ORIGINAL ARTICLE

Oman Medical Journal [2023], Vol. 38, No. 4: e530

Maternal, Perinatal, and Neonatal Outcomes of COVID-19 Severity in Pregnant Women: A Retrospective Study from Oman

Istaqlal Al Ghaithi[1], Bushra Ahmed[2], Tamima Al Dughaishi[2], Nihal Al Riyami[3], Rahma Al Haddabi[2] and Vaidyanathan Gowri[3]*

[1]Obstetrics and Gynecology Residency Training Program, Oman Medical Specialty Board, Muscat, Oman
[2]Department of Obstetrics and Gynecology, Sultan Qaboos University Hospital, Muscat, Oman
[3]Department of Obstetrics and Gynecology, College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman

ARTICLE INFO

Article history:
Received: 19 November 2022
Accepted: 7 January 2023

Online:
DOI 10.5001/omj.2023.90

Keywords:
COVID-19; Pregnancy; Neonate; Perinatal; Severity; Oman.

ABSTRACT

Objectives: To evaluate the effect of COVID-19 severity on maternal, perinatal, and neonatal outcomes in pregnant women infected with SARS-CoV-2. We also aimed to assess the effect of medical comorbidities on the severity of COVID-19. ***Methods***: A retrospective cohort study was conducted on women who became infected with SARS-CoV-2 during pregnancy and delivered at Sultan Qaboos University Hospital, Oman, from 1 March 2020 to 31 December 2021. ***Results:*** A total of 118 pregnant women with COVID-19 and their 118 newborns were included in the study. Mean maternal age was 32.0 years, with 60.2% of women infected in the third trimester. The majority of the participants had mild symptoms. Eleven (9.3%) women had moderate infection needing inpatient care. Six (5.1%) with severe infection were admitted to intensive care unit. The chronic diseases among the participants were hypothyroidism, obesity, sickle cell disease, epilepsy, and diabetes. The mean gestational age at delivery was 37.0 weeks with 20.9% of women delivering by cesarean section out of whom 37.5% had moderate-to-severe COVID-19. The most common complications associated with COVID-19 severity were preterm labor ($p = 0.002$), preeclampsia ($p = 0.002$), and intrauterine fetal death ($p = 0.089$). Of the total 118 newborns, 111 were singletons and six were twins. One fetus died and three singletons were lost to miscarriage. Placental histopathology conducted in 64 patients had no COVID-specific findings in most cases. ***Conclusions:*** Most pregnant women with COVID-19 infections had mild symptoms. The majority of women with moderate-to-severe infection were admitted for COVID-19 pneumonia. There was no direct effect of COVID-19 severity in neonatal outcomes or placental histopathology changes.

The first two years of the COVID-19 pandemic rocked the world healthcare system to the core as never before.[1,2] Oman was no exception. From February 2020 to December 2021, the country had 305 489 cases leading to 4116 deaths.[3,4] Even though the pandemic has subsided in Oman, new variants of SARS-CoV-2 continue to emerge in different parts of the world, the latest being the fast-spreading omicron.[5] Thus, the war against this pathogen is far from over.

Clinical severity of COVID-19 ranges from asymptomatic or mildly symptomatic patients to critical situations with bilateral pneumonia leading to multiorgan failure. There are many risk factors specific to pre-existing conditions that may predispose an individual to the severe attack of the disease. For women, a prominent risk factor for severe COVID-19 is being pregnant, on which this paper focuses.

Pregnancy is an independent risk factor for COVID-19 severity, as it further increases the risk of susceptibility of both mother and fetus.[6] The vulnerability is due to the pregnancy-induced anatomical-physiological changes in the female body, such as high metabolic demand and immune-suppressive status.[6,7] The dysregulation of the renin-angiotensin-aldosterone system in pregnant women with COVID-19 might be experienced as preeclampsia -like symptoms, leading to complicated pregnancy.[8] Moreover, pregnant women with pre-existing conditions such as hypertension and diabetes mellitus (DM) are at higher risk of developing severe COVID-19.[9] The most frequent maternal

*Corresponding author: ✉gowri@squ.edu.om; gowrie61@hotmail.com

outcomes were increased cesarean sections (CSs) (23–96%) and preterm deliveries (14–64%). The most frequent neonatal outcome, apart from more preterm deliveries, was low birth weight (5–43%). The odds ratio for such newborns being admitted to neonatal intensive care unit (ICU) was 3.13 (95% CI: 2.05–4.78).[10] However, the risk of vertical transmission of the virus has not been confirmed.[6,10]

