Care of the Pregnant Woman with COVID-19 in Labor and Delivery: Anesthesia, Emergency cesarean delivery, Differential diagnosis in the acutely ill parturient, Care of the newborn, and Protection of the healthcare personnel

Dr Balakrishnan Ashokka, FANZCA, Assistant Prof May-Han Loh, MMED Anesthesiology, Adjunct Associate Prof Cher Heng Tan, FRCR, Associate Prof Lin Lin SU, MRCOG, Dr Barnaby Edward Young, MRCP, Associate Prof David Chien Lye, FRCP, Prof Arijit Biswas, FRCOG, Prof Sebastian E Illanes, MD, Associate Prof Mahesh Choolani, FRCOG

PII: S0002-9378(20)30430-0

DOI: https://doi.org/10.1016/j.ajog.2020.04.005

Reference: YMOB 13198

To appear in: *American Journal of Obstetrics and Gynecology*

Received Date: 25 March 2020

Revised Date: 3 April 2020

Accepted Date: 3 April 2020

Please cite this article as: Ashokka B, Loh M-H, Tan CH, SU LL, Young BE, Lye DC, Biswas A, E Illanes S, Choolani M, Care of the Pregnant Woman with COVID-19 in Labor and Delivery: Anesthesia, Emergency cesarean delivery, Differential diagnosis in the acutely ill parturient, Care of the newborn, and Protection of the healthcare personnel, *American Journal of Obstetrics and Gynecology* (2020), doi: https://doi.org/10.1016/j.ajog.2020.04.005.

Title page

Care of the Pregnant Woman with COVID-19 in Labor and Delivery: Anesthesia, Emergency cesarean delivery, Differential diagnosis in the acutely ill parturient, Care of the newborn, and Protection of the healthcare personnel

Dr Balakrishnan ASHOKKA, FANZCA [1, 2]
Assistant Prof May-Han LOH, MMED Anesthesiology [1, 2]
Adjunct Associate Prof Cher Heng TAN, FRCR [3, 5]
Associate Prof Lin Lin SU, MRCOG [2, 6]
Dr Barnaby Edward YOUNG, MRCP [4, 5, 7]
Associate Prof David Chien LYE, FRCP [4, 5, 7]
Prof Arijit BISWAS, FRCOG [2, 6]
Prof Sebastian E ILLANES, MD [8]
Associate Prof Mahesh CHOOLANI, FRCOG [2, 6]

1 Department of Anesthesia, National University Hospital, Singapore
2 Yong Loo Lin School of Medicine, National University of Singapore
3 Department of Diagnostic Radiology, Tan Tock Seng Hospital, Singapore
4 Tan Tock Seng Hospital, Singapore
5 Lee Kong Chian School of Medicine, Nanyang Technological University
6 Department of Obstetrics & Gynaecology, National University Hospital, Singapore
7 Department of Infectious Diseases, National Centre for Infectious Diseases
8 Facultad de Medicina, Universidad de los Andes

Author contribution

Balakrishnan Ashokka, May-Han Loh, Mahesh Choolani conceived the idea of the manuscript and oversaw the direction of it. Cher Heng Tan provided input on aspects regarding diagnostic radiology and the diagnostic workflow. David Chien Lye and Barnaby Edward Young enhanced the infectious diseases perspectives of the manuscript, Lin Lin Su provided inputs from the workgroup for delivery suite management and Arijit Biswas and Sebastián Illanes supported the revisions of the manuscript.

Disclaimer: Authors report no conflict of interest

Financial support: No financial support was sought or received for this manuscript

Address for Reprint and Correspondence:
Balakrishnan Ashokka
Department of Anesthesia, National University Hospital Singapore
Main building, 5 Lower Kent Ridge Road
Singapore. 119074
Mobile: +6597118855; Office +6567724208

Word count including line, reference and figure legend: 6115
Word count with tables and figures removed: 4232
Number of Figures: 3
Number of Appendix: 1
Number of References: 59

Acknowledgement
We acknowledge the pediatric infectious diseases inputs from Dr Chan Si Min,Pediatrics, National University Hospital Singapore. The authors thank Dr Pradip Dashraath and Dr Wong Jing Lin Jeslyn, Department of Obstetrics and Gynecology, National University Hospital Singapore for their inputs during the initial discussion about the direction of the manuscript.

