound was unremarkable. Fetal movements were present and regular cardiac activity was recorded.

4) Diagnostics

Laboratory values revealed neutrophilic leukocytosis, lower erythrocyte count and slightly elevated MCV and MCH. Also, liver enzymes were elevated (ALT (GPT) 91 U/I; AST (GOT) 59 U/l), urea was low, and inflammatory markers were elevated. D-dimers were taken as nonspecific markers, which were also elevated.

Abdominal ultrasound revealed increased biliary volume without other pathology. Thus, the diagnosis of intrahepatic pregnancy cholestasis was confirmed. Further gynecologic ultrasound was unremarkable. Fetal movements were present and fetal heart activity was recorded. Furthermore, urinalysis and fecal examination were performed during hospitalization. The urinalysis showed ketones in the urine.

5) Therapy and course

The 40-year-old patient was diagnosed with intrahepatic pregnancy cholestasis, which was treated with Ursodeoxycholic acid (Ursofalk; 250 mg TID), adequate rehydration, Lepicol powder and Nadroparinum calcium infusion were administered.

Fetal movements were observed, and the liver enzymes were controlled.

The outcome was satisfactory. The patient was discharged in a stable condition after an inpatient stay of 10 days with a NEWs index of 0. Pulse, blood pressure and temperature were normal. On room air, oxygen saturation was 97% and eupneic. An appointment for follow-up was set for 7 days after discharge.

Patient 2, 30-year-old woman

1) Current reason for presentation with symptoms

A 30-year-old pregnant woman, at 30 weeks was admitted to the hospital with bilateral COVID- 19 pneumonia in mid-May 2021 for 7 days. She received her first positive SARS-CoV-2 rapid Ag test four days before the hospital admission. COVID-19 infection manifested with fever, general fatigue, dry cough, and dyspnea when lying down or during physical activity.

2) Anamnesis

There were no known pre-existing risk factors or diseases, and she was not on any long-term medications.

3) Physical examination findings

Upon arrival at the hospital, the patient was awake, communicative, and oriented. She had subfebrile temperature at 37.8°C, tachycardia (113 bpm), and normal blood pressure (124/79 mmHg). The patient had dyspnea and required supplemental oxygen 4 l/min. By this she had an oxygen saturation of 97%. Fetal movements were normal.

Subsequently, however, in addition to bilateral pneumonia, gestational diabetes, nonspecific urinary tract infection, and hypokalemia were diagnosed.

4) Diagnostics

Laboratory diagnostic showed an increased CRP (134.2 mg/l). The complete blood count revealed borderline low WBC (4.29*10^9/l), RBC (3.64*10^12/l) and a slight anemia (Hb 112 g/l). Despite the increased inflammation marker and the slight deprivation in the CBC were the laboratory results unremarkably. Urinalysis detected protein, urobilinogen, ketones, leukocytes, and bacteria in the urine. Moreover, fecal examination was unsuspicious. Ultrasound examinations and CTG were performed and confirmed the wellbeing of the fetus. Despite the current pregnancy, a thorax x-ray was performed due to the symptomatic presentation and revealed a viral associated bilateral pneumonia.

5) Therapy and course

The urinary tract infection and the bilateral pneumonia was treated with cefuroxime for 7 days (750 mg BID). As venous thromboembolism prophylaxis she received anticoagulation with nadroparinum calcicum for 7 days (0.3 ml BID). Additionally, infusion therapy for 5 days, as well as KCl for electrolyte correction for a total of 9 days was administered. The oxygen demand was initially 4 l/min and was gradually reduced to 1 l/min over the course of five days until no longer needed. The dry cough developed into productive cough until the latter also diminished. An additional symptom was diarrhea (up to six times a day) for four days.

Due to gestational diabetes, diet had to be adjusted and glycemic targets were set according to guidelines. Controls with an endocrinologist and gynecologist were to take place. It was recommended that fetal movements be self-monitored.

After a seven-day hospital stay, the patient was discharged in an improved general condition. Treatment was to be continued on an outpatient basis. Self-isolation was still required, but her well-being was good and symptoms such as cough, dyspnea, and diarrhea resolved. The patient did not require supplemental oxygen and had a saturation of 96% on room air at discharge. Additionally, more than ten fetal movements per hour were recorded.

Patient 3, 27-year-old woman

1) Current reason for presentation with symptoms

A 27-year-old woman, 38 weeks + 6 pregnant. She was tested positive for COVID-19 by PCR around in November 2021 with the following symptoms: general weakness, sore throat, fever, muscle pain, productive cough, abdominal pain, diarrhea, and nausea. She was hospitalized electively one week later due to the planned induction of labor because of intrahepatic pregnancy cholestasis.

2) Anamnesis

She was expecting her first child (G1, P0, A0). Regarding her medical history, she had a known history of intrahepatic pregnancy cholestasis during the current pregnancy and reported endometriosis; otherwise, no other pre-existing conditions or possible risk factors for a severe course of COVID-19.

3) Physical examination findings

On admission, she was in moderate condition, alert, oriented, and hemodynamically stable. She had no fever,

normal blood pressure (106/66 mmHg), tachycardia (96–120 bpm), eupnea (15 / min), and oxygen saturation of 98% on room air. Fetal movements were normal.

4) Diagnostics

Laboratory values on admission showed elevated liver enzymes as expected, as well as elevated serum phosphate, low urea, elevated eGFR. Potassium levels were borderline. Additionally, D- dimers were determined, which were also elevated. ACS normal. Pre-eclampsia signs were within normal range. The ultrasound examination and CTG were unremarkable. Additionally, a chest x-ray was performed and revealed a bilateral pneumonia.

5) Therapy and course

During the hospitalization, the patient did not require supplemental oxygen. For cholestasis, she received ursodeoxycholic acid. For prophylaxis for peptic ulcer omeprazole 20 mg in the morning, and for prophylaxis of DVT Sol. Nadroparinum calcicum 0.6ml QD subcutaneously. Furthermore, infusion therapy (Ringer solution 1000 ml QD; glucose 5% 500ml QD) was administered and her borderline hypokalemia was treated with 20 ml of 10% KCl.

