



CLINICAL CHARACTERISTICS AND FETO-MATERNAL OUTCOMES IN PREGNANT WOMEN WITH COVID-19 INFECTIONS

Obstetrics & Gynaecology

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ABSTRACT

Background and objectives:- COVID-19 is ongoing pandemic, caused by novel Corona Virus. There is very scarce information is available about clinical features and feto-maternal outcomes of COVID-19 in pregnancy. Therefore, this study was aimed to determine clinical characteristics and feto-maternal outcomes of pregnant women with COVID-19. **Methods-** In this retrospective study, we included all pregnant women admitted with COVID-19 over three months. Clinical features, laboratory findings and feto-maternal outcomes were assessed. **Results:-** The mean age of the patients was 24 years. Hypertensive disorder of pregnancy was most common associated co-morbidity. Majority of patients (81%) were asymptomatic. Lymphocytopenia was seen in 58% of the patients and 47% had elevated levels of CRP. All patients who presented in first trimester had spontaneous abortion. There is relatively higher rate of preterm birth (21%) and cesarean delivery (43%). All the neonates were tested negative for COVID-19. **Conclusion;-** There is relatively higher rate of cesarean delivery. Overall feto-maternal outcome was good and there was no evidence of vertical transmission.

KEYWORDS

COVID-19, feto-maternal outcomes, clinical chrecterstics, vertical transmission.

Introduction –

Novel coronavirus (SARS CoV-2) was identified as a cause of respiratory tract infection in December 2019, first at Wuhan, China. Within a very short of time, it engulfed the whole globe and hence the WHO declared it as pandemic on March 11, 2020^[1]. Globally, till today there have been 35,347,404 confirmed cases of COVID-19, including 1,039,406 deaths, according to WHO.^[2]

Novel corona virus (RNA virus) infects both humans and animals. Till now, seven different strains of the virus have been identified. Out of them MERS COV (beta corona virus) caused middle east respiratory syndrome of 2012 or MERS, SARS COV (beta corona virus) caused severe acute respiratory syndrome of 2003 or SARS and SARS COV 2 (novel corona virus) causing this COVID – 19 of 2019-2020.^[3] COVID-19 is person to person transmissible and can be transmitted by direct contact, indirect contact and droplet. Feco-oral transmission might be possible as virus has been identified in the stool of the infected personnel.^[4] Even neonates were found to be infected with COVID-19 as reports came from China and London, although it is still unclear whether disease was transmitted in-utero or after birth.^[3]

Many studies till now have shown that pregnant women are not more susceptible to COVID – 19 infection than general population, but despite mounting international experience with COVID-19, the clinical characteristics, feto- maternal outcomes and vertical transmission potentials of COVID-19 infection in pregnant women are still unknown. So it is very important to know the clinical presentation, feto-maternal outcomes and vertical spread of COVID-19 infection in pregnant women, so that we can frame appropriate prevention and management policies for the safety of both baby and mother in pregnant women. Therefore, to facilitate efforts in managing COVID-19 infection in pregnant women we collected and analyzed detailed clinical data and feto-maternal outcomes of pregnant women with confirmed COVID-19 infection at a tertiary care center in Rajasthan, India.

In this study, we present clinical characteristic, laboratory findings and feto-maternal outcomes of pregnant women with confirmed COVID-19 infection.

Methods-

This study is retrospective observational study, conducted at tertiary care center in Rajasthan, India, in the department of obstetrics and gynecology over three months between 27th may 2020 and 27th august 2020 after getting approval from local Ethical Committee.

In this study all pregnant women with confirmed COVID-19 infection, in the defined duration were included. The demographic details including age, parity, period of gestation, associated co-morbidities, clinical characteristics, laboratory investigations and feto-maternal outcomes were noted retrospectively from the medical records kept at medical record section. The data were analyzed for the desired results.

