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Review Article

Critical Care Management in Covid 19 Infection in Pregnancy

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Abstract

Novel coronavirus (SARS CoV-2) has been creating a havoc since its advent in 2019. It was first identified in Wuhan, China and has now spread over several countries and affected millions of population. Several variants of SARS CoV-2 have come to light till date, the latest being the Omicron variant.

Keywords: COVID-19; SARS CoV-2; Pregnancy

Introduction

Pregnancy is a known condition for aggravated obstetric and neonatal risks due to viral infections. The cardiovascular and respiratory components of these changes along with the development of immunological adaptations that allows the maternal body to tolerate the antigenically diverse fetus- inflate the risk towards the development of severe respiratory disease [1]. Pregnant women are more prone to severe COVID-19 infection particularly in the third trimester, particularly those with pre-existing comorbidities like chronic hypertension, diabetes, non white ethnicity, advanced maternal age and high BMI [2,3].

Epidemiology

According to surveillance data released by CDC in November 2020, in a study conducted on 400,000 reproductive aged women with confirmed COVID-19 infection, it has been found that pregnant women had significantly higher rates of ICU admission, mechanical ventilation, ECMO and death as compared to non pregnant women of same age, race, ethnicity and underlying medical conditions. The increased risk for severe disease was most significant in women aged 35-44 years who were almost four times likely to be mechanically ventilated and twice as likely to die as non pregnant women of same age [4]. Preterm births (6.4%) and increased rate of caesarean delivery were found to be more rampant in pregnancy with severe to critical disease [5].

Maternal and fetal effects of critical illness in covid-19

The delta variant has been linked to increased risk of severe-critical disease, ICU admission, need for ventilation and death in pregnant patients [6]. 1:10 symptomatic women being admitted to hospital with alpha variant needed intensive care whereas 1:7 symptomatic women with delta variant needed similar care [7]. However, the higher rate of ICU admissions in such cases may be due to lower threshold for the same in pregnancy compared to non pregnant state [8]. The omicron variant is usually associated with less severe disease than the delta variant. Unvaccinated patients are more prone to infection, even with delta variant due to its higher infectious nature. Unvaccinated women have 88% more chance of admission to hospital even with omicron variant infection in pregnancy, than those who have taken at least 2 doses of vaccination [9]. Patients with severe to critical disease are found to have higher rate of preterm delivery and stillbirths compared to mild to moderate or asymptomatic illness infected with the delta variant. Hence, CDC has included pregnancy as an "increased risk" category for severe COVID-19 infection.

Case definition of severe to critical illness in covid-19 infection

Triaging severity of symptoms in COVID-19 infection for critical care management is of utmost importance.

According to NIH guidelines, severe disease due to COVID-19 can be defined as when there is any of the following-

- Respiratory rate >25 breaths/min
- Spo2 <94% (on room air) at sea level
- Pao2/ Fio2 < 300
- Lung infiltrates >50% on chest radiograph

Critical illness due to COVID-19 can be defined as when there is any of the following-

- Respiratory failure
- Septic shock
- MODS

These patients exhibit the following lab parameters

Lab parameter	Values [10]
D-dimer	>1000ng/ml (normal range <500 ng/ml)
CRP	>100mg/L (normal range <8.0 mg/L)
LDH	>245 units/L (normal range 110-210 units/L)
Troponin	>2 times the upper limit of normal (0-9 ng/L)
Ferritin	>500 mcg/L (normal range 10-200 mcg/L)
CPK	>2 times the upper limit of normal (40 to 150 units/L)
Absolute lymphocyte count	< 800/microL (normal range 1800 to 7700/microL)

Table 1

We should often do a qSOFA scoring before admitting patients with COVID-19 for critical care management in which more than 1 of the following should be present-

- SBP < 100 mmHg
- Respiratory rate > 22
- GCS <15

Critical care management in covid-19 infection

After assessment of severity of COVID-19 symptoms, a multidisciplinary team approach should be done including a consultant obstetrician, anaesthesist, neonatologist, intensivist, respiratory physician and nurse-in-charge. The delivery in such patients should preferably be conducted in a tertiary care centre.

Respiratory support

Hourly observation of temperature, respiratory rate and spo2 should be done. Target spo2 ≥ 94%. Young women can compensate for deterioration in respiratory function by increasing their respiratory rate whilst keeping spo2 normal. Hence a rising trend of respiratory rate should raise an alarm. ABG should be done every 4-6 hourly for monitoring. Respiratory support includes-

- Low/high flow o2 (through nasal cannula/ face mask)
- Prone position (upto 28 weeks) along with pillows/paddings to ensure no pressure is exerted on gravid uterus
- Noninvasive ventilation
- Mechanical ventilation
- Higher PEEP strategies, pulmonary vasodilators and ECMO as last resort.

