



## “CLINICAL AND LABORATORY PROFILE OF PREGNANT WOMEN WITH SARS-COV-2 INFECTION AND PRE-ECLAMPSIA: CASE SERIES FROM A TERTIARY CARE HOSPITAL”.

### Obstetrics & Gynaecology

**Dr.Sowmya Shree Thimmappa\***

Assistant Professor, Department of Obstetrics and Gynaecology, JSSMC, JSS AHER, Mysore, Karnataka, India. \*Corresponding Author

### ABSTRACT

SARS-CoV-2 infection in pregnancy is associated increased maternal and fetal complications .Pre eclampsia is one of the complication frequently seen in association with COVID-19 infection .With the available literature to date it is still uncertain whether pre eclampsia risk is increased in pregnancy with COVID-19 infection or pre eclampsia like syndrome is caused due to COVID-19 infection .This is a case series of seven pregnant women with COVID-19 infection and pre eclampsia/pre eclampsia like syndrome from a tertiary care hospital. Four of these women presented with increased severity of preeclampsia and three patients were newly diagnosed cases of preclampsia /preeclapmsia like syndrome. Maternal complications seen in this series included HELLP syndrome,abruption placenta ,imminent eclampsia ,preterm delivery .Fetal complications included prematurity , IUGR,intrauterine fetal demise ,meconium aspiration syndrome .

### KEYWORDS

SARS-CoV-2, Pre eclampsia, Pre eclampsia like syndrome, Pregnancy

### INTRODUCTION:

Preeclampsia refers to the new onset of hypertension and proteinuria or the new onset of hypertension and end organ dysfunction with or without proteinuria after 20 weeks of gestation or postpartum in a previously normotensive women.<sup>1</sup> It is one of the leading causes of maternal and neonatal morbidity and mortality worldwide. Coronavirus disease 2019 (COVID19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and was first reported in China in December 2019.<sup>2</sup> Whereas COVID-19 is primarily a respiratory infection, it has important systemic effects including hypertension, kidney disease, thrombocytopenia and liver injury.<sup>3,4,5</sup> Women infected by COVID-19 had higher rates of preeclampsia.<sup>6</sup> Misdiagnosis, however, might have occurred in some of these cases, as COVID-19 and PE have overlapping clinical features. Therefore, differential diagnosis might be challenging in COVID-19 pregnant women presenting with hypertension and proteinuria, thrombocytopenia or elevated liver enzymes.<sup>6</sup> This study includes case series of pregnancy complicated by preeclampsia or preeclampsia like syndrome and COVID-19 infection .

### Case series:

**Case 1:** 26-year-old Gravida 4 Para 2 Living 2 Abortion 1 with 31 weeks 4 days of gestation in breech presentation with previous 2 lower segment caesarean section, presented with headache and vomiting for 1 day. She tested positive for COVID-19 RTPCR on admission. Patient was diagnosed with non severe preeclampsia at 29 weeks of gestation and was on antihypertensive medication. On admission her blood pressure was 160/110 mm hg ,SpO<sub>2</sub> -99%.On obstetric examination uterus corresponded to 30 weeks of gestation and FHS was good. Obstetric Ultrasound examination with umbilical artery doppler was normal .Patient was treated with injection labetalol 20 mg iv ,injection MgSo<sub>4</sub> seizure prophylaxis and 2 doses of betamethasone for fetal lung maturity .Preeclampsia laboratory workup did not show any abnormalities .She was further started on anti-hypertensive medication for control of blood pressure and discharged after Covid isolation period .There were no COVID related complications. On follow up anti-hypertensive medication was tapered and stopped. Patient was delivered by elective repeat caesarean section at full term.

**Case 2:** 27 year old Gravida2 Para1 Living1 with 34 weeks of gestation presented with decreased fetal movements since one day, cough and fever since 3 days. Patient was diagnosed with pre eclampsia since one month. On examination moderate pallor was noted, blood pressure - 140/90 mmHg, SpO<sub>2</sub> -98% and obstetric examination revealed intrauterine fetal demise. Patient tested positive for COVID-19. On investigation preeclampsia workup was found to be normal. Moderate anaemia and increased blood sugars were noted. Inflammatory markers remained within normal range. Dead male baby was delivered following induction of labour. Injection MgSO<sub>4</sub> was started for eclampsia prophylaxis. Blood sugars were controlled with regular insulin. There was no worsening of cough and no further episodes of fever. Blood pressure normalised following delivery.