For the cough, she received Ambroxol hydrochloride 30 mg per day. At this point, it is worth noting that Ambroxol hydrochloride should be prescribed with caution during pregnancy and lactation. Ambroxol hydrochloride is a category C pregnancy drug and is not recommended for pregnant women, especially during the first 3 months. In addition, Ambroxol hydrochloride can also be excreted into breast milk and therefore should not be taken during breastfeeding.

Since the pneumonia was most likely a viral infection, antibiotic therapy was not initiated. Delivery was induced with a mechanical cervical dilator and synthetic prostaglandins (received a total of 7 doses of tab. Cytotec 25 mcg every 2 hours). For pain, she received epidural analgesia. At birth, there was a first-degree perineal tear; otherwise, the birth was without complications. The baby was born in term with a weight of over 3000g and a height of 50cm. The Apgar score was 9/10. After birth, the tear was sutured, and the patient was given Diclofenac and Nadroparinum calcicum for the first days after.

Despite the bilateral pneumonia, the patient had a mild course of COVID-19. She was discharged in good general condition. No fever, blood pressure of 106/84 mm Hg, mild tachycardia (109 bpm), and oxygen saturation of 99% on room air. No leg edema was noted, and the abdomen was soft and painless on palpation. For follow-up, she was advised to present to an obstetrician-gynecologist as an outpatient, and liver enzymes should be controlled.

Patient 4, 33-year-old woman

1) Current reason for presentation with symptoms

A 33-year-old pregnant woman, in 31 weeks + 5 of pregnancy. In mid-December 2021, she tested positive for SARS-CoV-2 with a PCR test and was hospitalized five days later. The reason for her hospitalization was the COVID-19 infection during pregnancy, fever, general weakness, and anxiety concerning the fetus. In addition to the fever and weakness, she had symptoms of nausea and decreased appetite.

2) Anamnesis

This was her fifth pregnancy (G5, P2, A2). Besides the pregnancy, there were no additional risk factors for severe COVID-19 progression, and no pre-existing conditions were mentioned.

3) Physical examination findings

On admission, she was in acceptable condition, awake, oriented, and responsive. She was hemodynamically stable with a blood pressure of 125/77 mm Hg and an elevated heart rate of

134 bpm. She had a subfebrile temperature of 37.9 °C. Her oxygen saturation on room air was 96%. No leg edema was present. Fetal movements were normal. During the course, uterine spasms were induced by fever, but there was no preterm labor activity.

4) Diagnostics

At admission laboratory results showed an elevated CRP, LDH decreased, and potassium and sodium levels were at the lower limit. In addition, the D-dimers were elevated. The urinalysis was unremarkable. A chest x-ray showed a slight infiltration in the upper lobe of the right lung. Ultrasound and CTG were performed during a gynecological consultation and the results were unsuspicious.

5) Therapy and course

During the inpatient treatment, there was no requirement for supplemental oxygen. In the dynamics, the inflammatory indicators (CRP) were increasing, an antibacterial treatment (Cefuroxime 1500 mg TID) was applied. In case of fever (>38 °C) she received 1 000 mg Paracetamol. As thromboembolism prophylaxis she received Nadroparinum calcicum 0.6 ml QD. Fluid therapy was also administered. To control the electrolyte imbalance, she received KCl 10% 20 ml. For sedation she was given valerian on the day of admission. Furthermore, she received a nutridrink (protein) on the day of hospitalization. For nausea, she received Metoclopramidum 10 mg and for gastric protection, Omeprazole 20 mg.

The use of Metoclopramidum by women of childbearing age or during pregnancy has not been associated with an increase in malformations or other direct or indirect adverse effects on the fetus, according to current knowledge [8]. Anyhow, if possible, the use during the first and third trimesters should be avoided. In addition, monitoring for extrapyramidal syndrome and methemoglobinemia is recommended in neonates who have been exposed during the third trimester and/or birth. An important note is that there may be a relatively high risk of postpartum depression after delivery and that Metoclopramidum may cause depression as a side effect [8].

Summary of Case Reports of Pregnant Women Infected with SARS-CoV-2

A total of four pregnant women with SARS-CoV-2 infections from the Infectious Diseases Department of the Vilnius University Hospital Santaros klinikos (VUH SK) were subject of this report illustrating the course of COVID-19 in pregnancy. The infections occurred between spring and winter in 2021. In all patients the SARS-CoV-2 infection occurred during the third trimester of their pregnancy. They were admitted to VUH SK due to severe respiratory distress as inpatients for further treatment.

The patients were 27, 30, 33, and 40 years old. As risk factors for severe COVID-19 progression, the patients had in common their current pregnancy and the lack of vaccination against SARS-CoV-2 in common. However, the first patient had additional risk factors for complications due to her age (> 35 years) and complicated gynecologic history.

As the described, infections occurred between spring and winter 2021, it could be assumed that the SARS-CoV-2 delta variant was the causative strain based on the timing [9].

In summary, the four pregnant patients had a low-complication COVID-19 course although they were not immunized. After the hospitalization of 6 to 11 days, all could be discharged in a good general condition and the follow-up visits could be performed on an outpatient basis. During hospitalization, the third patient had an induction of labor (due to intrahepatic pregnancy cholestasis) unrelated to her SARS-CoV-2 infection.

Literature review

To understand and categorize the clinical context of these case reports, it is necessary to take a broader perspective on the epidemiologic significance, the pathophysiologic basis of SARS-CoV-2 infection, and the study evidence of the vulnerability of pregnant women as a risk group.

General information about SARS-CoV-2 infection

The incubation period of COVID-19 lasts an average of 4 to 6 days, with an expected average duration of infection of 8 to 10 days [2]. Typical clinical manifestations include according to the German Public-Health-Institute „Robert Koch Institute (RKI)“ symptoms such as cough (42%), fever (26%), common cold (31%), anosmia and/or ageusia (19%) [2]. Additional symptoms such as headache, fatigue, sore throat, and diarrhea should be considered, although presentation may vary, as reported by the Center of Disease Control and Prevention (CDC) [7]. In addition, the co-occurrence of symptoms such as anosmia, fatigue, and cough has been shown to most likely indicate acute SARS-CoV-2 infection [10].

