

Outcome of Pregnancy in COVID-19 Positive Pregnant Women: A Retrospective Observational Study

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ABSTRACT

Introduction: Pregnant women have also been affected globally due to the Coronavirus Disease 2019 (COVID-19) pandemic. As foeto-maternal unit is involved, hence it is important to know possible manifestations and outcome of COVID-19 affected pregnant women. The findings of the study can be a guide for betterment of COVID-19 affected antenatal patients care.

Aim: To find the outcome of pregnancies affected by the COVID-19 infection of the Antenatal care (ANC) patients who presented to the tertiary care hospital in terms of laboratory parameters, treatment of the infection, mode of delivery, adverse outcome if and presence of documented infection in newborn.

Materials and Methods: This was a retrospective observational study done from May 2020 to December 2020 conducted on the admitted pregnant women to the tertiary care hospital who tested positive for the COVID-19 virus were included in the study. Data collection (symptoms, reports and treatment) from these pregnant COVID-19 positive patients was done. Patients who were discharged before delivery were contacted telephonically and were asked the relevant information.

Results: During the study period, total 1150 COVID-19 positive patients were admitted to the hospital. Amongst these, there were 441 female patients including pregnant and non pregnant women. Amongst the 441 COVID-19 infected female patients, 20 were pregnant. Majority of the patients were in the age group of 21-30 years. An 85% of women were in their third trimester at the time of admission. Pre-eclampsia and Hypothyroidism were the major co-morbidities observed. Six maternal Intensive Care Unit (ICU) admissions were noted. Breathlessness was the main symptom seen followed by sore throat, fever and cough. Previous Lower Segment Caesarean Section (LSCS) and foetal distress were cited as the main reasons for undergoing LSCS. No vertical transmission of virus was seen in the study. There were two neonatal ICU admission. Low Molecular Weight Heparin (LMWH) was administered to 33% patients. Fifty percent of the patients were prescribed steroids.

Conclusion: Advanced gestational age, pre-eclampsia, hypothyroidism, elevated levels of d-dimer, Neutrophil/Lymphocyte (NL) ratio and C-reactive protein were seen as the main findings. Mother to child transmission was not observed in this study.

Keywords: Coronavirus disease-2019, C-reactive protein, D-Dimer, Ferritin, Inflammatory markers, Vertical transmission

INTRODUCTION

The COVID-19 pandemic has affected the healthcare system on a global level and has become a public health challenge. The virus which was first detected in December 2019, in Wuhan province of China eventually has spread across the world [1]. This viral outbreak has mostly affected the elderly population [2]. Physiological changes in the respiratory system, makes pregnant women more vulnerable to respiratory viral infection during pregnancy. Also pregnancy is a state of altered immunity which helps the developing foetus maternal environment [3,4]. Anatomical changes in pregnancy lead to a decrease in the Expiratory Reserve Volume (ERV) and Functional Residual Capacity (FRC) [5]. These maternal adaptations result in increased susceptibility of the pregnant mother to airway tract infections [6]. Respiratory Tract Infections with Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS-CoV2) have previously shown to affect pregnant women and have led to obstetric complications resulting in poor maternal and foetal outcomes [4].

Previous pandemic with H1N1 influenza virus affected pregnant women more seriously requiring intensive treatment [7]. Pregnant women being amongst the vulnerable population are also affected with SARS-CoV2 virus [1,8]. During pregnancy, changes in "T" cells occur such as decrease in numbers of helper T cells, reduced lymphocyte cytotoxic activity, and synthesis of substances that can block maternal recognition of foetal major histocompatibility antigens [9,10]. There is paucity of Indian studies, regarding the effect of COVID-19 infection on pregnancy. The study aims to find out the

effect of COVID-19 infection in pregnancy, laboratory characteristics maternal and foetal outcome.

