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Review Article

Managing Pregnancy in Covid-19 Pandemic

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ABSTRACT

Introduction: The outbreak Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a highly contagious and lethal beta coronavirus SARS-CoV-2, which has spread fast to become a pandemic. Pregnancy alters body physiology and immune systems, can have worse effects of some respiratory infections and due to limited research and published data we still are in dilemma of appropriate management guidelines. This article covers the updated guidelines for infection prevention and control (IPC), screening, sampling ,, antenatal visit schedules, risk scoring, triaging, supportive care, delivery, postpartum care and care of the newborn. Aim and Objectives: This article aims to provide up-to-date information as per recent guidelines of various association which would serve as guidance in managing pregnant women and newborn with suspected or confirmed COVID-19. Material and Method: All the published papers till date, NCPRE [i], WHO Interim guidelines [iii], RCOG [iv], FOGS GCPRI [vi], Medical Council of India [vii], ICMR [xiii], MOFHW [xv], CDC [xxxv], ACOG [xxxvi] guidelines are referred to compile this article to reach to a conclusion of evidence based management of pregnant ladies during Covid-19 pandemic. Conclusion: Data is very limited and hence very difficult to accurately define clinical management strategies and needs to be constantly updated.

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Introduction

The outbreak Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a highly contagious and lethal beta coronavirus SARS-CoV-2, started in Wuhan, China in December 2019 which has spread fast to become a global public health threat.^{1,2}

WHO situation reports as provided on July 3rd,2020 as total of 10 357 662 cases and 508 055 deaths. The epidemic has spread to more than 213

countries around the world.³

Research is currently underway and because of limited data it is difficult to differentiate the impact of COVID-19 pregnant woman and general population as pregnancy leads to changes in their bodies and immune systems, can have worse effects of some respiratory infections. Pregnancy is a condition with altered immunologic and physiological state hence women with suspected or confirmed COVID-19 should have a rational step wise approach while treating them on outpatient basis or requiring indoor patient management Although guidelines and recommendations are constantly being revised and updated by various association and bodies this article aims to enlighten with updated clinical management protocol which could serve as guidance in managing pregnant women and newborn with suspected or confirmed COVID-19 and by no means it is meant to replace clinical judgement or specialist consultation. This article covers the not only infection prevention and control (IPC) guidelines, screening and sampling guidelines, antenatal visit schedules, risk scoring, triaging but also in-patient supportive care, delivery, postpartum care and care of the newborn.

Effect of COVID 19 Infection on Mother and foetus

Pregnancy is an immuno-compromised condition and hence might be that due to altered immunological and physiological condition some viral respiratory infections cause more severe symptoms like pneumonia and marked hypoxia and this might be the same for COVID-19.⁴ This is particularly true in 3rd trimester of pregnancy and specifically those having comorbidities such as diabetes, chronic lung disease, hypertension, obesity and advanced age. ^{5,6}

But with currently we have no proven evidence to certify that pregnant women are more susceptible to COVID 19 infection than other healthy general population. Majority of pregnant women are asymptomatic or present with influenza like illness.⁸ Considering that the potential of SARS-CoV-2 to cause severe obstetric and neonatal adverse outcomes is unknown,

rigorous screening of suspected cases during pregnancy and long-term follow-up of confirmed mothers and their neonates are needed.8 No reliable evidence has been provided in support of the possibility of vertical transmission of COVID-19 infection from mother to baby. The outcomes are consistent with previous reports. But all these studies only assessed a small number of cases.^{19,10} Virus has not been detected in Amniotic fluid, cord blood, neonatal throat swabs, placenta swabs, genital fluid and breast milk samples of COVID-19 infected mothers.^{6,10} No published data suggesting Covid-19 infection might increase chance of foetal loss or teratogenicity if mother acquired infection at time of organogenesis¹¹ hence there is no rationale for recommending amniocentesis to detect foetal infection at this time.9 Though Liang et al quoted that infection if acquired in later gestational age may increase chance of premature rupture of membranes, preterm delivery, foetal tachycardia and foetal distress more data awaited to finally confirm this finding.¹² Prematurity can be iatrogenic due to maternal medical condition.

