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Perinatal outcomes of COVID-19 affected pregnant women in a tertiary care center of eastern India

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ABSTRACT

Background: Pregnancy is an immune-compromised state and pregnancy affected with COVID-19 infection is at a higher risk of adverse perinatal results. Data on fetomaternal outcomes in pregnancies infected with COVID-19 is sparse, which makes it difficult to draw conclusions on vertical transmission.**Objectives:** To study the perinatal outcomes of COVID-19 affected pregnant women.**Materials and Methods:** A prospective observational study was conducted over eighteen months, on 320 COVID-19 positive antenatal patients. Clinical manifestations of pregnancies with COVID-19, demographic profile, pregnancy outcomes were recorded. Important laboratory parameters were assessed along with COVID-19 inflammatory markers like serum ferritin, D-Dimer, CRP etc. Neonatal outcomes assessed included APGAR score, fetal deaths, birth weight, NICU admissions. Neonatal infections were screened by testing for SARS-CoV-2 positivity in neonatal throat swab samples.**Results:** 61.5% of patients complained of pain abdomen, followed by bleeding PV in 1.9%. 52.19% of the patients were asymptomatic for COVID-19 symptoms, followed by fever in 34.69%. Most common risk factor associated was hypothyroidism. Anemia was found in 22%, coagulation parameters were elevated in 30% and COVID-19 inflammatory markers were raised in more than 90% cases. Maternal and neonatal ICU admission rates were 4.69% and 30.34% respectively. Neonatal infection rate was 3.1%.**Conclusion:** COVID-19 was mainly seen in primigravida, without affecting the birth weight of babies. Coagulation profile and renal parameters were deranged in 30 percent of the patients, without any life threatening complications. COVID-19 specific inflammatory markers showed derangement in more than 90% cases, although majority of them were asymptomatic. The rate of COVID-19 positivity among newborns was 3.1%.This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.For reprints contact: reprint@ipinnovative.com

1. Introduction

COVID-19 was discovered in December 2019, at Wuhan province in China.^{1,2} It was brought on by a novel strain of coronavirus SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), which was a single-stranded RNA

virus, likely originating from bats.³ As of 11 December 2022, there were 645 million confirmed cases and over 6.6 million globally reported deaths.

Pregnant women have adaptation changes in their immune systems which render them more susceptible to infections.⁴⁻⁶ They have worse prognosis and more severe clinical presentations of viral and respiratory infections, compared to non-pregnant women.⁷

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Data on expectant mothers and newborns with COVID-19 is still sparse. Protocols to manage antenatal women, intrapartum events and newborn care in COVID-19 suspected or confirmed cases is often fragmented.^{8,9} In newborns, the prevalence of COVID-19 is currently at 1.5%, as depicted by a positive screening of nasopharyngeal swab for SARS-CoV-2.¹⁰ A paucity of data on COVID-19 pregnancies makes it difficult to draw conclusions on vertical transmission, which appears to be infrequent, but yet does happen.¹¹

2. Materials and Methods

A prospective observational study was conducted over eighteen months, on 320 COVID-19 positive antenatal patients between 18 to 44 years of age, admitted to the SUM COVID-19 dedicated hospital, Bhubaneswar, Odisha, India. The study was approved by IEC (Ref.no/IEC/IMS.SH/SOA/2021/206.) and participants were recruited after obtaining informed consent. Non probability convenient sampling was used.

Selection criteria included:

1. Pregnant women symptomatic for COVID-19, with gestational age 5-41 weeks of pregnancy.
2. Cases of laboratory confirmed infection by COVID-19 by use of quantitative Real Time Polymerase Chain reaction (q-RT-PCR) on samples from the maternal naso-pharyngeal & nasal swab specimens.

Maternal characteristics like clinical manifestations of COVID-19 in pregnancy, demographic profile, mode of delivery, pregnancy complications, need of ICU support for both the mother and newborn were recorded. Important laboratory parameters which were assessed were complete blood counts, blood sugar, liver function tests, renal function tests and COVID-19 inflammatory markers like serum ferritin, D-Dimer, serum procalcitonin, CRP and ESR.