Fluids

Hourly fluid input-output monitoring to be done with the aim to maintain a neutral fluid balance. Boluses in volumes of 250-500ml should be instilled according to requirement with proper assessment for prevention of fluid overload.

Antibiotics should be started if there is clinical suspicion of bacterial infection or sepsis (total lymphocyte count is elevated). Even when COVID-19 infection is confirmed, possibility of coexisting conditions should be kept in mind and full sepsis screening to be done.

Investigations

- Chest X-ray, Chest CT imaging are essential for critical care management and to be done with abdominal shield.
- ECG, Echocardiography, CTPA angio can be done to rule out pulmonary embolism or heart failure, if patient presents with symptoms like chest pain, worsening hypoxia or where breathlessness persists after expected recovery from COVID-19.
- Serum ferritin, CRP, D-dimer are usually elevated in COVID-19 hence not useful in the assessment of venous thromboembolism [11].
- Coagulation profile to be monitored keeping in mind the chance of disseminated intravascular coagulation.
- Routine tests like complete blood count, LFT, KFT, serum electrolytes to be monitored on a daily basis.

The intensive care management should be escalated if any signs of decompensation develop [12,13]

- Increase in Fi02> 35%
- Increase in respiratory rate >25 breaths/min
- Decrease in urine output
- Acute kidney injury (s. creatinine levels >75µmol/L in patients with no known renal disease)
- Drowsiness, even if spo_2 is normal

Medical management of severe-critical COVID-19 infection

Steroids

- If steroids are indicated for fetal lung maturity, Inj dexamethasone should be given IM 12mg 24 hours apart 2 doses followed by oral prednisolone 40mg/once a day or IV hydrocortisone 80mg twice daily and to complete total 10 days or until discharge, whichever is sooner.
- If steroids are not indicated for fetal lung maturity, treatment should be given with oral prednisolone 40mg once a day, or IV hydrocortisone 80mg twice daily for 10 days or until discharge whichever is sooner.
- Those who are postpartum and choose not to breastfeed or unable to breastfeed (as in critically ill patients) Inj Dexamethasone given once a day for 10 days [14-16].

Remdesivir

It can be given for critical patients who are deteriorating or for those who are stable but not improving. In breastfeeding women, its use should be restricted to patients requiring 02 therapy and not who are mechanically ventilated. Multidisciplinary team in accordance with the patient should take decision in such cases. Dosage is 200mg IV on day 1 followed by 100mg daily for 5-10days [17].

IL-6 receptor antagonists

Tocilizumab has been shown to improve survival in patients with hypoxia and evidence of systemic inflammation (CRP≥ 75mg/dl) [18]. It is secreted in very low levels in breast milk [19]. Sarilumab is similar other agent but with minimal data in pregnancy [20]. Though there is controversy regarding timing of BCG vaccination for babies of mothers receiving Tocilizumab, it is used only as short dose and is unable to affect baby. Hence it is recommended that patients who have received Tocilizumab early in pregnancy should have their babies vaccinated with BCG at the appropriate time [21].

Monoclonal antibodies

Pregnant and breastfeeding women who have been hospitalized due to COVID-19 infection and are found to have no antibodies to SARS C0V-2 virus, are recommended strongly as indication for administering monoclonal antibodies [22]. COVID-19 infection with coexisting active malignancy, primary immune deficiencies, HIV with high viral load and with history of solid organ transplantation in pregnancy is considered to be very high risk condition and Sotrovimab, a neutralizing monoclonal antibody, has been indicated in such cases [23].

Molnupiravir, hydroxychloroquine, ivermectin, lopinavir/ritonavir and azithromycin have been shown to be ineffective in treating COVID-19 infection in pregnancy [24]. Evidences suggest that administration of convalescent plasma in such patients is of little clinical benefit and hence not recommended as yet in pregnancy or breastfeeding [15].

JAK inhibitor

Baricitinib may be used in critically ill patients with pregnancy, but there is minimal information on feal effects [26].

VTE prophylaxis

Pregnancy is a known hypercoagulable state and COVID-19 infection aggravates the condition.

- All pregnant women with COVID-19 including those in critical care should be promptly started on prophylactic LMWH unless birth is imminent in next 12 hours. It should be continued till 10 days following hospital discharge or 6 weeks postpartum in women with persistent morbidity [24].
- Aspirin prescribed for pre-eclampsia prophylaxis should be withheld for the duration of infection or there is significant risk of hemorrhage [27].
- Thrombocytopenia may be associated with severe COVID-19 infection [28]. For those with platelet count <50,000 aspirin and LMWH should be discontinued and patient should be put on intermittent pneumatic compression.

