



# Preeclampsia in COVID-19: A Masquerading Errant—An Exploration of Foeto-Maternal Outcome from a Tertiary Care Hospital In India

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## Abstract

**Background** COVID-19 pandemic has shown that the multisystem involvement in COVID-infected patients is beyond the usual clinical manifestations of other respiratory viral illnesses. This study aims to evaluate the upshots of COVID-19 in women with preeclampsia.

**Methodology** This descriptive study was conducted in department of Obstetrics & Gynaecology at VMMC & Safdarjung Hospital (May–November 2020), wherein a retrospective review of the medical records of laboratory confirmed SARS CoV2-positive pregnant women (as per ICMR), with preeclampsia (as defined by ACOG guidelines), was done in the dedicated COVID labour ward. Primary outcome was incidence of preeclampsia in SARS CoV2 positive gravid females. Secondary outcomes were socio-demographic and maternal characteristics, severity of COVID-19 and foeto-maternal outcome.

**Results** During these 7 months, 38/302 (12.58%) SARS COV2-positive women presented with pre-eclampsia, either before or at the time of admission; amongst them 47.37% were primigravida. Severe preeclampsia was chronicled in 65.71% women. Around 20% women had severe COVID-19. All women with severe COVID19 required ICU stay, 5 requiring intubation. Three of these patients succumbed to their illness. Out of the 40 babies born to these women (including 2 twin pregnancies), 36.84% were premature deliveries. Seventeen (42.50%) babies had low birth weight. Although 82.50% were live births, five (12.50%) were intrauterine demise and 2 were early neonatal deaths.

**Conclusion** Gravid women with preeclampsia infected with SARS CoV2 have comparative more severe illness, requiring more intensive care requirement and high maternal and neonatal morbidity.

**Keywords** Preeclampsia · COVID-19 · Foeto-maternal outcome

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## Introduction

Ever since the Corona Virus Disease-19 (COVID-19) pandemic has engulfed the world, a lot of research has been done on a spectrum of patients infected by this deadly severe acute respiratory illness corona virus 2 (SARS CoV-2). The effects of COVID-19 on the obstetric population have also continuously been investigated since then. Recent large studies from west suggest that COVID-19 infection has a mild-to-moderate course in pregnant women, but pre-existing health conditions or comorbidities, such as diabetes or high blood pressure, predisposed them for graver outcomes, irrespective of the pregnancy status [1–5]. A comprehensive understanding of such potential causes leading to worsening of the clinical conditions of SARS Co-V2-positive pregnant women is extremely pivotal to thwart maternal and perinatal morbidity and mortality.

Preeclampsia is one such frequent comorbidity that is a multisystem progressive disease characterized by new onset of hypertension and proteinuria or significant end organ dysfunction in the latter half of pregnancy/postpartum [6]. Around 4–6% of pregnancies worldwide are complicated by preeclampsia [6, 7]. Preeclampsia encompasses a wide gamut of symptoms and complications including epigastric or upper abdomen pain, pulmonary oedema, peripheral oedema, oliguria, neurological manifestations like headache, visual disturbances, hyper-reflexia or seizures. Women with preeclampsia are proven to be endangered with life threatening obstetric or medical complications [6, 7].

Work done by past pollsters has divulged that hyper-inflammatory state in COVID-19 is responsible for preterm birth and subsequently low birth weight amongst the babies [8]. Similarly in preeclampsia, the already compromised placental morphology is susceptible to the added inflammatory changes by COVID-19 infection [9]

This novel virus enters target cells by ACE-2 (angiotensin-converting enzyme-2) mediation, forming complexes with the receptor, and subsequent ACE-2 inactivation. Angiotensin 1–7 plasma levels are lower in pregnancies complicated by preeclampsia than in physiological normal pregnancies [1, 2, 9]. This puts the preeclampsia patients at higher risk of acquiring severe COVID-19 infection.

Keeping all this in mind, along with scarcity of research on preeclampsia in SARS CoV2 positive women, especially in India, the present study was conceived with the aim of determining the foetal and maternal outcomes in these women. Identification of this high-risk pregnant group by liberal testing for COVID-19 and relentless monitoring for its clinical manifestation is thus of utmost importance to save the susceptible population from acquiring severe disease.