Signs and symptoms of SARS-CoV-2 infection in pregnant patients

The signs and symptoms of COVID-19 are similar in pregnant and in non-pregnant individuals. A systematic review and meta-analysis of 192 studies by Allotey et al. [3] found that pregnant women with COVID-19 are less likely to have symptoms such as fever (odds ratio 0.66, 95% confidence interval 0.52 to 0.86; 15 studies, 2017808 women), cough (0.77, 0.65 to 0.91; 14 studies, 2016795 women), dyspnea (0.75, 0.59 to 0.97; 15 studies; 2017083 women), and myalgia (0.59, 0.44 to 0.80; 10 studies, 1752452 women). Despite of this, symptoms such as fever and cough seem to be prevalent in 36% of pregnant patients [3].

In general, laboratory and imaging findings are comparable to those of nonpregnant individuals, with elevated C-reactive protein levels (51%), elevated procalcitonin levels (32%), lymphopenia (33%), elevated leukocyte counts (28%) and elevated transaminases common in COVID-19-positive pregnant women (3,4). Nevertheless, it should be emphasized that some findings may overlap with other pregnancy-related conditions, such as thrombocytopenia and elevated liver enzymes in preeclampsia [6]. Moreover, symptoms such as fatigue and dyspnea may occur due to physiological changes during pregnancy not affected by COVID-19.

Susceptibility vs severity of COVID-19 in pregnant patients

In the context of vulnerability of pregnant women, it must be differentiated whether pregnant women are more susceptible to contracting the SARS-CoV-2 virus or whether there is only higher risk for a more severe course if infection occurs. According to the article „COVID-19: Overview of pregnancy issues“ published in the online paper UpToDate, Berghalla et al. described that pregnancy does not increase susceptibility to SARS-CoV-2 infection [6]. Regardless, it may worsen the clinical course of COVID-19 if infection does occur. The risk for rapid deterioration, severe illness, and death is higher in pregnant individuals compared to symptomatic non-pregnant, although approximately more than 90% of infected pregnant women recover without hospitalization [6]. The severity of infection is related to the predominant viral variant of SARS-CoV-2. Throughout the pandemic, the Delta variant has been associated with higher disease severity than the pre-Delta and Omicron variants [6].

Additional risk factors for pregnant women

Additional risk factors for pregnant women with SARS-CoV-2 infection for severe outcome include [3]:

1. Preexisting comorbidities

Table 1. **Overview of four case reports of pregnant women infected with SARS-CoV-2**

	Patient 1	Patient 2	Patient 3	Patient 4
Age	**40-years old**	**30-years old**	**27-years old**	**33-years old**
Timing of infection	March 2021	May 2021	November 2021	December 2021
Gestational Age at infection	30 weeks	30 weeks	38 weeks + 6 days	31 weeks + 5 days
Medical history	No chronic disease, no medication	No chronic disease, no medication	Endometriosis; Intrahepatic pregnancy cholestasis	No chronic disease, no medication
Obstetrical history	Complicated: G5, P2, A2, V1	No information	G1, P0, A0	G5, P2, A2
Additional risk factors	Pregnancy; Not vaccinated against SARS-CoV- 2; Age > 35 yrs.; Complicated gyn. history	Pregnancy; Not vaccinated against SARS- CoV-2	Pregnancy; Not vaccinated against SARS- CoV-2	Pregnancy; Not vaccinated against SARS- CoV-2
Clinical presentation during admission	General weakness, sore throat, fever episodes	Fever, general fatigue, dry cough, dyspnea when lying down or during physical activity	General weakness, sore throat, fever, muscle pain, productive cough, abdominal pain, diarrhea, nausea	Fever, weakness, nausea, decreased appetite; anxiety about fetus
Laboratory ● Infection marker, CBC ● CRP ● D-dimers ● ALT; AST	WBC 10.34*10^9/l NEU 8.01*10^9/l 13.6 mg/l 1545 ug/l ALT 91 U/l AST 59 U/l	WBC 4.29*10^9/l NEU 2.90*10^9/l 134.2 mg/l No information ALT 13 U/l AST 28 U/l	WBC 4.49*10^9/l NEU 3.00*10^9/l 27.4 mg/l 595 ug/l ALT 239 U/l AST 158 U/l	WBC 5.43*10^9/l NEU 3.78*10^9/l 14.6 mg/l 415 ug/l ALT 9 U/l AST 22 U/l
Diagnostics ● Chest X-ray ● Gyn. ultrasound ● CTG	No information Normal No information	Bilateral viral pneumonia Normal Normal	Bilateral pneumonia Normal Normal	Infiltration in upper lobe of right lung Normal Normal
COVID-19 related diagnosis	COVID-19 during pregnancy	Bilateral COVID- 19 pneumonia	Bilateral COVID- 19 pneumonia	Unilateral COVID-19 pneumonia (right upper lobe)
Additional side diagnosis	Pregnancy related cholestasis	Unspecific UTI; Gestational DM; Hypokalemia	First-degree rupture of perineum at birth	Fluid & electrolyte imbalance
Duration of hospitalization	10 days	7 days	11 days	6 days
Outcome	Discharged in stable condition	Discharged in stable condition	Planned induction of delivery because of intrahepatic pregnancy cholestasis; Discharged in stable condition	Discharged in stable condition

2. Chronic hypertension
3. Diabetes mellitus
4. Advanced maternal age (>35 years of age)
5. Obesity
6. Nonwhite ethnicity
7. Nonexistent vaccination coverage against SARS-CoV-2

A systematic review of Khan et al. (total of ten studies with 3,158 patients, three case-series) was published in the medical journal Biomedical Central (BMC) and compared the importance of the different additional risk factors in pregnant women [11]. Khan et al. described that hypertensive pregnant women with COVID-19 were even more likely to be symptomatic (OR 2.07; 95% CI 1.38 to 3.10; 3 studies, 2427 participants) than pregnant women with respiratory

disease (OR 1.64; 95% CI: 1.25 to 2.16; 3 studies, 2516 participants). There was no statistical difference between pregnant individuals with diabetes mellitus, hypothyroidism, or chronic cardiac disease for being symptomatic or asymptomatic. Obese pregnant women with COVID-19 have higher probabilities of being symptomatic (OR 1.37; 95% CI 1.15 to 1.62; 3 studies, 2516 participants).

