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Obstetric anaesthesia and analgesia for pregnant women with COVID-19: a narrative review with practical considerations

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**Obstetric anaesthesia and analgesia for pregnant women with COVID-19：a narrative review with practical considerations**


## Abstract

During the COVID-19 pandemic, labour and delivery are not going to be put on hold. Managing anaesthesia for patients with COVID-19 will be a challenge, but there is little available data. Having reviewed the literature and the recommendations of experts, and the knowledge gained from the SARS epidemic, this article examines contemporary thinking regarding COVID-19 and pregnancy, the advantages and difficulties of various forms of anaesthesia, and a number of practical considerations related to the management of obstetric analgesia and anaesthesia for pregnant women with the disease.


Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus, emerged as a highly contagious and is spreading globally at an accelerating rate. By April 11, 2020, COVID-19 had been shown to be responsible for 109,021 deaths across 210 countries, with a total of 1,786,157 cases identified. A significant number of the identified cases will inevitably be pregnant women. Although there is little information regarding the effects of COVID-19 in pregnancy, it is the duty of those providing obstetric care to ensure that the birth process has the highest possible level of safety. There are a number of significant challenges to anaesthetists, which include what types

of anaesthesia they should choose given the condition of the patient, how they can protect themselves from contracting the virus from the patient, and any identifiable risk that COVID-19 medication poses for either mothers or babies.

For this paper, a thorough search has been made of the literature available on PubMed, Google Scholar, medRxiv, and the academic research communication platform of the Chinese Medical Association related to COVID-19 research; all of these were searched for the period January 1 to April 12, 2020, using the keywords, in English or Chinese, as appropriate, novel coronavirus disease 2019, cesarean delivery, labor analgesia, obstetric anesthesia, pregnancy, COVID-19, SARS-CoV-2, 2019 nCoV. A review was also undertaken of the references from any articles found to look for further research. For a systemic analysis of managing anaesthesia in pregnant women, any literature that did not describe the method of anaesthesia employed was rejected. Two authors (WD/LB) undertook a review of the papers and made an independent selection of those articles suitable for review. This review aims to provide practical considerations for anaesthesia and analgesia care for pregnant women with COVID-19, bringing together the up-to-date understanding of COVID-19 and pregnancy.

**COVID-19 in pregnancy: current knowledge**

The majority of people suffering from COVID-19 will encounter mild to moderate respiratory symptoms and be able to recover without needing special treatment. Severe symptoms and/or fatal outcomes are more likely to occur in older people and those who have comorbidities[1]. It is believed that pregnant women have a greater susceptibility to viral infections such as influenza in comparison to non-pregnant women, caused by attenuation in cell-mediated immunity by T-helper 1 (Th1) cells to Th2 cells which become dominant for protection of the fetus[2, 3]. It has been shown that SARS-CoV-2 activates release of IL-6 (mostly a response from Th1)[4], which has theoretical associations with a notably greater

probability of infection with COVID-19. But till now, there are no evidences supporting the great possibility of SARS-CoV-2 infection during pregnancy. In addition, physiological adaptive changes that occur in the course of pregnancy (diaphragm elevation, raised oxygen consumption, and respiratory tract edema) make pregnant women more likely to catch viruses generally, and also increases the likelihood of swift progression towards respiratory failure if the respiratory system comes under attack[5]. At present, no evidence exists to demonstrate whether or not pregnant women are more susceptible to catching COVID-19, but all of the above must be kept in mind when managing any pregnancy affected by the virus.

Globally, a leading cause of maternal death is viral pneumonia. When SARS was prevalent, research concerning 12 pregnant women in Hong Kong demonstrated that 50% of pregnant women needed intensive care treatment, 33% needed mechanical ventilation, and there was a 25% mortality rate amongst these women[6]. Whilst SARS-CoV-2 has genetic links with SARS-CoV-1 (around 79.5% shared identity), outcomes for pregnant women who have tested positive for COVID-19 appear to be better than was the case with SARS, being on a level equivalent to occurrences for the population as a whole[7-9]. In our review of the literature, we found that a cohort of 98 pregnant women recovered from the virus without any lasting effects (Table 1)[5, 9-17]. Although these data demonstrated that pregnant women with COVID-19 did not experience any long-term damage, these findings should be treated carefully in view of the low number of women involved and the short time span. In view of the physiological vulnerabilities to viruses and their immune-compromised nature, pregnant women must still be regarded as a high-risk group requiring robust preventative/management strategies regarding COVID-19. Recent literature[18] from Iran detailed the case of a 27-year-old woman who died of multi-organ failure just over 30 weeks into her pregnancy; it is possible that this is the first confirmed COVID-19 maternal death recorded in literature. The patient's CT scan and chest x-ray did not show typical features of pulmonary infection by COVID-19.