## Materials and Methods

This descriptive study was conducted in Department of Obstetrics & Gynaecology at VMMC & Safdarjung Hospital from May to November 2020, wherein laboratory-confirmed COVID-19-positive expecting women (as per ICMR guidelines) with preeclampsia (defined by ACOG guidelines), admitted for delivery in the dedicated COVID labour ward were enrolled, after taking institutional ethical clearance [10, 11]. Women with other comorbidities, such as diabetes, cardiovascular disorders, seizure disorder, and hypothyroidism, were excluded from the study.

Sampling of the patients was done in accordance with the existing Indian council of medical research (ICMR) guidelines at the time of admission [10]. A laboratory-confirmed case was defined as a positive rapid antigen test (RAT) or RT-PCR test (reverse transcriptase–polymerase chain reaction) following nasopharyngeal or oral swab sample

collection. Women were further classified based on severity of COVID-19 as per the ICMR definitions [12].

Preeclampsia was defined as high blood pressure of more than 140/90 mm Hg at two separate occasions four hours apart with either proteinuria or features of end organ dysfunction in a previously normotensive woman. Preeclampsia was further categorized into mild and severe form as per the latest definitions [11].

The medical records were reviewed for detailed history at the time of presentation, clinical signs and symptoms, disease progression, hospital stay, maternal and foetal outcome. Obstetric management of the patients was done in accordance with the standard practicing guidelines [12–14].

All data were recorded in predesigned case proformas and decrypted at the end of study. The presentation of the categorical variables was done in the form of number and percentage (%), whereas continuous variables were presented as mean  $\pm$  SD and median values. The data entry was done in the Microsoft EXCEL spread sheet, and the final analysis was done with the use of Statistical Package of Social Sciences (SPSS) software version 27.0.

## Results

During this 7-month study period, 302 SARS CoV2-positive pregnant patients were admitted for delivery in the dedicated COVID 19 Super-speciality block at Safdarjung hospital. Amongst them, 38 females (12.58%) presented with pre-eclampsia, diagnosed either before or at the time of admission.

The mean age of SARS CoV2-positive women with preeclampsia was 26.63 years, ranging from 19 to 36 years. While 47.37% were primigravida, rest 52.63% were multiparous women. The mean period of gestation at the time of admission was 37 weeks 1 day (Table 1).

Almost 40.00% of the study populace were asymptomatic at admission. Scrutinizing the presenting symptoms suggestive of COVID-19, fever was the most common (48.57%) followed by shortness of breath (17.14%), cough (11.43%) and loose stools (2.86%) (Fig. 1).

Severe features of preeclampsia were recorded in 18 women (47.37%), out of which 4 (10.52%) patients presented with antepartum eclampsia, 1 (2.63%) with HELLP syndrome, and two (5.26%) with pulmonary oedema.

In terms of severity of disease, 78.95% women had mild disease, 2.63% had moderate, and 18.42% had severe disease (Fig. 2).

All women with severe COVID-19 required intensive care, of which 5 (13.15%) women were intubated and put on mechanical ventilator, while the other two (5.26%) required high oxygen support. Analysing the mode of delivery, 23 (60.53%) underwent lower section caesarean section

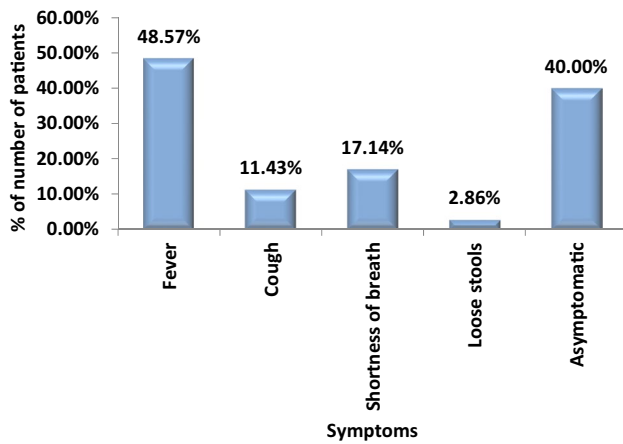
**Table 1** Distribution of socio-demographic characteristics of study subjects

Socio-demographic characteristics	Frequency
Age (years)	
Mean ± SD	26.63 ± 4.1
Median (25th–75th percentile)	26 (23.5–30)
Range	19–36
Parity	
Primigravida	18 (47.37%)
Multigravida	20 (52.63%)
Period of gestation (weeks)	
Mean ± SD	36.8 ± 2.85
Median (25th–75th percentile)	37.57 (35.538.857)
Range	29.71–40.57

