



STUDY OF CORONA VIRUS DISEASE IN PREGNANT WOMEN AT TERTIARY CARE HOSPITAL.

Gynaecology

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ABSTRACT

Objective: To study the course of SARS-Co-V-2 infection in pregnant women and to study the maternal and perinatal outcome in affected women.

Material & Methods: This was a prospective observational study conducted at Government Medical College & Hospital, Aurangabad during study period of 3rd May to 13th June 2020. All SARS-Co-V-2 infected pregnant women admitted in hospital were included in the study. Clinical history, examination, laboratory findings and imaging records were reviewed and documented. The course of disease was monitored and managed as per standard operative procedures of the department. Maternal outcome and perinatal outcomes were noted. The data was collected and analyzed using appropriate statistical test.

Results: 54 cases were confirmed to have SARS-Co-V-2 infection. Asymptomatic pregnant women were noted to be 77.77%. The course of disease was severe in 3.70% and critical in 1.85% mothers. Preterm delivery was noted in 24.07%. The caesarean section was done in 29.72% cases for obstetric indication. One maternal mortality (1.85%) was attributed to uremic encephalopathy with cytokine storm. Out of 5 (14.82%) babies admitted in NICU, 4 recovered and one died. Two (5.71%) babies were found to be infected with SARS-Co-V-2 infection on 5th day of birth.

Conclusion: SARS-Co-V2 infection during pregnancy was not associated with an increased risk of severity of the disease progression and did not affect the course of pregnancy and perinatal outcome. Vaginal delivery did not increase the risk of mother to child transmission of infection. Exclusive breast feeding with appropriate hand hygiene was being practiced safely.

KEYWORDS

COVID 19 pandemic, SARS-Co-V-2, pregnant women, maternal outcome, perinatal outcome

INTRODUCTION:

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global public health emergency. Coronaviruses are enveloped, non-segmented, positive-sense RNA viruses belonging to the family Coronaviridae, order Nidovirales¹. In December 2019, the novel coronavirus COVID-19 was first reported in Wuhan, Hubei province, China². The World Health Organization declared the same, a pandemic on 11 March 2020. We are well into the pandemic now, with the virus being at different stages of spread in different countries.

Viral pandemics threaten the general population including pregnant women. Pregnancy represents a unique immune condition that is modulated, but not suppressed. In previous pandemics such as SARS and H1N1, pregnant women were more susceptible to serious illness and had greater mortality rates than the general population³. The report from the World Health Organization (WHO) on March 3, 2020, estimated the global mortality rate of COVID-19 to be 3.4%⁴ although recent reports that have used appropriate adjustment for the case

ascertainment rate and time lag between symptoms onset and death suggest the mortality rate to be lower at 1.4%⁵. Pregnant women are especially susceptible to respiratory pathogens and severe pneumonia, because of the physiological changes in the immune and cardiopulmonary systems (eg, diaphragm elevation, increased oxygen consumption, and edema of the respiratory tract mucosa), which can render them intolerant to hypoxia. In 2003, it was reported that approximately 50% of pregnant women who received a diagnosis for SARS-Co-V were admitted to the intensive care unit (ICU), around 33% of pregnant women with SARS-Co-V required mechanical ventilation, and the mortality rate was as high as 25% for these women⁶. In 2009, pregnant women were reported to be at an increased risk for complications from the pandemic H1N1 2009 influenza virus infection, with a higher estimated rate of hospital admission than in the general population⁷.

There are still uncertain aspects of this novel infection even as research and medical trials are progressing furiously. Although data on COVID-19 continues to inform our understanding of this disease, pregnancy-specific information remains limited⁸.

Pregnant woman are a vulnerable group and as of now, not much is known about the vertical transmission of the virus in SARS-Co-V-2 positive mothers. Breastfeeding is one of the most important aspects of childbirth and transmission of the virus through it is yet to be evaluated.

Hence, to improve our understanding about the clinical characteristics of pregnant women with the disease and the impact of the current COVID-19 outbreak on the affected pregnant women in Marathwada region of Maharashtra, we, hereby, present our experience with SARS-Co-V-2 infected pregnant mothers.

Aims & Objectives:

- To study the course of SARS-Co-V-2 infection in pregnant women.
- To study the maternal outcome
- To study the perinatal outcome

Material & Methods:

This was a prospective observational study conducted in the Department of Obstetrics and Gynecology, Government Medical College & Hospital, Aurangabad between the study periods of 3/5/2020 to 13/6/2020.