Nevertheless, as she was suffering respiratory distress, her trachea was intubated and then under mechanical ventilation. The fetus was delivered with an Apgar score of zero and was unresponsive to neonatal cardiopulmonary resuscitation.

Pneumonia in pregnant women has associations with preterm labour, intrauterine growth restriction (IUGR), premature rupture of membranes, and neonatal mortality[19]. Such serious neonatal outcomes were found in the course of the SARS epidemic[6, 20]. Our review of the literature presents 11 articles consisting of 6 case report, 1 case series and 4 retrospective studies. 98 pregnancies produced 99 neonates (one set of twins). Our review showed that with COVID-19 neonatal complications included premature delivery and low birth weights[5, 11]. No solid evidence is currently available to indicate that SARS-CoV-2 is passed on by vertical transmission. There is a theoretical risk but given that both viruses undergo binding with the same receptor (angiotensin-converting enzyme II, ACE2)[21, 22], widely expressed in the umbilical cord and placenta [23], it may well be as low as that in the SARS-CoV-1 outbreak. Of the cases found in the literature up to April 12, 2020, two neonates had throat swabs showing a positive nucleic acid test a short time following delivery[9, 14], even though rigorous infection controls were employed in the course of delivery, which implied that SARS-CoV-2 found in the upper respiratory tracts of these neonates could be maternal in origin. However, it is not known if the neonates contracted the virus pre- or post-delivery. It was further reported that till March 8, 2020 three infants had SARS-CoV-2 IgM antibodies higher than the normal level (<10AU/mL), which could indicate in utero infection, as IgM antibodies cannot cross the placenta barrier and generally manifest between three to seven days post-infection. However, no ready explanation was available for the fact that nasopharyngeal swabs for these infants were repeatedly negative for PT-PCR[24, 25]. With reference to sample size limitations and a lack of full information, more research is needed to find whether SARS-CoV-2 infections can be vertically transmitted, particularly for neonates

where the mother became infected at an early stage of pregnancy. Whatever the risks may be, it seems that most children who contract SARS-CoV-2 only show mild respiratory symptoms[26].

**Choosing anaesthesia for pregnant women with COVID-19**

There are a number of differences in the way perioperative management for pregnant women differs to that for non-pregnant individuals. COVID-19 in pregnancy presents significant challenges to anaesthetists due to the low levels of information currently available regarding the management of anaesthesia. While there is a considerable degree of safety for general and neuraxial anaesthesia in obstetrics[27], with patients infected with COVID-19 very careful risk/benefit analysis must be undertaken regarding any interventions with either mother or fetus. It is vital that anaesthetists should take measures to prevent airborne infection in the course of anaesthesia and patient monitoring. The review of the literature[5, 9-17] found that publications cited were generally brief reports that did not contain detailed information regarding anaesthesia; they all described the anaesthesia and associated surgery as being straightforward and without complications.

Neuraxial anaesthesia

No evidence exists that there are contraindications for neuraxial analgesia or anaesthesia when COVID-19 is present. The Royal College of Anesthetists (RCOA)[28] recommended minimizing the risk that general anaesthesia will be required with pregnant women having either suspected or confirmed COVID-19 by using neuraxial techniques. While neuraxial anaesthesia may lead to a reduction in the risk of aerosol exposure, certain potential problems should be noted.

The most significant concern for pregnant women having COVID-19 who need a neuraxial block is hypotension. Significantly, 12/14 (86%) of pregnant women with COVID-19 exhibited hypotension following epidural anesthesia, though no adverse outcomes were observed either for mother or child[15]. One possible reason for this is that the key for the SARS-CoV-2 infection is the way its S protein binds with ACE2 receptors[21, 22] which have a central part in regulating the circulatory system[29]. Maternal hypertension has associations with a number of symptoms that could lead to a worsening of COVID-19 symptoms, e.g. nausea, vomiting, dyspnea, and dizziness, and is correlated with decreased uteroplacental flow resulting side effects on fetus, including lower Apgar scores and umbilical acidosis[30]. Thus, fluid therapy should be prepared along with drug therapy before undertaking neuraxial procedures to maintain systolic arterial pressure (SAP) at ≥ 90% baseline or avoid a drop of pressure < 80% baseline[30].