MATERIALS AND METHODS

This was retrospective observational study, involving pregnant women who were admitted to COVID ward with documented COVID-19 infection by the Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) swab test [11]. The study was commenced after approval from the Institutional Ethics Committee (Ref. SKNMC/Ethics/App/2020/677). All hospitalised COVID-19 positive pregnant women between the periods from May 2020 to December 2020 were in the study, analysis of the retrospective data was done and completed by February 2021 and informed consent was duly obtained from the included patients.

Inclusion criteria: All pregnant women who were admitted to the hospital and who tested positive for the COVID-19 virus by RT-PCR test were included in the study.

Exclusion criteria: Non pregnant female patients were excluded from the study.

Study Procedure

During the study period, total 1150 COVID positive patients were admitted to the hospital. Amongst these, there were total 441 female patients, of which 20 were pregnant. Pregnant women who showed symptoms suggestive of COVID-19 infection and were awaiting their results were shifted to the COVID-19 suspect ward/ICU. Out of these women who were later tested positive for COVID-19 infection

were shifted to COVID wards and only such confirmed COVID-19 positive pregnant patients were included in the study.

Patient information was collected from the COVID wards, COVID ICU registers, medical records, telephonic contact with the patients. The data was collected for the gestational age, maternal age, parity, obstetric risk factors, clinical characteristics, laboratory parameters and co-morbid conditions relevant to COVID-19. Mode of delivery, neonatal birth weight, neonatal nasopharyngeal swab report tested for COVID-19 virus by RT-PCR was also collected. Anaemia was classified into three categories viz., mild (10-10.9 gm/dL), moderate (7-9.9 gm/dL) and severe anaemia (<7 gm/dL) as per World Health Organisation (WHO) classification [12].

STATISTICAL ANALYSIS

The data collected was compiled and analysed using Excel (Windows 10 Version 16051.13426.20332.0).

RESULTS

Out of 20 COVID-19 positive pregnant patients admitted to the hospital, majority (n=14 (70%)) were in the age group of 20-30 years. A total of twelve women had obstetric risk factors, five women had hypertensive disorders of pregnancy, one patient had pre-existing diabetes mellitus while other one patient had gestational diabetes mellitus. One patient had rheumatic heart disease with mitral regurgitation. Three women had hypothyroidism. Under the COVID-19 relevant co-morbidities, one patient had asthma, two were diabetic and five patients had hypertensive disorders of pregnancy [Table/Fig-1].

The overlapping of patients in two categories was due to the fact that conditions like diabetes, hypertensive disorders and asthma are obstetric risk factors as well as co-morbid conditions relevant to COVID-19. Patient demographic characteristics and risk factors along with number of patients are mentioned in [Table/Fig-1].

Maternal characteristics	Number of patients (n=20)
1. Age (In years)	≤20: 2 21-30:14 >30: 4
2. Gestational age at admission (according to Trimester)	1 st Trimester- 0 2 nd Trimester-3 3 rd Trimester-17
3. Gravidity	Primigravida: 7 Multigravida: 13
4. Obstetric high risk factors (Hypertensive disorders in pregnancy, Diabetes, Heart diseases, Thyroid disorders)	12
5. Co-morbidities relevant to COVID-19 (Diabetes mellitus, Childhood asthma)	8

[Table/Fig-1]: Maternal characteristics with respect to age, parity, gestational age, obstetric risk factors and co-morbid conditions in 20 COVID-19 positive mothers. There were patients who had more than one obstetric high risk factor or co-morbidity relevant to COVID-19 hence there has been an overlap in such cases.

[Table/Fig-2] shows the clinical and laboratory characteristics of each patient. Eight patients (40%) were asymptomatic, at the time of admission. These eight patients were tested and were found to be positive for SARS-COV-2 as they were close contacts of confirmed COVID-19 positive patients. Fever, cough and breathlessness were most common presenting symptoms in remaining 12 patients with varying combination. Two patients had fever and breathlessness, two patients had fever and dry cough, while two patients had all three symptoms. Patient 5 and 11 had breathlessness as the only symptom while Patient 7 had only cough as presenting symptom.