**Case 3:** 28 year old Gravida2 para1 living 1 with 34 weeks of gestation with preeclampsia presented with complaints of blurring of vision,

headache for one day. She was diagnosed with non severe preeclampsia at 33 weeks of gestation .On examination blood pressure was 170/110 mm hg .COVID-19 RTPCR was positive on admission .Her TLC (15640Cells/cumm) ,AST(208U/L) and ALT ( 99U/L), uric acid (8.0mg/dl),LDH (594U/L), Urine albumin was 4+ on admission .Obstetric scan showed early onset intrauterine growth restriction (IUGR).She was started on intravenous labetalol and Mg So<sub>4</sub> infusion followed by emergency LSCS in view of severe preeclampsia with imminent signs of eclampsia. She delivered a live male baby of 1.4 kg by caesarean section. Platelet count was reduced to 0.97Lakh/cumm on 3rd post operative day. D Dimer (4.5µg FEU/ml) and ferritin (370.0ng/ml) were elevated. Patient was continued on oral antihypertensive agents and oral prednisolone and monitored with inflammatory markers and discharged. There were no other COVID-19 related complications.

**Case 4:** 21 year old primigravida with 38 weeks of gestation presented with history of fever for 3 days and bilateral swelling of lower limbs for one week. She was referred in view of hypertension in pregnancy and started on tablet labetalol and nifedipine for the past 2 days. On examination her blood pressure was 130/90 mm Hg. On investigation there was elevated D dimer (1.2µg FEU/ml), CRP (239.45mg/l), 2+ urine albumin. Pre eclampsia work up was normal. She underwent emergency LSCS for the non-reassuring NST and delivered a live male baby of 3.28 kg through meconium-stained amniotic fluid. Covid -19 RTPCR was positive. Patient maintained saturation on room air and had no further complications of Covid-19.

**Case 5-Gravid5 Para2 living2 abortion2** with 30 weeks of gestation presented with history of headache , fever ,cough and high blood pressure recording .On examination her blood pressure was 180/110 mm hg and SPo<sub>2</sub> -94%.On investigation patient was diagnosed with COVID-19 bronchopneumonia .Preeclampsia work up was normal , inflammatory markers LDH 302U/L ,CRP 14.47mg/l were elevated with positive COVID 19 RT PCR .She underwent emergency LSCS in view of severe pre-eclampsia with imminent signs of eclampsia .Delivered live male baby of 1.1 kg. Patient was treated with standard COVID-19 management protocol .Patient maintained saturation on room air and had no further complications .

**Case 6–20 year old primigravida** with 39 weeks of gestation presented in latent phase of labour. On examination her blood pressure was 160/100 mm hg. Pre-eclampsia work was normal and with raised CRP (25.8 mg/L) and trace urine albumin. Patient delivered live female baby of 2.62 kg by vacuum assisted vaginal delivery. Patient had no other complication of COVID 19.

**Case 7 -28 year old primigravida** with 38 weeks of gestation presented with fever and cough since 3 days, decreased perception of fetal movements since 1-day, abdominal pain and bleeding per vagina since 6 hrs. On examination her blood pressure was 120/80 mm hg, fetal heart sound was absent and was diagnosed with abruptio placenta with partial HELLP in active stage of labour with COVID -19 broncho pneumonia. On investigation coagulation profile was deranged with decreased platelet count(62000lacs/cumm), raised PT (20.2secs), INR

(1.67), APTT (>3mins) and raised inflammatory markers with D-dimer- >8.7, CRP -26.71mg/l, LDH - 779u/l. She delivered a dead female baby of 3.8 kg by vaginal route. Standard COVID-19 treatment was followed. Patient was treated with 2 fresh frozen plasma and 2 pints of PRBC. There was no further complication of COVID-19.

Table 1: Maternal and fetal outcome in pregnant women with hypertensive disorders of pregnancy and COVID -19 infection

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Hb (gm/dl)	12	9	13	12	12	12	12
Total count (Cells/cumm)	6440	11000	15640	8210	7940	16270	22490
Neutrophils (%)	78	79	77	62	77	75	88
Lymphocytes (%)	15	18	19	32	18	21	8

Platelet count (lakh/cumm)	2.84	2.8	1.41	2.13	1.51	2.34	0.62
LDH(U/l)	151	329	594	216	302	211	779
D Dimer (mcg/ml)	0.3	2	4	1.2	0.2	0.4	>8
Serum Ferritin (mcg/l)	30.5	70	50	92	117	30	321
AST(U/l)	31	25	208	20	20	5	63
ALT(U/l)	18	8	99	6	16	4	14
Serum creatinine (mg/dl)	0.43	0.46	0.72	0.64	0.79	0.74	0.47
Uric acid (mg/dl)	2.9	3.2	8	6.5	6.5	4.5	4.7
Urine albumin (dipstick)	nil	nil	4+	2+	1+	1+	2+