Assessment and risk scoring in pregnant women (not in labour) with COVID-19 infection

Proper screening of patients, a good systemic and obstetric examination to rule out co morbidities and ensure safe confinement. The criteria for testing are same for antenatal women as for the general population and is as per ICMR guidelines to ensure uniformity in assessing and treating the patients^{6,13}

The WHO - Global surveillance for COVID-19 (Interim guidance 20 March 2020) and Ministry of Health and Family Welfare has defined who are suspect, contacts, and confirmed cases.^{14,15}

Clinical Presentation of COVID-19 in Pregnancy

Incubation period ranges from 5 to 11 days of exposure[]. Most common presentation would be influenza like illness like fever, fatigue, sore throat running nose, nasal congestion myalgia, dry cough, and shortness of breath. As per Medical current Indian Council of Medical Research updates some might also present with abdominal pain, diarrhoea,

nausea, vomiting, cough with expec-toration haemoptysis and chest pain. Those with comorbid or immuno-compromised may develop severe acute respiratory illness (SARI), hypoxia requiring ventilatory support.¹⁷

The disease severity is classified by WHO based on the clinical symptoms.¹⁸

Pregnant women suspected of COVID-19 (history of international travel, close contact of confirmed covid-19 case <1 metre distance and >15 min exposure, living together or exchange of body fluids) should be promptly isolated and further investigated and depending upon severity of illness on clinical evaluation should be triaged and put into following categories:^{12,19}

- 1. **Mild** symptomatic patient with stable vital signs.
- 2. **Severe** respiratory rate >30 per minute, resting saturation (SaO2) <93% oxygen concentration (FiO2) <300 mm HG.
- 3. Critical- shock with organ failure, respiratory failure requiring mechanical ventilation or refractory hypoxemia requiring extracorporeal membrane oxygenation.

Pregnant women admitted in Intensive care Unit need to be assessed using Quick sequential organ failure assessment score qSOFA score as an adjunct for decision making in management of these in patients.⁶

Test methods and facilities

Patients with suspected/confirmed COVID19 positive (by RT-PCR) both symptomatic and asymptomatic needs to be immediately admitted to a negative pressure isolation ward Covid hospital with adequate facilities and multi-disciplinary expertise to manage critically ill patients.¹² The recent ICMR guidelines released in May, 2020 is now recommending home isolation for asymptomatic patients and those with mild illness but with strict isolation guidelines and to see medical care if symptoms appear or worsens. Once suspected or admitted the CDC recommends collection of a nasopharyngeal swab specimen to test for COVID-19¹⁹ but sample can also be obtained

from saliva, oropharyngeal or if required from lower respiratory tract (sputum, endotracheal aspirate, or bronchoalveolar lavage).SARS-COV-2 the etiologic agent of COVID-19, viral nucleic acid is detected by reverse-transcription polymerase chain reaction (RT-PCR) which is the gold standard for diagnosis of active infection. Many rapid and easy -to-use devices are being developed but they still need to be validated before use.^{13,20} There are more than 114 ICMR approved public laboratories government has permitted testing in private laboratories from 22 March 2020.^{13,21}

Other tests:

- 1. Rapid diagnostic tests based on antigen detection detects the viral proteins expressed by the COVID 19 virus in a sample from respiratory tract.
- 2. Rapid diagnostic test based on host antibody detection detects the presence of antibodies in the blood of believed to be infected with COVID-19.²²⁻²⁴

Assessing the disease process

Peripheral white blood cells lymphocyte count, platelet count remains normal and then may reduce in later stages. C-reactive protein, liver enzymes and creatine phosphokinase may be increased. Radiographic investigation pertaining to COVID19 e.g. Chest Xray and CT scan are a part of initial assessment and shouldn't be delayed because of foetal concerns. Radiological pictures of viral pneumonia were found in many COVID-19 infected pregnant women.25 Computed tomography (CT) scan of the chest without contrast is useful tool to confirm or rule out viral pneumonia and must be performed in suspected cases with abdominal shield to avoid radiation exposure to the foetus. Recently it has also been reported greater sensitivity of chest CT in diagnosing COVID-19 than that of RT-PCR (98% vs 71%).²⁶

