CORONAVIRUS (COVID-19) INFECTION IN PREGNANCY

Clinical guidelines
Department of Obstetrics and Gynecology
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AUTHORS:

Dr. Mohamed Aseel Jaleel, MD, Senior Consultant OBGYN and Head of Department of OBGYN

Dr. Jabeen Ali Shareef, DGO, Consultant OBGYN

Dr. Thasneem Farooq, MS, Senior Consultant OBGYN

Dr. Hawwa Hana, MS, Senior Consultant OBGYN

Dr. Shirmeen Mohamed, MD, Consultant OBGYN

Dr. Shanaz Dole, MD, Consultant OBGYN

Dr. Mariyam Ahmed, MD, Consultant OBGYN

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Dr. Niyasha Ibrahim, MD, Senior Consultant and Head of the department, Department of Child Health.

Dr. Hawwa Ashfa, MD, Consultant, Department of Child Health

Dr. Isneen Hilmy, MD, Internal Medicine

Dr. Fathimath Mishfa Waseem, MBBS, Medical Officer, Department of Obstetrics and Gynecology.

Cover Page: This scanning electron microscope image shows SARS-CoV-2 (round magenta objects) emerging from the surface of cells cultured in the lab. SARS-CoV-2, also known as 2019-nCoV, is the virus that causes COVID-19. The virus shown was isolated from a patient in the U.S. Image captured and colorized at NIAID’s Rocky Mountain Laboratories (RML) in Hamilton, Montana. Credit: NIAID
**TABLE OF CONTENTS:**

1. Introduction 4
2. General guidance 6
3. Diagnostic criteria and clinical classification 6
   3.1 Definition 6
4. Radiological examination of chest during pregnancy 8
5. Intrapartum and postpartum care of non-COVID women during the pandemic 8
   5.1 General measures 8
      A: wearing of masks and other PPE 8
      B: Visiting policy 8
   5.2 Timing of birth 9
   5.3 Admission considerations 9
   5.4 Intrapartum Care 10
   5.5 Postpartum care and discharge from hospital 10
6. Care of suspected or confirmed COVID-19 patient during antepartum, intrapartum and postpartum period 11
   6.1 Admission consideration and timing of delivery 11
   6.2 Mode of delivery 12
   6.3 Medical management 13
      6.3.1 Investigations 13
      6.3.2 Laboratory value changes of concern 14
      6.3.3 General measures 14
      6.3.4 Treatment 14
      6.3.5 Monitoring and further management 14
   6.4 Management during labor 15
      6.4.1 General measures 15
      6.4.2 Fetal monitoring during labor 15
      6.4.3 Intrapartum Oxygen use 15
      6.4.4 Drug consideration 16
   6.5 Anesthesia considerations during labor and Cesarean sections 19
   6.6 Cesarean for suspected or confirmed COVID-19 patients 20
   Flow chart for roles, equipment's and PPE in preparation for Cesarean delivery of suspected or confirmed COVID-19 patients 21
   6.7 Postpartum care 22
      6.7.1 Care of the mother 22
      6.7.2 Care of the newborn 22
7. Care of severe and critically ill pregnant COVID-19 patients 24
   7.1 General guidance 24
   7.2 Specific management 24
Annex 1 26
Annex 2 27
References 28
**ABBREVIATIONS:**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABG</td>
<td>Arterial Blood Gases</td>
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<tr>
<td>ACE 2</td>
<td>Angiotensin-Converting Enzyme 2</td>
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<td>ARI</td>
<td>Acute Respiratory Infection</td>
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<td>ARDS</td>
<td>Acute Respiratory Distress Syndrome</td>
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<td>CDC</td>
<td>Centers for Disease Control</td>
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<tr>
<td>CFR</td>
<td>Case Fatality Rate</td>
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<td>CK – MB</td>
<td>Creatinine Kinase - MB</td>
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<td>CRP</td>
<td>C – reactive Protein</td>
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<tr>
<td>CTG</td>
<td>Cardiotocography</td>
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<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<td>DH – 16</td>
<td>Dharumavantha Hospital Floor 16</td>
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<tr>
<td>DIC</td>
<td>Disseminated Intravascular Coagulation</td>
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<td>DNA</td>
<td>Deoxyribonucleic Acid</td>
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<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
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<tr>
<td>EMA</td>
<td>European Medicines Agency</td>
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<td>FDA</td>
<td>Food and Drug Administration</td>
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<td>HPA</td>
<td>Health Protection Agency</td>
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<tr>
<td>ICU</td>
<td>Intensive Care Unit</td>
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<td>IGMH</td>
<td>Indira Gandhi Memorial Hospital</td>
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<tr>
<td>IPC</td>
<td>Infection Prevention and Control</td>
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<tr>
<td>LDH</td>
<td>Lactate Dehydrogenase</td>
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<td>LFT</td>
<td>Liver Function Test</td>
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<td>LMWH</td>
<td>Low Molecular Weight Heparin</td>
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<td>MERS</td>
<td>Middle East Respiratory Syndrome</td>
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<td>mGy</td>
<td>Milligray</td>
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<tr>
<td>NSAID</td>
<td>Non – Steroidal Anti – Inflammatory Drugs</td>
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<tr>
<td>PPE</td>
<td>Personnel Protective Equipment</td>
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<tr>
<td>PPH</td>
<td>Post – Partum Hemorrhage</td>
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<tr>
<td>PaO2</td>
<td>Partial Pressure of Oxygen</td>
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<tr>
<td>RCOG</td>
<td>Royal College of Obstetrics and Gynecology</td>
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<tr>
<td>RFT</td>
<td>Renal Function Test</td>
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<tr>
<td>RHC</td>
<td>Reproductive Health Center</td>
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<tr>
<td>RT – PCR</td>
<td>Reverse Transcriptase – Polymerase Chain Reaction</td>
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<tr>
<td>SARI</td>
<td>Severe Acute Respiratory Infection</td>
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<tr>
<td>SARS-CoV-2</td>
<td>Severe Acute Respiratory Syndrome Corona Virus - 2</td>
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<tr>
<td>VTE</td>
<td>Venous Thromboembolism</td>
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<tr>
<td>UKOSS</td>
<td>UK Obstetric Surveillance System</td>
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<td>WHO</td>
<td>World Health Organization</td>
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PRACTICE RECOMMENDATIONS FOR COVID-19 IN PREGNANCY

1. INTRODUCTION:

This guideline is developed to provide guidance to the multidisciplinary team involved in the management of pregnant women with suspected or confirmed COVID-19 to provide safe care to women during pregnancy and childbirth and to reduce transmission of infection. COVID-19 is rapidly evolving, and this guidance will be updated as and when new information becomes available.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as a novel coronavirus in Wuhan, China, in December 2019. This virus belongs to the coronavirus family of viruses, which causes the common cold (HCoV 229E, NL63, OC43, and HKU1), Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV).

