

COVID19 and pregnancy- Two lives at risk

Abstract

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) is an infectious disease with rapid and efficient human-to-human transmission. Pregnancy is relatively an immunocompromised state, which makes it more vulnerable to infections, thus corona virus infection can be hazardous to both mothers and their fetuses. The management of parturients infected with COVID- 19 requires special considerations, including caring for critically ill pregnant and postpartum women to protecting health care workers from exposure. Therefore preparation and awareness regarding anesthetic management of pregnant women with COVID 19 is paramount. The goal of this review is to update the anesthesiologists caring for parturients during this pandemic and opt for best clinical practice for management of such patients, when evidence is limited.

Keywords: COVID19, pregnancy, anaesthetic management

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Synopsis

1. SARS-CoV-2 is an infectious disease with rapid human-to-human transmission.
2. Pregnancy being an immunocompromised state is more vulnerable to infections.
3. The management of parturients infected with COVID- 19 requires special considerations, including caring for critically ill pregnant and postpartum women to protecting health care workers from exposure.
4. There is a lot of anxiety and fear amongst pregnant healthcare professionals also.
5. Preparation and awareness regarding anesthetic management of pregnant women with COVID 19 is paramount.

Introduction

Severe acute respiratory syndrome coronavirus (SARS-CoV-2) is an infectious disease (COVID-19) which originated in Wuhan city, China in December 2019 and spread throughout the world.^{1,2} USA has been affected most severely till now. Symptomatology in COVID-19 appears to be similar to SARS epidemic in 2003.³ The virus spreads readily, through close contact, respiratory fomites or fecal route. Parturients have relatively compromised immunity which makes them more vulnerable to infections, thus corona virus infection can be hazardous to both mothers and their fetuses.⁴ World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) have provided some recommendations, based on previous outbreaks of coronaviruses.^{5,6} However, there is limited data regarding the management of pregnant women and neonates with COVID-19. As COVID-19 is rapidly spreading, more pregnant women are likely to get infected, therefore, it is important that the anesthesiologists

need to be updated as they are frontline warriors and will encounter such patients both in operating room and ICU.

Clinical course of the disease during pregnancy

Effect on the mother

Although, the incubation period of virus is around 2-14 days but transmission through respiratory droplets is possible even before the infected persons become symptomatic. The pertinent symptoms of COVID-19 are cough, fever, shortness of breath, fatigue and myalgias but most of the women will present only with mild to moderate flu like symptoms such as nasal congestion, rhinorrhea, sore throat. However, few patients may experience diarrhea, loss of smell or taste. Elderly people, immunocompromised and those with comorbidities including diabetes, cancer, chronic lung disease may have severe clinical presentation with COVID-19. Such as pneumonia and marked hypoxia. Pregnant women may even experience severe symptoms like pneumonia and marked hypoxia which requires prompt recognition and treatment. There is limited data related to the impact of COVID-19 in first and second trimesters of pregnancy. But in the third trimester of pregnancy it has been associated with preterm delivery, premature rupture of membranes, fetal distress and fetal tachycardia. Deaths as a result of respiratory complications from SARS-CoV-2 infection has been reported in two infected mothers, post delivery.⁷

Effect on the fetus

There has been no evidence of vertical transmission therefore fetal development is unlikely to be affected. Neonatal throat swab, cord blood, amniotic fluid and breast milk samples of infected mothers were found to be negative for SARS-CoV-2 in studies done in China and Iran, suggesting that there is no transplacental transmission.⁷⁻⁹ Furthermore, in another case series, three infants of symptomatic mothers were tested negative for the coronavirus.¹⁰

Role of anesthesiologists

History and education of the patient

History of travel, contact or COVID-19 within prior 14 days must be taken from parturient. Anesthesia written informed consent must be taken in the isolation ward or operation theatre to avoid repeated contact if patient has to undergo cesarean section. Personal protective equipment (PPE) must also be worn by the health care providers. But donning PPE may impact the decision to delivery interval as it is a time-consuming process, therefore parturient and their relatives must be informed about the possible delay and informed consent for the same should be taken. The whole staff including maternity, domestic, pediatric must get trained through simulation exercises in using PPE, a back up team must be informed and prepared beforehand to avoid possible delays.

