

RAMIFICATION OF COVID-19 INFECTION AT THE TIME OF DELIVERY

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Background- For successful management of Covid-19 pregnancy, adequate information and understanding of its clinical presentation and impact of the disease on pregnant mothers and their newborns is required.

Aim- To describe the clinical manifestations of COVID -19 infection in pregnant women during peripartum period and to study the clinical outcomes of neonates born to these mothers.

Methods- This prospective study was conducted at a COVID-19 Hospital of North India, from May 2021 to July 2021. All Covid-19 positive pregnant women who presented at the time of labor (symptomatic or asymptomatic) were included in the study. Follow up of these women and their newborns was done till discharge and neonates were further followed up till 28 days of life.

Results- Total 70 patients were included in the study (24.2% symptomatic and 75.7% asymptomatic). Eighteen (25.7%) were NVD and 52(74.2%) were LSCS. LSCS was done more in symptomatic subjects ($p < 0.05$). Frequency of AFD is higher in symptomatic subjects ($p \text{ value} < 0.05$). Co morbidities noted were PIH, GDM, hypothyroidism and anemia in 15(21.4%), 2(2.8%), 11(15.7%) and 22(31.4%) respectively. All study women were successfully discharged. There were 69 live births(53(76.8%) term and 16(23.1%) preterms)and 1 IUD. Two (2.8%) babies were tested positive for COVID19 . Both remained asymptomatic and discharged. Total 11 neonates required NICU admission due to non covid reasons . Number of deaths among neonates were 2 (2.8%). During follow-up visits 5(9.09%) neonates required readmission in NICU . Inadequate weight gain was seen in 3(5.4%) babies. None developed COVID related symptoms.

Conclusion- COVID 19 infection during pregnancy is not associated with severe clinical presentation, high mortality and morbidity. There may be an association between symptomatic COVID19 pregnant women and AFD. There is high incidence of prematurity and LBW in neonates born to COVID positive mothers.

INTRODUCTION-the outbreak of novel corona virus disease (COVID-19) was initially reported in Wuhan city in China in late December 2019 and since then it has now spread worldwide. In Jan 2020, WHO has declared this outbreak as “Public Health Emergency of International Concern”. Many research papers have elucidated the varying effects of COVID-19 infection depending on patient’s characteristics like age and associated co morbidities. Very little data is on its implication during pregnancy and delivery. SARS-COV-2 infection has also been reported in pregnant women and neonates

and the possibility of vertical transmission can't be denied. The impact of COVID-19 on perinatal outcome is also uncertain.

Aim The purpose of this study was to describe the clinical manifestations of COVID-19 infection in pregnant women during peripartum period and to study the clinical outcomes of neonates born to these mothers.

Methods- This prospective study was conducted at the COVID-19 Hospital of a tertiary care referral center of North India, from May 2021 to July 2021 after taking approval from the institutional ethical committee. In our center we routinely do COVID-19 screening via RAT and RTPCR of all the pregnant women, whether symptomatic or asymptomatic, who presented to Obstetrics And Gynaecology department of our center at the time of labor either our booked case or referred from peripheral hospitals. The samples taken from patients for COVID testing were nasopharyngeal swabs and were collected according to Ministry of Health and Family Welfare Government of India guidelines(1). Among them, all pregnant women who turned COVID positive were shifted to COVID-19 Hospital of our center and were included in the study. The study site was a designated health care facility for COVID-19 patients, where all types of COVID patients were admitted. The COVID-19 severity was divided into three categories on the basis of clinical and/or radiological features; mild, moderate and severe according to Ministry of Health and Family Welfare Guidelines of may 2021 for Covid-19 in adults(2). On the basis of severity: mild, moderate or severe, the patients were admitted in the isolation ward, high dependency Unit or intensive care unit respectively. Study subjects were managed according to current Guidelines of Ministry of Health and Family Welfare of Government of India(2). Data related to age, gestational age, parity, associated co morbidities, risk factors, presenting complaints, mode of delivery and symptoms related to COVID19 were recorded. The study subjects were followed till discharge. The severity of the illness, respiratory involvement, type of respiratory support, and duration of respiratory support were all taken into consideration. The length of hospital stay, recovery and mortality were monitored outcomes among pregnant women.

All neonates born to study subjects were managed according to NNF guidelines of Perinatal-Neonatal management of COVID-19 of May 2020(3). All these neonates were followed up in hospital facility till discharge and thereafter on OPD basis till 28 days of life. Data regarding gestational age, sex, birth weight, COVID testing, requirement of NICU admissions and its indications, requirement of respiratory support, intensive care interventions were evaluated during hospital stay. Data regarding development of COVID related symptoms, weight monitoring, feeding difficulties and NICU readmissions were collected during follow up on OPD basis. The length of hospital stay, recovery, mortality cause of death and adequate weight gain during follow up were monitored outcomes among neonates.