Many studies have focused on the obstetric and neonatal outcomes of infected pregnant women. The evolution of pregnancies in women diagnosed with SARS−CoV−2 infection through laboratory tests,[7] clinical presentation, risk factors, pregnancy and perinatal outcomes,[11,12] and pathobiological risk[6] have been described. This enabled formulation of management guidelines for pregnant COVID-19 patients.[13,14] Studies on placental histology have not shown any significant difference between women with and without COVID-19.[15]

This is a cohort study of maternal and neonatal outcomes of women infected with SARS-CoV-2 who delivered in a tertiary care center in Oman. We aimed to study the relations between the severity of infection and obstetrical and neonatal complications, as well as placental histology.

METHODS

This retrospective cohort study included all pregnant women who were infected with SARS-CoV-2 as confirmed by reverse transcription-polymerase chain reaction, and subsequently gave birth at Sultan Qaboos University Hospital from 1 March 2020 to 31 December 2021. Ethical approval was obtained from the Medical and Research Ethics Committee at the College of Medicine and Health Sciences, Sultan Qaboos University (Reference: mReC#2378).

The following data were collected: (1) maternal demographics: age, gravidity, parity, and miscarriage (obstetric history); (2) COVID-19-related data: gestational age at infection, severity of infection, admission to hospital, and reason for hospitalization; (3) past medical history; (4) obstetric outcomes: preeclampsia, intrauterine growth restriction, oligohydramnios, preterm premature rupture of membranes, fetal distress, intrauterine fetal death (IUFD), and mode of delivery; (5) neonatal outcomes: birth weight Apgar score.

The levels of COVID-19 severity were categorized into three levels: (1) mild: symptoms with no hospital admission; (2) moderate: symptoms requiring inpatient care in obstetric wards; and (3) severe: symptoms requiring ICU admission.

Collected data were analyzed using IBM SPSS Statistics (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 27.0. Armonk, NY: IBM Corp). For descriptive purposes, categorical variables were presented with frequency and percentages. Categorical variables were compared with severity using chi-square test. A p-value of < 0.05 were considered to have statistical significance.

RESULTS

We retrospectively identified 118 pregnant women with confirmed COVID-19 infection who delivered during the study period. The mean age of pregnant women included in the current study was 32.0 years (range = 20–44) and the mean gestational age at diagnosis was 33.0 weeks (range = 4–40). The most common comorbidity was hypothyroidism. Most pregnant women's COVID-19 symptoms were mild (101; 85.6%). Eleven (9.3%) patients developed moderate symptoms and required hospital admission. Only six (5.1%) patients had severe infection requiring ICU admission. Among the 17 women with moderate-to-severe symptoms, 11 were admitted for COVID-19 pneumonia. Four patients with sickle cell disease (SCD) needed admission for vaso-occlusive crisis during COVID-19 infection. One patient (5.9%) was admitted in ICU for encephalitis and one (5.9%) had fever and admitted in the ward [Table 1]. Pregnancy complications, mode of delivery, and placental findings are described in Table 1.

The majority 71 (60.2%) of patients were diagnosed with COVID-19 during the third trimester of pregnancy, among whom 12 (16.9%) developed moderate-to-severe symptoms. In comparison, among those infected during the first trimester, only one of 12 (8.3%) developed moderate symptoms ($p = 0.007$). The only chronic comorbidities significantly associated with the severity of COVID-19 were obesity ($p = 0.025$) and SCD ($p = 0.001$). Other chronic diseases did not reveal any statistically significant association [Table 2].

All women aged 20–24 years had mild symptoms. With increasing age, a slight tendency towards moderate-to-severe infections was apparent, though lacking in statistical significance ($p = 0.412$) [Table 2].

Table 1: Demographic and clinical characteristics of pregnant women with COVID-19 (N = 118).

