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Maternal and Fetal Outcomes in Pregnancies with Covid-19: A Retrospective Analysis

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ABSTRACT

Objectives: To study the sociodemographic features, obstetric profile and clinical disease patterns in pregnancies with COVID-19, and to correlate with maternal and fetal outcomes.

Methods: A retrospective analysis,from1st April 2020 to 15th August 2020, on a cohort of pregnant/ postpartum (within 6weeks) subjects with COVID-19 infection confirmed either by RT-PCR test for SARS-CoV-2 on nasopharyngeal and oropharyngeal swabs or by rapid antigen test kits. Information was collected from department data base and case record files. All women seen in the emergency either because they were showing clinical symptoms of COVID 19 or in labor or did not have home quarantine facility and were admitted. They were classified into – Asymptomatic/Mild category: minimal symptoms, no respiratory distress, RR 12-15/min, fever < 100 F, SPO2 > 95%; Moderate category: RR 15-30/min, Fever 100- 101.5 F, SPO2 90-94%, pneumonia on clinical/radiological examination; Severe category: Severe respiratory distress, shock, subnormal mentation, RR >30/min, fever >101.5 F, SPO2 <90%, ARDS, septic shock.

Results: 99 women with Covid-19 infection were included in the study-; 82 testing positive by RTPCR and remaining 17 had positive rapid antigen test. Three women underwent medical MTP, 2 underwent laparotomy for ectopic pregnancy,39 delivered vaginally and 36 by LSCS while 19 were still undelivered. The majority were young (median age 26.76 years), educated, urban and sedentary (not practicing yoga/exercise). Obstetric profile- Most of the patients were multiparous, presented in third trimester with no major associated medical or obstetric complications or complaints. Anaemia was commonest medical complication in 58 patients, pre-eclampsia in 11, preterm labor in 3, and transient liver dysfunction was observed in 3 subjects. Clinical profile- Asymptomatic/Mild disease: 92, moderate disease: 4, severe disease: 3. Majority (65) had no COVID symptoms, fever (21), breathlessness (8), atypical symptoms like diarrhoea (2) and headache (1) were present in these numbers. The mean SpO2 at admission was 98.17%. Most of the participants had no clinical findings in chest. Majority had normal TLC and platelet count and no covid changes on CXR. In treatment, more than 80% received Hydroxychloroquine & Azithromycin, 7.10% were put on Oxygen, 10.10% received steroids and LMWH was given to 75.75% patients. There were 3 maternal mortalities; all had associated pre-eclampsia and anaemia and underwent emergency caesarean section. No neonate had asphyxia/ mortality. Testing for SARS-CoV-2 was performed on all neonates, with only one testing positive by RTPCR.

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Conclusion: The present data on Indian population do not suggest an increased risk of severe disease among pregnant women, as has been observed with earlier influenza infections. However certain factors like pre-eclampsia, anaemia and emergency caesarean section may predispose them to severe morbidity/mortality.

Keywords: *Covid-19, Infections in Pregnancy, Maternal and Fetal outcomes*

INTRODUCTION

With over a million individuals infected, the global pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been growing at an accelerating rate.1 The increasing mortality rate warrants identification and protection of the vulnerable populations in society. The knowledge gained from previous human coronavirus outbreaks, namely, the severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome Coronavirus (MERS-CoV), suggests that pregnant women and their fetuses are particularly susceptible to poor outcomes.2

The physiologic and immunologic changes that occur during pregnancy make the mother more vulnerable to severe outcomes. Anatomical changes such as an increase in the transverse diameter of the thoracic cage and an elevated level of the diaphragm, decrease maternal tolerance to hypoxia.3 Lung volume changes and vasodilation can lead to mucosal edema and increased secretions in the upper respiratory tract.4 In addition, alterations in cell-mediated immunity contribute to the increased susceptibility of pregnant women to be infected by intracellular organisms such as viruses.5 The immaturity of the innate and adaptive immune systems makes them highly susceptible to infections. Though evidence of COVID-19 in pregnant women is still insufficient, identification of factors affecting Feto- maternal outcomes of COVID-19 pregnancy is of utmost importance during thispandemic.6-8

MATERIALS&METHODS

Information was collected from department data base and case record files of 99 pregnant/ postpartum (within 6 weeks) women with COVID-19 infection who were treated at our hospital from 1stApril to 15thSeptember, 2020.All women seen in the Obstetrics Emergency Room either because they were showing clinical symptoms (eg, persistent fever, dyspnea, radiological diagnosis of pneumonia, or oxygen saturations <95%) or they were in labor or not having facility for home quarantine were admitted as per hospital policy.