Unexpected, the meta-analysis of Khan et al. also reports that pregnant women who smoked seem to have lower odds for a symptomatic course (OR 0.50; 95% CI: 0.36 to 0.71; 2 studies, 2367 participants). In addition, they found a higher rate of symptomatic infections among Blacks (OR 1.48; 95% CI: 1.19 to 1.85; 2 studies, 2367 participants) and Asians (OR 1.64; 95% CI: 1.23 to 2.18; 1study, 1148 participants). In contrast, persons with White ethnicity were less likely to be symptomatic (OR 0.63; 95% CI: 0.52 to 0.76; 2 studies, 2367 participants) [11]. The study covered the timeframe between December 2019 and November 2020. Therefore, these data stand most likely for the Alpha and Beta variants.

Complications of COVID-19 in pregnant patients

Especially in pregnant women with additional risk factors, there is a higher probability of a severe COVID-19 course with complications. Complications associated with COVID-19 include [6]:

1. Respiratory diseases: pneumonia, respiratory failure, ARDS
2. Cardiac diseases: cardiac arrhythmias, acute cardiac injury
3. Thromboembolic events
4. Secondary infections
5. Acute renal failure
6. Neurological disorders: headache, dizziness, myalgias, olfactory and gustatory disturbances, strokes
7. Skin diseases: morbilliform rash, urticaria
8. Gastrointestinal and liver diseases
9. Psychiatric disorders: anxiety disorder, depressive disorder, insomnia disorder, PTBS Symptomatic pregnant patients would be at higher risk of requiring intensive care unit treatment and/or invasive ventilation compared to non-pregnant women of reproductive age as shown by Zambrano et al. in a CDC report [3,12]. After adjustment for age, race/ethnicity, and medical comorbidities, SARS-CoV-2 infected that pregnant women have a significantly higher risk of ICU admission than SARS-CoV-2 infected nonpregnant women (10.5 versus 3.9 per 1,000 cases; adjusted risk ratio [aRR] = 3.0; 95% confidence interval [CI]=2. 6–3.4). Same applies for invasive ventilation (2.9 versus 1.1 per 1,000 cases; aRR=2.9; 95% CI=2.2–3.8), extracorporeal membrane oxygenation (ECMO) (0.7 versus 0.3 per 1,000 cases; aRR=2.4;

95% CI=1.5–4.0), and death (1.5 versus 1.2 per 1,000 cases, aRR=1.7, 95% CI=1.2–2.4). Differentiation of risk by subgroups becomes apparent after sorting these analyses by age and ethnicity.

A retrospective cohort study by Molina et al. evaluated a total of 301,880 pregnant patients (≥35 years old) treated at 463 US hospitals [13]. Primary outcomes included preterm or term delivery, mortality outcomes, and mode of delivery, and secondary outcomes described relative changes in pregnancy-related complications and length of stay. During the pandemic period, the rate of live birth decreased by 5.2% compared to the pre-pandemic rate. Furthermore, the rate of Maternal death during delivery hospitalization raised from 5.17 to 8.69 deaths per 100,000 pregnant patients (odds ratio [OR], 1.75; 95% CI, 1.19–2.58).

The changes in mode of delivery were small (vaginal: OR, 1.01; 95% CI, 0.996–1.02; primary cesarean: OR, 1.02; 95%CI, 1.01–1.04; vaginal birth after cesarean: OR, 0.98; 95% CI, 0.95-1.00; repeated cesarean: OR, 0.96;95% CI, 0.95–0.97).

During the pandemic period decreased the length of stay in hospital for delivery by 7% (rate ratio, 0.931; 95% CI, 0.928–0.933). Even though, the adjusted odds of gestational hypertension (OR, 1.08; 95% CI, 1.06–1.11), obstetric hemorrhage (OR, 1.07; 95% CI, 1.04–1.10), preeclampsia (OR, 1.04; 95% CI, 1.02–1.06), and preexisting chronic hypertension (OR, 1.06; 95% CI, 1.03–1.09) increased slightly during the pandemic period.

Moreover, an England wide population-based cohort study by Gurol-Urganci et al. published in the „American Journal of Obstetrics and Gynecologyô, supports the findings of the previously described studies [14]. Women were included in a national database of hospitalizations with a recorded single birth between May 29, 2020, and Jan 31, 2021. In the analysis, 342,080 women were involved, of whom 3527 had laboratory-confirmed COVID-19 infection. Fetal deaths (adjusted odds ratio, 2.21; 95% confidence interval, 1.58-3.11; P<.001) and preterm births (adjusted odds ratio, 2.17; 95% confidence interval, 1.96-2.42; P<.001) occurred more frequently in SARS-CoV-2 infected pregnant women with COVID-19 compared to non-infected women. The risk of preeclampsia or eclampsia (adjusted odds ratio, 1.55; 95% confidence interval, 1.29e1.85; P<.001), delivery by emergency cesarean section (adjusted odds ratio, 1.63; 95% confidence interval, 1.51–1.76; P<.001) was higher in women with SARS-CoV-2 infection. Pregnant women with SARS-CoV-2 had a prolonged post-partum hospitalization (adjusted odds ratio, 1.57; 95% confidence interval, 1.44–1.72; P<0.001). There were no significant differences (P>0.05) in the rate of other maternal outcomes. The risk of adverse neonatal outcome (adjusted odds ratio, 1.45; 95% confidence interval, 1.27–1.66; P<.001), the need for specialized neonatal care (adjusted odds ratio, 1.24; 95% confidence interval, 1.02–1.51; P=0. 03), and prolonged neonatal admission after birth (adjusted odds ratio, 1.61; 95% confidence interval, 1.49–1.75; P<0.001) were all significantly higher for infants with COVID-19-infected mothers. All these neonatal complications were associated with preterm birth. When the analysis was restricted to pregnancies delivered at term (37 weeks), there were no significant differences in neonatal adverse outcome

(P=0.78), need for specialist neonatal care after birth (P=0.22), or neonatal readmission within 4 weeks of birth (P=0.05). However, neonates born at term with COVID-19 positive mothers were more likely to have prolonged admission after birth (21.1% compared with 14.6%; adjusted odds ratio, 1.61; 95% confidence interval, 1.49–1.75; P<0.001).