Inclusion criteria: All SARS-Co-V-2 infected pregnant women admitted in hospital and willing to participate in study.

Exclusion criteria: SARS-Co-V-2 infected mothers delivered outside and then referred to our hospital and brought dead cases.

All pregnant women coming from high containment area were tested for SARS-Co-V-2 infection as per Indian Council of Medical Research (ICMR) guidelines. Maternal nasopharyngeal swabs were collected and sent to Viral Research and Diagnostic Laboratory, Department of Microbiology, Government Medical College, Aurangabad in appropriate viral transport media (VTM) and tested for RT-PCR Biorad

cfx96. After applying inclusion & exclusion criteria and after obtaining the written informed consent, all SARS-Co-V-2 infected pregnant women were included in the study and admitted in isolation ward where PPE kit, N-95 face mask and face shield was compulsorily used by on duty health care providers (HCPs) and surgical face mask by infected mothers. Clinical history, examination, laboratory findings and imaging records were reviewed and documented. All cases underwent in-depth verbal interview regarding the source of contact. The course of disease was monitored and managed in co-ordination with physician and labour was monitored and managed as per standard operative procedures of the department. The decision for mode of delivery was taken by the senior obstetrician. The laboring women were given the freedom of choice regarding birthing positions. Only one birth companion was allowed and she was counseled regarding the importance of social distancing, appropriate hand hygiene, wearing of N-95 mask along with the danger signs and symptoms of labour. The mothers were counseled about the breast feeding practices to avoid perinatal transmission of infection like breast feeding with appropriate hand hygiene practices, expressed breast milk and formula feeding. The breast feeding practices opted by mother were respected. The neonate throat swab was tested at the end of 24 hours of birth and on day 5.

Maternal outcome was noted in the form of gestational age at the time of delivery, mode of delivery and maternal morbidity & mortality. For academic purpose, maternal nasopharyngeal swabs were tested on day 10 and if positive repeated on day 14 of admission.

After diagnosis of every case, risk assessment of HCPs was performed by institutional committee and testing was done as per risk assessment score.

Neonatal outcome was noted in the form of weight of baby, Apgar score, neonatal morbidity and mortality and SARS-Co-V-2 infection.

The data was collected and analyzed using appropriate statistical test.

Observations:

Table1: Baseline Characteristics of SARS-Co-V-2 infected pregnant mothers:

Characteristics	Number of SARS-Co-V-2 infected pregnant mothers (n=54)	Percentage (%) of SARS-Co-V-2 infected pregnant mothers (n=54)
Age in years	≤30	43
	>30	11
Parity	P0	21
	P1	10
	P2-P4	15
	≥P5	08
Gestational age in weeks at the time of diagnosis	≤12	04
	>12-28	06
	>28-37	14
	>37-42	30
Co morbidities	Heart disease	01
	Hypothyroidism	02
	Obesity	09
COVID positive contact	Known	07
	Unknown	47
H/o receiving Flu Vaccination	Received	00
	Not received	54
Symptoms	Asymptomatic	42
	Dry cough	01
	Sore throat	02
	Dyspnea	02
	Fever	06
	GI symptoms	03
	Malaise, headache, fatigue	02
Signs	Respiratory rate >20/min	03
	Heart rate >100/min	02
	Oxygen saturation <95%	03
	Temperature >100.04 F	06
Laboratory Parameters	Hemoglobin <11 gm	28
	D-dimer >250 ng/ml,	03
	LDH ≥220U/L	02
	Coagulation profile deranged	02
Treatment received	Antibiotics	28
	Antiviral	02
	Hydroxychloroquine	10

	Oxygen support	03	5.55
	Ventilator support	01	1.85
	Any Other(Dialysis)	01	1.85

Table 2: Distribution according to Maternal Outcome:

Maternal Outcome			Number of SARS-Co-V-2 infected pregnant mothers	Percentage (%)of SARS-Co-V-2infected pregnant mothers
Gestational Age at the Time of termination of pregnancy in weeks (n=41)	≤24		04	9.75
	>24-37		13	31.70
	>37-40		21	51.21
	>40		03	7.31
Course of Pregnancy (n=54)	Tubal Pregnancy		01	1.85
	Abortion		03	5.55
	Preterm delivery		13	24.07
	Full term delivery		24	44.44
	Ongoing pregnancy		13	24.07
Mode of Delivery (n=37)	Vaginal Delivery		26	70.27
	Caesarean section		11	29.72
Maternal Complication (n=54)	No complication		51	94.44
	Complication	Abruptio with DIC	01	1.85
		AKI	01	1.85
		Hypoxemia	01	1.85
Maternal Mortality			01	1.85