COVID-19 is the infection caused by SARS-CoV-2 and was recognized as a Pandemic by WHO on 11th March 2020. The virus has, till date infected approximately 6,79,9731 people globally and caused about 3,97,388 deaths so far1. As of 12th June 2020, there have been 2003 confirmed cases detected in the Maldives. Up to date information can be obtained from HPA Maldives2. So far, in the Maldives, most pregnant women are detected incidentally on contact tracing.

The transmission of COVID-19 infection from person to person occurs mainly through the respiratory spread, as droplets produced during coughing and sneezing and through aerosol generation. Aerosol particles that are smaller in size than droplets can remain suspended in the air for prolonged periods. And this can lead to exposure of a greater number of individuals to possible infection at a greater distance from the source. The infection may also be spread from touching contaminated surfaces and objects.

Commonly reported symptoms of COVID-19 in the general population include dry cough, fever, fatigue, and shortness of breath, which is reported in most people. In a systematic review which included 33 studies and 356 cases in pregnant women, the most frequent symptoms were fever (67 %), cough (66 %), dyspnea (7%), sore throat (7%), fatigue (7%), and myalgia (6%)3. Rhinorrhea/nasal congestion, anorexia, nausea/vomiting, headache, and abnormalities in smell and taste have also been reported.

The Chinese Center for Disease Control and Prevention reported in >44,500 confirmed infections the severity of the disease as4:

*Mild to Moderate* - 81% - *mild symptoms up to mild pneumonia.*

*Severe disease* - 14% - *dyspnea, hypoxia, or >50 percent lung involvement on imaging within.*

*Critical disease* - 5% - *respiratory failure, shock, or multi-organ dysfunction.*

The incubation period is 1 – 14 days (WHO).
Pregnant women are more susceptible to other severe diseases of the respiratory tract due to the physiological changes that occur during pregnancy. However, according to RCOG, all available data suggest that pregnant women with SARS-CoV-2 infection are at no greater risk of becoming seriously unwell compared with other healthy adults\(^5\).

Although COVID-19 is highly transmissible, the CFR of COVID-19 appears to be lower than that of SARS (9.5\%) and MERS (34.4\%), but higher than that of Influenza\(^6,7\).

Data on SARS and MERS in pregnancy are limited. However, many of the cases involved severe morbidity, including the need for intensive care, cardiorespiratory support, and several maternal mortality cases. The only published case-control study showed that pregnant women with SARS experienced worse outcomes than non-pregnant women of similar age\(^8,9,10\).

Women infected with SARS and MERS in the first trimester reported spontaneous abortion as well. Similarly, in the second trimester stillbirths, intrauterine growth restriction, and preterm birth were noted. However, it is essential to note that several pregnancies had good outcomes despite maternal infection with SARS or MERS. Experts believe that adverse pregnancy outcomes are most likely related to the severity of maternal respiratory compromise\(^8\)-\(^14\).

The most commonly reported adverse pregnancy outcomes in COVID-19 has been spontaneous and iatrogenic preterm labor. One stillbirth has been reported, and this occurred in the case of severe maternal illness reported\(^15\).

There are currently no data suggesting an increased risk of miscarriage or early pregnancy loss in relation to COVID-19. As there is no evidence of intrauterine fetal infection with COVID-19, it is currently considered unlikely that there will be congenital effects of the virus on fetal development. Iatrogenic delivery was predominantly for maternal indications related to the viral infection, although there was evidence of fetal compromise and pre-labor premature rupture of membrane, in at least one report\(^12,13,14\).

There has been no definitive evidence of vertical (mother-to-infant) transmission in any cases of COVID-19. Viral DNA was not detected in amniotic fluid analysis, placenta and breast milk from pregnant women confirmed to have COVID-19 infection\(^16\).
2. GENERAL GUIDANCE

During the pandemic of COVID-19 infection, all pregnant women should be asked if they have a history of exposure to a suspected or diagnosed COVID-19 patient and symptoms consistent with COVID-19.

Any pregnant woman who, after screening, is suspected to be having COVID-19 infection should be jointly managed by a multidisciplinary team including Obstetrician, Pulmonologist, Physician, Pediatrician, Anesthetist, Radiologist, and Nursing team.

Admission of any pregnant woman suspected as or diagnosed with COVID-19 infection should be based on obstetric indication and severity of illness. This decision should be made by the joint consultation of Obstetrician and Pulmonologist/Physician. COVID-19 patient with mild symptoms usually do not require admission to a hospital.

Chest radiography such as Chest X-ray and Chest CT has important reference value for the evaluation of COVID-19 infected pregnant women.

Antenatal care, delivery and postnatal care of women with COVID-19 infection should be carried out in isolation. Healthcare providers are recommended to employ strict infection prevention and control (IPC) measures and should wear appropriate personnel protective equipment (PPE).

Staff engaged in obstetric related work should have completed training in new updated COVID-19 infection control protocol.

3. DIAGNOSTIC CRITERIA AND CLINICAL CLASSIFICATION:

3.1. Definition:

COVID-19 CASE DEFINITION FOR A SUSPECTED CASE (as of 17th March 2020)

Patient with any acute respiratory illness (fever* and at least one sign/symptom of respiratory disease (e.g., cough, shortness of breath),

AND

No other etiology that fully explains the clinical presentation

AND

A history of travel to or residence in a location reporting local Transmission of COVID-19 disease during the 14 days prior to symptom onset.

