

Sars Cov2 Infection and Vascular Complications during Antepartum Period in Pregnancy

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Abstract

Background: COVID 19 infection is the profanation for the mother in late gestation in respect to vascular complication due to sharing of the same Pathophysiology.

Aim: To evaluate the incidence of vascular complications in covid positive mothers in late gestation.

Objectives:

- To study the incidence of Preeclampsia, Fetal growth restriction, obstetric Doppler changes in covid positive mothers.
- To correlate the patho physiology of COVID 19 and vascular complication in pregnancy.
- To correlate the clinical and biochemical findings of Covid 19 infections with vascular complications in pregnancy.

Settings and Design: This was the observational study carried out in a tertiary health care center.

Materials and Method: A prospective observational study was conducted with 103 covid positive pregnant women who were presented to the department of obstetrics and gynaecology, Bharati Vidyapeeth deemed university, Pune between June 2020 to May 2021. Covid positive mothers with the onset of

vasculopathies and other related complication have been observed. COVID 19 infection and pregnancy vascular pathology have been correlated.

Conclusion: In our study, inflammatory markers has been observed significantly raised in covid positive women who were symptomatic with vasculopathies as compared to symptomatic covid positive women without vasculopathies.

Clinical Significance: In present Covid era pregnant women are vulnerable to obstetric complications in late gestation as IUGR, Preterm labour with premature rupture of membranes, colour Doppler changes, Oligohydramnios, Preeclampsia .It is due to sharing the same patho physiology of Covid 19 and vasculopathies in late period of gestation.

Keywords: Covid 19; Vasculopathies; Pregnancy; CRP; D dimer.

Introduction

COVID 19, Coronavirus is the infecting agent residing in the respiratory tract predominantly, belonging to the Nidovirales order, includes Coronaviridae, Arteriviridae, Mesoniviridae, and Roniviridae families. These are the enveloped, non-segmented positive sense RNA viruses.

Pregnant women are more vulnerable to COVID 19 infection due to altered immune system during pregnancy occasionally related to severe symptoms. The risk to the mother increases mostly in the last trimester, reported with the complication of preterm birth, vascular and placental pathology, perinatal depression and anxiety in covid positive mother. The infection has led to a great impact on the mental health of pregnant covid positive women. The vertical transmission from mother to fetus antepartum and intrapartum is probable and proportion of pregnancies affected and the effect to the neonate yet to be determined. There are no recorded cases of vaginal secretion being tested positive or transmission through milk secretions as stated by WHO.¹

The currently available data has not proven the risk of early pregnancy losses, teratogenicity. But still, the pathogenesis of COVID 19 has been seen to have a drastic impact on pregnancy in the late trimester.¹

The SARS CoV 2 infection attacks on endothelial cells leading to the formation of micro thrombi thus increasing angiogenesis and rise of neutrophils extracellular traps (NETs). These NETs are the protein like material which are released to destroy extracellular bacteria which in turn plays important role in COVID-19 related immune thrombosis and endothelial damage leading to vascular and placental complications. The alpha 1 antitrypsin (AAT) is shown to protect preeclampsia through smad2 and inhibiting DNA binding 4 in placental tissue.² The consequence of placental dysfunction due to intravascular inflammation associated with infection leading to a pro thrombotic state in the placenta. The infection seems to reduce the number of lymphocytes relative to inflammatory monocytes induces cytokines storm leading to acute respiratory distress and multi-organ failure. The increase in pro-inflammatory cytokines and interleukins seems to be affecting early embryo development. The placenta shows increase deposition of fibrin and infiltration of monocytes and neutrophils in subcortical space.¹

Materials and Methods

A Prospective observational study was carried out in 103 women visiting gynaecological OPD with covid positive status (opportunistic screening). The data was collected from Bharati Hospital, OPD, department of Obstetrics and Gynaecology, Pune between June 2020 to May 2021. The purpose and the procedure of the study was explained to them and a written consent was obtained.

Inclusion Criteria

All pregnant women with covid positive status without any prediagnosed morbidity.

Exclusion Criteria

Prediagnosed diabetes mellitus and chronic HTN

Once the woman is recruited in the study she is observed for the onset of pre-eclampsia, FGR, signs of preterm labour, oligohydramnios in antenatal period. Biochemical markers for covid (CRP, D dimer, S.LDH, Pro calcitonin, Serum ferritin) and pre eclampsia panel (SGOT, SGPT, Serum alkaline phosphate, Serum creatinine, Serum uric acid, Serum urea, Prothrombin time, activated partial prothrombin time, S.LDH) has been correlated with the adverse or any unwanted outcomes. The severity of the adverse events was observed and correlated with medications offered as treatment protocol for covid such as anticoagulants, steroids.