Post-dural puncture meningitis (PDPM) is one of the other concerns, particularly if the patient has untreated viremia. With these patients depressed immune status is a risk factor along with other significant complications such as sepsis, caused by the virus and steroid therapies[31]. To date, there have been no reports indicating neurologic sequelae following neuraxial procedures with such patients[32]. Lumbar punctures are a diagnostic procedure for patients exhibiting fever and changed mental states. PDPM occurs rarely with these procedures, with one case of meningitis in around 53,000 (0.2/10,000) following the procedure[33]. "Under very rare circumstances" micro-bleeding in the course of spinal anaesthesia can cause hematogenous spread[31]. With the patient who developed meningitis following a lumbar puncture, this is thought to have been due to the bacteria/virus' pathogenic nature, not as a result of them being seeded within the subarachnoid space. Current data showed that there is a very low risk of encephalitis or meningitis being caused by neuraxial procedures, even amongst patients who are infected[34]. 49 patients with COVID-19 in a recent observational study were given spinal anaesthesia and none had any adverse reactions either intraoperatively or post-

operatively[7]. We also found that in every instance of dural puncture (spinal anaesthesia 47/70, CSEA 23/70) that no neurologic sequelae were present (Table 1). Regarding the limitation of the sample size and incomplete information, further studies are warranted to assess the risk of dural puncture in COVID-19 pregnant women, particularly the likelihood of SARS-CoV-2 infection in early pregnancy, if this is the case, then doing a neuraxial procedure would not introduce virus since it is already there. Nevertheless, because there is still a possible risk involving PDPM, standard epidural techniques that do not employ dura puncture could be preferable.

During the SARS epidemic, cerebrospinal fluid taken from a 32-year-old woman in the 26$^{th}$ week of her pregnancy showed positive for SARS-CoV-1, which implies that it is possible for the virus to infect the central nervous system (CNS)[35]. The outcomes of autopsies have also demonstrated that it is highly likely that SARS-CoV-1 is present in the CNS[36]. In the same way as SARS-CoV-1, SARS-CoV-2 enters the cell through interactions with ACE2 receptors that have one expression across a number of systems, which includes the CNS[37]. Recent research demonstrated that SARS-CoV-2 had a binding affinity with ACE2 10 to 20 times higher than with SARS-CoV-1[38]. Research reviewing 214 patients infected with COVID-19 found that 78 of them displayed neurologic manifestations (both 6.4%), which implies that SARS-CoV-2 could attack the CNS[39]. While this evidence should not be regarded as absolutely ruling out spinal anesthesia, it would appear to be wise to be cautious in this area. However, greater understanding of the neurotrophic potential of SARS-CoV-2 is urgently required so that optimal customized anaesthesia management and treatment protocols can be delivered to patients, particularly women in pregnancy.

Dependent on severity, thrombocytopenia has for a long time been regarded as a relative/absolute contraindication for neuraxial techniques. One third of patients in a case series from Wuhan developed thrombocytopenia (platelet count$<150{,}000 \times 10^6$/L)[40] in comparison with pregnant

patients' rate of 7% to 12%[41]. When the platelet count is below 70,000 × $10^6$/L, the risk of vertebral canal hematoma should be considered, although it is very low[42]. An individual decision based on risks and benefits should be made. Recent meta-analysis[43] has demonstrated that lower platelet counts have associations with an increasing risk of severe outcomes or mortality for patients infected with COVID-19. During the SARS outbreak, viral infection and mechanical ventilation caused endothelial damage which triggered platelet activation, aggregation, and thrombosis in the lung, leading ultimately to platelet consumption[44]. Nevertheless, according to WHO reports[45], there are notable differences between SARS and COVID-19 which suggest that the pathophysiologic mechanisms of the two infections may be different. Generally, thrombocytopenia in COVID-19 patients is associated with adverse outcomes. While various institutions set varying levels for interpreting the limits of thrombocytopenia, a review of platelet count prior to any neuraxial procedures and/or epidural catheter removal would seem to be sensible[46].

General anesthesia

For pregnant women suffering from COVID-19, general anaesthesia should not be employed except in cases of absolute necessity[28, 46]. If tracheal intubation has already taken place, general anaesthesia may be employed in the course of cesarean delivery (CD)[47]. Amongst the possible risks of general anaesthesia are aerosol transmission of virus and pulmonary complications. As the lung is the chief organ targeted by SARS-CoV-2, patients having hypoxia and other problems caused by pregnancy-related respiratory changes are more likely to be prone to development of additional pulmonary complications, e.g. atelectasis, pulmonary edema, and respiratory failure caused by mechanical ventilation and intubation. It is notable that there has been long-standing recognition of the fact that managing the airway in obstetrics presents unique challenges and there is a greater likelihood of failure with tracheal intubation[48]. The most common cause of maternal morbidity/mortality is a

failure of intubation and associated inadequacies of ventilation[49]. In the course of intubation, extubation and caring for the airway in pregnant patients, there is a considerable risk of virus exposure for anaesthetists and their co-workers[50]. Thus, if it is absolutely necessary to use general anesthesia, robust precautionary measures must be taken in advance.

**Considerations related to anaesthesia and analgesia with pregnant women**

There are numerous points to consider related to the perioperative management of pregnant women suffering COVID-19, so a number of essential factors have been listed that the healthcare providers should integrate to their institutional protocols (Table 2). There are certain essential points with which anaesthetists should familiarize themselves.

