

Impact of COVID-19 Infection on the Maternal and Perinatal Outcome of Pregnancies Associated with Preeclampsia

Original
Article

Reham Elkhateeb and Hashem Fares

Department of Obstetrics and Gynecology, Faculty of Medicine, Minia University, Egypt

ABSTRACT

Objectives: To compare the severity and complications of preeclampsia in the presence and absence of COVID-19 infection

Methods: A cross-sectional study was carried out at Minia Governate isolation Hospitals which have a standard procedure for monitoring and testing COVID-19. The study enrolled 345 pregnant women after considering eligibility criteria. One hundred fifteen cases were positive for COVID-19 infection compared with randomly chosen control cases with a ratio of 1:2 of COVID-19-negative pregnant women.

Result: The incidence of preeclampsia in COVID-19-infected pregnant women was 31.3% (36 cases), while 42 cases in the non-COVID-19 group had preeclampsia with an incidence of 18.3%. There was a high incidence of maternal complications in the study group (ICU admission incidence was 72.2% versus 45.2%, and maternal mortality was 41.6% versus 38%). Fetal complications were higher in the study group.

Conclusion: The development of preeclampsia in COVID-19 patients is associated with hazardous maternal and fetal outcomes. It increases the need for ICU admission, invasive ventilation support, maternal and perinatal mortality.

Key Words: COVID-19; hazardous pregnancy complications; hypertensive disorders; preeclampsia.

Received: 10 October 2022, **Accepted:** 15 October 2022

Corresponding Author: Reham Elkhateeb, Department of Obstetrics and Gynecology, Faculty of Medicine, Minia University, Egypt, **Tel.:** +20 10 9065 0463, **E-mail:** rehamelkhateeb68@gmail.com

ISSN: 2090-7265, November 2022, Vol.12, No. 4

INTRODUCTION

SARS-COV-2 is a newer strain of coronavirus that causes COVID-19, and it was first identified by the end of 2019 in Wuhan city, China^[1]. COVID-19 has rapidly spread worldwide, making pregnant women and their fetuses a high-risk group during illness epidemics due to the presence of physiological and anatomical changes that increase susceptibility to infection in pregnant women^[2].

Many studies have shown that a preeclampsia-like syndrome developed at severe SARS-COV-2 infection that's resolved after infection improvement^[3], and another study suggests an increased risk of preeclampsia in COVID-19-infected patients, even if asymptomatic due to similar placental pathology proposed in both^[4]. However, confounding common risk factors of both preeclampsia and COVID-19 infection could be explained by the following: COVID-19 and preeclampsia have the same pathophysiology and etiological pathway. They sometimes also share some diagnostic criteria^[5].

Management of pregnant women with COVID-19 in patients with preeclampsia-like syndrome admitted at hospitals must be well studied according to the severity of cases using oxygen flow to maintain saturation of more than 94%, IV fluids to maintain hydration, antibiotics, steroids,

prophylactic LMWH after venous thromboembolism assessment, antiviral medications and antihypertensive medications^[6]. According to recent research, pregnancy does not appear to increase vulnerability to COVID-19 infection, but it does seem to aggravate COVID-19's clinical course when compared to women who are not pregnant and are the same age^[7,8].

Preeclampsia and COVID-19 infection during pregnancy are linked, and both of these conditions enhance the likelihood of severe maternal and neonatal outcomes^[9,10,11]. According to one of the papers reviewed in the systematic review, preeclampsia and prenatal COVID-19 infection are linked to various unfavorable pregnancy outcomes^[12]. Patients with both preeclampsia and COVID-19 infection had an increased risk of preterm delivery, small-for-gestational-age neonates, and worse maternal and perinatal outcomes than patients with either preeclampsia or just COVID-19 infection. Healthcare providers must be aware of the elevated probability for preeclampsia among pregnant women with COVID-19 infection, even in asymptomatic patients. Due to the additive effect of COVID-19 infection and preeclampsia, close monitoring of the affected pregnancy must be planned, and early effective interventions that can lower risks to mothers and their fetuses or newborns must be adopted^[13].

METHODS

A cross-sectional study was conducted at Minia Governorate Hospitals, which have a universal COVID-19 testing policy and admission to labor and delivery. The study was conducted from the 1st of April 2020 to the 30th of October 2021. The study enrolled 345 pregnant women after considering eligibility criteria. One hundred fifteen cases were positive for COVID-19 infection compared with randomly chosen control cases with a ratio of 1:2 of COVID-19-negative pregnant women. COVID-19 was diagnosed with the standard testing protocol.

Cases that developed preeclampsia during COVID-19 infection (confirmed with nasopharyngeal swabs) were considered in the study group, while cases with preeclampsia and COVID-19 negative were considered in the control group. Patients with unavailable data records were excluded.

The incidence of preeclampsia in COVID-19-infected patients and non-COVID-19 patients was calculated. Demographic characters and maternal and fetal outcomes were statistically analyzed.

Statistical analysis

The Statistical Package for the Social Sciences (SPSS software version 25.0) program was then used to input the data and perform analysis of both groups to define the incidence of preeclampsia, its severity, and maternal and fetal complications. The outcomes were compared between two groups.