Labor epidural analgesia

There is neither any evidence suggestive of epidural analgesia or anesthesia being contraindicated, nor any incidence of increased aerosolization during labor in a patient of coronavirus infection. Continuous epidural or combined spinal-epidural (CSE) is therefore recommended before, or early in labor, to minimize the possibility of general anesthesia in case of urgent delivery. Approximately, one-third of patients in a case series from Wuhan developed thrombocytopenia (platelet count < 1,50,000), so it would be prudent to check the platelet count before insertion of epidural or spinal and even before removal of epidural catheter. Sterile PPE to be opted. Hat, fluid resistant surgical mask and eye protection to be worn outside the room of theatre, anesthesiologist to be scrubbed up and put on disposable fluid resistant sterile gown and sterile gloves. After performing epidural and ensuring its working, gloves to be removed, hands to be cleaned with gel, eye protection, gown to be removed and turned inside out, disposed off in clinical waste bin and further hands to be cleaned with gel. Again, fluid resistant surgical mask (avoiding touching outside) and hat to be removed outside the room and disposed off in clinical waste bin. Hands to be washed with soap and water thereafter.

The use of Entonox has not been considered as an aerosol generating procedure, however it should be used cautiously with a single patient microbiological filter. While using Entonox, women should be encouraged to breathe in and out through the mouthpiece, rather than breathing out directly into the room.

Perioperative management

Parturient must wear surgical mask and transferred in specific negative pressure vehicle. In the operating room, routine monitoring including non-invasive blood pressure, electrocardiography, respiratory rate and pulse oximetry must be done. The mode of delivery depends on parturient's condition and advice of the obstetrician. Since, there is no evidence of transmission of virus to the fetus during vaginal delivery, therefore cesarean section should be limited to obstetric indication, fetal distress and choice of the parturient. However, the ideal time at which Cesarean section must be performed is important as the virus can cause rapid deterioration of maternal lung condition.

Operating room preparation

Negative pressure operating rooms (minimum of 6 air changes per hour) must be used for operative delivery of infected women with COVID-19. Risk of transmission is high in a closed environment especially when exposed to high concentrations of aerosols for a long

time. Every medical personnel should follow the principles of clean area, contaminated pollution area and buffering zones¹¹ while entering and exiting the operating theatre, with the use of appropriate personnel protection equipment (PPE) in different zones. Biosafety level-3 (BSL-3) protective medical equipment including N95 masks, goggles, protective suits, disposable medical caps and rubber gloves must be worn. The anesthesiologist should use a powered air-purifying respirator ideally while performing intubation.¹² Equipments in theatre should be minimum to avoid contamination and trays/plastic bags with drugs/diluents/syringes/needles/labels likely to be used (for a single patient) should be put together and kept in theatre to minimize the need to leave theatre or open the cup- boards/fridge during the case.

GA drug tray

Regional drug tray

Emergency drug tray

Additional drugs tray (uterotonics, tranexamic acid, antiemetic, antibiotics, paracetamol)

Elective cesarean section

Both neuraxial and general anesthesia have been considered safe,¹³ however, as lung is the primary target organ in COVID-19 infection, the decision about anesthesia for cesarean section is critical. In case of elective cesarean section, spinal anesthesia is the preferred choice of anesthesia as it avoids the risk of endotracheal intubation which can cause or aggravate pulmonary complications in pregnant women infected with coronavirus. In a study in China, in pregnant women with COVID-19 undergoing neuraxial anesthesia, the time of onset of sensory - motor blockade, height of sensation, degree of motor block and quality of anesthesia was similar as in non-infected pregnant women.¹¹ However, it has been reported that 86% of infected women who were given epidural anaesthesia had intraoperative hypotension, probably due to binding of S protein of virus with angiotensin converting enzyme II (ACE2) receptor.^{14,15} But since the duration of the surgery is short, no end-organ damage or significant hemodynamic changes were apparent. The risk of conversion of spinal anaesthesia to general anaesthesia is minimal in non-urgent cases. Therefore, sterile PPE and eye protection based on risk assessment to be worn inside the theatre, at least 2 m away from the patient.

Emergency cesarean section

Neuraxial anesthesia is preferred choice but risk of conversion to general anesthesia is high in emergency situations. Therefore, aerosol generation procedure (AGP) PPE from the outset based on clinical and patient consideration is required. Anesthetist performing neuraxial block must use sterile PPE including hat, fluid resistant surgical mask, fluid resistant disposable gown, sterile gloves and eye protection based on risk assessment.