OR
Patient with any respiratory illness
AND
Having been in contact with a confirmed or probable COVID-19 case in the last 14 days prior to the onset of symptoms.
OR
Patient with SARI
AND
No other etiology that fully explains the clinical presentation.
SARI is defined as an acute respiratory infection (ARI) with a history of fever* or measured temperature ≥38°C and cough, with onset within the last 14 days and requiring admission to hospital. *Absence of fever does NOT exclude viral infection².

PROBABLE CASE: A probable case is a suspected case for whom the report from laboratory testing for the COVID-19 virus is inconclusive.

CONFIRMED CASE: A confirmed case is a person with laboratory confirmation of infection with the COVID-19 virus, irrespective of clinical signs and symptoms².

The following infections and non-infectious diseases should be considered during the diagnosis of COVID-19 infection:

- Influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, SARS coronavirus, and other known viral pneumonia.

- Mycoplasma pneumonia, chlamydia pneumonia, and bacterial pneumonia.

- Non-infectious diseases, such as vasculitis, dermatomyositis, and organizing pneumonia.
4. RADIOLOGICAL EXAMINATION OF CHEST DURING PREGNANCY:

For pregnant women with COVID-19 infection, a Chest X-ray or a chest CT may be required depending on the clinical course. The impact of X-ray and CT on the fetus is related to the gestational age and the radiation dose during the examination\(^{17}\). According to the American Radiological Association, a pregnant woman undergoing a single Chest X-ray will receive a fetal radiation dose of 0.0005 - 0.01 mGy. A chest CT will receive a fetal radiation dose of 0.01 – 0.66 mGy.

There have been no reports of fetal malformation, growth restriction, or miscarriage at a radiation dose of <50 mGy. However, pregnant women must sign informed consent and take necessary abdominal protection measures before undergoing chest X-ray and chest CT\(^{18}\).

5. INTRAPARTUM AND POSTPARTUM CARE OF NON-COVID WOMEN DURING THE PANDEMIC:

5.1 General Measures - Consider any patient getting admitted to labor ward/general wards/rooms during the pandemic:

a. Wearing of masks and other PPE:
Considering the high percentage of asymptomatic carriers who could potentially transfer infections, all patients getting admitted to antenatal ward, labor induction unit, and delivery ward/suites should be provided with a surgical mask (3 ply), regardless of the COVID-19 status of the patient. It should be worn at all times.

Full droplet precautions with level 2 PPE should be used when attending to any patients with respiratory symptoms\(^{19}\).

When attending to any patient undergoing any aerosol-generating procedure, including the second stage of labor, level 3 PPE, which includes an N95 mask, should be utilized.  
(For levels of PPE refer to annex 1)

b. Visiting Policy:
There is a significant risk of transmission of infection between patients, healthcare workers, and visiting family members. Hence strict restrictions should be applied to visiting the hospitals during the pandemic.

One caregiver/family member per patient can be permitted (to be decided as per hospital protocol). The caregiver should wear face mask, practice hand hygiene, and social distancing from others at the hospital. The switching of the caregiver should be discouraged.
5.2. Timing of birth:

Termination of pregnancy and timing of birth for all patients should be individualized based on obstetrics/medical indications.

Induction of labor for antenatal patients with medical/obstetric indication of non-COVID patients should not be postponed or rescheduled.

5.3. Admission considerations:

Where possible, all patients getting admitted to the hospital should be screened for COVID-19 with RT PCR, to reduce the risk to other patients and health care workers. It will help prevent the spread of infection and to contain the disease\textsuperscript{20, 21}. However, all emergency and required care should not be delayed (while waiting for COVID-19 result), and care should be carried out with appropriate precaution using PPE.

Special consideration should be given to limit women's movements from one care area to another (e.g., triage room to the antenatal ward to labor room)\textsuperscript{19}.

Patients getting admitted for induction of labor and delivery should be directly transferred to delivery suite/induction units without waiting in triage/ER.

All confirmed COVID-19 patients should be transferred to designated isolation units/facilities for such patients as soon as possible.

However, any patient who requires urgent delivery for obstetrics/fetal indications (e.g., a patient coming in 2\textsuperscript{nd} stage of labor or having fetal distress) should be managed in the institution where she reported. Designated isolation units/areas for giving care to such emergency patients should be set up in all health care facilities catering to regular delivery services.

If admission at IGHM is required for any reason, all COVID-19 positive/suspected patients should be transferred to Dharumavantha Hospital (DH 16 – isolation unit).
5.4. **Intrapartum care:**

In general, management of all stages of labor for all COVID-19 negative patients/asymptomatic COVID-19 positive patients should not be altered from routine practice.

However, special consideration should be given to the following:

- Wearing of appropriate PPE (*Annex 1*).
- Adequate hydration by oral administration of water and clear fluids.
- All efforts should be made to shorten all stages of labor. Hence, strict use of partograph and careful monitoring of labor should be done. And special consideration should be given for appropriate and timely augmentation of labor with oxytocin/early amniotomy.
- For the prophylaxis of PPH, in addition to standard Oxytocin and Inj. Methergin, Inj. Tranexamic Acid and Misoprostol\(^{19}\) may be considered as every effort should be made to minimize blood loss, particularly in setups where facilities for blood and blood products are limited.

5.5. **Postpartum care and discharge from hospital:**

To limit the transmission of infection to the patients themselves, other patients and staff, discharge of all uncomplicated deliveries should be expedited, and women should be counseled and notified on this ideally at the time of admission.

If the health care facility is burdened, following uncomplicated vaginal deliveries, women may be discharged before the standard 24 completed hours of hospital stay after ensuring no contraindication to early discharge.

For all uncomplicated cesarean deliveries, discharge can be considered on 2\(^{nd}\) postoperative day or late 1\(^{st}\) postoperative day after a full evaluation to rule out any contraindication to early discharge.

At the time of discharge, a postpartum visit by teleconsultation (with photo upload option) should be discussed. When suture removal is required, an arrangement should be made to make the patient have minimal contact with other staff and patients.
6. CARE OF SUSPECTED OR CONFIRMED COVID-19 PATIENTS DURING ANTEPARTUM, INTRAPARTUM AND POSTPARTUM PERIOD:

6.1. Admission considerations and timing of delivery:

Pregnant women with suspected or confirmed COVID-19 infection with mild symptoms do not require hospital admission or specific management. Hence, they should be managed at the designated isolation facilities. Admission to the hospital should be based on the severity of illness, underlying co-morbidities, and clinical status of the patient.