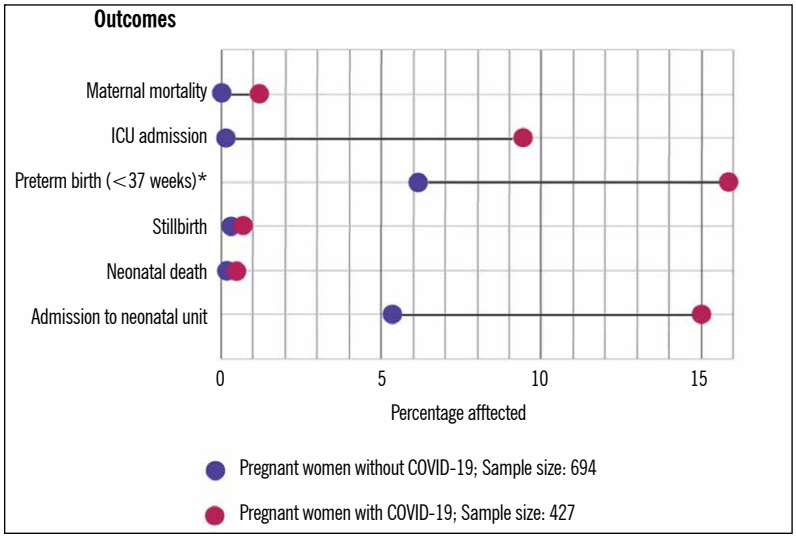
Ferrara et al. conducted a population-based cohort study involving 43886 pregnant women (mean [SD] age, 30.7 [5.2] years) with longitudinal data from electronic health records from conception to birth who delivered at Kaiser Permanente Northern California between March 1, 2020, and March 16, 2021. This cohort study, similar to previous studies, shows that SARS-CoV-2 infection during pregnancy was associated with an increased risk of severe maternal morbidity, preterm birth, and venous thromboembolism.

Women with SARS-CoV-2 infection (1332 [3.0%]) were more likely to be younger, Hispanic, perennial, have a higher neighborhood deprivation index, and be obese or have chronic hypertension. After adjustment for demographic characteristics, comorbidities, and smoking status, individuals with SARS-CoV-2 infection had a higher risk of severe maternal morbidity (HR, 2.45; 95% CI, 1.91–3.13), preterm birth (<37 weeks; HR, 2.08; 95% CI, 1.75–2.47), and venous thromboembolism (HR, 3.08; 95% CI, 1.09–8.74) than individuals without SARS-CoV-2. SARS-CoV-2 infection was also associated with an increased risk of medically indicated preterm birth (HR, 2.56; 95% CI, 2.06–3.19), spontaneous preterm birth (HR, 1.61; 95% CI, 1.22–2.13), and early (HR, 2.52; 95% CI, 1.49–4.24), moderate (HR, 2.18; 95% CI, 1.25–3.80), and late (HR, 1.95; 95% CI, 1.61–2.37) preterm birth. Of those with SARS-CoV-2 infection, 76 (5.7%) were hospitalized; gestational diabetes (HR, 7.03; 95% CI, 2.22–22.2) and Asian or Pacific Islander race and ethnicity (HR, 2.33; 95% CI, 1.06–5.11) and black (HR, 3.14; 95% CI, 1.24–7.93) were associated with increased risk of hospital admission. Pregestational diabetes and race and ethnicity as of Asians or Pacific Islanders and Blacks were associated with increased risk of hospitalization [15].

Table 2. **Overview of possible maternal and fetal complications associated with COVID-19**

Maternal complications	Fetal complications
• Hospitalization; ICU admission • Invasive ventilation • ECMO • Morbidity and mortality • Small changes in delivery mode; increased rate of cesarean section	• Hospitalization • Preterm birth; associated with neonatal death and stillbirth
• Gestational hypertension, obstetric hemorrhage, preeclampsia and preexisting chronic hypertension • Venous thromboembolism	

Figure 1. **An analysis of 77 clinical trials of Mullins et al. found that pregnant women who contract COVID-19 are more likely to require intensive treatment than those who are not infected. Their babies are more likely to be born prematurely, although the risk of death was low in babies born to both groups (adapted from 16)**



** Sample sizes: 44 pregnant women with COVID-19; 295 pregnant women without COVID-19.*

Discussion

Pathophysiology

To understand the context of the potential impact on the mother and the fetus, it is important to understand the pathophysiology behind it. Such as vulnerability during pregnancy, possible effects on placental function and whether vertical transmission may occur.