Variables	n (%)
Age, years, mean ± SD (range)	32.0 ± 5.1(20–44)
Gravidity, mean ± SD (range)	3.0 ± 1.8 (1–9)
Parity, mean ± SD (range)	2.0 ± 1.5 (0–8)
Gestational age at diagnosis in weeks, mean ± SD (range)	33.0 ± 9.3 (4–40)
Comorbid conditions	
Obesity	5 (4.2)
Diabetes mellitus	2 (1.7)
Sickle cells disease	6 (5.1)
Epilepsy	3 (2.5)
Hypothyroidism	7 (5.9)
Severity of COVID-19	
Mild	101 (85.6)
Moderate	11 (9.3)
Severe	6 (5.1)
Reason for admission (n = 17)	
Vaso-occlusive crisis	4 (23.5)
COVID-19 pneumonia	11 (64.7)
Fever	1 (5.9)
Encephalitis	1 (5.9)
Adverse pregnancy outcomes	
Preeclampsia	10 (8.5)
Intrauterine growth restriction	9 (7.6)
Oligohydramnios	3 (2.5)
Preterm premature rupture of membrane	3 (2.5)
Fetal distress	12 (10.42)
Gestational age at delivery, weeks (n = 115)	
≥ 37	94 (81.7)
< 37	21 (18.3)
Mode of delivery (n = 115)	
Vaginal	91 (79.1)
Cesarean section	24 (20.9)
Placental histopathology (n = 64)	
Unremarkable	34 (53.1)
Fibrin deposition	3 (4.7)
Infarction	14 (21.9)
Chorionitis	7 (10.9)
Coagulative necrosis	6 (9.4)

Preeclampsia and prematurity were the most common complications related to COVID-19 severity (p = 0.002 for both). Six (35.3%) of 17 cases with moderate-to-severe infections were complicated by preeclampsia. Preterm deliveries were more frequent (58.8%) among moderate-to-severe symptomatic patients. CS rates were also higher in the moderate-to-severe symptomatic group (52.9%; p = 0.004). IUFD occurred in one patient with severe COVID-19 infection (5.9%; p = 0.089). Other complications did not show any significant association with COVID-19 severity [Table 3].

Table 2: Relation between maternal characteristics and COVID-19 severity.

Characteristics	Mild n (%)	Moderate/ severe n (%)	*p*-value
Age group, years			
2 (20–24)	7 (100)	0 (0.0)	0.412
3 (25–29)	29 (87.9)	4 (12.1)	
4 (30–34)	31 (86.1)	5 (13.8)	
5 (35–39)	21 (75.0)	7 (25.0)	
6 (≥ 40)	13 (92.9)	1 (7.1)	
Gestation stage at diagnosis of COVID-19			
First trimester	11 (91.6)	1 (8.3)	0.007
Second trimester	31 (88.5)	4 (11.4)	
Third trimester	59 (83.1)	12 (16.9)	
Obesity			
No	99 (87.6)	14 (12.4)	0.025
Yes	2 (40.0)	3 (60.0)	
Diabetes mellitus			
No	100 (86.2)	16 (13.7)	0.160
Yes	1 (50.0)	1 (50.0)	
Sickle cell disease			
No	100 (89.3)	12 (10.7)	0.001
Yes	1 (16.7)	5 (83.3)	
Epilepsy			
No	99 (86.1)	16 (13.9)	0.448
Yes	2 (66.7)	1 (33.3)	
Hypothyroidism			
No	94 (84.7)	17 (15.3)	0.324
Yes	7 (100)	0 (0.0)	

Neonatal clinical outcomes are shown in Table 4. There were 117 live neonates born for 118 pregnant women including three sets of twins. There was one IUFD and three miscarriages. No neonatal death was reported.

The majority (88; 75.2%) of neonates had a normal birth weight of 2500–4000 g. Only five (4.2%) newborns had Apgar scores ≤ 7 at one minute. The total number of neonatal admissions was nine; five for prematurity, two for intensive phototherapy, and two for respiratory distress syndrome.

The rate of neonatal admission was significantly high in moderate-to-severe symptomatic mothers (four of 11; 26.7%), compared to five of 97 (4.9%) in the mild symptomatic group (p = 0.012) [Table 5].

Table 3: Relation between perinatal and intrapartum outcomes and COVID-19 severity.

Outcome	Mild (n = 101) n (%)	Moderate/severe (n = 17) n (%)	*p*-value
Preeclampsia	4 (4.0)	6 (35.3)	0.002
Intrauterine growth restriction	8 (7.9)	1 (5.8)	0.610
Oligohydramnios	3 (3.0)	0 (0.0)	0.620
Reduced fetal movements	1 (1.0)	11 (64.7)	0.310
Preterm premature rupture of membranes	3 (3.0)	0 (0.0)	0.620
Fetal Distress	10 (9.9)	2 (11.8)	0.094
Intrauterine fetal death	0 (0.0)	1 (5.9)	0.089
Premature birth (< 37 weeks)	14 (13.9)	10 (58.8)	0.002
Caesarian section	15 (14.9)	9 (52.9)	0.004

Table 4: Clinical outcomes of neonates born to pregnant women with COVID-19 (N = 118).