General anesthesia for caesarean delivery

General anesthesia is opted in case of maternal or fetal emergencies, patients with contraindication to regional techniques or failure of intrathecal anesthesia. There is no evidence that general anesthesia has any adverse effect on maternal or neonatal outcome with COVID19 infection. However, safe donning of PPE by the staff takes priority over starting the case if GA is to be performed in urgent situations. Since it has been associated with a high risk of aerosolization, so aerosol generation procedure PPE should be worn by all staff who will be in theatre at the time of intubation and extubation. Only essential

staff must be present in theatre during AGPs. Use of AGP PPE causes difficulty in communication, therefore, intubation checklist should be used with closed loop communication, keeping background noise to minimum. Preoxygenation should be performed with four vital capacity breaths with 100% oxygen, ensuring tight seal to avoid aerosolization followed by rapid sequence induction. High flow nasal oxygenation (HFNO) should not be used for pre-oxygenation or apneic oxygenation. For intubation, video-laryngoscopy is preferable and must be done by the most experienced anesthetist available. Do not ventilate until cuff inflation is confirmed. While performing intubation anesthetists are likely to get their gloves contaminated with respiratory secretions, so wearing a second pair of gloves must be considered and the outer pair to be removed once the ETT is secured. The position of ETT must be determined by chest wall expansion and end tidal CO_2 , thus without using auscultation method. Extubation is a high-risk procedure for aerosol generation, so coughing to be avoided during extubation.

Postoperative care

At the end of the case patient to be asked to clean hands with gel and put fluid resistant surgical mask, oxygen mask to be attached further and patient to be kept for 20 minutes in operation theatre. Thereafter patient to be handed over to clean team who must be wearing PPE to transfer and PPE to be removed as per doffing procedure. After that hands have to be cleaned with soap and water again. If the patient has any concern related to respiratory distress, transfer to ICU may be appropriate. While there is no clear data regarding safety of Ibuprofen in Covid-19, so NSAIDS and also opioids for post-operative analgesia must be avoided. Fluid balance must be meticulously observed to avoid fluid overload. The newborns must be shifted to radiant warmer bed in a separated area in operating room and further transferred to neonatal intensive care unit if required, by designated staff wearing PPE.

Post natal management

Maternal assessment should be done as per institutional protocol, including monitoring of oxygen saturation hourly postoperatively. If oxygen saturation is low, oxygen therapy should be commenced to maintain oxygen saturation $>94\%$. The critical care team must be informed early if oxygenation cannot be maintained above 94% despite facemask oxygen therapy. It is recommended to perform early endotracheal intubation in a controlled manner while taking all precautionary measures, to minimise exposure and hassle in urgent situations. There is limited information available regarding postnatal management of newborns of mothers infected with COVID-19. Literature from China reports two cases of neonates infected with COVID-19 at 36 hours and 17 days of birth, who appeared to get infected postnatally.¹⁶ therefore it is recommended that newborns should be temporarily separated from infected mother for at least 14 days to minimize the risk of viral transmission. The neonate should be closely monitored for any sign of infection in isolation ward and managed as per Royal College of Paediatrics and Child Health (RCPCH) guidelines. The pumped breast milk to be given to the baby by a non infected caregiver and SARS-CoV-2 RT-PCR viral test by taking nasal swab samples should be performed, on the day of delivery followed by the day before discharge.

Disinfection

The anesthesia workstation must be disinfected with anesthesia circuit sterilizer (containing 12% hydrogen peroxide) for two hours after the surgery. To clean the floor of operating room and surface of

anesthesia workstation and monitors, Chlorine containing disinfectant (2,000 mg L-1) can be used. The air purification system must be shut down for 20 minutes after the patient has left, followed by fumigation of the room for 2 hours with small amount of 3% hydrogen peroxide. The negative pressure ventilation of the operating room to be started again after fumigation.

Critical care management

General principles

Parturients diagnosed with COVID-19 must be immediately admitted in a negative pressure isolation room and critically ill patients should be managed by multi-disciplinary team including obstetrician, neonatologist, intensivist, microbiologist and anesthesiologist. Patients should be categorized based on clinical evaluation.

mild (symptomatic with stable vital signs)

severe (respiratory rate $\geq 30/\text{min}$, $\text{SaO}_2 \leq 93\%$, partial pressure of arterial blood oxygen (PaO_2) / inspiratory oxygen concentration (FiO_2) $\leq 300 \text{ mmHg}$)

critical (shock with organ failure, respiratory failure requiring mechanical ventilation or refractory hypoxemia requiring extracorporeal membrane oxygenation)

Every medical staff involved in the care of COVID-19 infected patients must be wearing PPE including N95 masks, gown, goggles and gloves. Special consideration must be kept in mind regarding physiological changes in pregnancy while managing parturients infected with COVID-19.