Staff and equipment

Staff numbers should be kept to the lowest necessary level, and a dedicated team should be made responsible for caring for pregnant women with COVID-19. To prevent crash situations and drug contamination in the working environment for anesthesia, it is recommended that COVID-19 kits should be prepared containing all the drugs needed for CD and labour analgesia[46]. If problems with the airway are expected, resources and equipment must be prepared to allow for airway rescue and for implementation of a "can't intubate can't oxygenate" (CICO) situation[48, 51]. All requisite equipment and medication must be available within the room when the procedure takes place, as staff entering and exiting the room may lead to an increased risk of viral transmission[52]. It could be useful to prepare a checklist of necessary materials appropriate for obstetrics with COVID-19 patients[51]. The anaesthesia personnel with the greatest experience should undertake procedures such as airway management and neuraxial anaesthesia in order to offer the best chances of first-time success[53]. Additional staffing may be required due to the fact that COVID-19

patients require time-intensive care, which includes the time for dressing/undressing personal protection equipment (PPE), and it would be wise to have backup strategies in place[46]. It should be noted that when a pregnant woman is asymptomatic but has a confirmed SARS-CoV-2 infection, there may be a crossover between manifestations of the illness and pregnancy symptoms. It was shown in a recent report that for 210 pregnant women showing no symptoms of COVID-19 in New York, USA, 29 (13.7%) were found to be positive for SARS-CoV-2 when tested upon admission for delivery[54]. COVID-19 transmission via asymptomatic carriers presents significant challenges in terms of containment; every health worker should note this and ensure that proper protective procedures are followed at all times during the pandemic. Testing every pregnant woman for SARS-CoV-2 when they are admitted will offer guidance on the deployment of PPE.

Precaution strategies

The Association of Anaesthetists of Great Britain recently released guidelines[55] with a focus on perioperative management for COVID-19 patients. These communications mentioned certain similar issues, among them the use of PPE, proper hand hygiene practices, and the safe management of airways. While it is believed that COVID-19 is chiefly transmitted through droplets and contact, when such close physical proximity/contact as prevails during labour and delivery, there is the potential for airborne transmission. This means that special precautions should be taken for minimization orientation risk in the labour/delivery room. Patients who have either confirmed or suspected COVID-19 must wear surgical masks and be treated in a designated room, ideally an airborne isolation room (i.e., a single room with negative pressure in which the air is frequently changed); warning signs should be used outside the room to prevent unnecessary staff exposure[53]. Before entering the room all medical personnel should don appropriate eye protection and other PPE for protection against contact and/or droplet transmission[46]. During

the aerosol-generation medical procedures (e.g., tracheal intubation, non-invasive ventilation, manual ventilation before intubation, extubation and bronchoscopy), strict protection for anaethetists are needed, including PAPRs or double gloves[52, 56]. Once emergent CD is indicated, the degree of PPE for anaesthetists need to be weighed in respect of categorization of urgency. For example, category 1 CD under epidural top-up has a significant risk of GA conversion, therefore airborne precautions are warranted from the outset (there will not be time to don intra-operatively if the block fails).

Oxygen supply

18% of patients presenting with COVID-19 present with shortness of breath[57]. It may be problematic to distinguish between pathologic dyspnea and the usual physiologic shortness of breath normally found in labour caused by high maternal oxygen requirements. Individual evaluation of each patient should take place for consideration of how aerosolization at the airflow rate should be balanced for the mistreatment or maintenance of optimal oxygen saturation levels, and when conversion to invasive mechanical ventilation should take place. It is recommended that oxygen therapy put in place at an early stage ($O_2$ saturations$\geq$ 95% and/or $PaO_2 \geq 70$ mmHg should be targeted)[58]. Pregnant women exhibiting mild COVID-19 symptoms in the course of labour/delivery may be provided with supplemental oxygen if necessary through a nasal cannula; surgical masks should be worn above the cannula for reduction of droplet transmission risk[52]. Patients displaying severe respiratory systems might need mechanical ventilation to increase maternal oxygen levels (target $PaO_2 > 70$ mmHg rather than 55 to 80 mmHg) and to decrease carbon dioxide levels (target $PaCO_2$ 28 to 32 mmHg) to mitigate the risk of respiratory failure and fetal hypoxemia[59]. High flow nasal oxygen (HFNO) and non-invasive ventilation (NIV) may present small risks of aspiration during pregnancy and the two increase risk of aerosol generation dependent on

airflow rate, ventilator pressure, and how cooperative the patient is[51]. Because of this, such equipment should be deployed within airborne isolation rooms and administering personnel must be equipped with close-fitting PPE during such procedures. If HEPA breathing circuit filters are available at least one should be employed between the endotracheal tube and the breathing circuit so that the virus cannot infiltrate the anaesthesia equipment[50].