Short title

COVID-19: Peripartum care of the acutely ill parturient

Condensation

Stepwise approach for managing acutely ill parturients to improve maternal outcomes and minimizing disease transmission

Keywords

COVID-19, Coronavirus disease 2019, SARS-CoV-2, pandemic, coronavirus, virus, MERS, SARS, severe acute respiratory syndrome, ACE2, acute respiratory distress syndrome, ARDS, obstetric management, maternal morbidity, acutely ill, pregnancy, vertical transmission.

Introduction

Coronavirus Disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). SARS-CoV-2 are the largest among the ribonucleic acid (RNA) viruses. [1] The World Health Organization (WHO) has now declared COVID-19 a pandemic. The elderly are at greatest risk. [2] Current evidence suggests that pregnant women are no more at risk of COVID-19 than other adults, [3] nor is the condition thought to be more severe in them. [4] A case series of nine pregnant women at term, and late preterm (36 weeks and above), reported good maternal and fetal outcomes. [5] However, all these cases had short time-intervals between diagnosis of COVID-19, and cesarean deliveries, and the true impact of the disease on pregnant women should not be extrapolated from this descriptive study. Indeed, when a larger cohort of 147 pregnant patients was evaluated (WHO-China Joint Mission Report), [6] up to 8% of the cohort were either severely ill (tachypnoea ≧30 breaths/min, or oxygen saturation ≤93% at rest, or PaO_2/FiO_2 <300 mmHg) or 1% critically ill (respiratory failure requiring mechanical ventilation, shock, or other organ failure that requires intensive care). This rate of presentation of severe illness in pregnancy was less than that observed from influenza (H1N1) pandemic. [6] This statistic came from a country that is now recognized globally to be dealing with the COVID-19 outbreak admirably, having gained experience from the 2003 severe acute respiratory syndrome (SARS) epidemic. It is uncertain whether other health systems would experience an under-10% severe maternal morbidity, or instead, severe illnesses in pregnant women being closer to 25% as was observed in other coronaviral infections such as the Middle east respiratory syndrome (MERS) and SARS. [1, 7]

Moreover, the SARS-CoV-2 virus has been shown to have an 85% similarity with SARS coronavirus (SARS-CoV) and MERS coronavirus (MERS-CoV). Both the SARS and the MERS

epidemics had significant adverse effects on pregnant women including preterm deliveries, stillbirths, respiratory complications and maternal mortality. [1] Preexisting physiological factors such as basal atelectasis from gravid uterus, lower lung reserves (reduced functional residual capacity), and increased oxygen consumption (30%) [8] predispose the parturient to poor outcomes during respiratory illnesses, such as coronaviral pneumonias. On the other hand, there is reasonably good evidence to suggest that vertical transmission from the pregnant patient to the fetus is unlikely. [2, 9] Recommendations are in place for managing suspect or confirmed COVID-19 patients who are pregnant, ensuring the safety of their neonates, other parturients in the delivery suite, and healthcare workers caring for them. [3, 10, 11]

It is known that disease transmission and case fatality rate (2.3%) [12] are lower in health systems that had better systematic pandemic preparedness strategies, [13] and with experience managing coronaviral outbreaks. As of March 25, 2020, Singapore has hospitalized 631 cases of COVID-19 confirmed by real-time reverse transcriptase–polymerase chain reaction (RT-PCR) of which 3 were pregnant. Of these 631 patients, 160 have fully recovered from the infection and have been discharged from hospital. There are have been two mortalities from complications due to COVID-19. One of this was an imported case who was ill before coming to Singapore, and admitted to the intensive care unit (ICU) upon arrival. [14] Singapore was taken by surprise during the 2003 SARS epidemic, but has since build capacity and capability within the country to manage global infectious disease emergencies with protocols in place for non-gravid and pregnant patients.

Clinical presentation

COVID-19 can present with a spectrum of clinical manifestations that range from mild symptoms and signs [15] such as fever, cough, sore throat, myalgia and malaise to severe illness including pneumonia with or without acute respiratory distress syndrome (ARDS), [2] renal failure, and multi-organ dysfunction that may require immediate advanced critical care support. Clinical presentations in COVID-19 pregnant patients could be atypical with normal temperature (56%) and leukocytosis. [16]