Any patient requiring admission to the hospital due to obstetric indication/worsening of symptoms should be admitted to the designated center/isolation units.

The timing of delivery for women with suspected or confirmed COVID-19 should be decided based upon obstetric indications, the period of gestation, and severity of illness.

For women in early gestations, especially those with mild symptoms who are expected to recover well, no alteration to the usual delivery time is indicated.

For women in the third trimester, based on the severity of illness, fetal lung maturity, as well as the case burden of the facility, timing of delivery, may be individualized. If the faculty is burdened by a large number of cases, it may be reasonable to schedule the timing of delivery (prepone or postpone).

For women in their third trimester/at term and having mild symptoms, the delivery may be postponed (provided no other medical/obstetric indications arise) until a negative RT-PCR result is obtained or quarantine restrictions are lifted.

Studies on non-pregnant as well as pregnant COVID-19 patients\textsuperscript{22} show that the severity of the disease peaks at the second week of infection, with admission to the hospital on day 7 of the disease and intubation on day 9 of the disease. With this in mind, for patients at term/more than 34 weeks, especially for those with other comorbid factors such as advanced maternal age, obesity, cardiac and respiratory disease, induction of labor, and expediting the delivery in the early days of the disease may also be considered.
6.2. Mode of delivery

Effects on the fetus and vertical transmission:
In the initial phase of the pandemic, there were few reports of cases that suggested an increased risk of fetal distress in labor. Subsequent studies, including those on pregnant women with COVID-19 pneumonia, did not find any evidence of adverse perinatal outcome.

In a review of 10 articles of case reports and case series done by Ana Cristina Simoes e Silva and Caio Ribeiro Vieira Leal and published on Frontiers of Pediatrics; serum samples, swabs from newborn's pharynx, samples of breast milk, samples of products of conception (placenta, amniotic fluid, and cord blood) were collected at birth. The virus was not detected in any of these samples. The mother's infection occurred in the 3rd trimester, and only one newborn in one study by Zhu et al. had a neonatal death, whose nasopharyngeal swab collected at birth was negative for SARS-CoV-2. In all other studies, there were no cases of fetal death, neonatal death, or severe intrauterine asphyxia. The authors concluded that unlike pregnant women infected with SARS-CoV or MERS-CoV, those infected with SARS-CoV-2 are not prone to unfavorable pregnancy outcomes.

Similarly, in a retrospective study done by Enrico Ferrazi et all on women with COVID-19 who delivered at various centers of Northern Italy, the findings suggested that vaginal delivery is associated with low risk of intrapartum transmission of COVID-19 to the newborn. (57% of women in this study delivered vaginally).

The most recent evidence came from the interim report of UKOSS (UK Obstetric Surveillance System), where data of 427 pregnant women (largest cohort of pregnant COVID-19 women to date) was analyzed and compared with the data of 694 in the comparison group. And in this study, twelve infants (5%) tested positive for SARS-CoV-2 RNA, six of these infants within the first 12 hours after birth. (of the six infants with early-onset SARS-CoV-2 infection, 2 were unassisted vaginal births, four were born by cesarean, three were pre-labor.)

2% of infants did have evidence of viral RNA on a sample taken within 12 hours of birth, which suggests that vertical transmission may have occurred. However, there was no evidence as to whether IgM was raised in these infants and, therefore, whether the infection was acquired before or during birth, but three infants tested positive following pre-labor cesarean section, suggesting vertical transmission as the possible mode of transmission to these three infants.

Hence, with the current limited available evidence showing that COVID-19 is associated with only a probable or minimal to no risk of vertical and intrapartum transmission as well as no significant adverse perinatal outcomes; the mode of delivery for all COVID-19 positive patients who are not critically ill should be individualized based on obstetric factors, available resources and case burden of the individual facilities.

Until and unless further evidence emerges against it, vaginal deliveries are encouraged and should be carried out as much as possible and to reduce the exposure to health care workers optimize the use of PPE.
6.3. Medical management.

Once the patient is settled in the isolation room, a full assessment of maternal and fetal condition should be carried out, and this should include:

- Evaluation of the severity of COVID-19 symptoms by the multi-disciplinary team.
- Maternal observations, including temperature, respiratory rate, and oxygen saturation.
- Confirmation of the onset of labor, as per standard care.
- Where available electronic fetal monitoring using a cardiotocograph (CTG).
- If the woman has signs of sepsis, investigation and treatment should be carried out according to the multidisciplinary team's guidance.
- Ultrasound assessment of the fetus should be discussed with the radiologist and carried out as indicated.

6.3.1. Investigations

Nasopharyngeal and oropharyngeal and, if possible, sputum sample.
SARS-CoV-2 RT- PCR, Influenza screening, and gram staining.
Cultures: Urine, Blood, Sputum
Complete blood count
LFT
RFT
Coagulation profile
Urine routine
Type and cross match blood based on the plan of delivery/termination of pregnancy.
For patients with moderate, severe and critical COVID-19: CRP, LDH, D-dimer, Ferritin, Lactate, Sodium, Potassium, Magnesium, Calcium, ABG, 12 lead ECG, Chest X-ray, Troponin and CK-MB (if applicable).
6.3.2. Laboratory value changes of concern.

Normal physiological changes that occur during pregnancy lead to specific changes in some of the laboratory values. Normal pregnancy is often associated with mildly elevated transaminases and mild thrombocytopenia. Further increase in transaminases, thrombocytopenia, an increase in creatinine level, and altered coagulation parameters may be observed in pregnant patients with pre-eclampsia and eclampsia.

COVID-19 is also associated with the same laboratory value changes; special consideration should be given when interpreting these values.

6.3.3. General measures.

Adequate sleep, adequate caloric intake to suit patients' needs and preferences, water, and electrolyte balance should be ensured. A dietician should be engaged where required.

6.3.4. Treatment:

At present, there are no approved safe and effective drugs for the treatment of COVID-19, which are proven to be safe and effective by clinical trials. Many antiviral and other drugs are under clinical trials. *(For more details, please refer to the section on drug considerations).*

Treatment will depend on the severity of the illness, and the multidisciplinary team should make the decision to start treatment.