RESULTS

A comparison of demographic data between the two groups is shown in (Table 1). The incidence of preeclampsia in COVID-19 patients was 31.3%, and the incidence of preeclampsia in the control group was 18.3%. Regarding severity, 77.8% of cases of preeclampsia with COVID-19 were severe, while the incidence of severity of preeclampsia in cases without COVID-19 was 42.9%. The other maternal complications in both groups are shown in (Table 2). Fetal complications were higher in COVID-19 patients, as demonstrated in (Table 3).

Table 1: Comparison of demographic data between the two groups

		Preeclampsia		P-value
		COVID-19 (n=36)	Non-COVID-19 (n=42)	
Age	Mean \pm SD	29.4 \pm 6.4	28.7 \pm 7.3	0.623
Body mass index	Mean \pm SD	26 \pm 2.3	27.9 \pm 2.5	0.001*
Mean arterial pressure	Mean \pm SD	110 \pm 7	105.7 \pm 4.9	0.002*
Duration of marriage	Median (IQR)	10 (2.3-13.8)	5 (1.8-10.5)	0.100
Parity	Median (IQR)	2 (0-3)	1 (0-3)	0.297

Table 2: Comparison of severity of preeclampsia and maternal complications between the two groups

		Preeclampsia		P-value
		COVID-19 (n=36)	Non-COVID-19 (n=42)	
Severe preeclampsia & eclampsia		28 (77.8%)	18 (42.9%)	0.002*
HELLP syndrome		12 (33.3%)	14 (33.3%)	1
Renal affection		5 (13.9%)	7 (16.7%)	0.735
Postpartum hemorrhage		3 (8.3%)	0	0.094
Impaired liver function		17 (47.2%)	14 (33.3%)	0.211
Maternal mortality		15 (41.6%)	16 (38%)	0.916

Table 3: Comparison of fetal complications between the two groups

	Preeclampsia		P-value
	COVID-19 (n=36)	Non-COVID-19 (n=42)	
Intrauterine growth retardation	1 (2.8%)	4 (9.5%)	0.366
Intrauterine fetal death	5 (13.9%)	5 (11.9%)	1
Early neonatal death	3 (8.3%)	0	0.094
Respiratory distress	24 (66.7%)	19 (45.2%)	0.058
Incubation	25 (69.4%)	19 (45.2%)	0.032*
Preterm labor	16 (44.4%)	18 (42.8%)	0.888
Low birth weight	9 (25%)	8 (19%)	0.526

DISCUSSION

This study showed that there was a significant difference as regards the severity of preeclampsia in both groups. Mean arterial blood pressure (MAP) was 110 ± 7 in the study group (preeclampsia with COVID-19) versus 105 ± 4.9 in the control group (preeclampsia without COVID-19).

The incidence of severe preeclampsia in COVID-19 patients 77.8%, while was 42.9% of preeclampsia were without COVID-19 patients. The study group had a higher maternal and fetal complications incidence than the control group. Our findings are consistent with three meta-analyses that compared the adverse outcomes for mothers and babies in both COVID-19 -infected and uninfected pregnant women^[8,14,15]. According to the findings of this research, pregnant women with COVID-19 infection are significantly more likely to have a risk of maternal death, ICU admission, premature birth, and stillbirth than those who don't have an infection. Furthermore, compared to children born to moms without the illness, kids born to mothers with COVID-19 infection were more likely to be admitted to the neonatal ICU. The prevalence of hypertensive disorders of pregnancy was 18.8%, 23.8%, and 40.4%, respectively, among women with asymptomatic COVID-19 infection, mild or moderate disease, and severe or critical disease, according to comprehensive cohort research by Metz *et al.*^[16]. Patients with light, moderate, or severe disease had a higher risk of developing hypertensive disorders of pregnancy compared to asymptomatic patients (adjusted RR, 1.24; 95% CI, 0.98-1.58 for mild, moderate disease; and adjusted RR, 1.61; 95% CI, 1.18-2.20 for severe, critical disease). These facts strongly imply a dose-response relationship.

The current study showed an increased rate of incidence of maternal ICU admission at 77.8%, with increased incidence of eclampsia, HELLP (hypertension, elevated liver enzymes, low platelet count), postpartum hemorrhage, and maternal mortality. The adverse maternal and perinatal outcomes between pregnant women with and without COVID-19 infection were evaluated in meta-analyses, and our findings were consistent with those findings^[8,14,15].

Regarding fetal complications, the current study showed a statistically significant difference for neonatal incubation, 69.4% for the group of preeclampsia with COVID-19, while the incidence was 45.2% for the control group. As regards intrauterine growth retardation, intrauterine fetal death, early neonatal death, and respiratory distress syndrome were higher in the study group, but the difference is not statistically significant, which agrees with a study done by Papageorgiou *et al.*, 2021^[17].

CONCLUSION

Development of preeclampsia in COVID-19-infected patients worsens maternal and fetal outcomes. Since preeclampsia and COVID-19 infection have hazardous outcomes for pregnant women, we must establish a protocol for of management of this high-risk group of patients.