Tracheal intubation, extubation, and airway management

The intubation of patients suffering COVID-19 is a significant challenge for an anaesthetists, particularly if the patient is pregnant. There is always a desire to deliver the fetus as rapidly as possible which can militate against good preparation, assessment, planning and/or communication procedures. Most problematic airway issues and failed intubations in obstetrics are a result of emergency situations and time pressure[48]. A number of essential elements should be in readiness in case a crash occurs (Table 3). Routine assessment of airways must take place.

WHO[45] recommend that COVID-19 patients are suitable for rapid sequence induction (RSI) that is standard procedure for general anaesthesia induction in obstetrics. If patients can't cope with a short apnea period, or their alveolar-arterial gradient is very high, ultra-rapid modified RSI-transnasal humidified rapid-insufflation ventilatory exchange technique (THRIVE) may be required[60]. Anaesthetists should consider five minutes of preoxygenation at 100% oxygen using a tight seal to mask before RSI, for the avoidance of manual ventilation and possible aerosol generation. Should manual ventilation be needed, a small tidal volume should be applied. Although HFNO has been suggested and developed as a methodology for obstetric pre-oxygenation and provides apneic oxygenation[48], these have only been assessed in non-obstetric population[61].

And there is controversy about how safe this procedure is with COVID-19 patients[28, 62]. Of more pressing article concern is the adequate protection of caregivers from possible aerosol generation. It is recommended that RSI is performed using a video laryngoscope[60, 63]. Muscles must be sufficiently relaxed for the prevention of coughs in the course of tracheal intubation. Fiber-optic intubation on awake patients should be avoided unless there is a specific reason for it. For those circumstances that oxygenation and manual ventilation may not be guaranteed once anaesthesia has been induced in pregnant women, it is advisable to employ awake intubation, with every precaution being closely adhered to. Particular preparations for this may involve the employment of topical anaesthesia and adequate sedation. It would be best if awake intubation/anaesthesia was provided by an anaesthetist and surgical team with prerequisite airway specialty knowledge.

However, tracheal extubation carries high risks of aerosol generation. Coughing can be effectively reduced without inducing significant side-effects with COVID-19 patients through intravenous Lidocaine administration before tracheal extubation[64]. The fewest possible number of staff should be present in the room. A plan will be required for pre-extubation, with several issues to be considered, including how respiration will be supported following extubation[65].

Timing of delivery

Delivery timing choice should be customized to the patient after a comprehensive assessment of conditions for both mother and fetus and the gestational age. Nevertheless, if the mother's condition is so severe that treatment cannot improve it, the CD threshold can be reduced[45, 47]. Emergency CD should be prompted by fetal distress, acute organ failure, or septic shock. During late pregnancy, delivering the placenta and fetus will decrease oxygen demands by as much as 50 mL/min, a critical amount in acute respiratory distress syndrome (ARDS) patients[66].

Reviewing the literature of COVID-19 cases, the majority of CDs were undertaken for obstetric indications. In 7 cases CD was implemented due to the risk of the mother suddenly clinically deteriorating and the effect that the virus and associated medication could have on fetal development[9]. Chen[5] suggested that a contributory factor was uncertainty about the chances of intrapartum vertical transmission through vaginal delivery. Generally speaking, COVID-19 does not, in and of itself, indicate a pregnancy should be ended. Maternal and fetal/infant safety has to override the potential risks of surgery.

Prophylaxis for nausea and vomiting

Vomiting and nausea occurs more frequently in CD than in other, non-obstetric surgeries. A number of reasons exist for this. Spinal anaesthesia induces hypotension which could either activate the gastrointestinal tract[67], and COVID-19 could make the hypotension more severe[15]. Certain surgical procedures (e.g., intra-abdominal saline irrigation, uterine exteriorization) , anaesthetic causes (e.g., hypotension, increased vagal activity) and medications (e.g., uterotonics, antibiotics) are contributory factors[68, 69]. Intra-operative nausea and vomiting (IONV) and post-operative nausea and vomiting (PONV) are major stressors for women and families. Operating surgeons may find IONV significantly challenging and there is a risk of possible aspiration. Vomit is an environmental contaminant and increases risks of exposure to the virus. When patients with COVID-19 undergo CD, it is recommended that they be given antiemetics[46].