Neonatal outcomes which were assessed included APGAR score, neonatal death/stillbirths, birth weight, NICU admissions, neonates with COVID-19 infection. Evidence of neonatal infection were assessed by screening for SARS-CoV-2 positivity in neonatal throat swab samples.

The data were recorded using Microsoft Excel 2019 and statistical analysis was done using SPSS version 25.0.

3. Results

Table 1 shows the baseline demographic data of COVID-19 affected pregnant women. Mean age of the patients was found to be 26.62 ± 4.4 year with 260 patients below 30 years (81.2%). The mean gestational age was found to be 36.8 ± 4.8 weeks. 57.5% of women included in the study were primigravida and 42.5% were multigravida.

Table 2 shows that the chief obstetric complaint in 61.5% of patients was pain abdomen, followed by bleeding PV

Table 1: Baseline demographic data of COVID-19 affected antenatal women

Demographic Characteristics		
A) Age wise distribution	Study participants N=320	Percentage (%)
< 30 years	260	81.2
>30 years	60	18.8
B) Mean Age (years)	26.62 ± 4.414	
C) Mean POG at admission (weeks)	36.8 ± 4.8	
D) Parity	N (Total=320)	Percentage (%)
P1	184	57.5
P2	97	30.3
≥P3	39	12.2

in 1.9%. Symptoms like headache, head-reeling, epigastric pain, chest-pain, leg pain, vomiting were present in 19.4% of the patients. On evaluation of the COVID-19 symptoms, 52.19% of the patients were asymptomatic followed by fever in 34.69%, cold and cough in 23.1% and 10.3% patients respectively.

Table 2: Obstetric complaints and clinical symptoms of COVID-19 affected pregnant women

A) Chief obstetric Complaints	N	Percentage (%)
Pain Abdomen	197	61.5
Bleeding P/V	6	1.9
Others	62	19.4
No complaints	55	17.2
B) COVID-19 symptoms	N	Percentage (%)
Asymptomatic	167	52.19
Fever	111	34.69
Cold/ flu-like symptoms	74	23.13
Cough	33	10.31
Myalgia	16	5.00
Diarrhoea	7	2.19
Breathlessness/ Dyspnea	7	2.19
Others	10	3.13

Table 3 shows the various maternal risk factors among study participants. 6.56% of patients had hypothyroidism, followed by Rh-negative pregnancy in 4.06%, gestational hypertension in 3.44% and gestational diabetes in 2.81%. Other risk factors were twin pregnancy (2.50%), pre-eclampsia (1.25%), bronchial asthma (1.25%), severe anemia (1.25%), cholestasis of pregnancy (0.63%), placental abruption (0.63%), eclampsia (0.31%).

Table 4 shows the blood parameters in the study participants. Average hemoglobin level was 11.0 gm/dl with SD 1.66 gm/dl. Total platelet count had a mean of $245 \times 10^3 /\mu\text{L}$ and SD of $94 \times 10^3 /\mu\text{L}$. Total WBC count had a mean

Table 3: Risk factors associated with COVID-19 infected pregnant women

Maternal Risk Factors	N	Percentage (%)
Hypothyroidism	21	6.56
Rh negative pregnancy	13	4.06
Gestational hypertension	11	3.44
Gestational diabetes mellitus	9	2.81
Twin pregnancy	8	2.50
Pre-eclampsia	4	1.25
Bronchial asthma	4	1.25
Severe Anaemia	4	1.25
Cholestasis of pregnancy	2	0.63
Placental abruption	2	0.63
Eclampsia	1	0.31
Total	79	24.68

and SD of $10.39 \times 10^3 / \mu\text{L}$ and $4.23 \times 10^3 / \mu\text{L}$ respectively. ESR values had a mean and SD of $55\text{mm}/1^{\text{st}}$ hr and $26\text{mm}/1^{\text{st}}$ hr respectively.