Consent waiver for this retrospective study was obtained from IEC-HR of the institution.

Inclusion criteria

All pregnant or post-partum (Within 6 weeks) patients with COVID-19 confirmed either by a reverse transcription polymerase chain reaction (RT-PCR) test for SARS-CoV-2 on nasopharyngeal and oropharyngeal swabs or by rapid antigen test (RAT) kits were included in the study. Strong clinical suspects and symptomatic patients if negative by RAT were subjected to RT-PCR test for confirmation. All confirmed COVID-19 infection patients are classified as: (a) mild (b) moderate (c) severe according to hospital policy. Mild category (category 1) - minimal symptoms, no respiratory distress, RR 12-15/min, fever < 100 F, SPO2 > 95%.Moderate category (category 2) - RR 15-30/min, Fever 100-101.5 F, SPO2 90-94%, pneumonia on clinical/radiological examination of lung. Severe category (category 3) - Severe respiratory distress, shock, subnormal mentation (disoriented/unconscious), RR >30/min, fever >101.5 F, SPO2 <90%, ARDS, septic shock.

The protocols implemented for treatment at our hospital were as follows: (a) for asymptomatic/ mildly asymptomatic patients: rest at home (if facility for home quarantine available) and 500 mg of paracetamol every 8 hours or as needed for fever and general discomfort; and multivitamins specially Zinc, Vitamin C& Vitamin D3 (b) Oseltamivir,and Hydroxychloroquine (after normal ECG) with or without Azithromycin was given to most patients and they were closely monitored for symptoms and oxygen saturation (c) Moderate to severe category patients were managed in consultation with medicine and critical care departments for oxygen therapy, antiviral drugs, steroid and therapeutic anticoagulation treatment. Prophylactic

anticoagulation (LMWH) was given to all admitted antenatal, postnatal, post caesarean and post abortion and severe category disease for 7-10 days. Caesarean section was carried out for obstetric indication or severe respiratory disease. Delivery care was performed by obstetricians and all delivery staff followed the precautions and recommendations on infection prevention and control. Data on socio- demographic characteristics, obstetric parameters, delivery& neonatal details, COVID disease profile variables were collected on a case record proforma from clinical case sheets. For the purpose of analysis, study population was divided into two group- Group A: asymptomatic/ mild disease and Group B: moderate to severe disease, morbidity including complications like sepsis, thromboembolism, ARDS etc and mortality.

Statistical Analysis

Data was coded and recorded in MS Excel spreadsheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Data were presented in a graphical manner wherever appropriate for data visualization using histograms/box-and-whisker plots/column charts for continuous data and bar charts/pie charts for categorical data. Group comparisons for continuously distributed data were made using independent sample 't' test when comparing two groups. If data were found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon Test were used for these comparisons. Chi- squared test was used for group comparisons for categorical data.Incase the expected frequency in the contingency tables were found to be <5for> 25% of the cells,Fisher's Exact test was used instead. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was kept at $p < 0.05$

RESULTS

99 pregnant women with Covid-19 infection were included in the study-; 82 testing positive by RTPCR and remaining 17 had positive rapid antigen test. There were 62 antenatal and 37 postnatal patients. In this study,3 women underwent medical MTP, 2 had laparotomy for ectopic pregnancy, 39 delivered vaginally and 36 by LSCS while 19 remained still undelivered. The majority were young (median age 26.76 years), educated, urban, sedentary (not practicing yoga/exercise). Obstetric profile- Most of the patients were multiparous, presented in third trimester with no major associated medical or obstetric complications or complaints. Anaemia was the commonest medical complication present in 58 patients, pre- eclampsia in 11, preterm labor in 3, and IHCP/ transient liver dysfunction was observed in 3 subjects. Clinical profile- Asymptomatic/Mild disease: 92, moderate disease: 4, severe disease: 3. Majority (65) had no COVID symptoms while fever (21), breathlessness (8), and atypical symptoms like diarrhoea (2) and headache (1) were present in others. The mean SpO2 at admission was 98.17%. Most of the participants had no clinical findings in chest. Majority had normal TLC and platelet count and no covid changes on CXR. In treatment, more than 80% received Hydroxychloroquine & Azithromycin, 7.10% were put on Oxygen, 10.10% were on steroids and LMWH was given to 75.75% patients.