Corticosteroids

As steroids could potentially promote viral rebound and are associated with adverse events, including ARDS[70], for patients with suspected/confirmed COVID-19, dexamethasone is not recommended for prophylaxis against PONV for these patients[46]. This is in line with the

present WHO interim guidelines[45] but do not recommend that corticosteroids should routinely be employed to manage COVID-19 patients. In theory, a corticosteroid might be able to suppress inflammation in the lungs, inhibiting pathogen clearance and immune responses[71]. Despite this, a team of doctors working on the frontline in China has opposed such liberal deployment of corticosteroids as the current evidence is methodologically limited; and they counsel prudent use in low to moderate dosage for patients who are critically ill from COVID-19 [72]. However, decisions as to whether to use corticosteroids for the acceleration of fetal maturity and to improve outcomes for both mother and child in instances of expedited preterm delivery must be taken on a case-by-case basis[2]. Careful assessment of the risk/benefit analysis regarding corticosteroid should be made and the decision should be taken in conjunction with the patient and her family.

NSAIDs

It is common to add non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen to post-operative analgesic regimes in tandem with opioids for pain relief following CD with the aim of reducing the consumption of opioids[73]. However, there are concerns that the symptoms of COVID-19 will be worsened by NSAIDs. It is feared possible that NSAIDs could enhance the expression of ACE2 and thus make it more likely that severe/fatal COVID-19 may develop[74]. One study[75] demonstrated that individuals with community-acquired pneumonia (non-COVID-19 related) had their symptoms worsened and illnesses prolonged following administration of NSAIDs. But actually, up to April 10, 2020, there have been no articles on Pubmed reporting the connection between the use of NSAIDs and the severe adverse events of COVID-19 (e.g., acute health care utilization, long-term survival, or quality of life of COVID-19 patients) [76].Until robust evidence exists, pain patients should continue to take their NSAIDS rather than turn to opioids[77]. While the WHO guidelines do not currently prohibit the use of NSAIDs on the basis of the

information available at present, when treating postpartum pain in patients symptomatic for COVID-19, caution should be employed[45]. The decision to use NSAIDS should be based on a risk/benefit analysis.

Nitrous oxide

Nitrous oxide is frequently used in obstetrics to control pain. Due to risks of aerosolization, it should not be given to patients with either suspected or confirmed COVID-19. There is presently too little evidence to make assumptions regarding how safe nitrous oxide may be in such contexts[46]. Epidural analgesia or patient-controlled analgesia (PCA) should be preferred for pain control at present[78].

Thromboembolism prophylaxis

Recent research has shown an association between COVID-19 and high D-dimer levels which are present in between 36% and 43% of positive instances of the virus[79]. Pregnant women are at greater risk of venous thromboembolism (VTE) which was 4-5 fold higher than those who are not pregnant. It has been proposed that D-dimer levels increase progressively over the course of pregnancy[80]. However, D-dimer levels are not regarded as a reliable means of screening for VTE during pregnancy or postpartum as it is not a reliable diagnostic tool[80]. In a retrospective analysis, 1,026 non-obstetric patients with COVID-19 were included for evaluation of the risk of VTE. 40% of them had a high risk and most of VTE can be prevented. The author suggested that among COVID-19 patients with a high risk of VTE, anticoagulation drugs and mechanical compressions should be considered[81]. Recently, the Royal College of Obstetricians and Gynaecologists (RCOG) updated the comment on VTE from COVID-19. It was recommended to use low molecular weight heparin in prophylaxis to reduce the risk of VTE in patients with COVID-19 during pregnancy, and to consider pulmonary embolism if women with COVID-19 suddenly deteriorate[82].There are doubts over the usefulness

of D-dimer in diagnostic management in obstetrics, but in relation to the risk factors, for the prevention of VTE, pneumatic compression/early mobilization should be employed for all postpartum women.

Mental health care

Having to practice social distancing and isolation from their newborn will clearly have an impact on mother-infant bonding and initiation of milk supply, and may even provoke negative emotions. It has been illustrated that widespread disasters, environmental, traumatic, natural, inevitably lead to increases in depression, PTSD, and many other behavioral/mental disorders[83]. Even in times of relative calm and peace, one in seven women suffers peripartum depression[84]. Because of this, those providing obstetric care should be taking steps to prevent and/or intervene to effect reductions in the influence the current pandemic has on mental health or postpartum patients. Physical care should be supplemented by psychological and emotional support systems. Patients should be provided with a means of remotely communicating throughout their pregnancy and afterwards, e.g. by SMS, video calling, et cetera, so that physical contact can be minimized. An assessment should be made regularly so that the levels of pain relief required can be correctly and effectively assessed; effective communication and the right levels of peripartum anaesthesia could play a significant part in preventing the onset of mental health disorders.