Renal parameters like urea showed a mean value of 21.6 mg/dl, with standard deviation of 19 mg/dl and it was reduced in 14.38% of the study participants. Mean creatinine levels were 0.6 mg/dl and were found to be reduced in 24.38% of the patients.

Liver function tests showed a mean total bilirubin of 0.93 mg/dl and mean SGOT and SGPT values of 43.8 U/L & 49.3 U/L respectively. The mean alkaline phosphatase levels were found to be 175.9 mg/dl.

Table 5 shows the deranged blood parameters in the study population. Anemia was present in 22.19% cases, coagulation parameters like PT, APTT and INR were elevated in 30%, 30.3% and 29.3% cases respectively. SGOT and SGPT were elevated in 43.75% and 70% respectively.

In Table 6 COVID-19 inflammatory markers in the study population is shown. 98% (314) patients had an elevated CRP followed by elevated D-Dimer in 93.1%(298). LDH levels were elevated in 80.6% (258) of the patients and serum pro-calcitonin was elevated in 59.37%(190) patients.

Table 7 shows the method of delivery and maternal outcomes of COVID-19 affected antenatal women. Caesarean section was done in 234 cases (73.12%), while normal vaginal delivery was done in 30 cases (9.37%). 28 (8.75%) patients underwent vaginal delivery with right mediolateral episiotomy. Expulsion was recorded in 2 cases (0.63%). Conservative treatment was adopted in 26 cases (8.13%). There were 15 (4.69%) cases which required ICU support and there were two maternal deaths during the study period (0.62%).

Table 8 shows the fetal outcomes among the study participants. 198 (67.34%) babies born were term babies. Prematurity was seen in 57 babies (19.4%), while 39 (13.26%) were postdated babies. Intra-uterine death was seen in three cases (1.02%) and still birth in one case

(0.34%). Low birth weight (<2.5 kg) was seen in 48 newborns (16.32%).

Mean APGAR score at 1 min for the newborns (n=290) was 6.9 (SD of 0.97) while at 5 min it was 8.2 (SD of 1.01).88 (30.34%) babies had NICU admission. 9 newborns were found to be COVID-19 positive (3.1%).

4. Discussion

In our study the mean age of antenatal women was 26.6 years, with the majority being below 30 years of age and it is consistent with the meta-analysis finding of Wilkinson et al., where among the 43,000 pregnancies included for analysis, the median age was found to be 26 years.¹² Fakari et al., concluded that pregnant women are prone to contract COVID-19 at an earlier age than the general population due to changes during pregnancy.^{13,14}

In our study, the period of gestation varied between 32 to 40 weeks which is consistent with the meta-analysis finding of Parums et al., which stated that maternal SARS-CoV-2 infections occurred mostly during the last trimester of pregnancy.¹⁵ Similarly, a study done by Yan et al., showed the median gestational age to be 38 weeks.¹⁶

In our study, primigravida were more common than multigravida. This contrasts the findings by Nowacka et al., where COVID-19 infections were more common in multigravid women, due to lowered immunity amongst them.¹⁷

In our study, pain abdomen followed by bleeding per vaginam were the most common obstetric complaints in COVID-19 positive pregnant women. Priyadharshini et al., found that most(67.2%) of their study participants were asymptomatic.¹⁸ In a study by Pettiroso et al., asymptomatic infection was detected in 43.5%-92% when universal testing was performed, similar to our study, where 52.19% patients were asymptomatic for COVID-19 symptoms, although Y. Breslin and Kayem et al., identified fewer asymptomatic patients amongst their research group.¹⁹⁻²¹ In our study, among the patients who manifested COVID-19 symptoms, fever was seen in 34.69% and 10% had cough and other minor symptoms. This is compliant with findings of Chen et al., where fever, cough, myalgia, sore throat, and malaise were the most prevalent symptoms experienced by pregnant women.²² Similarly, Melissa Chao et al., in a systematic review found that cough (16.02%), fever (11.31%), myalgia (9.61%), headache (7.78%), and dyspnea (7.66%) were the most prevalent COVID-19 symptoms in pregnancy.²³