Amongst the patients complaining of breathlessness (n=6), three patients had oxygen saturation of less than 95% on room air. All these three patients required oxygen support [Table/Fig-3].

Additionally, myalgia and diarrhoea were found in one patient each. (Patient 13 and 14, respectively). Majority of the patients had deranged inflammatory markers (18 out of 20), which included serum ferritin, D dimer, C-Reactive Protein and NL ratio. Patients 1, 5 and 14

Patient	Fever	Cough	Breathlessness	SpO ₂ at time of admission (%)	Laboratory characteristics	Mode of delivery	Term/Preterm/Post-term delivery	Birth weight (gm)
1	Yes	Yes	No	96	Elevated D-Dimer, Ferritin, CRP	LSCS	Preterm	2400
2	Yes	No	Yes	94	Elevated NLR, D-Dimer, CRP	LSCS	Term	3000
3	Yes	Yes	Yes	98	Anaemia, Elevated NLR, D-Dimer, CRP	LSCS	Term	2700
4	No	Yes	No	96	Elevated NLR	LSCS	Term	3200
5	No	No	Yes	98	Elevated D-Dimer, Ferritin, CRP	LSCS	Term	2700
6	No	No	No	98	Elevated D-Dimer	FTNVD	Term	3800
7	No	Yes	No	97	Anaemia, Elevated NLR, D-Dimer, Leukocytosis	LSCS	Term	2268
8	No	No	No	100	Anaemia, Elevated D-Dimer	LSCS	Term	2300
9	No	No	No	99	Elevated NLR, D-Dimer	LSCS	Term	2660
10	No	No	No	97	Elevated D-Dimer, CRP	LSCS	Term	3245
11	No	No	Yes	94	Elevated NLR	FTNVD	Term	3400
12	Yes	Yes	Yes	98	Anaemia, Elevated D-Dimer, CRP	LSCS	Term	4234
13	No	No	No	99	Anaemia, Elevated NLR	FTNVD	Term	2845
14	Yes	Yes	No	98	Anaemia, Elevated D-Dimer, Ferritin, CRP	FTNVD	Term	2880
15	No	No	No	97	Anaemia	LSCS	Term	2300
16	No	No	No	97	Elevated D-Dimer, CRP	LSCS	Term	2780
17	No	No	No	98	Normal S	FTND	term	2875
18	Yes	No	Yes	93	Anaemia, Elevated NLR	LSCS	Preterm	1700
19	No	No	No	100	Elevated D-Dimer, CRP	FTNVD	Term	3000
20	No	No	No	98	Anaemia, Elevated NLR, D-Dimer, CRP, Leukocytosis	LSCS	Preterm	2600

[Table/Fig-2]: Clinical and Laboratory characteristics of patients.

CRP: C reactive protein; LSCS: Lower segment caesarean section; NLR: Neutrophil to lymphocyte ratio; FTNVD: Full term normal vaginal delivery; FTND: Full term normal delivery

Treatment	Number of patients (n=20)
Antiviral drugs	5
Antibiotics	12
Low molecular weight heparin (Enoxaparin)	7
Steroids	8
Maternal Intensive Care Unit (ICU) admissions	6
Oxygen Support	Yes-3 No-17

[Table/Fig-3]: Treatment received by COVID-19 infected patients.

Some patients were prescribed multiple drugs. Antiviral drugs used were Remdesivir or Favipiravir; Most common Antibiotics were Amoxicillin+Clavulanic Acid or Azithromycin or Doxycycline; Steroids Methylprednisolone/Prednisolone; LMWH (enoxaparin)

had elevations in all three inflammatory markers. Ten patients had raised NL ratio. The highest NL ratio was seen in patient 20 with a value of 12.71. The maximum value of elevated serum ferritin of 5639.2 ng/mL was seen in patient 14. This patient had asthma as associated co-morbid condition.