Other investigations like Electrocardiography, Computed Tomography Pulmonary Angiogram, full sepsis screen should be used in indicated cases to assert the differential diagnosis.²⁶

Arterial blood gas, serum lactate, Renal Function Test, Liver Function Test and cardiac enzyme assessment are also indicated to our septic shock, acute kidney injury or virus-related cardiac injury.^{12,26}

Management of Covid-19 pregnant

- Supportive therapy

Titration of oxygen flow can be done to keep saturation level > 94% among pregnant patients with inhaled oxygen (60-100% concentration at an initial rate of 4 L/min which can be increased up to 10-15 L/ min. Some cases like ARDS or patients with SARI may warrant intubation, , extra-corporal membrane oxygenation (ECMO), with lateral decubitus positioning to maintain oxygenation.^{13,26-28} High flow Nasal Oxygen (HFNO) and Non-invasive ventilation (NIV) should be reserved for patients with hypoxemic respiratory failure.²⁹

Fluid management can be started with bolus doses of 250-500ml of crystalloid fluid. Caution should be applied with regular assessment of fluid overload.^{26,29} Apart from fluid management adequate rest, nutritional support and electrolyte balance should be ensured.^{6,13}

- 3. Symptomatic management with NSAIDS like paracetamol is safe and preferred.¹³
- 4. Antibiotics can be started if there is indication with raised white cell counts or suspicion of secondary bacterial pneumonia.^{6,8,26}

Steroid i.e. betamethasone 12 mg IM is indicated in preterm delivery (especially before 30 weeks) as there is no documented evidence of harm in context of COVID-19.^{13,26,28,29} However, the use of steroids needs to be individualized. On one hand Steroid use in COVID 19 pneumonia has shown to delay the viral clearance on the other hand short-term (3-5 days) administration of methylprednisolone (1-2 mg/Kg body weight per day) has been used frequently in China in SARI to suppress virus induced lung inflammation causing hypoxaemia, dyspnoea and ARDS.^{13,23,29}

6. Covid specific therapy- Combination therapy for oral capsule of antiproteases Lopinavir/ Ritonavir (200 mg/50 mg per capsule) twice daily together with nebulization with áinterferon inhalation (5 million IU in 2 mL of sterile water) twice a day has been the preferred drug regimen being relatively safe in pregnancy but still being investigated for efficacy.^{6,19} CDC as updated on 16th June 2020 recommends use of Remdesivir in hospitalized patients with severe Covid19.³⁰

Hydroxychloroquinein a dose of 600 mg (200 mg thrice a day with meals) and Azithromycin (500 mg once a day) for 10 days has been shown to give virological cure on day 6 of treatment in 100% of treated patients in one study. Alternative dosage regimens for hydroxy-chloroquine are, to give 400 mg twice a day on day 1 and then 400 mg once a day for the next four days. Chloroquine as an alternative at a dose of 500 mg twice a day for 7 days can also be used. Oseltamivir 75 mg twice daily along with hydroxychloroquine for five days is another regime of trial in covid-19 patients.^{28,29} The current CDC guidelines as updated on June 16th, 2020 recommends use of Hydroxychloroquine only for prophylaxis and does not to be given routinely for treatment of Covid 19 patients.

Antepartum Care of Pregnant Patients: As per ICMR Guidance for Management of Pregnant Women in COVID-19 Pandemic and supported by FOGSI GCPR.⁶ Telehealth needs to be promoted and to cut down necessary antenatal visits to minimum of 3-4 at the discretion of the maternal care provider at 12, 20, 28 and 36 weeks of gestation, unless they meet current self-isolation criteria. (8 weekly check-up).

For women who have had symptoms, defer routine antenatal check-up until 7 days after the start of symptoms, unless symptoms (aside from persistent cough) become severe. DFMC to be maintained. For women who are self-quarantined due to any possible reasons and not developing any symptoms of COVID-19, next appointment should be after 14 days but if any woman did not turn up for more than 3 weeks of their scheduled visit must be contacted.

Any women previously tested negative for COVID-19 but develops with symptoms again she would be treated as COVID-19 suspected case.