Hypothyroidism was the most common risk factor associated with COVID-19 positive pregnant women in our study. Pregnancy-related physiological processes like growth and functioning of the placenta, fetal development and expression of neuropeptides at labor initiation are regulated by thyroid hormones. Hence, the risk of adverse pregnancy outcomes increases due to alterations in maternal

Table 4: Blood parameters among COVID-19 affected pregnant women

Blood Parameters	Mean	SD	Study Participants N=320		
			Normal N (%)	Decreased N (%)	Increased N (%)
Hb (g/dl)	11	1.66	248 (77.50)	71 (22.19)	1 (0.31)
TPC ($\times 10^3/\mu\text{L}$)	245.18	94.27	256 (80)	45 (14.06)	19 (5.94)
TWBC ($\times 10^3/\mu\text{L}$)	10.39	4.23	175 (54.69)	8 (2.50)	137 (42.81)
ESR($\text{mm}/1^{\text{st}}$ hr)	55	26	33 (10.31)	0 (0)	287 (89.68)
Coagulation parameters					
	Mean	SD	Normal N (%)	Decreased N (%)	Increased N (%)
PT (sec)		11.06			1.85
Elevated PT			96 (30%)		
APTT		27.6			3.5
Elevated APTT			97 (30.3%)		
INR		1.02			0.17
Elevated INR			94 (29.3%)		
	Mean	SD	Normal N (%)	Decreased N (%)	Increased N (%)
RBS (mg/dl)	107.30	34.35	225 (70.31)	50 (15.62)	45 (14.06)
Urea (mg/dl)	21.6	19.01	271 (84.68)	46 (14.38)	3 (0.94)
Creatinine (mg/dl)	0.6	0.43	240 (75)	78 (24.38)	2 (0.63)
INR	1.02	0.17	226 (70.63)	0 (0)	94 (29.37)
Other Blood investigations					
	Mean	SD	Normal N (%)	Decreased N (%)	Increased N (%)
Total Bilirubin (mg/dl)	0.93	1.23	283 (88.4)	0 (0)	37 (11.6)
SGOT (U/L)	43.83	26.962	180 (56.25)	0 (0)	140 (43.75)
SGPT (U/L)	49.34	28.223	95 (29.69)	1 (0.31)	224 (70)
ALKPO4 (U/L)	175.93	75.061	268 (83.75)	37 (11.56)	15 (4.69)

Table 5: Deranged blood parameters in COVID-19 affected pregnant women

Blood Parameters	Mean value	Result
Hemoglobin	11 gm/dl	Decreased in 22.19%
Total White Blood Cells	10.39×10^3	Elevated in 42.81%
Prothrombin Time (PT)	11.06	Elevated in 30%
APTT	27.6	Elevated in 30.3%
INR	1.02	Elevated in 29.37%
SGOT	43.83 U/L	Elevated in 43.75%
SGPT	49.34 U/L	Elevated in 70%

Table 6: COVID-19 inflammatory markers in infected pregnant women

COVID-19 specific inflammatory parameters	Mean	SD	Study Participants N=320		
			Normal N (%)	Decreased N (%)	Increased N (%)
CRP (mg/L)	21.5	20.25	6 (1.87)	0 (0)	314 (98.12)
D-dimer (microgram FEU/ml)	868.38	920.24	22 (6.9)	0 (0)	298 (93.1)
LDH (U/L)	328	203	61 (19.06)	1 (0.31)	258 (80.63)
Serum Procalcitonin (ng/ml)	0.44	0.51	130 (40.62)	0 (0)	190 (59.37)
Serum Ferritin (ng/ml)	203.61	217	172 (53.75)	18 (5.62)	130 (40.62)

Table 7: Mode of delivery and maternal outcomes in COVID-19 affected pregnant women

1) Mode of Delivery	Study Participant (N=320)	Percentage (%)
Caesarean section	234	73.12
Normal Vaginal Delivery	30	9.37
Vaginal delivery with RMLE	28	8.75
Expulsion	2	0.63
Conservative Management	26	8.13
2) ICU Admission (Mothers)		
Present	15	4.69
Absent	305	95.31
3) Maternal Deaths	2	0.62
4) Mean Duration of stay in hospital	8.5 ± 2.9 days	