Outcome	n (%)
Fetuses	118
Alive	117 (99.2)
Intrauterine fetal death	1 (0.8)
Neonatal death	0 (0.0)
Singlet	111 (94.1)
Twin	6 (5.1)
Miscarriage	3 (2.5)
Sex (n = 117)	
Male	51 (43.6)
Female	66 (56.4)
Birth weight, g (n = 117)	
2500–4000	88 (75.2)
< 2500	25 (21.4)
< 1500	4 (3.4%)
Reason for neonatal admission (n = 9)	
Prematurity	5 (55.6)
Respiratory distress syndrome	2 (22.2)
Intensive phototherapy	2 (22.2)
Apgar score	
≤ 7 at 1 minute	5 (4.2)
> 7 at 5 minutes	117 (99.2)

Table 5: Relation between COVID-19 severity of mothers and neonatal outcomes.

Outcome	Mild n (%)	Moderate/severe n (%)	*p*-value
Birth weight, g			
2500–4000	81 (79.4)	7 (46.7)	0.001
< 2500	21 (20.6)	8 (53.3)	
Neonatal admission			
No	97 (95.1)	11 (73.3)	0.012
Yes	5 (4.9)	4 (26.7)	

Placental histopathology was examined in 64 patients during their pregnancy, which yielded normal results for 34 women while 30 were found to have abnormal placenta. The commonest histopathological abnormalities were infarction and chorangiosis. Six of the tested patients had moderate-to-severe COVID-19 infections of whom placental histopathology reports of five were normal. Only one patient with moderate-to-severe symptoms had abnormal placental histopathology. Among 56 women who had mild COVID-19 symptoms, 50.0% had normal and 50.0% had abnormal placental histopathology. Abnormalities in placental histopathology were classified into four groups: fibrin deposition (4.7%), infarction (21.9%), chorionitis (10.9%), and coagulative necrosis (9.4%). Their rates of prevalence were not associated with COVID-19 severity [Table 1].

DISCUSSION

The current study investigated the effects of COVID-19 severity on maternal, perinatal, and neonatal outcomes in 118 pregnant women with COVID-19 infection. The age of the participants (mean = 32.0 years; range = 20–44) had no significant impact on severity of infection. Other studies have associated maternal age of ≥ 35 years with higher COVID-19 severity risk.[9,16]

Most (n = 71) of our participants were diagnosed with COVID-19 in their third trimester, 12 women as late as the 38th week. It was noted that there was a significant increase in the severity of infection with advanced gestational age. In later stages of pregnancy, reduction in total lung capacity and reduced ability to clear secretions due to elevation of

the diaphragm by the gravid uterus can make women more susceptible to severe respiratory infection.[5] A multicenter study identified a significant increase of composite adverse obstetric outcomes at > 20 weeks gestation and of composite adverse neonatal outcomes at > 26 weeks gestation ($p < 0.001$) in the COVID-19 exposed group.[17]

Our results show that in most cases the clinical course of infection in pregnant women was not complicated. Similar results were found in the literature review with different inclusion criteria. Two different studies in New York reported that COVID-19 disease severity in pregnant women—86% mild, 9.3% severe, and 4.7% critical—was similar to that in non-pregnant adult women.[17,18]

Six hospital admissions in the current study were due to COVID-19 pneumonia. Five were admitted in ICU, including four sickle cell crisis cases and one for encephalitis. Pneumonia-like symptoms are known to be a global characteristic of SARS-CoV-2 infection, for which patients with various comorbidities are most at risk. Critical conditions may develop in individuals with hypertension, DM, chronic obstructive pulmonary disease, heart diseases, malignancies, and HIV.[4,6,19] The comorbidities among our participants were obesity (5; 4.2%), DM (2; 1.67%), SCD (6; 5.1%), epilepsy (3; 2.5%), and hypothyroidism (7; 5.9%). Their rates of prevalence were comparable to other studies.

Among our two DM patients, one was infected severely and the other mildly. Two meta-analyses have identified DM as a risk to pregnancy outcomes even without COVID-19.[20,21] The insignificant *p*-value (0.160) we obtained could be attributed to the small sample size.