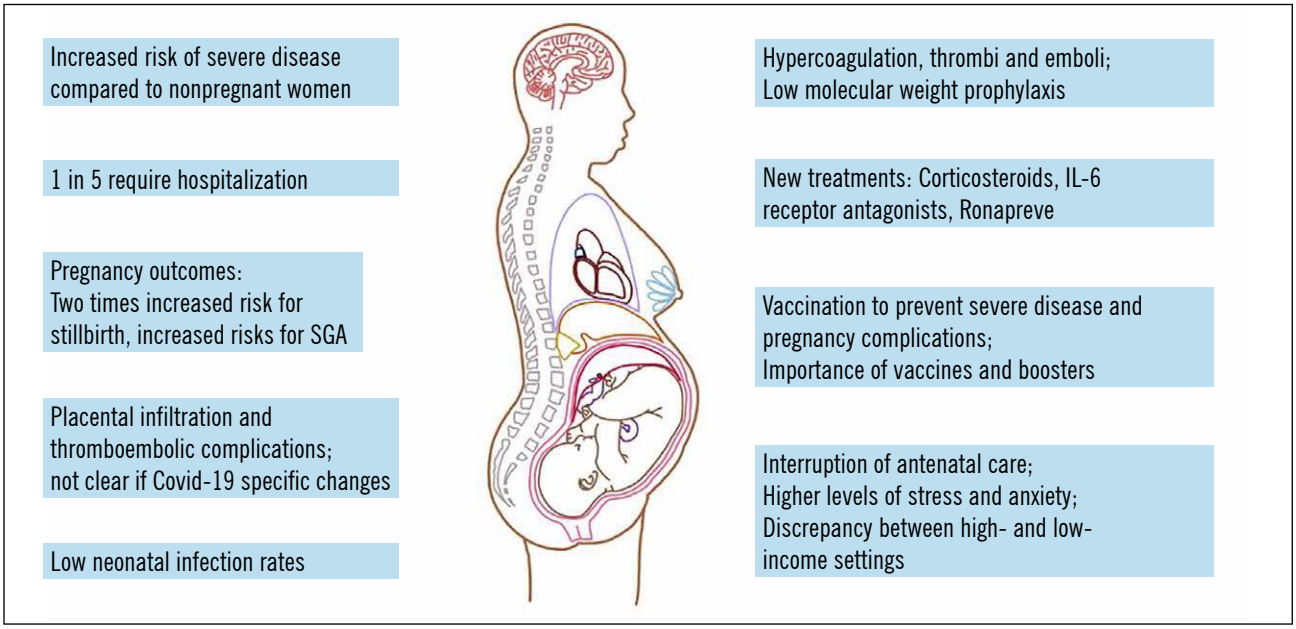
Vulnerability of pregnant women due to anatomical and physiological changes

The vulnerability of pregnant women to a severe course of SARS-CoV-2 infection can be explained by the anatomic and physiologic changes that occur during pregnancy. Pregnancy- related changes include increasing transverse diameter of the chest, elevation of the diaphragm, alteration of lung volume, and vasodilation followed by mucosal edema, which reduces maternal tolerance to hypoxia [11].

Possible effect of SARS-CoV-2 on placental function

In previous reviews, Reynold et al. speculated on possible mechanisms by which SARS-CoV-2 might affect placental function (see Figure 2) [17]. Since the virus SARS-CoV-2 acquires access to human cells by attaching to the

Figure 2. **This figure graphically illustrates that pregnant women are at increased risk for severe COVID-19 compared to non-pregnant women. The consequences shown include hospitalizations, risk of stillbirth, low pregnancy weight, and placenta-associated complications. A low risk of infection for newborns is also indicated. In addition, anticoagulation prophylaxis, new treatments, and vaccinations are emphasized [17]**



angiotensin-converting enzyme-2 (ACE2) receptor, the virus may have effects on the placenta and fetus as the same receptors are presented on the maternal placenta. Reynolds et al. has compared two systematic reviews and meta-analyses in which nearly 1500 placentas were histologically examined for changes due to SARS-CoV-2 infection during pregnancy.

More than 80% of placentas had abnormalities, both vascular and inflammatory lesions, suggestive of placental hypoperfusion and inflammation [17]. An elemental question was whether invasion and infection of the placenta by SARS-CoV-2 was associated with the development of preeclampsia, fetal growth restriction, or other complications of COVID-19 in pregnancy. The meta-analysis (1452 cases from 30 publications) by Suhren et al. showed that there were no COVID-19 specific placental changes, and the incidence of vascular and inflammatory lesions were comparable to those in pregnancies without COVID-19 [18]. To distinguish the effects of acute maternal illness with maternal-fetal hypoxia associated with pneumonia from virus-specific effects would require further investigation. Although SARS-CoV-2 virus may be detected in the placenta, it is not yet known whether this results in fetal infection. Because there is disagreement in the literature about whether the placenta co- expresses ACE2 and transmembrane protease serine 2 (TMPRSS2), it remains unclear whether transmission of the virus from mother to fetus is even possible [17]. Because SARS-CoV-2 uses ACE2 as the entry receptor and TMPRSS2 as the viral entry-associated serine protease for S- protein priming, both proteins are necessary for infection [19].

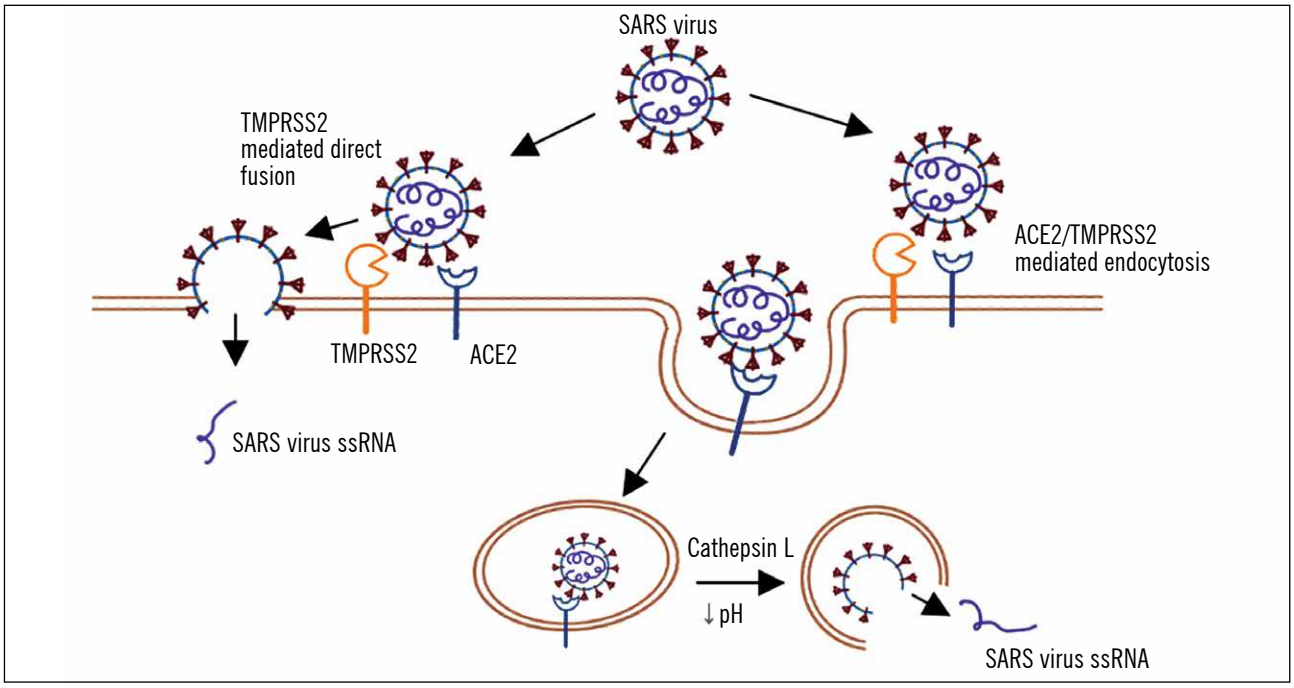
Vertical transmission of SARS-CoV-2

The risk for vertical transmission is considered low (3–6%) and would occur predominantly in the third trimester [17].