Table 8: Fetal outcomes in COVID-19 affected pregnant women

1) Gestational age at delivery	Study Participants N(294)	Percentage(%)
Pre-Term (32 weeks to 36 weeks)	57	19.4
Term (37 weeks to 40 weeks)	198	67.34
Post -dated (> 40 weeks)	39	13.26
2) Pregnancy outcomes	N (294)	Percentage (%)
Very Low Birth Weight (VLBW)	2	0.68
Low Birth Weight (LBW) (<2.5 kg)	48	16.32
Normal Birth Weight	240	81.63
Still birth	1	0.34
Intra Uterine Death (IUD)	3	1.02
	294	
3) APGAR scores	Study Participants N=290	
	Mean	SD
1 min APGAR Score	6.9	0.97
5 min APGAR Score	8.2	1.01
4) NICU admission	Study Participants N=290	
	N	Percentage (%)
Present	88	30.34
Absent	202	69.65
5) COVID-19 positive babies	Study Participants N=290	Percentage (%)
Yes	9	3.1
No	281	96.89

FT4 concentration due to significant stress such as a COVID-19 outbreak. Gestational hypertension, GDM, pre eclampsia, eclampsia were seen in less than 5% of the patients in our study and Wei et al., found that these were all linked to COVID-19 infection.²⁴

In our study 22% of the patients were anemic which is a risk factor for increased severity and poor outcomes in patients with SARS-CoV-2 infection.²⁵ In pregnant women and fetuses, cytokine affects iron redistribution between tissues and thus hypoxia is caused by erythrocyte breakdown brought on by acute inflammation.²⁶ Coronavirus disease is commonly accompanied by thrombocytopenia, which is a recognized indicator of the disease's progression.^{27,28} In our present study only 14.06% of the mothers had thrombocytopenia and there was no intrapartum or postpartum hemorrhage. Platelets are proposed to play a leading role in inducing inflammation, remodeling and tissue repair.²⁹ In our present study elevated

platelet counts were seen in 5.94% of the patients, which may be an indicator of a reactive process.³⁰

In our study, more than 40% of patients had an elevated WBC count, consistent with findings of Vakili et al., and Wu et al.^{31–33} This can be utilized as a marker for active infection in patients included in the study.

Although in previous studies COVID-19 has been shown to initiate liver injury, the LFT derangement was usually mild in COVID-19 infected antenatal patients and did not increase their hospital stay.³⁴ In our present study the mean values of liver function were within normal range with no significant liver injury.

COVID-19 inflammatory markers like CRP levels were high in almost all the patients in our study. Studies have shown CRP levels fluctuated significantly along the clinical course of COVID-19 infection in pregnant patients and thus support its use as an effective tool for monitoring the evolution of the disease.³⁵ Serum ferritin level was found

to be elevated in 40% of our study population. Similarly, Chen et al., observed median values of serum ferritin at 337 µg/L among their patients with moderate COVID-19 infection.³⁶ Thus, it can be inferred that the inflammation caused by SARS-CoV-2 leads to an increase in levels of serum ferritin in pregnant patients, but this increase is not substantial due to its physiological low levels encountered in pregnancy. Other inflammatory markers of COVID-19 such as serum pro-calcitonin, LDH and D-Dimer were also elevated in majority of the patients.

73.12% of patients had caesarean section, which was the most common modality of delivery in our study and is consistent with results of a meta analysis by D Liu et al., where majority women underwent caesarean section, with the most common indication being COVID-19 positive status.³⁷ Only 15(4.69%) mothers needed ICU support and maternal mortality was seen in only 2 patients. However, in a study by Hantoushzadeh et al., there have been 7 maternal deaths out of 9 pregnant women infected with COVID-19 pneumonia.³⁸ Parums et al., in a systematic review concluded that most maternal COVID-19 infections occur during the last trimester and result in a slight increase in hospital admission, ICU admission, mechanical ventilation, preterm delivery, and cesarean sections.¹⁵ Bellos et al., in their study reported that severe illness affected 11% of women & there were two maternal mortalities.¹