Education/training

COVID-19 is a global public health emergency the like of which has not been seen for many decades. Healthcare providers on the front line are at a high risk of infection with SARS-CoV-2. Of the 44,672 infections reported, over 3,000 were in some way related to the medical profession[85]. There is little data as to how many anaesthetists have contracted the infection; one single-center study stated that SARS-CoV-2 RT-

PCR showed positive in 5/44 anaesthetists (11.4%)[17]. Those providing anaesthesia face significant dangers of infection, so preventative and control measures of the essence. Education regarding COVID-19 patient management should be regular, interdisciplinary, and held in departments. Ideally education sessions should be supported with multimedia visual aids and practical exercises[86]. Simulated drills should be gone through for a number of different scenarios, e.g. transporting patients between operating room and labour rooms, putting on and taking off PPE, conversion to general anaesthesia and accompanied tracheal intubation, extubation patients and promoting their recovery. It must be borne in mind that undertaking standard obstetric procedures, e.g. neuraxial anaesthesia, will be more complex and take more time when it is necessary to wear PPE[87]. In many ways the COVID-19 outbreak has been a valuable wake-up call to the anesthesiology profession to be prepared for all eventualities.

**Conclusion**

This narrative review has focused on managing obstetric anaesthesia for pregnant women infected with COVID-19; specialist literature regarding clinical features and obstetric and neonatal outcomes for patients infected with the virus have been excluded. This methodology could be useful in excluding the possibilities of overlapping data supplied by more than one department in the same hospital facility, e.g. a report by Zhang et al[88] was not included because its data represented collected figures from three Wuhan medical institutions that had already been registered individually.

When pregnant women have suspected/confirmed COVID-19, this represents a special case requiring expert knowledge of the disease's pathophysiology. This review has presented the optimal knowledge currently available to address the challenges of COVID-19, ranging from its

clinical virology and action in pregnancy to anesthetic choices. The details given above of perioperative management strategy and essential practical considerations for pregnant women should be carefully considered. It must be understood that COVID-19 knowledge and practice is in a continual state of flux and so all the recommendations above may be subjected to modification. At present it is extremely difficult to draw some conclusions regarding analgesia and anaesthesia for pregnant women infected with COVID-19. As more and more data is gathered and case series published globally, we will have an improved idea of the action of COVID-19 in pregnant women and how analgesia and anaesthesia should be deployed with them; this will help us create ever more efficient strategic plans. With many thousands of researchers globally researching COVID-19, it is to be hoped that the optimal interventions to fight this deadly pathogen will soon be revealed.

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**Table 1**: **Anesthetic management and clinical characteristics of pregnant women with COVID-19**

| Author | Cases (n, mother/ neonates) | Gestational Age, w | Mode of delivery (Vaginal/CD) | Indication for CD (OB/Virus) | Anesthetic regimen (GA/ Neuraxial) | Oxygen Support | Fever prior to delivery | PLT | D-dimer | Respiratory status at time of delivery | Neonatal outcomes | Potential Vertical Transmission Evidence |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Chen et al., 2020, China[5] | 9(9) | 36 0/7 to 39 4/7 | CD | OB (7); virus (9) | 9(100%) Epidural anaesthesia | 9(100%) Nasal Cannula | 7/9 (78%) | NR | NR | 9(100%) CT Evidence of pneumonia | 2(22%) low body weight 4 (44%) Premature delivery | All negative |
| Yu et al., 2020, China[9] | 7(7) | 37 0/7 to 41 2/7 | CD | Virus (7) | 6(85%) CSEA, 1(15%) GA | 7(100%) Nasal Cannula | 6 (86%) | 2 (29%) below normal | 7(100%) above normal range | 7(100%) CT Evidence of pneumonia | Normal | 1 neonates nucleic acid+ (36h, |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | rang e | | | | throat swab) |
| Xia et al., 2020, China[10] | 1(1) | 36 5/7 | CD | OB | CSEA | Face mask (3L/min) | 1(100% ) | NR | NR | CT Evidence of pneumonia SARS-CoV-2 Nucleic Acid in oropharyng eal swab + | Normal | negati ve |
| Wang,e tal., 2020,C hina[11] | 1(1) | 30 6/7 | CD | OB | CSEA | Face mask (5L/min) | Normal | NR | 1(100 %) above norma l range | 1(100%) CT Evidence of pneumonia | Prematu re, 1830g, | negati ve |
| Lee et al., 2020, Korea[12] | 1(1) | 37 6/7 | CD | OB | Spinal anaesthesi a | No oxygen supply | Normal | NR | NR | 1(100%) CT Evidence of pneumonia | Normal | negati ve |
| Kang et al., 2020, China[13] | 1(1) | 35 2 | CD | OB | Epidural anaesthesi a | Nasal Cannula | 1 | 96× $10^9$/ L | 1(100 %) 3139u g/L | 1(100%) CT Evidence of pneumonia SARS-CoV-2 Nucleic | Normal | negati ve |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Acid in Throat Swabs + | | |
| Wang et al., 2020, China[14] | 1(1) | 37 3 | CD | OB | Spinal anaesthesia | Face mask | 1 | 114 $\times 10^9$ /L | NR | 1(100%) CT Evidence of pneumonia SARS-CoV-2 Nucleic Acid in Throat Swabs + | Normal | 1 neonate nucleic acid+ (36h, throat swab) |
| Chen et al., 2020, China[15] | 17(17) | ≥37 (14) < 37 (3) | CD | OB | Epidural (14), GA(3) | Nasal Cannula | 4(24%) | NR | NR | CT Evidence of pneumonia SARS-CoV-2 Nucleic Acid in Throat Swabs + | Normal | negative |
| Yue et al., 2020, China[16] | 14(15) | 38±0.4 | CD | OB | CSEA | NR | 4(28.6 %) | NR | NR | CT Evidence of pneumonia SARS-CoV-2 Nucleic Acid in | Normal | Negative |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | Throat Swabs + | | |
| Song et al., 2020, China[89] | 1(1) | 36 3 | CD | OB | CSEA | Face mask (5L/min) | 1 | NR | NR | CT Evidence of pneumonia SARS-CoV-2 Nucleic Acid in Throat Swabs + | Normal | Negative |
| Zhong et al., 2020, China[17] | 45(NR) | NR | CD | OB | Spinal anaesthesia | Nasal Cannula | 45 | NR | NR | CT Evidence of pneumonia 13 (26.5%) with Positive RT-PCR for SARS-CoV-2 | NR | NR |