Women with SCD are more prone to severe COVID-19 infection and complicated pregnancies with obstetrical and fetal complications.[22] This is due to increased metabolic demands, hypercoagulable state, and vascular stasis associated with pregnancy,[22] which was observed in our cohort also. On the contrary, some reports claim mild COVID-19 symptoms in women with SCD.[23]

Obesity is a risk factor for almost all pregnancy complications and maternal death. It is also an independent prognostic factor for the severity of COVID-19 and almost reached significance in our population. Other chronic diseases did not reveal anything statistically significant.[24,25]

It was noted that 51 out of 114 patients had an active infection during labor, 14 (27.5%) of whom delivered preterm (< 37 weeks). The severity of COVID-19 was highly associated with gestational age at delivery. This is supported by meta-analyses,[10,12] which also found greater odds of preterm birth in women with COVID-19.

Eight (33.3%) of 24 CSs in this cohort were performed in response to fetal distress. This is a much higher percentage of CS than those performed for fetal distress in non-COVID-19 women.[26]

In the current study, seven out of 12 women with active infection had fetal distress. As infection with SARS-CoV-2 has been shown to cause hypoxemia, these changes may lead to accumulation of oxygen free radicals, changes in intracellular pH, accumulation of lactic acid, electrolyte changes, and further cellular damage that lead to fetal distress and expedite delivery.[12] Other studies have shown an increase in CS deliveries, but indications were not fully studied.[13] One systematic review reported more CS deliveries by COVID-19 patients contributing to raising the preterm delivery numbers; half of CS deliveries were conducted on women with COVID-19 pneumonia.[27]

A study in New York compared pregnancy outcomes in African American women with and without COVID-19. Surprisingly, they found no difference in perinatal outcomes between the two groups,[28] despite the fact that African American ethnicity is associated with a higher tendency for vascular conditions such as hypertension and coronary artery diseases.[29,30]

Vertical transmission of SARS-CoV-2 has been reported by some studies, while others did not confirm it.[27,31] Positive SARS-CoV-2 testing in neonates correlated with direct contacts.[11,31] One study detected SARS-CoV-2 in breast milk,[27] while in another study, placental, cord blood, and amniotic fluid samples were negative for the virus.[32] Most of the studies demonstrated healthy or mild symptomatic neonates born from COVID-19-positive mothers, though there was a tendency for low birth weight (< 2550 g).[32,33] Increase in neonatal ICU admissions has been reported,[27,31,33] usually due to respiratory distress, hyperbilirubinemia, possible sepsis, and prematurity.[32,34] In another systematic review, birth asphyxia and respiratory distress syndrome also accounted for 1.8% and 6.4% of neonate admissions, respectively.[31]

In our study, no impact was observed of COVID-19 infection in the neonates' Apgar scores. There was an increase in low-birth-weight rates (< 2500 g) due to prematurity, as 55.6% of our low-birth-weight newborns were born < 37 weeks. Perhaps placental hypoperfusion contributes to the likelihood of low birth weight.

Placental histopathology was examined in 64 pregnant women. Most of the abnormal placental histology was in mild symptomatic infection as severe infection resulted in termination of pregnancy (three miscarriages, one fetal death, and six preterm deliveries). No specific histopathology changes were observed linked to the severity of infection nor to the gestational age at the time of infection. Different reviews concluded the same findings; no specific changes in the placentas of SARS-CoV-2-infected pregnant women.[15,35,36] Some changes could be related to placental hypoperfusion with different variables like DM and high body mass index.[37] One study showed prominent lymphohistiocytic villitis, attributable to SARS-CoV-2 infection of the placenta.[37]

There were limitations to our study. First, the prevalence of COVID-19 infection in patients who delivered in Sultan Qaboos University Hospital could not be estimated due to the lack of screening of asymptomatic patients. Second, the study was conducted at a single center so the small sample size may not have sensitively reflected the impact of comorbidities. Third, being a retrospective study, some information regarding patient history, investigations, and outcomes was unavailable. Further, this study pertained to cases that emerged during the two-year period when knowledge of the pandemic and its management were evolving rapidly, so the effect of different variants of COVID-19 was not studied and the impact of any vaccines taken by the patients was not taken into account.