6.3.5. Monitoring and further management.

Vital signs, oxygen saturation, arterial blood gas analysis, and chest imaging (if required), blood routine, urine routine, liver enzymes, myocardial enzymes, kidney functions, and coagulation function should be closely monitored.

In a patient suspected for COVID-19, if the result of the first sample is negative, then the patient can be discharged, and if COVID-19 infection is confirmed, further testing and follow up should be done according to the latest guideline.
6.4. Management during labor.

6.4.1. General measures.

- Infection prevention - to prevent nosocomial infection, any facility managing COVID-19 patients should ideally have a separate floor or a section of the floor with a delivery isolation room designated for admitting labor patients with suspected or confirmed COVID-19 and such patients should be transferred to this room avoiding contact with other patients.

- Accompanying guardian/family members are discouraged from entering the isolation room.

- PPE - the patient should be provided with a surgical (3 ply) mask as discussed in the previous section, and caregivers should wear level 2 or level 3 PPE according to availability.

- The number of caregivers should be minimized as much as possible.

6.4.2. Fetal monitoring during labor.

Based on 2 Chinese series\(^1\) showing a significant rate of fetal compromise, RCOG recommends EFM for patients with COVID-19\(^5\). Although significant adverse fetal and neonatal outcomes are not observed in subsequent studies, EFM should be used in facilities where it is available.

6.4.3. Intrapartum oxygen use.

Oxygen therapy (giving high flow oxygen to the mother) is often used in our labor wards/suits to reverse suspected fetal acidosis, which is clinically observed as abnormal fetal heart tracings.

However, various studies have demonstrated that intrapartum oxygen use (or hyper oxygenation of the mother) as a form of intrauterine resuscitation is not beneficial, or may even cause harm, and a study has also shown that room air is superior to oxygen in improving fetal metabolic status\(^2\). Although some studies have demonstrated a positive effect on the fetal heart rate following oxygen administration, the outcomes of Apgar score, umbilical artery blood gas, free oxygen radicles, and mode of delivery did not show any significant difference with the control\(^3\).

Giving oxygen through a nasal cannula or mask does not involve aerosol generation; however, due to contamination by the upper respiratory secretions, handling will pose the risk of contracting the virus.
During the pandemic, the health care worker must avoid performing any procedure that involves the risk of transmission of infection unless that procedure is proven to benefit the patient or will cause harm to the patient if neglected.

Latest evidence shows no beneficial effect for the fetus by giving oxygen to the mother. Giving oxygen should be avoided as long as the mother’s SpO₂ remains normal.

Oxygen therapy should be reserved for abnormal fetal heart tracing associated with a drop in mothers SpO₂ level and for the critically ill patients with severe COVID-19 requiring oxygen to maintain SpO₂ level.

6.4.4. Drug considerations.

The use of some drugs in patients with COVID-19 has become controversial and is under scrutiny, and some of these drugs are commonly used in pregnant women.

**NSAIDs.**

NSAIDs are commonly used in pregnant women, particularly for postoperative pain relief.

Some reports and articles hypothesized that as pathogenic coronaviruses bind to their target cells through ACE 2 receptors, expression of these receptors may be increased by drugs such as thiazolidinediones and NSAIDs such as Ibuprofen³⁰ thereby worsening the disease. But according to EMA (European Medicines Agency), US FDA and WHO, currently, there is no definitive evidence proving this theory³¹ and both WHO and US FDA recommends to continue to use NSAIDs in patients with COVID-19.

**BETAMETHASONE AND DEXAMETHASONE.**

Various studies done on patients with viral pneumonia, particularly on Influenza, failed to demonstrate any beneficial effects of systemic corticosteroids in the treatment of pneumonia. These studies showed that systemic corticosteroid administration increased the overall morbidity and mortality rate of these patients, the main contributing factor being hospital-acquired secondary pneumonia and longer duration of ICU stay and mechanical ventilation³², ³³, ³⁴.

This led to the concern that the administration of Betamethasone/Dexamethasone to pregnant women with preterm labor may have a similar detrimental effect. CDC recommends to avoid glucocorticosteroids in the general population with COVID-19 but has not addressed the issue of antenatal administration of steroids.

With COVID-19, the studies conducted so far are non-conclusive, some reporting that Methylprednisolone has a beneficial effect on patients with severe disease³⁵.
It should be noted that the dose of corticosteroids used for fetal lung maturity in preterm labor is much lower than the dose used in the studies of viral pneumonia and patients with mild symptoms of COVID-19, clinical benefits of antenatal corticosteroids will outweigh the risks of potential harm to the mother.

Based on these facts and the recommendations of WHO\textsuperscript{36} use of Betamethasone/Dexamethasone should be continued for patients with mild symptoms (who are less than 34 weeks), after assessing the gestational age accurately, and discussing with the woman the benefits versus harm to the preterm newborn and the mother respectively.

For patients with severe disease or patients who are critically ill and less than 32 weeks, the benefits to the preterm newborn again might outweigh the potential risk to the mother. And steroids may be given after discussing with the multidisciplinary team, including the Pediatrician.

For patients with severe disease or those who are critically ill and more than 32 weeks’ gestation, if the NICU facilities are reasonably good, the potential risk to the mother might outweigh the benefit to the newborn. In this situation, it may be reasonable to withhold giving corticosteroids. However, the decision again should be taken after consulting the Pediatrician, multidisciplinary team as well as the woman’s guardian.

**CHLOROQUINE AND HYDROXYCHLOROQUINE.**

Both Chloroquine and Hydroxychloroquine (HCQ) have been widely used to treat Malaria and some autoimmune diseases. Reviews of studies on the use of Chloroquine and HCQ during pregnancy showed no significant increase in congenital anomalies, spontaneous abortions, preterm birth, and intrauterine fetal death\textsuperscript{37, 38, 39}. Hence both Chloroquine and HCQ appear to be safe to use during pregnancy.

However, emerging data on the use of Chloroquine and HCQ in the treatment of COVID-19 is non-conclusive. Some reports have documented severe dysrhythmias in patients with COVID-19 treated with Chloroquine or HCQ, often combined with Azithromycin and other medicines that prolong the QTc interval.