Obstetric monitoring

- Obstetric ultrasound (for fetal well being, placental position) should be done once the patient is stable.
- GBS cultures in patients ≥ 23 weeks should be sent and penicillin should be started pending culture results, following standard indications.
- Fetal heart rate and uterine contraction monitoring to be done according to gestational age.
- Individualized delivery planning is of utmost importance.

Timing of delivery

- In both intubated and non-intubated patients, attempt is made to continue pregnancy till 32-34 weeks, keeping spo2≥95% with maximum respiratory support [29].
- However, in case of deteriorating maternal and fetal health, multidisciplinary team approach to be done for determining iatrogenic preterm birth. In such cases, antenatal corticosteroids and $MgSO_4$ for neuroprotection to be considered till 33^{+6} weeks of gestation [30].

Mode of delivery

- There are no evidences to suggest one mode of delivery as preferable to the other, due to presence of COVID-19. The severity of the condition of the patient dictates need for IOL or emergency caesarean section in order to expedite the resuscitation of the mother. In patients>28 weeks of gestation who have cardiac arrest, resuscitative perimortem caesarean section is advocated.
- Epidural and spinal analgesia can be recommended for such patients. General anaesthesia is not also contraindicated in times of requirement.
- In case of labouring patients with ICU admission, continuous electronic fetal monitoring to be done as there have been evidences of fetal compromise in such patients [31].
- Fetal blood sampling or using fetal scalp electrodes are not contraindicated in fetal acidosis in such patients.
- Delayed cord clamping and skin to skin contact have been advocated [32].

Management of undelivered patients recovered from severe-critical COVID-19 infection

- For mothers who have recovered following hospital admission for serious or critical COVID-19 illness, the planning for timing and place of birth should be decided beforehand with priority.
- The consultant obstetrician should review any growth scan conducted following this period of illness
- If the interval between resolution of illness and presentation for birth is insufficient for conducting growth scan, then the assessment of patient and fetus should be taken accordingly. (RCOG- Expert Consensus).

Postpartum management

Breastfeeding and rooming in of babies born to SARS CoV-2 positive women should be done according to BAPM guidelines.

- Breastfeeding is encouraged to all patients with COVID-19.
- When a woman is critically ill or baby is in NICU, the woman should be supported to express her breast milk by hand or personalized breast pump.
- Women who are unable to express breast milk due to critical illness, should consider wet nursing (donor breast milk) or formula feeding.
- Patients who have been in critical care and discharged after delivery, should complete a period of 20 days isolation since the appearance of symptoms and then should be permitted access to NICU [33].
- According to ICMR guidelines, a separate isolation room should be available for the baby. However, if due to limitation of facility or mother's wishes, the baby is "rooming in" (also called as co-location of mother and baby) then measures like proper sterilization of hands, sterilization of bottle and wearing face mask by the mother should be strongly encouraged to prevent infection of mother to baby [34].

Management of covid-19 infected patients in critical care [35]

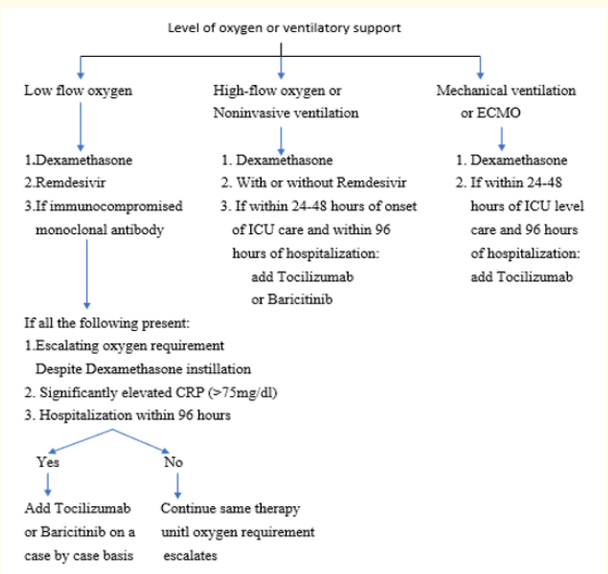

Figure 1

Conclusion

COVID-19 infection in pregnancy can be life threatening.. Guidelines have changed regarding critical care management in pregnancy and will continue to evolve with light on new information on COVID-19 with the passage of time. Hence, obstetricians should possess an optimum level of awareness to detect severity of such illness and enhance intensive care management so as to prevent progression to fatality and thereby improve the overall feto-maternal outcome.

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