Antenatal ultrasound services for foetal growth surveillance not to be done unless actually indicated and needs to be deferred for 14 days following recovery from acute illness.⁹

Timing and mode of delivery

Separate delivery room and operation theatres along with neonatal resuscitation corners located at least 2 m away from the delivery table need to be identified in Covid block of hospitals for delivering suspected or confirmed COVID-19 pregnant women in presence of neonatologist.^{6,12}

The use of tocolytic drugs in patients with preterm labour is as such contraindicated and only to be given for 48 hours for steroid cover to attain foetal lung maturity. Beta-mimetic agents should be avoided in case of pulmonary involvement.⁴ Inj. Betamethasone 12mg intramuscularly followed by repeat dose after 24 hrs should be given for foetal lung maturity if patient <34 weeks and having mild symptoms.³¹ Low molecular weight heparin needs to be started unless imminent delivery is suspected within next 12 hours in all infected or suspected COVID-19 pregnant patients to avoid thromboembolism.^{14,16} Oxygen saturation must be maintained above 94%, titrating oxygen therapy accordingly.⁴³⁰

Timing of delivery should be individualized based gestational age and foetal conditions and also on disease severity with existing comorbidities such as pre-eclampsia, diabetes, cardiac diseases etc.^{6,18} In mild and stable cases responding to treatment and in the absence of foetal compromise pregnancy may be continued to term under close surveillance of foetal heart rate monitoring and Ultrasound if required assuring foetal wellbeing.²⁷ In critical cases possible benefits of immediate induction or surgical intervention needs to be weighed against the possible risk guided by proper assessment of patient condition, gestational age, available infrastructure, risk of exposure to health care personnel and the couple's wishes to save the life of mother and baby both by reducing extra metabolic load.^{16,31}

As such the pregnant women with COVID-19 infection if decided to give trial of normal vaginal delivery and indications for intervention should follow standard obstetric practice and continuous electronic foetal monitoring during labour is suggested if such facilities are available.⁴ The second stage of labour should be cut short specially in those with respiratory involvement to prevent hypoxaemia and maternal exhaustion.⁴ Epidural anaesthesia is preferred over spinal during emergency caesarean section to avoid the use of general anaesthesia.^{4,18}

Test for newborn and breastfeeding and newborn care

There were few case reports from China pointing at postnatal transmission due to close contact.^{10,32} Hence testing protocol for COVID-19 is advised only to those neonates who are born to mothers who have contracted the infection between duration of 14 days prior to delivery till 28 days post-delivery. If first report comes negative, testing should be repeated after 2 days.^{6,15}Nasopharyngeal and throat swabs are the routinely testing specimens but in case of mechanical ventilation tracheal aspirate is collected in viral media abiding by all standard protocols followed by disposal at concerned laboratories.6,33 Rectal swabs of sick neonates with prolonged admission are also collected in institution where facilities are available.³¹ There is no documentation of transmission via breast milk directly though infection transmission risk is attributed to close contact between neonate and mother. $^{\scriptscriptstyle 6,10,15,31,33\cdot36}$ As breast milk confers immunological protection, in present scenario, its benefits outweigh risks of transmission, hence breastfeeding is allowed after taking precautionary measures like hand hygiene, mask wearing, milk pump disinfection etc before and after every feed with strict maintenance of 2 meters distance between the mother and neonate in the same room.³³⁻³⁶ Expressed breast milk should be used if the mother is infected or suspected with pending reports.^{33,34} Temporary separation is permitted if the mother wishes so however it may be implemented as per gravity of the situation under the clinical guidance of local health advisory.^{34,35} Since there is dearth of sufficient data and notified cases, protection of newborn is imperative in sync with evolving guidelines and shared knowledge. **Discharge of Patient:** CDC³⁵ recommends either Time based Strategy or Test based Strategy to discharge or end isolation of Covid positive patients and institute can develop its own policies as per the circumstances in that particular region.

Outpatient assessment and management for pregnant women with suspected or positive COVID-19 is summarized in the following flowchart adopted from ACOG and modified on the basis of RCOG, ICMR. WHO, &CDC guidelines. [FIGURE 1]



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