**Table 2** Distribution of maternal outcome of study subjects

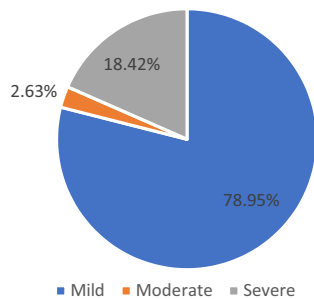
Maternal outcome	Frequency (percentage)
Need for O2	
No	33 (94.29%)
Yes	2 (5.71%)
ICU stay	
No	31 (81.58%)
Yes	7 (18.42%)
Need for ventilation	
No	33 (86.84%)
Yes	5 (13.16%)
Maternal mortality	3 (7.89%)
Need for blood transfusion	
No	29 (76.32%)
Yes	9 (23.68%)
Surgical site infection	
No	35 (92.10%)
Yes	3 (7.90%)
Mode of delivery	
Vaginal	15 (39.47%)
LSCS	23 (60.53%)

**Distribution of symptoms of study subjects**



**Fig. 1** Distribution of symptoms of study subjects

**Distribution of disease severity of study subjects**



**Fig. 2** Distribution of COVID-19 disease severity of study subjects

(LSCS), whereas 15 women (39.47%) were delivered by vaginal route. Foetal distress was the predominant indication in 12 (52.17%) followed by failed induction in 6 (26.08%)

women. During their course in hospital, 7 (18.42%) women required blood transfusion due to co-existent anaemia, and in 2 (5.26%) women PPH triggered transfusion. 3 (7.89%) women developed surgical site infection, of which one required re-suturing, whereas the other wound healing was attained by secondary intention. There occurred three mortalities (7.89%) amongst these women: two due to AKI and the third owing to sepsis with antepartum eclampsia (Table 2).

Out of the 40 babies born to the study population (including 2 twin pregnancies), 36.84% were born premature. Seventeen (42.50%) babies had their birth weight lower than 2.5 kg, whereas 23 (57.50%) babies weighed more than 2.5 kg at birth. Ten babies (28.57%) required NICU stay, all in view of birth asphyxia. Although 82.50% were live births, five (12.50%) were intrauterine demise and 2 (5.00%) were early neonatal deaths. All live born babies were tested and monitored for vertical transmission of COVID-19 infection by RT-PCR nasopharyngeal sampling done within 24 h post-delivery as per the existing ICMR guidelines. All babies tested negative for infection suggesting no evidence of vertical transmission (Table 3).

### Discussion

The incidence of preeclampsia in SARS CoV2-positive pregnant women in the extant study was found to be 12.58%. This is significantly higher than the incidence in India as

**Table 3** Distribution of foetal outcome of study subjects

Foetal outcome	Frequency (percentage)
Baby weight ( <i>n</i> = 40)	
< 2.5 kg	17 (42.50%)
≥ 2.5 kg	23 (57.59%)
Mean ± SD	2.44 ± 0.73
Median (25th–75th percentile)	2.6 (1.905–3.05)
Range	0.92–3.82
Prematurity	
No	26 (68.42%)
Yes	14 (36.84%)
NICU stay ( <i>n</i> = 35)	
No	25 (71.43%)
Yes	10 (28.57%)
Neonatal outcome	
IUD	5 (12.50%)
Live baby	33 (82.50%)
NND	2 (5.00%)

reported by WHO (2–15%), average being 4.5% [15]. This makes the current exploration attach great significance, as being one of the very few COVID-19 researches in gravid women directed towards its systemic effects during pregnancy. The increased incidence could have been due to development of preeclampsia like syndrome in patients infected with COVID-19 as is shown in various studies [16, 17].

In one of the largest researches in India conducted by Aabhida et al. on 93 pregnant patients with preeclampsia, it was concluded that 67.74% patients had severe features, as opposed to 47.37% SARS COV2-positive study populace developing the same [18]. The authors in their study reported 5.37% cases of antepartum eclampsia in contrast to present research with 13.16% cases of eclampsia. Another study conducted by Sangeetha et al. in a tertiary care hospital at Bangalore reported a comparable incidence of antepartum eclampsia as 19.4% [19]. Therefore, it is concluded that SARS-COV-2 infection during pregnancy could cause a surge in the risk of suffering posterior reversible leukoencephalopathy or preeclampsia/eclampsia syndrome due to endothelial damage. Meticulous foeto-maternal surveillance followed by institution of effectual treatment to optimize the blood pressure in SARS CoV2-positive women thus becomes imperative for averting these complications.