Supportive care

Supportive treatment includes adequate rest, nutritional support and hydration. Maternal vital signs (heart rate, blood pressure, respiratory rate, temperature), urine output and oxygen saturation should be meticulously monitored. Patient may require high-flow nasal cannula, mechanical ventilation or extra-corporeal membrane oxygenation (ECMO) depending on severity of hypoxemia. Other complications may include acute kidney injury, septic shock and virus induced myocarditis. Therefore, it is crucial to get serial arterial blood gas analysis done, dynamic assessment of electrolytes, fluid balance and monitor liver function, renal function, electrocardiography, cardiac enzymes, echocardiography, depending upon clinical situation of the patient. X-Ray and CT scan of the chest must be performed when indicated as for non-pregnant adult and should not be delayed due to fetal concerns. Abdominal shielding may be used for fetal protection as per protocol. Fetal heart rate monitoring and ultrasound for assessment of fetal wellbeing is recommended.

Antiviral therapy

Antiviral treatment recommended includes combination therapy with 400mg of Lopinavir/100 mg of Ritonavir orally with α -interferon nebulization (5 million IU in 2 mL of sterile water for injection) twice a day. It has been found to be safe in pregnancy. Remdesivir, a nucleotide analogue and chloroquine, an antimalarial drug, are other drugs which have been found to inhibit COVID-19 virus *in vitro*.¹⁷

Antibacterial therapy

Antibiotics are advised only if there is suspicion of secondary bacterial pneumonia or sepsis. Empirical treatment with Ceftriaxone intravenously can be started till the reports of culture and sensitivity are available.

Cautious use of drugs

Routine use of corticosteroids is not recommended, however, methylprednisolone (1-2 mg/Kg of bodyweight per day) for 3-5 days has been frequently used in China in patients with severe dyspnea and hypoxemia to prevent acute respiratory distress syndrome. Although its efficacy and safety requires further assessment. Two doses of Betamethasone, 12mg intramuscularly stat and 24 hours later should be administered for fetal lung maturity if there is a risk of preterm delivery. There is a concern regarding the use of certain drugs including steroids, indomethacin for tocolysis, magnesium as neuroprotective agent, dexamethasone as antiemetic, as these drugs may worsen the clinical condition of a patient with COVID-19.¹⁸ Use of alternatives to these medications is suggested. In a case of postpartum haemorrhage, use of carboprost tromethamine has been related to immediate and prolonged bronchospasm in a patient with COVID19, therefore other drugs like oxytocin and methylergometrine should be the preferred uterotonic.^{19,20}

Timing of delivery depends on severity of infection, obstetric and fetal indication. Pregnancy may be continued to term under supervision in mild cases but in critical cases premature delivery or termination of pregnancy must be considered for safety of the mother after consultation with the patient and her family.

Pregnant healthcare professionals

Due to scarcity of information, there is a lot of anxiety and fear amongst pregnant healthcare professionals. However, it is advisable for all pregnant women to minimize social contact as a precautionary measure. Pregnant women are not more susceptible to catch the virus but infection with COVID-19 may have different course of disease in pregnancy and may pose risk to their unborn baby, should the mother become critical. Therefore, it is advisable for pregnant healthcare professionals to discuss their concerns with institutional department.

Conclusion

To conclude, planning and preparedness is need of the hour against COVID-19 pandemic. The goal must be the provision of pertinent clinical management to patients and importantly, with adequate protection of healthcare professionals. However, there may be different obstacles in different countries in accomplishing the goal, such as paucity of medicines, personal protective equipment kits and blood products (reduced blood donations), panic and lack of awareness amongst infected pregnant women leading to their admissions in hospitals in advanced stage of labor. The morbidity and mortality amongst healthcare professionals is also a serious concern. Improvement in governance of healthcare and also education of healthcare personnel in infection control and self-protection need to be emphasized. The clinical course and response to treatment of COVID19 may differ from previous outbreaks of SARS in 2003 and MERS, therefore recommendations on its management in pregnancy must be drawn on grounds of current experience. Guidelines will keep on evolving as more information becomes available with time.

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