Statistical Analysis

All statistical analyses were done by SPSS software with version 25. Quantitative variables results were shown by descriptive statistics. Qualitative variables results were shown by frequency and percentage. An independent t-test was used for a continuous variable that follows normal distributions. Mann Whitney U test was used for a continuous variable that follows a non-normal distribution. Chi-Square test was used to test the association between categorical variable. Throughout the results, a 5% level of significance was used. All results were shown with a 95% of confidence p value <0.05 was considered significant.

Results

One hundred and three women were included in our study. All COVID 19 positive mothers visited our institution were symptomatic or in late gestation.

Table 1: Mode of Delivery.

Mode of Delivery	Frequency (n)	Percentage (%)
Vaginal	19	18.4
LSCS	84	81.6
Total	103	100

The study was conducted on 103 covid positive women out of which 19 women (18.4%) delivered vaginally and 84 women (81.6%) delivered through LSCS.

Table 2: Complications in antepartum period and Post covid period.

		Frequency (n)	Percentage (%)
Antepartum Complications	Yes	16	15.5
	No	87	84.5
Post covid complications	Pneumonia	1	1.0
	No	102	99.0
Total		103	100.0

Among 103 covid positive women, 16(15.5%) women faced the challenge of vasculopathies during antepartum period, while 87(84.5%) had no complications. After recovery from Covid, only one woman experienced post covid complications as Pneumonia, rest all 102(99%) women had a good recovery from Covid.

Table 3: Types of Vasculopathies in Covid positive women.

Vascular Complication	Frequency (n)	Percentage (%)
Color Doppler Changes	4	25
IUGR	1	6.3
Oligohydramnios	4	25
Pre eclampsia	3	18.8
PROM with Preterm	4	25
Total	16	100

Out of 103 covid positive women, 16 (15.53%) had vascular complications out of those 16 women, 4 (25%) women had colour Doppler changes, 4 (25%) went into preterm labour with premature rupture of membranes. 1(6.3%) woman had late onset fetal growth restriction. 4(25%) women presented with decreased liquor (oligohydramnios) and 3(18.8%) women had pre-eclampsia.

Table 4: Need for supportive treatment for Covid management.

	Requirement	Frequency (n)	Percentage (%)
O2	Yes	16	15.53
	No	87	84.47
INJ PCM	Yes	1	0.97
	No	102	99.03
INJ Dexamethasone	Yes	40	38.83
	No	63	61.17
INJ LMWH	Yes	28	27.18
	No	75	72.82
INJ Remdesevir	Yes	10	9.71
	No	93	90.29
INJ CTRI	Yes	12	11.65
	No	91	88.35

Out of 103 women studied, Oxygen required was in 16(15.53%) women. Inj. Remdesivir was required for only 10 women (9.71%), 28 women (27.18%) required Inj. LMWH, while Inj. Dexa was given to 40(38.83%) women. Inj. CTRI was administered for 12 women (11.65%) while Inj. Dexamethasone was needed in only 1(0.97%) woman.

Table 5: Comparison of Women with and without Complications.

		Vascular Complications (n=16) n, (%)	No Complications (n=87) n, (%)
Type of Delivery	Vaginal	0 (0.00)	68 (78.16)
	LSCS	16 (100.00)	19 (21.84)
O2 Required	Yes	5 (31.25)	11 (12.64)
	No	11 (68.75)	76 (87.36)
INJ PCM	Yes	16 (100.00)	1 (1.15)
	No	0 (0.00)	86 (98.85)
INJ Dexamethasone	Yes	6 (37.50)	34 (39.08)
	No	10 (62.50)	53 (60.92)
INJ LMWH	Yes	7 (43.75)	21 (24.14)
	No	9 (56.25)	66 (75.86)
INJ Remdesevir	Yes	2 (12.50)	8 (9.20)
	No	14 (87.50)	79 (90.80)
INJ CTRI	Yes	0 (0.00)	12 (13.79)
	No	16 (100.00)	75 (86.21)

Inj Remdesevir requirement was there in only 2 (12.50%) women with vascular complications, on the other side 8 (9.20%) women without any complications required remdesivir injection.

While Inj LMWH was required by 7(43.47%) women having vascular complications and 21(24.14%) women having no complications. Steroids (Inj dexamethasone) were given to 6 (37.50%) women having complications and 34 (39.08%) women without any complications.

Inj. PCM was administered in all 16 (100%) women with vasculopathies and only 1 (1.15%) woman without any complications was in need of it. There were no requirement of Inj CTRI was observed in the women having complications and on the other hand 12 (13.79%) women without complications were in need of it.

Oxygen requirement was observed in 5 (31.25%) women having vascular complications and in 11 (12.64%) women having no complications.