CONFLICT OF INTERESTS

There are no conflicts of interest.

REFERENCES

- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *The lancet*. 2020 Feb 15;395(10223):497-506.
- Hu X, Gao J, Luo X, Feng L, Liu W, Chen J, Benachi A, De Luca D, Chen L. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vertical transmission in neonates born to mothers with coronavirus disease 2019 (COVID-19) pneumonia. *Obstetrics and gynecology*. 2020 Jul 1.
- Ferrer-Oliveras R, Mendoza M, Capote S, Pratcorona L, Esteve-Valverde E, Cabero-Roura L, Alijotas-Reig J. Immunological and physiopathological approach of COVID-19 in pregnancy. *Archives of gynecology and obstetrics*. 2021 Jul;304(1):39-57.

4. Dashraath P, Wong JL, Lim MX, Lim LM, Li S, Biswas A, Choolani M, Mattar C, Su LL. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *American journal of obstetrics and gynecology*. 2020 Jun 1;222(6):521-31.
5. Di Mascio D, Sen C, Saccone G, Galindo A, Grünebaum A, Yoshimatsu J, Stanojevic M, Kurjak A, Chervenak F, Suárez MJ, Gambacorti-Passerini ZM. Risk factors associated with adverse fetal outcomes in pregnancies affected by Coronavirus disease 2019 (COVID-19): a secondary analysis of the WAPM study on COVID-19. *Journal of perinatal medicine*. 2020 Nov 1;48(9):950-8.
6. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z, Lu G, Qiao C, Hu Y, Yuen KY, Wang Q. Structural and functional basis of SARS-CoV-2 entry by using human ACE2. *Cell*. 2020 May 14;181(4):894-904.
7. Ciapponi A, Bardach A, Comandé D, Berrueta M, Argento FJ, Rodriguez Cairoli F, Zamora N, Santa María V, Xiong X, Zarea S, Mazzone A. COVID-19 and pregnancy: An umbrella review of clinical presentation, vertical transmission, and maternal and perinatal outcomes. *PloS one*. 2021 Jun 29;16(6):e0253974.
8. Allotey J, Stallings E, Bonet M, Yap M, Chatterjee S, Kew T, Debenham L, Llavall AC, Dixit A, Zhou D, Balaji R. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *bmj*. 2020 Sep 1;370.
9. Abalos E, Cuesta C, Carroli G, Qureshi Z, Widmer M, Vogel JP, Souza JP, WHO Multicountry Survey on Maternal and Newborn Health Research Network. Pre-eclampsia, eclampsia and adverse maternal and perinatal outcomes: a secondary analysis of the World Health Organization Multicountry Survey on Maternal and Newborn Health. *BJOG: An International Journal of Obstetrics & Gynaecology*. 2014 Mar;121:14-24.
10. Martinez-Portilla RJ, Smith ER, He S, Torres-Torres J, Espino-Y-Sosa S, Solis-Paredes JM, Poon LC. Young pregnant women are also at an increased risk of mortality and severe illness due to coronavirus disease 2019: analysis of the Mexican National Surveillance Program. *American Journal of Obstetrics & Gynecology*. 2021 Apr 1;224(4):404-7.
11. Wei SQ, Bilodeau-Bertrand M, Liu S, Auger N. The impact of COVID-19 on pregnancy outcomes: a systematic review and meta-analysis. *Cmaj*. 2021 Apr 19;193(16):E540-8.
12. Conde-Agudelo A, Romero R. SARS-CoV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis. *American journal of obstetrics and gynecology*. 2021 Jul 21.
13. Huntley BJ, Mulder IA, Di Mascio D, Vintzileos WS, Vintzileos AM, Berghella V, Chauhan SP. Adverse pregnancy outcomes among individuals with and without severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): a systematic review and meta-analysis. *Obstetrics and gynecology*. 2021 Apr;137(4):585.
14. Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, Gan H, Sun YL, Fu W, Li W, Liang HL. Risk factors for severe and critically ill COVID-19 patients: a review. *Allergy*. 2021 Feb;76(2):428-55.
15. Lai J, Romero R, Tarca AL, Iliodromiti S, Rehal A, Banerjee A, Yu C, Peeva G, Palaniappan V, Tan L, Mehta M. SARS-CoV-2 and the subsequent development of preeclampsia and preterm birth: evidence of a dose-response relationship supporting causality. *American Journal of Obstetrics & Gynecology*. 2021 Dec 1;225(6):689-93.
16. Metz TD, Clifton RG, Hughes BL, Sandoval GJ, Grobman WA, Saade GR, Manuck TA, Longo M, Sowles A, Clark K, Simhan HN. Association of SARS-CoV-2 infection with serious maternal morbidity and mortality from obstetric complications. *JAMA*. 2022 Feb 22;327(8):748-59.
17. Papageorgiou AT, Deruelle P, Gunier RB, Rauch S, García-May PK, Mhatre M, Usman MA, Abd-Elsalam S, Etuk S, Simmons LE, Napolitano R. Preeclampsia and COVID-19: results from the INTERCOVID prospective longitudinal study. *American journal of obstetrics and gynecology*. 2021 Sep 1;225(3):289-e1.