Results:-

In present study, maternal age ranged between 19-40 years. Forty three percent of the patients were primigravida and 57% were multigravida. Most of the patients (85%) reported in the third trimester of pregnancy (28-41 weeks of POG). The most common chief complaint was pain abdomen (71%) followed by leaking per vaginam (LPV), bleeding per vaginam (BPV) and vomiting. One patient was referred for PPH from the periphery, and later she tested positive for COVID-19. Twenty one percent (07/32) of patients had associated co-morbidity. The most common associated co-morbidity was hypertensive disorder of the pregnancy (03/07) followed by hypothyroidism (02/07), bronchial asthma (01/07), appendicitis (01/07) and hepatitis B (01/07) as depicted below in table-1. One patient had both hypothyroidism and bronchial asthma.

Table:-1 demographic and clinical details of pregnant women with COVID-19 infection.

Sr. No.	Demographic and clinical details	No. of patients	Percentage (%)
1	Maternal age(years) (n=32)	Mean age 24 year	
2	Parity (n=32)	Primi gravida (14) Multi gravida (18)	43 57
3	Period of gestation (n=32)	≤ 12 weeks- 02 13-28 weeks- 03 29-41 weeks- 27	06 09 85
4	Chief complain on admission (n=32)	Pain abdomen -23 Leaking per vaginum- 03 Bleeding per vaginum- 03 Vomiting – 02 PPH – 01	72 09 09 06 03
5	Associated co morbidity (n=7)	Hypertensive disorder in pregnancy- 03 Hypothyroidism- 02 Bronchial asthma -01 Appendicitis- 01 Hepatitis B- 01	42.8 28 14 14 14

6	Symptoms: (n=32)	Asymptomatic-26	81
		Symptomatic - 06	19
		Fever -1	16
		Vomiting-2	32
		Diarrhea - 1	16
		Cough & cold- 1	16
		Headache- 1	16

In the present study, majority of patients (81%) were asymptomatic and 19% were symptomatic. The most common symptom was vomiting (02/06) followed by fever (01/06), diarrhoea (01/06), cough & cold (01/06) and headache (01/06).

Table-2 laboratory investigations of pregnant women with COVID-19 infection

Sr. No.	Investigation	Report	Percentage (%)
1	Hemoglobin	7-10 gm/dl - 24 >10 gm/dl - 8	75 25
2	Lymphocyte counts (n=29)	<20% - 17 >20% - 12 Not done for 3 patients	58 42
3	Serum CRP qualitative (n=19)	Positive- 09 Negative - 10 Not done in 13 patients	47 53
4	ECG (n=32)	Within normal limit-26 Sinus tachycardia - 2 T wave inversion- 2 Abnormal Q wave- 2 Arrhythmia- 1	80 06 06 06 03

CRP- C Reactive protein, ECG- electrocardiography

In the present study, we found significant alteration in the laboratory findings of pregnant women with COVID-19 infection. All the patients were anemic, 75% of the patient had moderate anemia, whereas 25% of patients had mild anemia, although none of the patients were severely anemic. Lymphocyte count was done for 29/32 patients, 58% of patients had lymphocytopenia. C- reactive protein (CRP) was done for 19/32 patient, elevated CRP level found in 09/19 (47%). Majority of patients (80%) had normal electrocardiography (ECG). ECG abnormality like sinus tachycardia (06%), T-wave inversion (06%), presence of Q wave (06%) and sinus arrhythmia (03%) were found.

Table-3 fetal-maternal outcomes of pregnant women infected with COVID-19 infection.

Sr. No.	Feto-maternal outcomes	No. of patients	Percentage (%)
1	Mode of delivery (n=32)	LSCS 14 NVD 14 SA 02 ANC 02	43 43 06 06
2	Neonatal COVID-19 RT-PCR report (n=21)	Negative - 21 Not done - 06	100
3	Neonatal maturity (n=29)	Preterm - 06 Term - 23	21 79
4	Neonatal status (n=29)	Shifted to mother side 26 NICU 01 IUD 02	90 03 07
5	Maternal ICU admission and death (n=32)	ICU admission 0 Death 0	

LSCS- lower segment cesarean section, NVD- normal vaginal delivery, SA- spontaneous abortions, ANC- ante natal care, NICU- neonatal intensive care unit, IUD- intra uterine death.