Table 2 - Laboratory Characteristics of pregnant women with hypertensive disorders of pregnancy and COVID-19 infection

		Case1	Case2	Case 3	Case 4	Case 5	Case 6	Case 7
Maternal characteristics	Maternal Age	26	27	28	21	25	20	21
	Gravidity	G4P2L2A1	G2P1L1	G2P1L1	Primigravida	G5P2L2A2	Primigravida	Primigravida
	Co morbidity	nil	GDM, Moderate anemia	Hypo thyroidism	Hypothyroidism	Hypothyroidism	Type 2 DM	NIL
	Previous history of pre-eclampsia	-	-	-	-	-	-	-
	Previous history of HTN	-	-	-	-	-	-	-
	Previous history of GDM	-	-	-	-	-	-	-
	Gestational age at diagnosis of PE (weeks)	29	30	33	38	30	39	38
	Severe pre-eclampsia	Yes		Yes		Yes		Yes
	Non severe preeclampsia		Yes		Yes		Yes	
	Imminent signs of eclampsia	Headache vomiting	NO	Headache Blurring of vision Pedal edema	NO	headache	NO	Headache Epigastric pain
	Gestational age at diagnosis of COVID 19 (weeks)	31	34	34	38	34	39	38
	Asymptomatic COVID -19	Yes	Yes	Yes			Yes	
Symptomatic COVID 19				Fever	Fever Cough		Fever Cough	
MATERNAL OUTCOME	Mode of delivery	Caesarean section at full term	Vaginal delivery	Caesarean section	Caesarean section	Caesarean section	Instrumental delivery	Vaginal Delivery
	Indication for caesarean section	Previous 2 Caesarean section	-	Imminent eclampsia with previous LSCS	Non reassuring CTG	Previous LSCS with imminent eclampsia	-	-
	ICU admission	No	No	No	No	Yes	No	Yes
	Preeclampsia complication	No	Abruptio placenta	Partial HELLP		No	No	Abruptio placenta, Partial HELLP
	Covid-19 complications	No	No	No	No	Broncho pneumonia	No	Broncho pneumonia
Fetal outcome	Birth weight	2.8	1.5	1.4	3.2	1.1	2.6	3.8
	Apgar score 5 min	8	-	5	7	8	8	-
	Apgar score 7min	9	-	6	8	9	9	-
	NICU admission	No	-	yes	Yes	Yes	No	-
Neonatal complications	Nil	Intrauterine fetal demise	Early onset IUGR	Meconium aspiration syndrome	Prematurity	Nil	Intrauterine fetal demise	

**RESULTS:**

Seven pregnant women with hypertensive disorders of pregnancy and COVID -19 infection are included in the present case series. 4 (57.14%) of the pregnant women were know patients of preeclampsia in pregnancy and presented with severe preeclampsia at the time of COVID -19 infection .3(42.85%) pregnant women were newly diagnosed with hypertension in pregnancy at the time of COVID -19 infection. All pregnant women were in the age group of 20 -30 years. 4(57.14%) women were multigravida and 3(42.85%) were primigravida. Associated co morbidities included hypothyroidism, gestational hypertension, type 2 diabetes mellitus and moderate anaemia. Common presenting symptom was headache among both

previously diagnosed preeclampsia patients and those diagnosed at the time of COVID -19 infection. Other presenting symptom included blurring of vision, epigastric pain and vomiting. 4(57.14%) patients were asymptomatic for COVID-19 infection and 3(42.85%) patients were symptomatic with fever and cough .2(28.57%) patients were delivered by caesarean section for the indication of severe preeclampsia with imminent sigs of eclampsia and the other patient for non-reassuring fetal heart rate. 2(28.57%) patients required ICU admission for COVID-19 broncho pneumonia. Both these patients had symptoms of fever and cough. One among these developed HELLP syndrome with abruptio placenta. HELLP syndrome, abruptio placenta, thrombocytopenia were the complications of preeclampsia

noted in 3(42.85%) patients. There was no maternal mortality in this case series. Three babies with IUGR, meconium aspiration syndrome and prematurity required NICU admission. there were two intrauterine fetal demise.

Most common laboratory abnormality was raised D dimer noted in 4(57.14%) followed by leucocytosis in 3(42.85%) patients, thrombocytopenia ,elevated LDH , raised AST in one (14.28%) patient each.