SARS-CoV-2: severe acute respiratory coronavirus, CD: cesarean delivery, OB: obstetric, CSEA: combined spinal epidural anaesthesia, GA: general anaesthesia, RT-PCR: Reverse transcription polymerase chain reaction, PLT: platelet count, CT: computerized tomography, NR: not reported

**Table 2: Peri-operative management elements of Cesarean Delivery in patients with COVID -19**

| | **Maternal surveillance** | **Neonatal surveillance** |
|---|---|---|
| Pre-operative | • T, BP, HR, RR, $SpO_2$ monitoring<br>• Chest imaging (high resolution CT-scan or X-ray), if necessary<br>• Routine evaluation<br>• Aspiration prevention, antibiotics prophylaxis | • FHR<br>• Growth + Doppler<br>• Fetal maturation (if necessary) |
| Precaution & Preparation | • Don PPE*, scrubs<br>• Assure instruments / equipment<br>• Transport patient to OR (with surgical facemask) | |
| Intra-operative | • BP, HR, RR, $SpO_2$ monitoring<br>• Oxygen supply: nasal cannula, mechanical ventilation, etc<br>• Face mask (if not intubated)<br>• PONV/IONV prophylaxis, consider avoiding dexamethasone<br>• Prevention and treatment of hypotension | • Early cord clamping<br>• Early cleaning of the newborn<br>• Isolation from mother after born<br>• SARS-CoV-2 RT-PCR of the newborn |

***PPE**

- Gown
- Gloves
- Face shield/ goggles
- N95 mask/ respirator
- PAPR
- Latex gloves

| | | |
|---|---|---|
| Post-operative | • Consider avoiding NSAIDS<br>• Intensive care unit admission if indicated<br>• No breastfeeding<br>• Thromboprophylaxis<br>• Post-operative visit via remote tools | • Monitoring in isolated room with negative pressure<br>• Isolating from mother until viral shedding<br>• Transport to NICU if indicated |

SARS-CoV-2: severe acute respiratory coronavirus，T: temperature, BP: blood pressure, HR: heart rate, RR: respiratory rate, $SpO_2$: oxygen saturation by pulse oximetry，NSAIDS：Non-steroidal anti-inflammatory drug，RT-PCR: Reverse transcription polymerase chain reaction, CT: computerized tomography, PONV: postoperative nausea and vomiting, IONV: intra-operative nausea and vomiting, PPE: personal protective equipment, NICU: neonatal intensive care unit, OR: operating room, FHR: fetal heart rate

**Table 3: Necessities in airway management for pregnant women with COVID-19**

| Precaution | Airway equipment | Medication |
|---|---|---|
| • Gown<br>• Gloves<br>• Face shield/ goggles<br>• N95 mask/ respirator<br>• PAPR<br>• Latex gloves<br>• Shoe covers | • Breathing circuit filters (HMEF or HEPA)<br>• ETT (various size), with stylet and syringe<br>• Suction catheter<br>• Supraglottic airway devices (2nd generation preferable)<br>• Video laryngoscope<br>• Fitted face mask<br>• Oral airway<br>• Nasal cannula<br>• PEEP valve<br>• Manual resuscitation bag | • Induction medication<br>• Rescue medication<br>• Uterotonics |

PAPR: powered, air-purifying respirator, HMEF: heat moisture exchanger filters, HEPA: high-efficiency particulate air, ETT: endotracheal tube