Six percent (02/32) of patient who came in the first trimester had spontaneous abortion, one of them was complicated by appendicitis for which post-abortion she got operated. Another one patient was presented with incomplete abortion and required dilatation and evacuation. Six percent (02/32) continued their pregnancy and were discharged as an antenatal patient. Forty-three percent of the patients had normal vaginal delivery, and equal number of patients (43%) had lower segment cesarean section (LSCS). Neonatal COVID-19 by nasal swab RT-PCR was done for 21/27 neonates and all were negative for

COVID-19. Twenty one percent (06/28) neonates were born as preterm, whereas 79% (22/28) of neonates were born as term. Only 04 % (01/26) of neonates required NICU admission, reason for NICU admission was respiratory distress syndrome on day one of delivery, 96% of neonates did not require any resuscitation and were shifted to mother side. Seven percent (02/28) of fetus were intra-uterine death (IUD). None of the patients required ICU admission and no maternal death occurred.

Discussion

As we all know pregnant women are particularly susceptible to respiratory tract infection because of their immune-compromised status and physiological adaptive changes like diaphragm elevation, increased oxygen consumption and edema of respiratory tract mucosa, which further increases their susceptibility to subsequent respiratory failure – a key concern in relation to COVID – 19 infections in pregnant women.^[5]

Among all 32 patients, maternal age ranged between 19-40 years. Mean age of the patients were 24 years. Antoun L et al^[6] did a prospective study, where mean age of the patients were 29 years (16-40). In the present study, 43% of the patients were primigravida, whereas 57% of the patients were multigravida. A study by Chen H J et al^[7] showed 52% were primigravida and 48% were multigravida. Whereas in a study by Munir SI et al^[4] only 20% of patients were primigravida and 80% of the patients were multigravida. This difference in the age and parity could be because of regional variation.

In our study, majority (85%) of the patients (27/32) were presented in the third trimester of pregnancy, 09% (03/32) of patients presented in the second trimester of pregnancy and only 06% (02/32) of patients presented in the first trimester of pregnancy. These results were similar to Antoun L et al^[6] where 83% of patients presented in the third trimester of pregnancy, while 17% of patients presented in the second trimester of pregnancy. In a study by Munir S I et al^[4] all patients presented in third trimester of pregnancy. In present study, majority of patients were admitted with chief complain of pain abdomen (72%) followed by leaking per vaginum (09%), bleeding per vaginum (09%) and vomiting (06%). One patient (03%) delivered at primary health care center later referred to our center in view of postpartum hemorrhage, tested positive for COVID-19.

In the present study, 21% of patients were found to be associated with co-morbidity. The most common associated co-morbidity was hypertensive disorder of pregnancy in 43% (03/07) of patients followed by hypothyroidism (02/07), asthma (01/07), one case of appendicitis (01/07) and HbsAg positive. Among these cases, one patient had both asthma and hypothyroidism. One patient got admitted with diagnosis of appendicitis for which later she got operated. These data were in-consistent with data from a study by Antoun L et al^[6] where 48% (11/23) of patients were associated with co morbidity; the most common associated co morbidity was diabetes mellitus (04/11), acute kidney injury (03/11), asthma (02/11), hyperthyroidism (01/11) and pyelonephritis (01/11). Results of our study were consistent with study by Nan yu et al^[8] where 29% of patient had chronic disease (hypothyroidism and PCOD), it has been documented that in general population COVID-19 patient with underlying medical condition like hypertension, diabetes mellitus, COPD, asthma and malignancy have shown increased hospital admission rates, ICU admission and mortality.^[9] so similarly pregnant women with underlying medical condition requires more liberal testing to prevent adverse fetal maternal outcomes associated with COVID-19 infection.

In our study, 81% of the total patients (26/32) were asymptomatic and presented to gynecology receiving room or OPD with labour related complains. As in our hospital, we recommended that all women presenting to the hospital for delivery to be tested for SARS CoV-2 by RT-PCR test on admission, so accidentally they were found to be positive and shifted to the designated ward for the same. So it is reasonable to suspect that asymptomatic COVID-19 presentation are common and responsible for substantial contribution to spread of disease and currently there is no easy way to predict COVID-19 infection in asymptomatic patients. Presenting symptoms were vomiting (02/06), fever (01/06), diarrhea (01/06), cold and cough (01/06) and headache (01/06). None of the patients complained for difficulty in breathing or myalgia. None of our patients required intensive care unit admission and no death occurred. These results are contrary to study by Munir S I et al^[4] where the most common

symptoms was fever, followed by cough, myalgia, diarrhea and shortness of breath. These results were again inconsistent with Antoun L et al^[6] where 17% (04/23) patients had severe adult respiratory distress syndrome, complications and required ICU support and one of these led to maternal death. This difference in the presenting symptom could be because of variation in population ethnicity and small study sample size.