4.1. Neonatal outcomes

The rate of pre- term delivery was found to be 19.4% in our study in contrast to Debrabendere et al., who showed a higher premature delivery rate in COVID-19 mothers.³⁹ Chi et al., in a comprehensive review of studies found the pre-term rate to be 24.74% which was comparable with the present study.⁴⁰ In a study by Ciapponi et al., premature birth rate was 14%-64%, low birth weight rate was found to be 5%-43%.⁴¹ 16.32% of the babies in our study had low birth weight, along with 3 cases(1.02%) of intra uterine deaths and 1 case of still birth (0.34%). Newborn deaths directly consequent to perinatal infection with SARS-CoV-2 is extremely rare.⁴² In a meta analysis by Lassi et al., it was found that in the newborn ICU, 23.4% neonates were preterm and 16.6% were low birth weight babies.⁴³

Majority newborns in our study had normal APGAR score at 1 min as well as at 5 min, which is consistent with the finding of a cohort study done by M. Prabhu, where there were no significant difference between APGAR scores at 1 min and at 5 min.⁴⁴ However in a cohort study by Kalahroudi et al., the risk of APGAR scores of less than 7 in the affected group was 25.4 times more than that in the unaffected group, which might be attributed to causes like fetal distress, preterm labor and prematurity seen frequently in the affected group.⁴⁵

69.65% of newborns in our study were shifted to mother side immediately after birth and 30.34% of babies

needed neonatal ICU support. Kalahroudi et al., stated that the NICU admission rates were not significantly different between COVID-19 positive pregnant women and healthy pregnant woman.⁴⁵ NICU admission criteria vary among various hospitals and this might have resulted in differences in the findings of other studies. Admissions to the NICU have mainly been performed for the purpose of monitoring the premature newborns or for isolation of newborns from their COVID-19 positive mothers.⁴⁶

COVID-19 positive status was seen in 9 babies (3.1%) in our study. Lassi et al., in their meta analysis found 3.5% newborns tested positive for COVID-19.⁴³ Facciola et al., stated various possible modes of transmission of SARS-CoV-2 from mother to newborn such as, vertical blood transmission through placenta, through contaminated birth canal, breast feeding or by respiratory droplets from an infected family member or health care worker.⁴⁴

In a case series by Patane et al., it was found that 2 out of 22 neonates tested screen positive for SARS-CoV-2 in nasopharyngeal swabs using RT-PCR and the virus was found in placental tissues as well.⁴⁷ In a study by Chi et al., 5 neonates had positive SARS-CoV-2 throat swab tests, while three exhibited increased IgM and IgG levels against SARS-CoV-2 out of the eight with negative throat swab tests.⁴⁰

5. Conclusion

In this study, all the maternal and neonatal parameters associated with COVID-19 infected pregnancy have been evaluated. COVID-19 was more commonly seen in primigravida than multigravida, but did not affect the birth weight of the babies. Deranged blood indices like anaemia, reduced platelet counts and increased WBC counts were quite common in mothers infected with COVID-19. Coagulation profile and renal parameters were deranged in about 30% of the patients but it did not cause any life threatening complications. COVID-19 specific inflammatory markers like CRP, serum procalcitonin and D-dimer showed derangement in more than 90% of the pregnant mothers, although majority of them were asymptomatic. LSCS was the most common mode of delivery and neonatal outcomes were normal in majority of the patients with term babies. The rate of COVID-19 positivity among newborns was 3.1%. Although this study has a good sample size; it is a single center study. Therefore, further studies are needed for the results to be generalized to the mass population.

6. Source of Funding

The authors did not receive any source of fund.

7. Conflict of Interest

There are no conflicts of interest.

8. Patient Consent

Patient consent was approved from the patient or from the patients' family members before enrolling them into the study.

9. Ethical Approval

This study was approved by IEC with approval no. Ref.no/IEC/IMS.SH/SOA/2021/206.


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