The COVID-19 Treatment Guidelines Panel (the Panel) of NIH, US recommends against using high-dose Chloroquine (600 mg twice daily for ten days) for the treatment of COVID-19\textsuperscript{40}. This recommendation was based on a randomized, double-blinded study comparing high-dose Chloroquine (600mg twice daily for ten days) versus low dose Chloroquine (450mg twice daily for one day followed 450mg daily for four days) in the treatment of COVID-19. This study was stopped due to safety concerns; however, the results of the small number of participants showed a significant increase in mortality in the high dose arm of Chloroquine regimen\textsuperscript{41}.

WHO recommends not to give Chloroquine or HCQ as either treatment or prophylaxis for COVID-19 outside of the context of clinical trials.
Based on these findings, if a decision is being made to add Chloroquine or HCQ to the treatment of pregnant COVID-19 patients, a low dose Chloroquine regimen or HCQ which appears to be safer than Chloroquine should be chosen, and it should be started only after an agreement is reached between the multidisciplinary team members.

**ANTIVIRALS.**

*Oseltamivir (Tamiflu)*
The neuraminidase inhibitor antiviral Oseltamivir was used empirically in several patients during the COVID-19 outbreak in China due to the overlap with peak influenza season\(^42\).

However, Oseltamivir has no documented in vitro activity against SARS-CoV-2 and is not expected to play a role in the management of COVID-19\(^43\).

*Remdesivir*
It is a novel nucleotide analog found to be having in vitro activity against SARS-CoV-2 and related coronaviruses (including SARS and MERS)\(^44\) has been used without reported fetal toxicity in some pregnant women with Ebola\(^45\).

Although not approved by their FDA, based on preliminary clinical trial data, the COVID-19 Treatment Guidelines Panel of NIH, UK (the Panel) recommends the use of Remdesivir for the treatment of COVID-19 in hospitalized patients with severe disease defined as SpO\(_2\) ≤94% on ambient air (at sea level), requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation\(^40\).

However, WHO recommends not to give antivirals (Remdesivir, Lopinavir, Umifenovir, Favipiravir) to patients with COVID-19, outside of the context of the clinical trial.

**MAGNESIUM SULPHATE**
Magnesium Sulphate is widely used in pregnancy as a tocolytic, in the treatment and prophylaxis of eclampsia and as a neuroprotective agent for the fetus, given to women considered to be at risk of preterm delivery. Effects of Magnesium Sulphate toxicity include respiratory depression; hence theoretically, its use may worsen the condition of a severe or critically ill COVID-19 patient with already compromised respiratory function.

At present, there are no reported data regarding the use of Magnesium Sulphate in COVID-19. However, given the potential respiratory complications with the use of Magnesium Sulphate, it should be used judiciously in cases of severe respiratory symptoms. And in this situation, careful consideration should be given to both total fluid administration and kidney function\(^19\).
**ANTICOAGULANTS**

Direct data on thromboembolic risk with COVID-19 are limited, but suggest an increased risk. The American Society of Hematology and the Society of Critical Care Medicine recommends routine pharmacologic venous thromboembolism prophylaxis in patients hospitalized with COVID-19 unless there is a contraindication (e.g., bleeding, severe thrombocytopenia).

RCOG also recommends VTE prophylaxis with LMWH following delivery for all patients with suspected or confirmed COVID-19 and advises to continue it for ten days postpartum.

If a decision is made to give VTE prophylaxis, LMWH should be used if delivery is not expected within 24 hours and if it has been started in the postpartum period.

In postpartum, the first dose should be administered as soon as possible after birth, provided there is no PPH, and regional anesthesia has not been used. If regional anesthesia has been used, it can be administered 4 hours after the last spinal injection or removal of catheter.

Unfractionated heparin can be used if faster discontinuation is needed (e.g., if delivery, neuraxial anesthesia, or an invasive procedure is anticipated within approximately 12 to 24 hours or at 36 to 37 weeks of gestation).

### 6.5. Anesthesia considerations during labor and cesarean section:

At present, there is no evidence that epidural or spinal analgesia/anesthesia is contraindicated in patients with COVID-19. However, considerations should be given to the following.

Some laboratory values may be altered in pregnant women with COVID-19 and of particular importance is platelet count and coagulation profile, as DIC may occur, especially in patients with severe disease. Hence, necessary investigations before a cesarean section in a patient with COVID-19 should include recently done platelet count and coagulation profile.

Careful assessment of the patient's general condition, including evaluation for any organ failure and cardiorespiratory status, should be done by the Obstetrician and Anesthetist before shifting the patient to the theater.

There is a high chance that a pregnant COVID-19 patient may require general anesthesia, either due to a compromised cardiovascular and respiratory status or due to failure of spinal or epidural anesthesia. Intubation and extubation are both aerosol-generating procedures, hence proper PPE, and if available, video-laryngoscope should be kept at hand.
6.6. Cesarean for suspected or confirmed COVID 19 patients.

Suspected or confirmed COVID-19 patients may require a cesarean section for either obstetric/fetal indications or due to worsening symptoms of a severe or critically ill patient.

And if a cesarean delivery is being performed, consideration should be given to the following:

a. Consent for cesarean should include the risk of exposure to COVID-19, despite the precautions being taken.

b. Designate a separate operating room (OR), which will be used only for all suspected or confirmed COVID-19 patients for the duration of the pandemic, and only the essential equipment should be kept in this OR.

c. Place appropriate PPE outside the OR to minimize the time required for donning.

d. Training on proper donning and doffing of PPE. Simulation exercises to prepare staff, build confidence, identify areas of concern, and to prepare for emergency transfers to operating room should be done.

e. Minimize the number of providers involved at each step, but adhering to a safe level of staffing and assign specific roles for each caregiver, including which level of PPE to be worn by each. And there should be no exchange of staff during the surgery.