CONCLUSION

Most pregnant patients with COVID-19 infections had mild symptoms. The majority of cases with moderate-to-severe infection were admitted for COVID-19 pneumonia. SCD and obesity were significantly associated with COVID-19 severity. Other comorbidities could not be studied due to the small sample size. The most common obstetric complications were preeclampsia, preterm deliveries, and fetal distress, which reflect the increase in the rate of CSs. Neonatal admission and low birth weight were correlated to the severity of COVID-19. There were no demonstrable placental histopathology changes.

Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

REFERENCES

1. World Health Organization. Archived: WHO timeline - COVID-19. 2020 [cited 2020 April 27]. Available from: https://www.who.int/news/item/27-04-2020-who-timeline---covid-19.
2. World Health Organization. Coronavirus disease (COVID-19) weekly epidemiological updates and monthly operational updates. [cited 2021 December 28]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
3. Khamis F, Al Rashidi B, Al-Zakwani I, Al Wahaibi AH, Al Awaidy ST. Epidemiology of COVID-19 infection in Oman: analysis of the first 1304 cases. Oman Med J 2020 Jun;35(3):e145.
4. Worldometer. Oman COVID - coronavirus statistics. [cited 2021 December 28]. Available from: https://www.worldometers.info/coronavirus/country/oman/.
5. Center for Disease and Control and Prevention. SARS-CoV-2 variant classifications and definitions. 2022 [cited 2022 November]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/variants/variant-classifications.html.
6. Naidu S, Clemens R, Pressman P, Zaigham M, Davies K, Naidu A. COVID-19 during pregnancy and postpartum. Journal of Dietary Suppl 2022 Nov;19(1):78-114.
7. de Oliveira KF, de Oliveira JF, Wernet M, Carvalho Paschoini M, Ruiz MT. COVID-19 and pregnancy: a scoping review on pregnancy characteristics and outcomes. Int J Nurs Pract 2021 Oct;27(5):e12956.
8. Sayad B, Mohseni Afshar Z, Mansouri F, Salimi M, Miladi R, Rahimi S, et al. Pregnancy, preeclampsia, and COVID-19: susceptibility and mechanisms: a review study. Int J Fertil Steril 2022 Apr;16(2):64-69.
9. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. BMJ 2020;370:m3320.
10. Ciapponi A, Bardach A, Comandé D, Berrueta M, Argento FJ, Rodriguez Cairoli F, et al. COVID-19 and pregnancy: an umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes. PloS One 2021 Jun;16(6):e0253974.
11. Mirbeyk M, Saghazadeh A, Rezaei N. A systematic review of pregnant women with COVID-19 and their neonates. Arch Gynecol Obstet 2021 Jul;304(1):5-38.
12. Lassi ZS, Ana A, Das JK, Salam RA, Padhani ZA, Irfan O, et al. A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity. J Glob Health 2021 Jun;11:05018.
13. Kazemi S, Hajikhani B, Didar H, Hosseini S, Haddadi S, Khalili F, et al. COVID-19 and cause of pregnancy loss during the pandemic: a systematic review. PloS One 2021 Aug 11;16(8):e0255994.
14. Pavlidis P, Eddy K, Phung L, Farrington E, Connolly M, Lopes R, et al. Clinical guidelines for caring for women

with COVID-19 during pregnancy, childbirth and the immediate postpartum period. Women Birth 2021 Sep;34(5):455-464.