Gesaka et al. reviewed 96 studies in a systematic literature review to clarify mediators, mechanism of entry, pathogenesis, identification, and placental pathology of SARS-CoV-2 [21]. Gesaka‘s review highlighted variable expression of the canonical mediators of SARS-CoV-2, angiotensin-converting enzyme-2 (ACE2), and transmembrane serine protease-2 (TMPRSS2) in different compartments of the placenta (e.g., villous cytotrophoblasts, syncytiotrophoblasts (STB), and extravillous trophoblasts (EVT)) during pregnancy. Gesaka reports that SARS CoV-2 virus RNA, proteins, and particles can be confirmed in syncytiotrophoblasts by in situ hybridization, immunohistochemistry, electron microscopy, and polymerase chain reaction. Gesaka concludes that the placenta exhibits a differential predisposition to SARS-CoV-2 infection over the course of gestational trimesters. This depends on the localization of SARS-CoV-2 receptors, proteases and genes encoding proteins that drive viral pathogenesis in the placenta [21].

According to the systematic review by Allotey et al. [22], a correlation is observed between severe maternal disease and positivity of the test in the offspring. This could be related to the detection of viral RNA in the blood, which is associated with the severity of the disease. However, there is currently no clear evidence of linkage between severity of maternal disease and excretion of SARS-CoV-2, but it can be hypothesized that the duration of excretion appears to be prolonged in individuals with severe COVID-19.

Figure 3. **This figure by I.S. Mahmoud and Y.B. Jarrar illustrates the TMPRSS2 mediated entry of SARS-CoV-2 into host cells. After the virus binds to the cell surface, TMPRSS2 could activate host cell entry through at least two major pathways. The left side of the figure shows that TMPRSS2 mediates proteolytic cleavage of the viral (S) protein, which initiates direct fusion of the viral and plasma membranes. This results in the release of viral ssRNA into the cytoplasm. The right side of the figure shows that TMPRSS2 cooperates with the host cell receptor ACE2 in the activation of the SARS-CoV-2 (S) protein, which then stimulates receptor-mediated endocytosis. Subsequently, SARS-CoV-2 terminates in endosomal compartments, where a decline in endosomal pH stimulates cathepsin-L enzymes, which proceed to cleave and activate the viral (S)-glycoprotein. Release of viral ssRNA into the cytosol is facilitated [20]**



It is difficult to rule out the possibility that positively tested newborns may not have contracted the disease from the mother or caregivers after birth if testing for COVID-19 is only obtained postnatally. Notably, Allotey et al. found no association between breastfeeding practices and SARS-CoV-2 positivity in newborns. This is in accordance with the rare findings of RT-PCR positivity in breast milk samples. Nevertheless, Allotey et al. found evidence of SARS-CoV-2 positivity in amniotic fluid, placenta, and vaginal secretions. These several biological samples could be associated with the potential for vertical infections. Despite these positive samples, there is no mandatory correlation with infection of the fetus. Nevertheless, the evaluation and classification of these samples is limited since it is unclear whether the maternal or fetal side of the placenta was swabbed [22].

Risk for severe maternal disease according to SARS-CoV-2 variant

In addition to the individual medical factors of the patient, another factor that contributes to the severity of the course of the disease is the SARS-CoV-2 variant.

Deng et al. compared the risks and outcomes of the different SARS-CoV-2 variants [23]. Preliminary data suggest that infection with the delta variant during pregnancy might be associated with a higher risk of severe maternal illness, placental dysfunction, and fetal impairment. Accordingly, both pre-Delta variants and the Omicron variant were associated with a lower risk. The risk of pneumonia was higher in pregnant women infected with the delta variant (B.1.617.2) in comparison to the pre-delta variants. However, the need for intensive care was higher for Alpha phase (B.1.1.7) infected pregnant women with, - higher than for the wild-type phase of the SARS-CoV-2 virus.

In contrast, the Omicron variant (B.1.1.529) leads to comparatively mild courses during pregnancy. Factors contributing to this trend include the lower virulence of the variant. However, also the higher vaccination rates, and the increased immunity within the community might contribute to this finding [23].

A recent publication (March 2023) of the COVI-PREG registry also confirmed that the risk of a serious maternal adverse event was higher in the delta period than in the pre-delta period (adjusted risk ratio (aRR)=1.8; 95% CI 1.1–3.2) and lower in the omicron period than in the pre-delta period (aRR=0.3; 95% CI, 0.1–0.8) [24].

Although Omicron is associated with milder courses and is currently the predominant SARS- CoV-2 variant worldwide, severe courses for pregnant women requiring ICU admission, respiratory support, or preterm delivery also occur with this variant [23]. Regardless, the risk of hospitalization for COVID-19-infected women was high in all variants – both in the pre- delta period and in the

delta period, but also in the Omicron period. Therefore, Omicron infection should not be trivialized [24].

Iatrogenic preterm birth

As all variants can cause preterm birth as one of the main complications of COVID-19 during pregnancy and as preterm birth is one of the main causes of further neonatal complications, as indicated in the section on „Complications of COVID-19 in pregnancy", it is necessary to distinguish between the different causes of preterm birth in order to improve the clinical management of the complication.