In the present study, 100% of patient were anemic although none of them had severe anemia, 25% of patients (10/32) had mild anemia whereas 75% of patients (22/32) had moderate anemia. Sixty percent of patient were anemic by a study by Munir S I et al^[4], so this suggests that anemia could be one of the important risk factors for the COVID-19 infection in pregnant women.

In our study, lymphocyte counts was done for 29/32 patients and 12/29 (41%) patients had lymphocytopenia, whereas 58.6% of the patients had normal lymphocyte counts. Serum C-reactive protein (CRP) was done for 19/32 patients among them 9/19 (47%) patients had elevated serum CRP levels. These results were contrary to study by Munir SI et al^[4] showed only 21% of patients had raised serum CRP and lymphocytopenia. Another study by Dong L et al^[10] showed lymphocytopenia was found in 59% of the patients and elevated CRP was found in 70% of patients. As human corona virus associated myocarditis is known and a number of COVID-19 related cases have been reported. A clinical finding of COVID-19 associated myocarditis includes changes in electrocardiography (ECG), cardiac biomarkers and impaired cardiac function so in our study ECG was done for all patients with COVID-19 infection. Although in our study, 26/32 (81%) patients had a normal ECG reading. Two out of six patients had sinus tachycardia, 02/06 had T wave inversion, Q wave was present in 02/06 patients and 01/06 patient had sinus arrhythmia.

In the present study, all the patients who presented in their first trimester had spontaneous abortion. Six percent patients (02/32) were discharged as antenatal patients. Forty three percent (14/32) of patients delivered by normal vaginal delivery and equal number of the patients (14/32) were delivered by lower segment cesarean section (LSCS). Indications for cesarean sections were antepartum hemorrhage (03/14), fetal distress (03/14), failed induction of labour (02/14), malpresentations (02/14), cephalo-pelvic disproportion (02/14) and previous cesarean section with scar tenderness (02/14). These finding of present study were not comparable to many studies where 100% of pregnant women with COVID-19 infection were delivered by cesarean section.^[6,4,8]

In this study, 21.4% (06/28) patients had preterm vaginal delivery whereas, 78.6% (23/28) patients delivered at term. In our study, cohort, we had 28 pregnant women with confirmed COVID-19 infection in their 3rd trimester, delivered 29 neonates (27 singletons and one twin) and out of them two neonates were still born. Nasal swab RT-PCR was performed for 21/27 (78%) neonates on day 5 of birth. All neonates were negative for COVID-19. RT-PCR could not be performed for 06/27 neonates because these patients had given the undertaking for home isolation and were early discharged on request and could not be followed up for neonatal COVID status.

Conclusion-

In our study, hypertensive disorder of pregnancy was the most common associated co-morbidity. Pregnant women with co-morbidity are slightly more prone to contract COVID-19 infection, so liberal testing of COVID-19 is required for these patients to prevent adverse fetomaternal outcomes. Majority of our patients were asymptomatic so we suspect that these are substantial contribution to disease spread and early identification of asymptomatic cases can be an important step towards minimizing spread of the disease. Anemia in pregnancy could be one of the important risk factors for COVID-19 infection as all (100%) of our patients were anemic. Pregnant women, in the first trimester had poor pregnancy outcomes as in our study, all patients, who presented with COVID-19 infection in their the first trimester of pregnancy had spontaneous abortion. There is relatively higher rate of preterm birth and cesarean section delivery in pregnant women with COVID-19 infection. It seems that COVID-19 infection is not vertically transmittable as all the neonates were negative for COVID-19 by RT-PCR, although our study sample size was small so further studies will be recommended to establish this. So ultimately, our finding can provide an additional guidance to enhance prenatal

counseling of the patients with COVID-19 infection during pregnancy.

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