15. Tasca C, Rossi RS, Corti S, Anelli GM, Savasi V, Brunetti F, et al. Placental pathology in COVID-19 affected pregnant women: a prospective case-control study. Placenta 2021 Jul;110:9-15.
16. Şahin D, Tanaçan A, Webster SN, Moraloğlu Tekin Ö. Pregnancy and COVID-19: prevention, vaccination, therapy, and beyond. Turk J Med Sci 2021 Dec;51(SI-1):3312-3326.
17. Badr DA, Picone O, Bevilacqua E, Carlin A, Meli F, Sibiude J, et al. Severe acute respiratory syndrome coronavirus 2 and pregnancy outcomes according to gestational age at time of infection. Emerg Infect Dis 2021 Oct;27(10):2535-2543.
18. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM 2020 May;2(2):100118.
19. Center for Disease and Control and Prevention. Underlying medical conditions associated with higher risk for severe COVID-19: information for healthcare professionals. 2022 [cited 2022 August 28]. Available from: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html.
20. DeBolt CA, Bianco A, Limaye MA, Silverstein J, Penfield CA, Roman AS, et al. Pregnant women with severe or critical coronavirus disease 2019 have increased composite morbidity compared with nonpregnant matched controls. Am J Obstet Gynecol 2021 May;224(5):510.e1-510.e12.
21. Grigoryan OR, Mikheev RK, Kurinova AN, Chernova MO, Sazonova DV, Akhmatova RR, et al. [Comparative impact analysis of risk factors on the course and outcomes of pregnancy with gestational diabetes mellitus]. Probl Endokrinol (Mosk) 2021 May;67(3):78-86.
22. Jain D, Atmapoojya P, Colah R, Lodha P. Sickle cell disease and pregnancy. Mediterr J Hematol Infect Dis 2019 Jul;11(1):e2019040.
23. Kolanska K, Vasileva R, Lionnet F, Santin A, Jaudi S, Dabi Y, et al. Sickle cell disease and COVID-19 in pregnant women. J Gynecol Obstet Hum Reprod 2022 Mar;51(3):102328.
24. Aljahdali EA. Impact of body weight on the outcome of pregnancy: a prospective cohort study. Saudi Med J 2021 Oct;42(10):1109-1116.
25. Price SA, Sumithran P, Nankervis AJ, Permezel M, Prendergast LA, Proietto J. Impact of preconception weight loss on fasting glucose and pregnancy outcomes in women with obesity: a randomized trial. Obesity (Silver Spring) 2021 Sep;29(9):1445-1457.
26. Qureshey EJ, Mendez-Figueroa H, Wiley RL, Bhalwal AB, Chauhan SP. Cesarean delivery at term for non-reassuring fetal heart rate tracing: risk factors and predictability. J Matern Fetal Neonatal Med 2022;35(25):6714-6720.
27. Jafari M, Pormohammad A, Sheikh Neshin SA, Ghorbani S, Bose D, Alimohammadi S, et al. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: a systematic review and meta-analysis. Rev Med Virol 2021 Sep;31(5):1-16.
28. Liu C, Andrusier M, Silver M, Applewhite L, Clare CA. Effect of SARS-CoV-2 infection on pregnancy outcomes in an inner-city black patient population. J Community Health 2021 Oct;46(5):1029-1035.
29. Jurgens P, Carr J, Terry J, Rana J, Jacobs D, Duprez D. Association of abdominal aorta calcium and coronary artery calcium with incident cardiovascular and coronary heart disease events in black and white middle–aged people: the coronary artery risk development in young adults study. Journal of the American Heart Association 2021;10(24):e023037.
30. Nunes JP. Arterial hypertension and sepsis. Rev Port Cardiol 2003 Nov;22(11):1375-1379.
31. Vizheh M, Allahdadian M, Muhidin S, Valiani M, Bagheri K, Borandegi F, et al. Impact of COVID-19 infection on neonatal birth outcomes. J Trop Pediatr 2021 Oct;67(5):fmab094.
32. Villar J, Ariff S, Gunier R, Thiruvengadam R, Rauch S, Kholin A. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the intercovid multinational cohort study. JAMA Pediatr 2021 Aug 1;175(8):817-826.
33. Lokken E, Huebner E, Taylor G, Hendrickson S, Vanderhoeven J, Kachikis A, et al. Disease severity, pregnancy outcomes and maternal deaths among pregnant patients with SARS-CoV-2 infection in Washington State. Am J Obstet Gynecol 2021 Jan 26;225(77):e1-e77.
34. Vouga M, Favre G, Martinez-Perez O, Pomar L, Acebal LF, Abascal-Saiz A, et al. Maternal outcomes and risk factors for COVID-19 severity among pregnant women. Sci Rep 2021 Jul;11(1):13898.
35. Shanes ED, Mithal LB, Otero S, Azad HA, Miller ES, Goldstein JA. Placental pathology in COVID-19. Am J Clin Pathol 2020 Jun;154(1):23-32.
36. Leal C, Maciel M, Junior M. SARS-CoV-2 infection and placental pathology infecção por SARS-CoV-2 e patologia placentária. Revista Brasileira de Ginecologia e Obstetrícia 2021 Sep 6;43(6):474-479.
37. Menter T, Mertz KD, Jiang S, Chen H, Monod C, Tzankov A, et al. Placental pathology findings during and after SARS-CoV-2 infection: features of villitis and malperfusion. Pathobiology 2021;88(1):69-77.