RESULTS – Total 70 patients were included in the study Maternal characteristics are given in table1. 53(75.7%) were RAT positive, 12(17.1%) were RTPCR positive and 5(7.1%) were both RAT and RTPCR positive. 17(24.2%) were symptomatic and 53(75.7%) were asymptomatic. Among symptomatic patients number of mild, moderate and severe cases were 5(7.1%), 10(14.2%) and 2(2.8%) respectively. Clinical presentation of patients in labour were Term Labor, Preterm Labor±PPROM, Leaking/PROM, Acute

Fetal distress, pre eclampsia/eclampsia ,APH and IUD as given in table1 . COVID related symptoms were cough, breathlessness, fever, palpitations and catarrh as shown in table 1. Out of 70 deliveries, 18(25.7%) were NVD and 52(74.2%) were LSCS. When compared for mode of delivery, LSCS was done more in symptomatic subjects as compared to asymptomatic ones and results were statistically significant ($p < 0.05$). LSCS was done due to obstetric indications (previous LSCS, severe pre eclampsia , eclampsia, non progression of labour, abnormal fetal presentation and CPD) in 26(37.1%) patients and due to fetal indications(Signs of fetal distress: decreased fetal movements, fetal bradycardia and inutro meconium) in 24(34.2%) patients . In remaining 2(2.8%) mothers indication of LSCS was worsening COVID-19 illness. Frequency of AFD is significantly higher in symptomatic as compared to asymptomatic mothers(p value < 0.05). Co morbidities noted were PIH, GDM, hypothyroidism and anemia in 15(21.4%), 2(2.8%), 11(15.7%) and 22(31.4%) respectively. Duration of hospital stay was ≤ 2 days in 30(42.8%) patients, 3-5 days in 29(41.4%) patients and 6-13 days in 9(12.7%) and ≥ 14 days in 2(2.8%) patients. Out of 17 symptomatic mothers, 6 required no respiratory support, 9 required oxygen via nasal prongs and 2 required high flow oxygen. Among 11 patients who were on oxygen support, 6 required oxygen for ≤ 7 days and 3 required oxygen support for 8 to 13 days and 2 required respiratory support for ≥ 14 days . All study subjects were successfully discharged.

Total 69 newborns were delivered from 69 COVID 19 positive mothers and 1 patient had intrauterine fetal demise. Neonatal characteristics are shown in table 2. Among the babies delivered, 39(56.5%) were females and 30(43.4%) were males. Out of 69 babies, 53(76.8%) were term babies and 16(23.1%) were preterms. One (1.44%) baby was ELBW, 4(5.7%) were VLBW and 22(31.8%) were LBW. Only 2(2.8%) babies were tested positive for COVID19 after birth. Both these babies remained asymptomatic and were discharged along with their mothers. Total 11 neonates required NICU admission . Indication for admission, requirement of respiratory support and intensive care interventions in these neonates is given in table 2. Total number of deaths among neonates were 2(1 MAS and 1 ELBW)(2.8%) and rest of the neonates were discharged successfully. Follow up after discharge on OPD basis was done in 55 neonates and remaining 14 were lost to follow-up and could not be contacted. During follow-up visits 4 neonates required readmission in NICU, 4 due to hyperbilirubinemia and 1 due to late onset sepsis. Inadequate weight gain was seen in 3 babies. None of the neonate developed COVID related symptoms during a period of 28 days after birth.

Discussion- In our study , total 70 COVID-19 positive pregnant women who presented to us in labor were included. 75.7% were asymptomatic and 24.7% were symptomatic. Out of symptomatic patients, 29.4% were presented with mild COVID-19 infection, 14.2% had moderate disease and 11.7% had severe disease. Similar results were found in study conducted by Vinita Singh et al., and Nayak AH et al(4,5). In both of these studies most of the study subjects were asymptomatic. We had only 2 pregnant women presented with severe COVID-19 infection who required ICU admission. Similarly many other studies that have shown lesser incidence of severe COVID-19 disease among pregnant women(4-7). But contrary to this, some studies have shown increased risk of severe COVID-19 disease in pregnant women(8,9).

Among symptomatic COVID-19 infected pregnant patients, 21.4% were having cough, 17.1% had breathlessness, 24.2% had fever, 4.3% had palpitations and 4.3% had catarrh. In Meta analysis conducted by Ioannis Bellos et al ,(which included 8 observational studies) fever was most common symptom followed by cough and breathlessness and the results were similar to our study(10).