Patient 3 had all three key symptoms of COVID-19 infection- fever, cough and breathlessness. The CRP level of 686 mg/L, in this patient was the highest value observed amongst all patients. Patient 20 shows leukocytosis. She also had a high NLR (highest in the cohort) at 12.71, and CRP value of >90 mg/L and raised D-dimer value. Yet, she showed no symptoms of COVID-19 infection clinically. Nine out of 20 patients were anaemic three had mild anaemia while six had moderate anaemia. Oxygen support was required by three patients, one of whom was admitted to the ICU [Table/Fig-3]. The others were managed at the COVID-19 positive ward.

[Table/Fig-2] also shows the maternal and neonatal outcomes in 20 mothers. Fourteen (70%) of the patients underwent LSCS while six (30%) had a vaginal delivery. Amongst these six women, one had forceps assisted vaginal delivery due to foetal distress with meconium stained liquor. Elective caesarean section was done in seven patients and other seven patients had emergency caesarean section. Out of the patients who underwent elective LSCS, three patients were previous caesarean section and were not willing for vaginal delivery. The other indications for elective LSCS were severe oligohydramnios (one patient), cephalo-pelvic disproportion (one patient), primigravida with breech presentation (one patient) and history of secondary infertility with oligohydramnios (one patient). Seven patients underwent emergency LSCS. Out of the seven patients who underwent emergency LSCS, four had foetal distress during labour. One patient had placenta accrete with vaginal bleeding and required emergency caesarean section along with obstetric hysterectomy. There was prolonged rupture of membranes with failed induction in one patient, while one patient had prolonged labour. None of the patients in the study required mechanical ventilation.

There were 17 term births and three preterm births, out of which two preterm births and three term births had a low birth weight neonate (total low birth weight neonates=5). Overall, 13 out of the 20 neonates were in the normal birth weight range i.e., 2500-3499 g and two were above normal birth weight (≥ 3500 g). APGAR scores of 12 neonates were available, out of which majority had a score of 8 at one minute and 9 at five minutes (7 and 6 neonates respectively).

Two neonates required NICU admission after birth for hypoglycaemia and low birth weight respectively in each baby. Meconium Stained Amniotic Fluid was found in three cases. Twelve neonates were tested for COVID-19 infection by RT-PCR of nasal and oropharyngeal swabs. Nasal swabs of all 12 neonates were negative for COVID-19 infection. Eight neonates were not tested for the infection at birth.

[Table/Fig-3] shows the various treatment modalities, number of maternal ICU admissions and mothers requiring oxygen support. Twelve patients received antibiotics, followed by steroids (8 patients) and Low Molecular Weight Heparin (7 patients). Six women were

prescribed antiparasitic drug (Ivermectin) and five patients were taking antivirals.

Antibiotics included were amoxicillin and clavulanic acid or doxycycline or cefixime while steroids included any one of methylprednisolone or prednisolone or betamethasone. Enoxaparin was the low molecular weight heparin used. Antiparasitic drugs prescribed included both hydroxychloroquine and ivermectin, oseltamivir and remdesivir were the antivirals used.

Three patients required oxygen support due to a low oxygen saturation. Two patients received oxygen at a rate of 2 L/min while the third required a rate of 4 L/min. There were six maternal ICU admissions during their pregnancy due to various obstetric and COVID-19 high risk factors. These included pre-eclampsia, diabetes mellitus, cardiomegaly, hypotension, decreased oxygen saturation and postcaesarean section with obstetric hysterectomy for postoperative monitoring.