There were 3 maternal mortalities; all three had associated pre-eclampsia and anaemia and underwent emergency caesarean section. No neonate had asphyxia/ mortality. Testing for SARS-CoV-2 was performed on all neonates, with only one testing positive by RTPCR.

TABLE 1: General patient characteristics

AllParameters	**Mean± SD||Median(IQR)||Min-Max|| Frequency(%)**
Age(Years)	26.76±5.47||26.00(23.00-30.00)||13.00-39.00
Age	
≤20Years	12(12.1%)
21-30 Years	68(68.7%)
31-40 Years	19(19.2%)

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Status	
ANC	62(62.6%)
PNC	37(37.4%)
POG	
1stTrimester	5 (5.1%)
2ndTrimester	5 (5.1%)
3rdTrimester	52(52.5%)
PNC	37(37.4%)
Residence	
Rural	25(25.3%)
Urban	74(74.7%)
Education	
Educated	73(73.7%)
Uneducated	26(26.3%)
BMI(Kg/m2)	21.55±2.23‖21.10(20.00-23.00)‖17.30-28.00
BMI	
<18.5Kg/m2	6(6.1%)
18.5-22.9Kg/m2	67(67.7%)

AllParameters	**Mean± SD‖Median(IQR)‖Min-Max‖ Frequency(%)**
23.0-24.9Kg/m2	19(19.2%)
25.0-29.9Kg/m2	7 (7.1%)
Parity	
Primigravida	43(43.4%)
Multigravida	54(54.5%)
Grandmultipara	2 (2.0%)
PresentingComplaints(COVID)	
Asymptomatic	65(65.7%)
Fever	21(21.2%)
Breathlessness	8 (8.1%)
Cough	2 (2.0%)
Diarrhoea	2 (2.0%)
Headache	1 (1.0%)
ObstetricComplaints	
None	71(71.7%)
LaborPain	14(14.1%)
LeakingPV	7 (7.1%)
DecreasedFetal Movement	4 (4.0%)
Bleeding PV	3 (3.0%)
MedicalHistory	
None	84(84.8%)
Hypertension	6 (6.1%)
Hypothyroidism	3 (3.0%)
TB	3 (3.0%)
Diabetes	1 (1.0%)
Diabetes+Hypertension	1 (1.0%)

Others	1 (1.0%)
ObstetricComplications	
None	75(75.8%)
Pre-Eclampsia	11(11.1%)
Others	6 (6.1%)
Oligohydramnios	3 (3.0%)
FGR	2 (2.0%)
GDM	2 (2.0%)

AllParameters	**Mean± SD||Median(IQR)||Min-Max|| Frequency(%)**
FamilyMember	
Affected	15(15.2%)
NotAffected/Tested	84(84.8%)
Diet	
Non-Vegetarian	21(21.2%)
Vegetarian	78(78.8%)
Smoking/Alocohol(Present)	0 (0.0%)
Yoga/Exercise(Yes)	4 (4.0%)
SpO2atAdmission(%)	98.17±3.40||99.00(98.00-99.00)||70.00-100.00
Chest	
NoFindings	94(94.9%)
Significant ClinicalFindings	5 (5.1%)
Anaemia(Present)	58(58.6%)
Thrombocytopenia(Present)	8 (8.1%)
TLC	
Leukocytosis	5 (5.1%)
Leukopenia	5 (5.1%)
Normal	89(89.9%)
CXR	
NoCOVIDChanges	89(89.9%)
COVIDChangesPresent	10(10.1%)
Outcomeof Pregnancy	
VaginalDelivery	39(39.4%)
LSCS	36(36.4%)
Undelivered	19(19.2%)
Medical Abortion	3 (3.0%)
Laparotomy	2 (2.0%)
OutcomeofDisease	
Mild	92(92.9%)
Mdoerate	4 (4.0%)
Severe	3 (3.0%)
BabyOutcome	
Affected	1 (1.3%)