Clinical Virology

The largest report to date on COVID-19 from China revealed 1% asymptomatic out of 72134 cases. Of 44672 cases confirmed by RT-PCR, 8% were in the age group between 20 to 29 years, versus 87% in 30 to79 years old. There was no further stratification in the 30 to 79 years age group to represent the reproductive age group 30 to 45 years. Of the 44415 cases with data on clinical severity, 81% was classified as mild, 14% severe (defined as dyspnea, tachypnea or oxygen saturation ≤93%) and 5% critical (defined as respiratory failure, septic shock or multiorgan failure). [12] Case fatality was 2.3% overall, 8% among those 70 to 79 years, 14.8% among those 80 years and older, and 49% among critically ill. [12] More detailed clinical information from 1099 patients revealed that fever was present in 43.8% on admission but developed in 88.7% during hospitalization. Cough was present in 67.8% but sputum production only in 33.7%, nasal congestion 4.8%, sore throat in 13.9% and diarrhea 3.8%. [17] The median time from illness onset to dyspnea was 8 days, to acute respiratory distress syndrome 9 days and intensive care unit admission 10.5 days. [15] Compared with non-ICU patients, ICU patients with COVID-19 were older with comorbidities, had higher temperature, more dyspnea and tachypnea, more leukocytosis, neutrophilia and lymphopenia, higher alanine and aspartate aminotransferase, bilirubin, creatinine, procalcitonin, troponin, D-dimer and lactate dehydrogenase. [15, 16, 18]

Diagnosing COVID-19

Confirmation of the disease is done using nucleic acid amplification tests (NAAT), such as real time reverse transcriptase polymerized chain reaction (RT-PCR). [13] The average RT-PCR testing needs up to 2 hours yet takes between six to ten hours for completion or even longer when batch testing is done by laboratories. [19]

Chest imaging

Imaging of the lungs is important in assessing the extent of COVID-19 pneumonia, and in the follow up. Evidence about ultrasonographic imaging of the lung in COVID-19 patients is evolving. In up to 85% of patients, abnormalities are found on imaging during the acute phase. [20] Radiological features of COVID-19 include patchy infiltrates on chest X-ray (CXR), and ground glass opacities (GGO) on chest computed tomography (CT). [21] CXRs can be rapidly performed at the bedside but may have reduced sensitivity in early stages of infection. Chest CT is more sensitive than CXR (Figure 1A and 1B), but its widespread use is limited by availability, and the practical but no less important consideration of the need for terminal cleaning to prevent nosocomial transmission, and acceptance by pregnant women. On chest CT, multilobar GGO are most commonly seen, whereas, lower lobe consolidation is more frequently encountered in patients with severe and prolonged disease (Figure 1C and 1D). [20] Its use as a first-line diagnostic tool has been cautioned against by the American College of Radiologists given its relatively untested specificity. [22]

<Insert Figure 1: Chest Imaging in COVID-19 Patients>

In an epidemic setting, where there is very high pre-test probability of COVID-19 infection, a positive result on chest CT may precede RT-PCR and may carry higher. [23] In a case series of fifteen COVID-19 pregnant patients who were exposed to between 2.3–5.8 mGy of ionizing radiation, all were found to have CT findings of mild disease, which did not worsen with pregnancy.[22] In some circumstances when an earlier diagnosis of COVID-19 would alter the management of an obstetric patient, particularly if the patient is in respiratory distress raising concerns about significant pneumonia or concomitant pathology (e.g. pulmonary embolism), chest imaging with CXR, and thereafter CT if needed, could be considered. A diagnostic workflow detailing the application of RT-PCR and chest imaging when assessing COVID-19 suspects is described (Figure2). In such instances, abdominal lead shielding may be applied to reassure patients of the minute risks of scatter radiation to the fetus. [24, 25]

<Insert Figure 2: COVID-19 SUSPECT Pregnant Patient Diagnostic Workflow>

Differential Diagnoses

COVID-19 is primarily a respiratory illness**.** As our understanding of the diagnostic imaging features of COVID-19 evolves, significant overlap with other viral and atypical pneumonias are increasingly reported. On CXR, COVID-19 pneumonia often presents with multifocal, bilateral airspace opacification.[2] This distinguishes it from the more common unifocal involvement noted in SARS, [26] but not from MERS.[27] When imaged by CT, the distribution seen in COVID-19 is similar to that noted in other viral and coronaviral [20] pneumonias, such as influenza,

parainfluenza, respiratory syncytial virus, and adenovirus. [28, 29] Even the multifocal GGO, described in more than 80% of COVID-19 pneumonias [30] are common features of atypical (e.g. Mycoplasma pneumoniae) and opportunistic (e.g. Pneumocystis jirovecii) pneumonias. [31, 32] As with other viral pneumonias, lymphadenopathy and pleural effusions are uncommon associated findings.[30] In the latter stages of COVID-19, confluent consolidation and interstitial thickening become more pronounced, with up to 20% patients developing features of ARDS. [18, 21] Given the significant overlap of imaging findings with other acute viral respiratory infections, imaging alone is unlikely to supplant the role of RT-PCR for the primary diagnosis of COVID-19.