The present study reports higher rate of LSCS delivery than former studies [4, 5, 18–20]. It can be speculated that SARS-CoV-2 infection in these hypertensive women with already existent vasoconstriction is more likely to result in maternal hypoxia or increased oxygen requirements, resulting in a non-reassuring foetal heart tracing, meriting expedited delivery. A high rate of prematurity of 36.84% and

low birth weight rate of 42.50% is derived at, when contrasted with 23.65% and 7.52%, respectively, in the study by Aabhida et al. [18]. Moreover, a 28.57% incidence of babies necessitating NICU admission, with neonatal mortality of 5%, was quite high in juxtaposition of 18.75% and 1.56%, respectively, in the research by Patel et al. on 64 women [20]. These diversities also substantiate higher rates of severe preeclampsia and poor neonatal outcome in the extant study amongst SARS CoV2-positive women with preeclampsia, as compared to previous reviews across the country on women with preeclampsia without a super added viral infection. The likely explanation for the same could be SARS CoV2 (by altering the expression of ACE2) causing a preeclamptic state via elevated angiotensin II level in the placental villi triggering vasoconstriction and restricted foetal blood flow.

When equating the current study findings with the most recent meta-analysis on maternal and neonatal outcome of SARS CoV2-positive gravid women, increased rates of ICU admission (18.42% vs. 4%) and need for mechanical ventilation in these women with preeclampsia were observed [3–5]. In congruence to the same, 13.16% women needed ventilator support in our study in contrast to 3% in their study. The neonatal outcome in current study showed a prematurity rate of 36.84% in contrast to 17% in the meta-analysis by Allotey et al. [3] and 26.94% in a study conducted on 141 patients by Nayak et al. in Mumbai [21]. The 12.50% still-birth and 5.00% neonatal mortality were way higher than 0.28% and 0.34%, respectively, in the study by Allotey et al. [3]. The NICU admission rate was found to be 25.00% which is higher than that of Allotey et al. [3] and Nayak et al. [21].

## Conclusion

This study illustrates that SARS CoV2 afflicted pregnant females presenting with preeclampsia develop a more severe illness, have intensive care requirement and higher maternal and neonatal morbidity as compared to patients with COVID-19 without preeclampsia and preeclampsia in general. This can be explained by higher inflammation, multi-system involvement and augmented deteriorating effects of COVID-19 in the background of preeclampsia. Prospective larger studies with more diverse regional or national representation would prove more information on this discussed clinical conundrum and help validate the aforesaid findings. This study does not differentiate between true preeclampsia and preeclampsia like syndrome due to non-availability of uterine artery PI Doppler and antigenic factors signifying the pathophysiology of preeclampsia in pregnant females as done by other studies. Incorporating them in the investigation panel would help in differentiating severe COVID-19 and pre-eclampsia, and hence timely

initiation of management directed to the virus would thwart its progression, to achieve an optimal foeto-maternal outcome. Till then obstetricians are advocated to be cognizant of women harbouring the SARS CoV2 virus at term, or even those reporting symptoms early in pregnancy.

## Declarations

**Conflict of interest** SM, AD, NMB, SP, SuM and NG all declare that there are no conflicts of interest amongst them.

**Research Involving Human Participants and/or Animals** This is a retrospective data analysis. No research is done on animals or human participants.

**Informed Consent** This is a retrospective analysis. Institutional ethics committee clearance has been taken for this study and consent waiver for the study was provided in view of retrospective study.

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## About the Author



**Dr. Sheeba Marwah** is working as Associate Professor in Department of OBGY at VMMC and Safdarjung Hospital and has many publications to her credit. She has been the nodal officer for COVID-19 in her department and was instrumental in establishing separate dedicated COVID facility for maternity patients. Having catered to around 400 COVID patients for more than 15 months (apart from non-COVID OBGY patients), she has been felicitated with numerous awards for her out-

standing work during COVID pandemic, noteworthy being “Smriti Pattika” by VMMC & MOHFW on Independence day 2020, and the International Women's Day theme award “Woman in leadership—achieving an equal future in COVID 19 world!”. She wishes to keep working for the noble cause in future as well, with special inclination for treating critically ill high-risk gravid women.