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AllParameters	**Mean± SD||Median(IQR)||Min-Max|| Frequency(%)**
NotAffected	75(98.7%)
APGAR(1Minute)	9.62±0.49|| 10.00(9.00-10.00)|| 9.00-10.00
BirthWeight(Kg)	2.68±0.37||2.60(2.40-2.90)|| 1.50-3.80
BirthWeight	
<2.5Kg	24(29.6%)
≥2.5Kg	57(70.4%)
EBF (Yes)	74(94.9%)
TypeofTest	
RTPCR	81(82.7%)
RapidAntigenTest	17(17.3%)

DISCUSSION

Wuhan, Wuhan, Hubei Province in China saw the first cases of COVID-19 pneumonia starting in December 2019. After that, the infection rapidly spread all over the world. As obstetricians began to identify cases of COVID-19 in pregnancy, some reports have appeared in the literature.4,5 This study summarizes the findings of 99 pregnancies with confirmed COVID-19 infection. We observed that COVID-19 infection in pregnancy is not associated with severe maternal morbidity or adverse outcome unless there is associated medical or surgical complication. Earlier,SARS-CoV-1 outbreak during 2002-2003 was associated with a high maternal mortality rate (case fatality rate of 25%), spontaneous miscarriages during the first trimester and intrauterine growth restriction in the second and third trimesters. Nevertheless, a recent editorial on COVID-19 in pregnancy argues that management guidelines should be based on data from the current epidemic rather than drawing on the limited experience from previous outbreaks, as their epidemiology, clinical course and response to treatment may differ.7,8 Indeed, our review of 99 pregnant women with confirmed SARS-CoV-2 infection showed only three cases of maternal intensive care admission (3%) and three fatalities.

In our study, in socio-demographic profile results, the majority of the patients were young, educated, urban women not practicing any of exercise. Anaemia was the most common associated medical complication seen in 59% patients followed by pre- eclampsia, pre-term labor and transient liver dysfunction. Low socio-economic status, high parity, nutritional deficiencies, phytate rich Indian diet, malaria, helminthic infestations and other infections which are responsible for high incidence of anaemia in Indian pregnant population, predispose them to any new infections including covid infection.

In our study, more than 90% patients were either asymptomatic or had mild disease. Milder symptoms in pregnant Covid-19 patients may be explained by the younger age and healthier population as compared to the general Covid-19 patient population. A previous study by Liu et al8 that compared pregnant and non-pregnant Covid-19 patients, also found similar results where more patients were classified as mild in pregnant population.

In the present study almost half of the delivered patients had LSCS done mostly for obstetric indications like non-progress of labor, fetal distress etc and not because pregnant women had Covid-19 infection. This is in contrast to a study conducted in Chinese population by Chen et al9 where LSCS was conducted for COVID infection in all patients. However, in another Indian study by Nayak et al10 also LSCS were conducted for obstetrical indications only.

In our study, all three maternal mortalities had associated pre-eclampsia, anemia and underwent emergency cesarean sections. A WHO report[11] also suggested that associated diseases such as pre-eclampsia are associated with adverse pregnancy outcomes in covid patients because respiratory syndromes may aggravate pulmonary edema and decrease oxygen saturation. Similar reports were found in a study conducted in India where patients with severe pneumonia had presented with a number of comorbidities such as anemia, pre-eclampsia, GDM etc[10].The two maternal ICU admissions reported by Breslin et al[6] involved mothers with high BMI (>35) and complicated medical history which leads one to

question whether COVID-19 increases the risk of severe morbidity in high-risk pregnancies.

Testing for SARS-CoV-2 was performed on all neonates by RT-PCR with only one neonate testing positive by RT-PCR. Many studies have suggested no increased risk of perinatal vertical transmission[2,3,5]. Our study findings are in concurrence with the findings of these studies.

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