Minimizing disease transmission

Person to person transmission is now known to occur via fomites, via droplets through close proximity aerosols,[33, 34] and prolonged close contact within two-meter perimeter.[13]A study showed that patients can continue to shed the virus as evidenced by RT-PCR remaining positive for up to 13 days after disease resolution. Stool sample remain positive in 50% of patients who have recovered.[35] Coronavirus epidemics in the past are known to have occurred with aerosolization from flushing of toilets.[1]

The spread of the infection has been reported from patients deemed asymptomatic, thereby making the early detection and containment of the disease difficult.[36] There is a possibility of dissemination of the virus when a patient is forcefully exhaling when in pain during active labor.[25] Hence it is prudent to consider early epidural analgesia for optimal pain control, and unmedicated natural labors should be cautioned against. In addition, all healthcare staff attending to women in active labor need to don full personal protective equipment (PPE).

Infection control

In a simulated aerosol generating experiment generated by 3-jet Collison nebulizer and fed into a Goldberg drum, SARS-CoV-2 could survive on plastic and stainless-steel surfaces for 72 hours, cardboard 24 hours and copper 4 hours. The median half-life of the virus in this simulated aerosol was 2.7 hours with 95% credible interval 1.65-7.24 hours. [34] In contrast, in a real-world experiment in Singapore, three patients' rooms were sampled at multiple sites including air samples, which revealed that bleach disinfection was highly effective in two rooms and fomite contamination was common in the third room. Notably, air samples, protective equipment, anteroom and corridor outside of anteroom were negative. [35] Additionally, a case report of emergency intubation in an unsuspected COVID-19 patient subsequently found to be positive showed that no healthcare workers on surgical or N95 masks were infected. [36] In summary, current recommendations for eye protection, N95 mask, splash-resistant gown and gloves with hand hygiene should be sufficient.

Managing COVID-19 patients in labor

A pregnant woman presenting to the delivery suite or emergency department needs to be triaged based on the presence of maternal and / or fetal compromise. (Appendix for workflow on management of the pregnant patient presenting with COVID-19). When there are imminent risks, emergency cesarean delivery must be performed. When there are other maternal and fetal conditions that require an early operative delivery, a coordinated team response is initiated for assessment and optimization of maternal oxygenation and infection control measures. Caesarean

deliveries may be indicated for maternal reasons, such as worsening condition of the mother related to COVID-19 and fulminant preeclampsia, or fetal indications such as non-reassuring fetal status. When an operative delivery is not planned, pregnant mothers need to be admitted into the delivery suite for detailed assessment, labor pain management, stratification of infection control precautions and plans for safe delivery of the fetus. In the presence of COVID-19, the threshold for cesarean delivery should be lower than usual so that infection control procedures can be more readily adhered to and disease transmission minimized

Safe and optimal care of the parturient in the peripartum period requires a multidisciplinary team approach.[37] The healthcare professionals that provide this coordinated care include obstetricians, neonatologists, anesthesiologists, midwives and support services at the delivery suite. Here, we highlight the acute care perspectives of the parturient, summarize existing evidence, and propose an algorithmic approach for the management of the acutely ill parturient.

Anesthesia in emergency cesareans for COVID-19 pregnant patients

An emergency cesarean delivery (decision-to-delivery within 30 minutes) mandates a systematic plan and preparedness for minimizing cross contaminations.[38] While emergency cesarean delivery needs to be done as soon as possible, there are instances where the decision to go for urgent cesarean delivery has some lead time. The possibilities of suspected COVID-19 patients requiring imminent operative deliveries have to be communicated to the operating room team so that they could be conducted in negative pressure operating rooms. [38]

When a COVID-19 parturient with desaturation (oxygen saturation decreases to ≤93%) presents for emergency cesarean delivery, general anesthesia needs to be administered. This is done with rapid sequence induction (RSI) and tracheal intubation with a cuffed tube. The airway team should don full PPE and powered air-purifying respirator (PAPR). Presence of systemic complications of COVID-19 such as renal failure and disseminated intravascular coagulation might warrant the use of invasive monitoring (intra-arterial blood pressure, central venous pressure).