Table 6: Risk of Complications between Symptomatic and Asymptomatic Covid Positive women.

	Symptomatic		Total	Chi-Square Value	P-value
	Yes	No			
Complication	Yes	5	11	0.114	0.736
	No	31	56		
Total		36	67		

There is no association between the complication among those who have COVID-19 complications and COVID-19 symptomatic women without complications the p-value shows insignificant value.

Table 7: Evaluation of inflammatory markers significance by using Mann whitney test.

		Mann-Whitney U Test		
Symptomatic with Complications		N	Median	p-value
CRP (mg/dl)	Symptomatic with Complications	5	57.95	0.207
	Symptomatic without Complications	31	40.00	
D-dimer (mcg/dl)	Symptomatic with Complications	5	857.00	0.657
	Symptomatic without Complications	31	656.00	
Procalcitonin (ng/dl)	Symptomatic with Complications	5	0.12	0.448
	Symptomatic without Complications	31	0.07	
Ferritin (mcg/l)	Symptomatic with Complications	5	115.76	0.667
	Symptomatic without Complications	31	110.55	

In our study, through the various inflammatory markers it has been observed that the inflammatory markers have significantly raised in covid positive women with vasculopathies rather than the covid positive women without vasculopathies. CRP showed median of 57.95 in symptomatic women with complications which is higher than 7.95 units than the symptomatic women without complications.

D dimer shows the significant rise in both categories with the median value of 857.0 Procalcitonin is mildly raised in symptomatic women

with vasculopathies with median value of 0.12. Ferritin has also minimal rise with median values if we compare both the groups which is statistically not significant. After the evaluations, no significant difference found in value of inflammatory markers between symptomatic women with vasculopathies and without vasculopathies.

Discussion

We observed 16 women out of 103 Covid positive who had vascular complications. There is vertical transmission of COVID 19 infections between mother and neonate.¹ COVID - 19 infections have been associated with hypercoagulability, ischaemic changes leading to disseminated intravascular changes. It is suggestive of disturbed placentation, endothelial dysfunction, end-organ damage with microthrombi and angiogenesis. The incidence of neutrophilic extracellular traps has been seen implicated in both COVID 19 infections and in the non-covid condition associated with Preeclampsia and IUGR.²

The physiological changes in pregnancy and vascular and metabolic changes in high-risk pregnancy with COVID 19 infections seems to worsen the condition. The pathophysiology of COVID 19 infections and vasculopathy in pregnancy shows a common denominator as endothelial injury.³

A prospective observational study was done in 2020 by Medoza M stated that among there 8 severe cases of covid positive women, 5 were having new onset of hypertension, proteinuria, thrombocytopenia with elevated liver enzymes which is similar to our study as well.⁴

The increased dysfunction in placenta and various pathogenic mechanism in COVID 19 is relatable to the pathogenesis of Pre eclampsia .women came with raised blood pressure and significant adverse maternal and neonatal outcomes noted.⁴ The alpha - 1 anti-trypsin plays a protective role in pre eclampsiaat molecular level.^{5,6}

There is a significantly raised d-dimer and LDH value signifies worsening of vascular complication in late pregnancy. D-dimer signifies the thrombotic events leading to the poor prognosis of vascular complications in pregnancy. Through CRP, Procalcitonin, ferritin seems to be non-significant markers in case of severity of disease.⁷

The thrombotic events can lead to more requirements for oxygen, steroid supplements and anti-coagulants, as the pregnancy is a state of the

altered immune system.⁷

There is an increased risk of stillbirth and preterm labour and intrauterine growth restriction with oligohydramnios with pre-eclampsia with colour Doppler changes.⁸

Khali.et.al in august 2020 has studied that there is more incidence of preterm birth, still birth, cesarean sections and admissions in NICU, 9%of women with covid positive status has incidence of still birth ,while in our study there were 25% women with vasculopathy had a preterm labour with zero perinatal mortality till now.⁸

There is increase incidence of maternal medical complications and obstetric complications in COVID positive women who has lead to increase the incidence of c-section and there is increase incidence of Preterm birth, low birth weight, C-section ,NICU admission than general population.⁹

In our study, there is no significant difference between covid positive women with vascular complications as compared to without any complications seen.

Conclusion

Covid 19 is the cuss in pregnant women during late gestation leading to the vasculopathies causing the risk of ICU admission, maternal and fetal morbidity and mortality. Proper measures must be taken to prevent the women by doing:

- Regular antenatal visits.
- Prevention through vaccines.
- Protection from influenza like diseases.
- Proper nutrition and maintain hygiene.

Goal is to protect every mother and baby from this deadly virus and its consequences .

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