Table 1 Demographic Profile of the study women

S.NO.	PARAMETERS	NO. OF PATIENTS (N)	PERCENTAGE (%)
1	Total COVID-19 Positive pregnant women	70	
2	Gestational age		
	a) < 28 weeks	1	1.4%
	b) 28-34 weeks	2	2.9%
	c) 34-37 weeks	13	18.6%
	d) 37-42 weeks	54	77.1%
	e) >42 weeks	0	0.0%
3	Parity		
	a) Primigravida	24	34.3%
	b) Multigravida	46	65.7%

Table 2: COVID Related Characteristics among study women

S. NO.	PARAMETERS	NO. OF PATIENTS (N)	PERCENTAGE (%)
1	Testing Positivity	70	
	a) RAT	53	75.71%
	b) RTPCR	12	17.14%
	c) Both	5	7.14%
2	Severity of Illness		
	a) Asymptomatic	53	75.71%
	b) Symptomatic	17	24.29%
	i) Mild	5	29.41%
	ii) Moderate	10	58.82%
	iii) Severe	2	11.76%
3	COVID Related Symptoms		
	a) Cough	15	21.43%
	b) Breathlessness	12	17.14%
	c) Fever	17	24.29%
	d) Palpitations	3	4.29%
	e) Catarrh	3	4.29%
4	Requirement of Respiratory Support Among		

	Symptomatic (n=17)		
	a) No Respiratory Support	6	8.57%
	b) Oxygen via Nasal Prongs	9	12.86%
	c) High Flow Oxygen	2	2.86%
	d) Mechanical Ventilation	0	0.00%
5	Duration of Respiratory Support		
	a) ≤ 7 days	6	8.57%
	b) 8 - 13 days	3	4.29%
	c) ≥ 14 days	2	2.86%

Table 3: Maternal Characteristics

S. NO.	PARAMETERS	NO. OF PATIENTS (N)	PERCENTAGE (%)
1	Presenting Complaints in Labour		
	a) Term Labour	30	42.86%
	b) Pre-Term Labour	16	22.86%
	c) Leaking/PROM	5	7.14%
	d) Acute fetal distress	12	17.14%
	e) Eclampsia/Pre-Eclampsia	5	7.14%
	f) APH	1	1.43%
	g) IUD	1	1.43%
2	Mode of Delivery		
	a) NVD	18	25.71%
	b) LSCS	52	74.29%
3	Indication of LSCS		
	a) Obstetrics	26	37.14%
	b) Fetal	24	34.29%
	c) Progressive COVID Illness	2	2.86%
4	Comorbidities		
	a) PIH	15	21.43%
	b) GDM	2	2.86%
	c) Hypothyroidism	11	15.71%
	d) Anaemia	22	31.43%
5	Duration of Hospital Stay		
	a) ≤ 2 days	30	42.86%
	b) 3 - 5 days	29	41.43%
	c) 6-13 days	9	12.86%
	d) ≥ 14 days	2	2.86%

Table 4: Neonatal Characteristics

S.NO.	PARAMETERS	NO. OF PATIENTS (N)	PERCENTAGE (%)
1	Total Live Births	69	
	a) IUD	1	1.45%
2	Gestational Age		
	a) <28 weeks	1	1.45%
	b) 28-34 weeks	2	2.90%
	c) 34-37 weeks	13	18.84%
	d) 37-42 weeks	54	78.26%
	e) >42 weeks	0	0.00%
3	Birth Weight		
	a) ELBW	1	1.45%
	b) VLBW	4	5.80%
	c) LBW	22	31.88%
4	Sex		
	a) Males	30	43.48%
	b) Females	39	56.52%
5	Testing Positivity		
	a) RAT	2	2.90%
	b) RTPCR	0	0.00%
6	Requiring NICU Admission	11	15.94%
7	Indication of NICU Admission		
	a) TTN	1	1.45%
	b) MAS	2	2.90%
	c) Prematurity	4	5.80%
	d) Birth Asphyxia with HIE	2	2.90%
	e) Sepsis	2	2.90%
8	Respiratory Support		
	a) Oxygen via Nasal Prongs	5	7.25%
	b) CPAP	3	4.35%
	c) Mechanical Ventilation	3	4.35%
9	Intensive Care Intervention		
	a) Antibiotics	6	8.70%
	b) Surfactant	4	5.80%
	c) Inotropics Support	2	2.90%
10	Follow up after discharge		
	a) Readmission	5	7.25%
	i)NNH	4	5.80%

	ii) LOH	1	1.45%
	b) Poor weight gain	3	4.35%
11	Mortality	2	2.86%
	a) ELBW	1	1.43%
	b) MAS	1	1.43%

In our study, 16(22.8%) subjects presented with preterm labour±PPROM. Study conducted by Vinita et al showed similar rate(28.69%) of preterm births(4). Meta analysis by Bellos et al showed results similar to our study with 29.7% of preterm births(10). High rates of preterm deliveries among SARS-COV-2 infected pregnant women were reported by many review articles and meta analysis(11,12). Similarly Allotey et al has also showed higher incidence of preterm births among pregnant women infected with COVID 19 in his meta analysis(8). However a systematic review of 33 studies by Elshafeey F et al showed lower rates of preterm birth (15.2%) among 385 pregnant women infected with COVID(13). Till now it is difficult to determine any relationship between spontaneous preterm labour and COVID19 infection in pregnancy due to scarcity of data.