DISCUSSION

Pregnant women have always been amongst the vulnerable population, the others being the elderly population, people with co-morbidities and children. Pregnancy is an immunosuppressive condition [13]. Also, during pregnancy there are physiological and anatomical changes in the respiratory system. There is reduction in functional residual capacity, due to elevation of diaphragm by the gravid uterus. Oedema of the respiratory tract in pregnant women leads to decrease in the caliber of the airway [6]. A physiological state of respiratory alkalosis due to increase in the tidal volume ensures transfer of oxygen from mother to foetus. All these changes place pregnant women at an increased risk of acquiring respiratory infections. Mortality rate due to COVID-19 in pregnant women was found to be around 1.6% [14].

Previous respiratory viral infections among pregnant women with H1N1, SARS-COV-1 and MERS-COV were associated with poor clinical course and outcome. Respiratory viruses like Influenza virus (H1N1) and the Coronavirus like SARS-COV and MERS-COV have previously caused severe respiratory illness leading to increased maternal morbidity and mortality [4,15]. Various studies have been published since the outbreak of the COVID-19 pandemic, studying the effect of nCoV-2 (SARS-COV-2) on pregnant women and the outcome of pregnancy as well as their clinical and laboratory characteristics. Systemic reviews from different studies conducted in multiple countries have reported that majority of the pregnant women present with mild symptoms, with fever and cough being the most common symptoms [16]. The mortality rate due to COVID-19 in pregnant women was found to be 1.6% [13].

In present study, fortunately, there was no maternal mortality amongst the 20 COVID-19 positive pregnant patients. Fever, cough and breathlessness were the most common reported symptoms in present study, similar to a study conducted by Chen N et al., which included 99 cases with COVID-19, suggested that the most common symptoms at presentation were fever, cough and breathlessness [17].

In another study, [18] evaluating the impact of coronavirus infection in pregnancy, amongst 141 COVID-19 positive pregnant women, 27 (19.14%) women had associated co-morbidities like pregnancy induced hypertension, eclampsia, anaemia. In present study, there were 8 patients (40%) with associated co-morbidities relevant to COVID-19. Half of the patients in present study had increased NL Ratio (50% had lymphopenia). Authors in other study [1], which included 118 COVID positive women, observed lymphopenia in 44% patients.

Seven out of 20 women (35%) underwent an elective LSCS, whereas seven had an emergency LSCS [Table/Fig-1]. Although, most of the elective LSCS done in these studies were due to the foetal concern of COVID-19 infection in pregnancy.

Six patients had vaginal delivery in present study. None of the new born in present study who were tested by RT-PCR was positive, suggesting less likelihood of the possibility of vertical transmission. In another study [1] on nine patients, samples from amniotic fluid, cord blood, neonatal throat swab and breast milk were taken and all of them tested negative for COVID-19 virus. All patients were delivered by LSCS. However, another study demonstrated that none of the newborns of five patients who underwent vaginal delivery tested positive for the virus [19].

In present study, there were six maternal ICU admissions [Table/Fig-3] due to obstetric and COVID-19 high risk factors including pre-eclampsia, diabetes mellitus, cardiomegaly, hypotension and decreased oxygen saturation. One patient was admitted for postoperative monitoring since she underwent an obstetric hysterectomy after delivery.

Limitation(s)

All neonates were not tested for the viral infection, as some patients were delivered at other hospital. High Resolution Computed Tomography (HRCT Thorax scan was not done on the pregnant patients, as per the institutional protocol.

CONCLUSION(S)

Most common clinical presentation in SARS-COV-2 affected pregnant women was fever, cough and breathlessness. Presence of these symptoms should prompt clinician to promptly test the ANC in patient to rule out possible COVID-19 infection.

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PLAGIARISM CHECKING METHODS: [Jan H et al.]

- Plagiarism X-checker: Mar 22, 2021
- Manual Googling: Jun 19, 2021
- iThenticate Software: Jul 22, 2021 (7%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:

- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 22, 2021**

Date of Peer Review: **Jun 04, 2021**

Date of Acceptance: **Jun 26, 2021**

Date of Publishing: **Aug 01, 2021**