(Refer to the flow chart for roles, equipment, and PPE in preparation for Cesarean delivery of suspected or confirmed COVID-19 patients).

f. An arrangement should also be made on how emergency drugs, blood, and equipment can be supplied into the OR if the need arises.

g. The electro-surgery unit should be set to the lowest possible setting for the desired effect. The use of monopolar/bipolar electro-surgery should be minimized, as these can lead to particle aerosolization. Use attached smoke evacuators if available.

h. Debriefing led by the surgeon after surgery should be done. Debriefing should include Obstetrician, Nursing team, Anesthetist and Pediatrician.

i. Following debriefing, condition of the patient should be explained to the patient and relatives.
FLOW CHART FOR ROLES, EQUIPMENT, AND PPE IN PREPARATION FOR CESAREAN DELIVERY OF SUSPECTED OR COVID 19 POSITIVE PATIENTS:

<table>
<thead>
<tr>
<th>PRE - OP</th>
<th>Ward RN - Level 1 PPE&lt;sup&gt;1&lt;/sup&gt; - Prepare patient in room (mask/cap).</th>
<th>OT In-charge RN - PPE cart outside OR - Mark OR as COVID positive - Log of providers.</th>
<th>OT floor RN - Level 2 PPE&lt;sup&gt;2&lt;/sup&gt; - Assist in patient transport.</th>
<th>Scrub RN - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt; - Scrub in&lt;sup&gt;4&lt;/sup&gt; - Prepare OR</th>
<th>OB + Assistant - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt; - Scrub in&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Anesthesia + RN - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt; - Scrub in&lt;sup&gt;4&lt;/sup&gt;</th>
<th>Pediatrics - Level 2 PPE&lt;sup&gt;2&lt;/sup&gt; - Minimize number in OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTRA-OP</td>
<td>Recovery RN - Level 1 PPE&lt;sup&gt;1&lt;/sup&gt; - Receive baby from OR - Can pass any required supplies through to OR</td>
<td>OT Floor RN - Level 2 PPE&lt;sup&gt;2&lt;/sup&gt;</td>
<td>Scrub RN - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt;</td>
<td>OB + Assistant - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Anesthesia + RN - Level 3 PPE&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Pediatrics - Level 2 PPE&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup> Level 1 PPE: Gown, gloves, surgical mask and face shield.  
<sup>2</sup> Level 2 PPE: N95 in addition to Level 1 PPE  
<sup>3</sup> Level 3 PPE: Full PPE with Hazmat suit and eye goggles.  
<sup>4</sup> Scrub in: Sterile surgical gown, sterile gloves over level 3 PPE

* In IGMH – Suspected/confirmed COVID cases or emergency cases with COVID unknown status will be done in EOT in Hiyala Wing.  
* Pediatric team will be outside the operating area.  
* In other centers, designated OT setup for such cases should be used.

| POST-OP | Ward RN - Level 1 PPE<sup>1</sup> to receive the patient | Recovery RN - Level 2 PPE<sup>2</sup> to receive the patient from OR | OT Floor RN - Level 2 PPE<sup>2</sup> to transfer the patient | Scrub RN - Appropriate wipe down of all surfaces, - Dispose anything out of PPE cart or uncovered during the case. | OB + Assistant - Appropriate removal of the outer layer of PPE inside OR - Level 2 PPE<sup>2</sup> to transfer the patient. | Anesthesia + RN - Appropriate removal of the outer layer of PPE inside OR - Level 2 PPE<sup>2</sup> to transfer the patient. | Pediatrics - Appropriate removal of all PPE. |

* COVID; Coronavirus disease, OB; Obstetrician, OR; Operating Room, PPE; Personal Protective Equipment, RN; Registered Nurse.

6.7. Postpartum care.

6.7.1. Care of the mother.

General postpartum care of women with suspected or confirmed COVID-19 with mild symptoms should follow the same principle as non-COVID patients discussed previously. The patient should be monitored closely for worsening symptoms and PPH.

The monitoring of vital signs and urine output should be done carefully in the first 24 hours.

VTE prophylaxis, where indicated, should be continued as discussed previously.

Pain relief - NSAIDs can be used for pain relief following cesarean section, as discussed previously.

Discharge from the hospital - if the symptoms of the mother do not worsen and her general condition and vitals remain stable, all spontaneous vaginal deliveries can be discharged from the hospital after 24 hours and shifted to an isolation facility/home isolation. Similarly, if the symptoms do not worsen, and there are no other medical/obstetric complications, mothers who underwent a cesarean section can be discharged after 48 hours.

Postpartum care following discharge - if no further complications develop, postnatal care should be continued as teleconsultation until the patient's infection clears (testing should be done according to National guidelines).

During the teleconsultations, it is essential to screen the patients for postpartum depression, which may be more common during this stressful time of the pandemic.

6.7.2. Care of newborn.

- Secretion of the virus in breast milk:
There are very few studies done to determine the presence of SARS-CoV-2 virus in breast milk; hence secretion of the virus in breast milk and risk of transmission through breastfeeding is not clear. Initially, several small case series reported that all samples of breast milk from mothers with COVID-19 tested negative for SARS-CoV-2. Others subsequently reported few samples of breast milk positive for the virus.

- Skin-to-skin contact:
With documented evidence of transmission of infection from mother to newborn infant through mother’s respiratory droplets, some have advocated the temporary separation of the newborn from the mother following delivery and avoiding skin to skin contact. However, this could pose problems in rooming-in and breastfeeding later on.
The World Health Organization (WHO) advocates that mothers who have suspected, probable or confirmed COVID-19 virus infection should be enabled to remain together with their infant and practice skin-to-skin contact.

On the other hand, the CDC (US) recommends deciding on a case-by-case basis using shared decision making between the mother and the clinical team. Factors to consider when making a decision include:

- The mother’s desire to breastfeed

- Whether the mother's infection is suspected or confirmed, and the infant's SARS-CoV-2 testing result (separation is not necessary if both the mother and the infant has a positive test)

- The clinical condition of the mother and the newborn.

Where feasible, all the newborns of both suspected and confirmed COVID-19 mothers should be tested for SARS-CoV-2, ideally at birth or within the 1st 12 hours. And if the test is negative, it should be repeated after 48 hours.

If skin-to-skin contact and breastfeeding have been allowed, and the newborn's COVID-19 status is unknown, the mother should strictly wear a mask and practice hand hygiene.

If a decision has been made to separate the mother and the newborn temporarily, the mother should express breast milk to establish and maintain milk supply. And if the milk is expressed under proper IPC measures, it can be fed to the newborn by a healthy caregiver.