Table 3: Distribution according to Perinatal Outcome:

Perinatal outcome		Number of SARS-Co-V-2 infected pregnant mothers	Percentage (%)of SARS-Co-V-2infected pregnant mothers
Nasopharyngeal swab test of Neonate (n=35)	Negative	33	94.28
	Positive	02	5.71
Baby weight in grams (n=37)	<500	01	2.70
	>500 -1500	02	5.40
	>1500-2500	10	27.02
	>2500	24	64.86
Apgar at 5' (n=35)	≤7	05	14.28
	>7-10	30	85.71
Admission to NICU	Required	05	14.28
	Not required	30	85.71
Perinatal complications (n=35)	Complication	01	2.85
	No complication	34	97.14
Perinatal Outcome (n=37)	Live Birth	34	91.89
	Still Birth	02	5.40
	Perinatal Death	01	2.70
Breast Feeding Practices opted by Mother (n=34)	Exclusive breast feeding	19	55.88
	Expressed Breast Milk	12	35.29
	Formula feed	03	8.82

RESULTS: Out of 509 pregnant women coming from high containment area, 54 cases were confirmed to have SARS-Co-V-2 infection by RT-PCR giving an incidence of 10.60%. Out of these 54 cases, 30 were at term and remaining 24 were admitted in hospital for various obstetric conditions.

TABLE 1: Amongst 54 SARS-Co-V-2 positive pregnant women, 43(79.62 %) were less than 30 years of age, 23(42.59 %) were multiparous and 44(81.42%) were diagnosed in third trimester. Obesity is the most common co-morbidity noted in 9(16.66%) cases. H/O known COVID positive contact was traced in only 7(12.96%) cases. Not a single women received flu vaccination during antenatal period. Forty two (77.77%) pregnant women were asymptomatic at time of diagnosis and 6 out of 12 symptomatic mothers reported with febrile illness. Oxygen saturation was less than 95% in 3(5.5%) pregnant women. D dimer was deranged in 3(5.5%) ,3(5.5%) cases required high flow oxygen and 1(1.85%) required ventilatory support. Chest X-ray finding were found to be within normal limits in women having respiratory symptoms.

TABLE 2: Out of 41 SARS-Co-V-2 positive pregnant women, 24(58.52%) delivered after 37 weeks of gestation, 13(31.70%) underwent preterm delivery, 3 (5.55%) were spontaneously aborted and one (1.85%) required exploratory laparotomy for ruptured ectopic pregnancy. Thirteen (24.07%) pregnant women were having ongoing pregnancy. Out of 13 cases of preterm delivery, 7 went in spontaneous labour and 6 required induction of labour for various obstetric

indications like preeclampsia, abruptio placenta, IUFD. Out of 37 delivered cases, 11(29.72%) required caesarean section for obstetric indication. The course of pregnancy was uneventful in 94.44% pregnant women and complications were developed in 3(5.5%) cases. Amongst them one case was an obstetrics complication and other 2 were due to SARS-Co-V-2 infection. Three cases (5.55%) required high flow oxygen supplementation with one of them requiring further ventilatory support. The one woman requiring ventilatory support also had acute kidney injury. She succumbed to uremic encephalopathy with cytokine storm.

TABLE 3: Amongst 37 babies delivered, 2 (5.40%) were still birth, 34(91.89%) were live births and one case of perinatal mortality(2.70%) due to severe perinatal asphyxia with GRADE 3 HIE. Around 24(64.86%) babies had baby weight >2500gm . APGAR<7 was noted in 5(14.28%) babies and these babies required NICU admission. Four babies who recovered were preterm and one died birth asphyxia.

Exclusively breast feeding was done in 19(55.88%) cases , Expressed Breast Milk in 12(35.29%) babies and formula feed was given in 3(8.82%). Two babies who were on exclusive breast feeding tested positive on day 5 for SARS-Co-V-2 and were managed conservatively.

Impact on Health care providers(HCPs): While managing these pregnant mothers, around 3 HCPs got infected. Out of them 2 were presented with fever and one required oxygen supplementation for hypoxia. All three HCPs recovered from this infection and doing well.