The literature research revealed an increased incidence of preterm births and, in some studies, also a higher rate of cesarean sections. However, when considering these study results, it should be emphasized that recommendations for the management and stabilization of COVID-19 positive pregnancies changed during the pandemic. Indeed, only a few studies reported the indication for cesarean section. However, it can be inferred from the data that the main reason for cesarean section was severe maternal pneumonia with the risk of decompensation and not primarily fetal distress [4]. There was the interim hypothesis that severe maternal respiratory illness would improve after birth [6]. This would further explain the trend in the incidence of C-sections and iatrogenic preterm births. However, the hypothesis has not been proven right as clinical improvement of pregnant women after delivery has not been observed [6]. Furthermore, rate of spontaneous premature delivery was in the expected range showing that severe maternal pneumonia due to COVID-19 in pregnancies does not justify iatrogenic preterm birth beyond spontaneous premature delivery, especially because premature delivery is one of the main causes of neonatal complications [4].

Contradictory data on the effects of COVID-19 on pregnancy outcomes: exploring factors contributing to variations in research findings

Overall, the data on this topic are complex. As an example, the question on the change in the rate of preterm births could be used. Molina et al. stated in 2022 that the overall births decreased however the mode of delivery and preterm births remained stable [13]. In contrast, Gurol-Urganci et al. said a year earlier (2021) that SARS-CoV-2 at the time of birth have a higher rate of fetal death and preterm birth [14]. In a later study, the result looks different. In 2022, Gurol-Urganci et al. found a very small decreases in preterm birth and small gestational age birth rates [25]. Yalçin et al. describes 2020 that there would be a significant reduction in preterm and LBW births possibly due to the indirect effects of the pandemic (in Turkey) [26]. In the same year, Reynolds et al. identified an increased incidence of small-for-gestational age babies in COVID-19 infected women [17]. The different results can be explained firstly by the fact that different virus variants predominated during the various studies. Secondly, there are differences in the respective inclusion criteria of the studies: in some, only cases detected with a PCR test was used, while in others an appropriation test or even the patient's statement was sufficient. Another limitation of most studies was that it was difficult to distinguish between behavioral and biological determinants of infection susceptibility. In addition, different health care and welfare systems in different countries might influence the reported outcomes.

Vaccination during pregnancy and in women of childbearing age

Regarding the benefit of vaccination against SARS-CoV-2, studies appear to be consistent. According to the CDC, there is a definite recommendation to vaccinate all persons six months of age and older against COVID-19 (+ booster), including pregnant and breastfeeding persons and persons who are trying to become pregnant. The recommendation to vaccinate pregnant women relies on data supporting the safety and efficacy of the vaccine in pregnant women, as well as data showing that pregnancy is associated with an increased risk of severe infection. The expected side effects are the same for pregnant and non-pregnant patients [27].

There were individual reports on social media of women reporting irregular menstrual cycles after vaccination [28]. This may have also triggered concerns There were unfortunately some concerns among young women that the vaccination could cause infertility or be harmful to a subsequent pregnancy. Since most clinical trials on vaccines exclude pregnant women there was only little data on the use during pregnancy. Regarding the increased risk of a severe course, most gynecological societies recommended vaccination with an mRNA vaccine for pregnant women from the second trimester onwards, - although prospective clinical studies or clinical data were lacking at that time. To date, there is no evidence of direct or indirect adverse effects on fertility, embryonic/fetal development, the course of pregnancy, delivery, or postnatal development of the offspring [6, 29].

mRNA vaccines and recombinant protein subunit adjuvanted vaccines are favored over vector-based vaccines. However, it is better to choose a vector-based vaccine than to abstain from vaccination against COVID-19 [30].

Because of the strong evidence of transplacental transfer of antibodies to the fetus following maternal COVID-19 vaccination during pregnancy, the vaccines seem to be beneficial for both the mother and the fetus [17]. Severe illness and infant deaths are rare in western countries and occurs mostly in unvaccinated populations.

The vast majority (98%) of pregnant women who suffered a serious infection and were admitted to hospital were unvaccinated [17].

Conclusion

To conclude, pregnant women with SARS-CoV-2 infection are at increased risk for rapid deterioration and severe illness. Especially pregnant women with additional risk factors are more vulnerable for complications such as maternal morbidity, admission to the intensive care unit, and in severe cases, maternal death, or adverse pregnancy outcomes such as preterm birth. Complications such as stillbirth and neonatal death occur particularly in association with preterm birth. The mechanisms underlying these risks are currently under investigation but may be related to the direct effects of SARS-CoV-2 on the placenta and fetus, as well as the indirect effects of systemic inflammation and cytokine storm. The study search has shown that especially the severe complications are attributed to the delta variant. In comparison, milder courses of disease occur under the predominant Omicron variant. Nevertheless, despite the officially announced end of the pandemic by the WHO, the risks and possible complications that can also arise from Omicron variant should not be underestimated. Pregnant women should be considered a vulnerable population, and preventive measures such as social distancing, hand hygiene, and mask wearing should be encouraged. Pregnant women with suspected or confirmed COVID-19 should receive prompt and appropriate medical care to minimize the risk of adverse outcomes.

Recommendations

1. Pregnant women should be advised to follow strict preventive measures such as social distancing, hand hygiene, and mask wearing to minimize the risk of SARS-CoV-2 infection.
2. Pregnant women who develop symptoms suggestive of COVID-19 should seek medical attention promptly, and healthcare providers should have a low threshold for testing pregnant women for SARS-CoV-2.
3. Pregnant women with confirmed COVID-19 should receive prompt and appropriate medical care, including close monitoring of maternal and fetal well-being, and management of symptoms and complications.
4. Healthcare providers caring for pregnant women with COVID-19 should be aware of the increased risk of adverse maternal and fetal outcomes and be prepared to manage these complications.
5. Pregnant women who have been vaccinated against SARS-CoV-2 should continue to follow preventive measures as recommended by public health authorities, as the duration and degree of protection provided by the vaccine during pregnancy are not yet well-understood. However, vaccination is strongly recommended for pregnant women as the benefits of protection against COVID-19 outweigh the potential risks.
6. Pregnant women who are at high risk of exposure to SARS-CoV-2, such as healthcare workers, should be given priority for vaccination.

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