*(For more information on newborn care and breastfeeding, please refer to Annex 2 and clinical guideline on management of COVID-19 in children)*.
7. CARE OF SEVERE AND CRITICALLY ILL PREGNANT COVID 19 PATIENTS:

Based on the severity of the disease, The Chinese Center for Disease Control and Prevention classified COVID-19 as:
- **Mild and Moderate** - 81% - mild symptoms up to mild pneumonia.
- **Severe disease** - 14% - dyspnea, hypoxia, or >50 percent lung involvement on imaging within 24 to 48 hours.
- **Critical disease** - 5% - respiratory failure, shock, or multi-organ dysfunction.

Existing data shows that pregnant women who develop COVID-19 pneumonia have almost the same rate of intensive care unit (ICU) admissions as in the non-pregnant population. Still, an increased risk of preterm and cesarean delivery rates is observed in patients with severe disease.

Some cases of maternal deaths from cardiopulmonary complications and due to multi-organ failure have been reported51.

7.1. General guidance:

A multidisciplinary team should manage hospitalized pregnant women with severe disease (with or without other co-morbidities) and on oxygen requirement and patients who are critically ill at a tertiary center with obstetric services and an adult intensive care unit (ICU).

Chest imaging is beneficial for evaluating patients with severe disease; hence if required, it should be done with an abdominal shield.

The decision to terminate a pregnancy should be individualized and based upon the condition of the fetus and the mother, the potential for improvement of the mother’s health following termination, and the gestational age of the fetus. And an informed decision should be taken by the multidisciplinary team and the woman’s guardian together.

7.2. Specific management

The respiratory rate, oxygen saturation, and other vital signs should be monitored carefully, and the patient should be observed for signs of decompensation.

(Signs of decompensation include an increase in oxygen requirement or FiO2 more than 40%, respiratory rate of more than 30, and a decrease in urine output.)

Input and output should be monitored carefully to detect decompensation as well as fluid overload.
IVF - Keeping in mind the risk of ARDS, IV fluids should be used cautiously, and fluid overload should be avoided. Giving boluses in volumes of 250 - 500 ml and then assessing for fluid overload before giving more fluids is one way of ensuring a fluid balance without overload.

During pregnancy, maternal peripheral oxygen saturation (SpO₂) should be ideally maintained at ≥ 95%, which is more than the oxygen delivery needs of the mother. If SpO₂ falls below 95%, an arterial blood gas should be obtained to measure the partial pressure of oxygen (PaO₂). Maternal PaO₂ greater than 70 mmHg is desirable to maintain a favorable oxygen diffusion gradient from the maternal to the fetal side of the placenta.

Oxygen should be titrated according to the SpO₂ level, to keep saturation above 92 - 95%.36

Prophylactic LMWH should be considered for all pregnant women admitted with severe disease/critically ill and in ICU.

The patient should be monitored clinically and by investigations to detect any developing complications such as ARDS, DIC, acute liver injury, acute kidney injury, and myocardial injury, and safe and effective supportive therapies should be initiated timely.36
ANNEX 1:
LEVELS OF PPE USED IN THE DEPARTMENT OF OBSTETRICS AND GYNECOLOGY:

<table>
<thead>
<tr>
<th>PROTECTIVE LEVEL</th>
<th>PROTECTIVE EQUIPMENT</th>
<th>SCOPE OF APPLICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LEVEL 1</strong></td>
<td>- Reusable gown</td>
<td>- Triage desk</td>
</tr>
<tr>
<td></td>
<td>- Surgical mask</td>
<td>- OBG ER (Green, yellow and red zone)</td>
</tr>
<tr>
<td></td>
<td>- Face shield</td>
<td>- Doctors from other department attending referrals</td>
</tr>
<tr>
<td></td>
<td>- Gloves</td>
<td>- Wards (doctors, nurses and attendants)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- RHC - OPD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Wound Clinic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Clinical assistants</td>
</tr>
<tr>
<td><strong>LEVEL 2</strong></td>
<td>- Disposable gown</td>
<td>- Examining confirmed/suspected isolated cases (OBG ER, main ER, Isolation ward, DH).</td>
</tr>
<tr>
<td></td>
<td>- N95 + surgical mask</td>
<td>- Surgical and other procedures with no risk of aerosol generation.</td>
</tr>
<tr>
<td></td>
<td>- Surgical cap</td>
<td>- Cleaning of surgical instruments used for confirmed/suspected cases.</td>
</tr>
<tr>
<td></td>
<td>- Face shield</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Double gloves</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Shoe cover</td>
<td></td>
</tr>
<tr>
<td><strong>LEVEL 3</strong></td>
<td>- Full PPE with Hazmat suit and eye goggle.</td>
<td>- Surgical and other procedure with risk of aerosol generation (Surgery, intubation, CPR).</td>
</tr>
</tbody>
</table>
ANNEX 2: BREASTFEEDING IN CONTEXT OF COVID-19:

Is Mother suspected or confirmed case of COVID-19?

- YES
  - Is mother well enough to express breastmilk or breast feed?
    - YES
      - Start feeding with expressed breastmilk (EBM) feeds:
        - Express breastmilk to establish and maintain milk supply.
        - A dedicated breast pump should be provided.
        - Wash hands before touching any pump or bottle parts and before expressing milk.
      - Option of direct breastfeeding according to parents wish:
        - Mother to wear mask and practice respiratory hygiene/ wash hands before and after touching baby/ disinfect surfaces.
      - Support mother to breastfeed.
        - For Newborn: initiate breastfeeding within first hour after delivery and practice skin-to-skin care as soon as possible.
        - For Infants < 6 months: support exclusive breast feeding.
        - Do not separate mother and baby.
        - > 6 months: Continue breastfeeding with safe and healthy complementary foods.
        - Advice to mother: wash hands frequently with soap and water or use alcohol-based hand rub before touching baby. - regularly clean and disinfect surfaces.
    - NO
      - Revert to direct breastfeeding when mother recovers.

- NO
  - Is mother well enough to express breastmilk or breast feed.
    - YES
      - Other options of feeding according to cultural/ religious norms.
    - NO
      - Is the mother willing to breastfeed after recovery?
        - YES
          - Assist mother with re-lactation when she is well enough to breastfeed.
        - NO
          - Continue alternative modes of feeding the baby.

*Taken from clinical guideline on management of COVID-19 in Children - IGHM*
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