DISCUSSION:

India-the world's second-most populated country is witnessing a rise in confirmed Covid-19 cases. The whole world has to be prepared for the ongoing transmission of infection for many months and for perhaps years to come.

The present study showed the clinical maternal evolution of SARS-Co-V-2 infection among 54 hospitalized pregnant women in Marathwada region of Maharashtra, India. Most pregnant women were diagnosed to be infected with SARS-Co-V-2 in third trimester (81.42%). Four pregnant women (7.40%) were admitted in first trimester of pregnancy, one of them required laparotomy for ruptured ectopic pregnancy and three underwent abortion. Known history of COVID positive contact was traced in 7 cases only. Majority of pregnant women were asymptomatic (77.77%). Symptoms at the time of diagnosis were reported in 16(29.62%) cases. The most frequent symptom noted was fever in 6(11.11%) followed by GI symptoms in 3(5.55%) cases.

Infection with SARS-Co-V-2 caused severe disease in 2(3.70%) cases and in one case (1.85%) developed critical illness and required intensive care management. She needed dialysis for acute kidney injury and ventilatory support and ultimately succumbed to uremic encephalopathy with cytokine storm.

In present study, the main co-morbidities associated with infection included obesity in 9 (16.66%) cases, hypothyroidism in 2(3.70%) and heart disease in 1(1.85%). No case of gestational or overt diabetes and chronic hypertension was noted. Anemia was the commonest medical disorder observed frequently in 28(51.85%) cases followed by hypertensive disorders in pregnancy in 4(7.40%) cases. Out of 13(24.07%) cases of preterm delivery, 7 cases underwent spontaneous labour and 6 cases required induction of labour for obstetric indication like pre-eclampsia, abruption, intrauterine fetal demise. No case was induced due to severe course of disease. It was noted that 70.27% cases infected with SARS -Co-V-2 had successful vaginal delivery and 11(29.72 %) required caesarean section. In all cases caesarean section was done for an obstetric indication. No case of maternal respiratory indicated urgent delivery was noted. Course of delivery was uneventful in 51(94.44%) cases and complications developed in 3(5.55%) cases. In one case abruption with DIC and in other two cases acute kidney injury and hypoxia were noted. It was observed in the study that 34 (91.89%) had live birth, 5(14.82%) required NICU admission and one early neonatal death occurred due to perinatal asphyxia with grade 3 HIE following emergency LSCS for obstructed labour. All live babies were tested for SARS-Co-V-2 and 2 (5.71%) babies were reported to be positive on day 5 swabs. Both these babies were infected probably due to violation of hand hygiene at the time of breast feeding.

There was no currently validated treatment to control SARS-Co-V-2 in pregnancy. All the cases were treated on individual basis as per the course of disease.

While managing all these cases, 3 HCPs developed symptoms and tested positive. Two of them had mild disease and one HCP developed severe disease requiring oxygen supplementation.

No study reported the impact of SARS-Co-V-2 infection on HCPs while managing pregnant women.

In a study of 77 cases conducted by Savasi et al⁹ from Italy, reported that 14 had severe disease (18%). Two thirds of the patients in the cohort were admitted during the third trimester, and 84% were symptomatic on admission. Eleven patients underwent urgent delivery for respiratory compromise (16%), and six were admitted to the ICU (8%). One woman received extracorporeal membrane oxygenation; no deaths occurred. Preterm delivery occurred in 12% of patients, and nine newborns were admitted to the neonatal intensive care unit. Patients in the severe subgroup had significantly higher presentational body mass indexes (BMIs) and heart and respiratory rates and a greater frequency of fever or dyspnea on admission compared with women with a nonsevere disease evolution. They concluded that one in five women hospitalized with COVID-19 infection delivered urgently for

respiratory compromise or were admitted to the ICU.