## DISCUSSION:

The prevalence of preeclampsia in pregnant women with SARS-CoV-2 infection is 8.2%.<sup>7</sup> Its occurrence among SARS-CoV-2-infected pregnant Asian women is higher than among women of other ethnicities.<sup>7</sup> Intrauterine infection caused by COVID-19 can alter ACE2 expression, promoting a preeclamptic state.<sup>8</sup> Both asymptomatic and symptomatic SARS-CoV-2 infections significantly increased the risk for preeclampsia.<sup>9</sup> Rosenbloom et al<sup>10</sup> hypothesized that SARS-CoV-2 infection that was diagnosed closer to term was not associated with a significant increase in the risk for preeclampsia because the time remaining to develop the clinical disorder was limited. A meta-analysis showed that SARS-CoV-2 infection diagnosed either at delivery or at any time during pregnancy was significantly associated with an increased risk for preeclampsia.<sup>11</sup> In our case series we had both term and preterm pregnancy patients with SARS-CoV-2 patients with preeclampsia.

Pregnant women with severe COVID-19 can develop preeclampsia features that might be distinguished from actual preeclampsia by a more detailed assessment. It might not be a placental complication and could resolve spontaneously after recovery from severe pneumonia.<sup>11,12</sup> Only one patient in this case series had resolution of preeclampsia symptoms and signs after recovery from COVID-19 infection who was delivered at full term. Intrauterine infection caused by COVID-19 can alter ACE2 expression, promoting a preeclamptic state. Mendoza, in his case series, postulates a preeclampsia-like syndrome in patients with severe SARS-CoV-2 infection, who meet the criteria for preeclampsia but who recover without delivery, only after the improvement of the respiratory condition.<sup>12</sup>

Recent studies have shown that angiogenic factors support the differential diagnosis between PE and some of its imitators.<sup>13,14,15</sup> PlGF and sFlt-1 are placenta-related angiogenic factors that are highly specific to placenta insufficiency.<sup>16</sup> sFlt-1/PlGF, UtAPI and LDH allow PE to be differentiated from the PE-like syndrome present in some of the pregnant women with severe COVID-19. This knowledge could improve management and reduce misdiagnosis in pregnancies with severe COVID-19.<sup>12</sup> Four patients in this case series were known case of pre-eclampsia, who had worsening of preeclampsia at the time of COVID-19 infection. Other three patients presented with raised blood pressure recordings with proteinuria at the time of COVID-19 infection. sFlt-1/PlGF, UtAPI reports were not available to differentiate between pre eclampsia and pre-eclampsia like syndrome. In these three patients' delivery was indicated as they presented at full term pregnancy with COVID-19 infection. There was resolution of pre-eclampsia/pre-eclampsia like symptoms following delivery.

SARS-COV-2 has been identified in brain endothelial cells.<sup>17</sup> Eclampsia, posterior reversible leukoencephalopathy and COVID-19 share a common pathophysiology affecting endothelial tissue.<sup>18,19</sup> Four patients in this case series had imminent signs of eclampsia. Three were preterm pregnancy and one term pregnancy. Two of these had COVID-19 broncho pneumonia and the other two had asymptomatic COVID-19 infection. One among these had resolution of symptoms of imminent eclampsia after recovery from COVID-19 infection and was delivered at term. None of the patients had eclampsia probably due to early intervention.

Intercovid study reported that, the risks of severe neonatal complications, including NICU stay for 7 days or longer, as well as the summary index of severe neonatal morbidity and its individual components, were also substantially higher in the group of women with COVID-19 diagnosis.<sup>20</sup> In our study there were two intra uterine fetal demise and three neonates required NICU admission.

In a case series by Coronado-Arroyo JC et al<sup>8</sup>, the most frequent findings in their laboratory tests were as follows: hyper transaminasemia, 40 %–65 %; leukocytosis, 30 %; lymphopenia, 15 %; and elevated C-reactive protein levels, 10 %. In our case series the most frequent laboratory abnormality was increased D dimer followed by leucocytosis.

## CONCLUSION:

Clinicians should be aware of the pre-eclampsia like syndrome in pregnant women with COVID-19 infection especially in pregnancies remote from term. PE-like syndrome might not be an indication for earlier delivery in itself, as it might not be a placental complication and could resolve spontaneously after recovery from severe pneumonia.<sup>12</sup> It is still uncertain whether COVID-19 manifests in pregnancy with a preeclampsia like syndrome or infection with SARS-CoV-2 results in an increased risk for pre eclampsia.<sup>20</sup> This case series indicates that there can be worsening of pre-existing preeclampsia and new onset preeclampsia like syndrome in SARS-COV-2 infected pregnant women. Well designed studies are necessary to study the association of pre eclampsia and pre eclampsia like syndrome with COVID-19 infection in this ongoing pandemic.

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