In our study commonly seen co morbidities were PIH(21.4%), GDM(2.8%), Hypothyroidism (15.7%) and anaemia(31.4%). Similar observations were made by Vinita et al and Nayak et al(4,5). In our study 7% subjects were presented with pre eclampsia/eclampsia. Similarly in study conducted by Antoun at al 10.5% of patients were presented with severe pre eclampsia(14). Meta analysis done by Bellos et al showed 5.4% of pre eclampsia patients(10). In our study,17% of COVID19 infected pregnant women had acute fetal distress which was significantly higher among symptomatic mothers. In a study by Vinita et al, 25.64% of patients presented with AFD which is comparable to our results(4). However Meta ananlysis conducted by Bellos et al showed 6.1% of COVID19 infected mothers presented with fetal distress(10).

In our study, 25.7% had NVD and 74.2% had LSCS. In study conducted by Vinita et al percentage of LSCS was 63.93%(4). Similar results were seen in other studies with higher rates of LSCS, among COVID19 infected pregnant women (12,13,15). In our study most of the LSCS were done for obstetric(37.1%) and fetal indication(34.2%).LSCS due to progressive COVID illness was done in only 2.8% of patients. Similarly in study conducted by Vinita et al ,LSCS was done mainly for obstetric and fetal indications(4).

In our study total 11 patients out of 17 symptomatic subjects required respiratory support. 12.8% required oxygen by nasal prongs who presented with moderate disease. Only 2 patients (2.8%) having severe progressive COVID illness required high flow oxygen and ICU care. Similar to our study, Sourya kanti Das et al found only 2.6% patients required high flow oxygen and ICU care(16). All COVID positive mothers in present study were discharged successfully.

In our study, total 69 live births delivered by 69 COVID 19 positive women and 1 had IUD. Out of these 69 live births, 23.1% were preterm. Along with high number of preterm births ,we also observed high incidence of low birth weight babies(39.1%). Percentage of IUD and neonatal deaths in our study were 1.4% and 2.8% respectively. Similar observations were made by other studies(4,5,8). In our study 2(2.89%) newborns

were tested positive for COVID19 at birth within 24 hours. Although we didn't take placental and amniotic fluid samples for COVID19 testing in these 2 cases but the possible explanation for this may be vertical transmission because in both these babies samples were taken immediately after birth. Similar observations were made by Vinita et al and Bellos et al(4,10). Both these babies didn't develop any symptoms, were roomed in with the mother and were discharged successfully along with mother. In our study 11(15.9%) neonates required NICU admissions due to reasons other than COVID. Radiological findings and laboratory investigations in these neonates were consistent with their primary diagnosis. Similarly in study conducted by Dumitriu et al, newborns who were tested positive for COVID remained asymptomatic and those who required NICU admission were COVID negative and were admitted due to other reasons(17). Number of neonatal deaths in present study was 2(2.8%). MAS and prematurity(ELBW) were the reason of these two mortalities. In our study 5 neonates required NICU readmissions. Out of these, 4 were readmitted due to hyperbilirubinemia and 1 due to late onset sepsis. All these 4 infants were born of symptomatic COVID19 positive mothers. Similar observations were made by Dimitriu et al in their study where maternal severe critical disease was associated with higher incidence of hyperbilirubinemia requiring phototherapy(17). Among 54 neonates who were followed up till 28 days of life, weight gain was not adequate in 3 neonates. The reason for poor weight gain was- 2 babies were not roomed in along with mother due to prolonged ICU stay of mother and were fed inadequately and 1 baby was erratically fed and developed sepsis

Strengths- The strength of our study is that it is prospective study done in a COVID dedicated Hospital of a Tertiary care center. Follow up of neonates born to COVID positive mothers was done till 28 days of life.

Limitations- Comparison of study subjects is not done with Non COVID19 positive patients. Biological samples(placental membrane swabs, amniotic fluid and peritoneal fluid) could not be taken to establish vertical transmission.

Conclusion- Our study concludes that COVID 19 infection during pregnancy is not associated with severe clinical presentation in pregnant women, high mortality and morbidity in pregnant women. There may be an association between symptomatic COVID19 pregnant women and AFD. More studies are required to confirm this association. There is high incidence of prematurity and LBW in neonates born to COVID positive mothers. Further, mostly neonates born to COVID positive mothers are asymptomatic and the risk of vertical transmission is very low and could not be ascertained in our study.

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