In a retrospective study of 116 cases conducted by Jie Yan et al¹⁰ from China, the median gestational age on admission was 38+0 weeks. Thirty eight cases(32.85) reported contact with infected persons. The most common symptoms were fever (50.9%) ,cough (28.4%) and 23.3% patients presented without symptoms. Of these 116 cases, there were 8 cases (6.9%) of severe pneumonia but no maternal deaths. One of 8 patients who presented in the first trimester and early second trimester had a missed spontaneous abortion. Of these 99 patients, 21 (21.2%) who delivered had preterm birth, including 6 with preterm premature rupture of membranes. The rate of spontaneous preterm birth before 37 weeks' gestation was 6.1% . One case of severe neonatal asphyxia resulted in neonatal death. Furthermore, 86 of the 100 neonates tested for SARS-Co-V-2 had negative results. They concluded that SARS-Co-V- 2 infection during pregnancy is not associated with an increased risk of spontaneous abortion and spontaneous preterm birth. There is no evidence of vertical transmission of SARS-Co-V-2 infection when the infection manifests during the third trimester of pregnancy.

In a study conducted by Chen L et al¹¹ from Chiana, the most common symptoms in 112 women were fever (in 75%) and cough (in 73%). A total of 109 of 118 women (92%) had mild disease, and 9 (8%) had severe disease (hypoxemia), 1 of whom received noninvasive mechanical ventilation (critical disease). Severe disease developed in 6 of the 9 women after delivery, and the woman who received noninvasive mechanical ventilation did so after delivery. There were no deaths. There were 3 spontaneous abortions, 2 ectopic pregnancies, and 4 induced abortions . A total 58% delivered during the study period and had 70 births (2 sets of twins). Of these 68 patients, 63 (93%) underwent a cesarean section; in 38 of 63cases (61%), the procedure was performed because of concern about the effects of Covid-19 on the pregnancy. A total of 14 deliveries (21%) were premature; 8 were induced (7 owing to concern about Covid-19). No babies had neonatal asphyxia. Testing for SARS-CoV-2 was performed on neonatal throat swabs of 8 newborns and breast-milk samples of 3 mothers. No positive results were reported.

In present study, the rate of caesarean section was less as compared with other studies^{9,10,11}. This may be attributed to counseling of the expectant mother helping them to understand the delivery process both physical and physiological , the presence of birth companion helps reduce anxiety and provide emotional support during delivery as well as identify warning signs and symptoms earlier, providing option for various birthing positions that suit the comfort of the mother give greater success in vaginal delivery. Training resident doctors and staff nurse in respectful maternity care bridge the communication gap between doctor and pregnant mother, these non-clinical interventions are cost effective ways to help reduce caesarean rates along with mild course of disease in most of pregnant mothers. Application of these protocols has helped us reduce caesarean sections conducted at the institute.

The rate of preterm deliveries and consistent with other studies was similar to other studies^{9,10,11}. The course of disease were severe and critical in studies from China and Italy as compared to our study as most of our pregnant mothers were asymptomatic. We reported one death while there were no deaths in studies from Italy and Chiana .

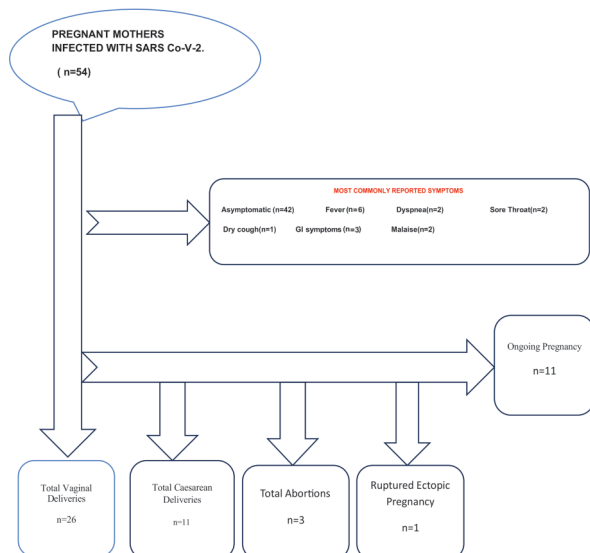
Limitations of study: The present study was of short duration, single centered. The follow up of 13 cases of ongoing pregnancy after resolution of SARS-Co-V-2 infection was not included in the study. We understand that during a pandemic, the intention to share data rapidly might have an impact on the quality of published primary reports but helps in quality improvement in management of infected mothers.

CONCLUSION:

SARS-Co-V-2 infection during pregnancy was not associated with an increased risk of severity of the disease progression. SARS-Co-V-2 infection apparently did not affect the course of pregnancy and perinatal outcome. Vaginal delivery did not increase the risk of mother to child transmission of infection. Caesarean delivery was required only for obstetric indication. Exclusive breast feeding with appropriate

hand hygiene was being practiced safely.

Flow Chart:



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