When the parturient's oxygen saturation is adequate (94% and above), [6, 10] regional anesthesia with epidural top up or single shot subarachnoid blockade, needs to be actively considered in place of general anesthesia[10] to minimize aerosolization and cross infection during airway management. Where there is a working epidural catheter in place for ongoing labor analgesia, administering a top up with potent local anesthetics (e.g. 10 to 15ml of 1.5% lignocaine, alkalinized with 8.4% sodium bicarbonate) achieves anesthesia plane for surgery with a rapid onset of 3.5 minutes. Rapid sequence spinal anesthesia [39] is described for emergency cesarean deliveries, where patients are transferred in a left lateral position with supplemental oxygen, and a single shot subarachnoid blockade is administered by the most experienced anesthetist who is pre-scrubbed. The surgical readiness time is comparable to general anesthesia and neonatal outcomes are better.[40]

Extubations after general anesthesia should be performed with the same precautions as with the conduct of intubations. [41] Patients tend be more agitated during emergence from anesthesia and extubation. This could result in higher chances of viral dissemination from coughing as compared to the intubation process.[42] During RSI and intubation, patients are anesthetized,

paralyzed and unable to cough. It is imperative that all operating room personnel wear full PPE until patients are safely extubated and transferred out of the operating room. [38, 41]

The disposition for COVID-19 patients after unplanned cesarean delivery should be decided at the earliest instance. Transferring these patients to the post anesthesia care unit (PACU) might compromise and cross contaminate other postoperative patients recovering there. Provisions should be made for suspected and confirmed patients to be recovered in the operating rooms where the cesarean deliveries were performed. Patients should subsequently be transferred directly to isolation wards post recovery.

The acutely ill parturient

When a parturient desaturates, there are multiple etiopathologies: infective (pneumonia with or without COVID-19), inflammatory (systemic inflammatory response syndrome), cardiogenic (peripartum cardiomyopathy, viral myocarditis) and non-cardiogenic pulmonary edema (hypertensive and non-hypertensive pulmonary edema). [43] A stepwise approach for systematic management of the acutely ill parturient is detailed (Figure 3).

< Insert Figure 3: Stepwise Approach to the Care of Acutely Ill Parturient>

If there is absence of maternal and / or fetal compromise, and emergency cesarean delivery is not indicated, further plans for management of the patient are then made (Figure 3). When parturients are acutely ill, it may be challenging to differentiate the etiologies based on the

presence of tachypnea and tachycardia. The percentage saturation of hemoglobin with oxygen (SpO_2) is non-invasive continuous monitoring that provides real time information on peripheral oxygen saturation. It also provides indirect information on adequacy of pulmonary gas exchange, cardiac function and intravascular volume status. There is correlation between oxygenation measured by SpO_2 and invasive arterial blood gas. An arterial partial pressure of oxygen (PaO_2) of less than 60mmHg corresponds to SpO_2 of less than 90%. [44] Delivery units need to be equipped with, and use continuous SpO_2 monitoring. Disposable low cost SpO_2 finger probes are commercially available and need to be considered when multi-parameter monitoring is not available. Knowing the (P-F ratio) which is the ratio between PaO_2 and fraction of inspired oxygen (FiO_2) is useful in predicting the degree of lung compromise.[6]

When SpO_2 has decreased to less than 94%, rapid clinical decisions must be made in the context of COVID-19. Patients with low SpO_2, and are hypotensive must be prioritized and systematically managed at the earliest, considering cardiac, non-cardiac and septic causes.

A practical and swift method for the assessment of hypotension is by bedside transthoracic echocardiography (TTE) in order to guide management.[45] A poorly contractile left ventricle signifies cardiac pump failure. In this situation, fluids should be restricted, and the use of inotropes should be considered. Hyperdynamic cardiac activity as evidenced by 'kissing' ventricular walls is suggestive of distributive shock such as in sepsis. This requires fluid resuscitation and the use of vasopressors. The TTE probe can also be used to image the inferior vena cava (IVC) to assess the patient's intravascular volume status. Avoidance of fluid mismanagement is crucial; fluid loading in cardiomyopathy can precipitate congestive cardiac failure that worsens lung oxygenation.

Cardiovascular causes of desaturation in COVID-19 include systolic failure from viral myocarditis, congestive cardiac failure and pulmonary edema. The SARS-CoV-2 surface glycoprotein interacts with the angiotensin converting enzyme 2 (ACE2) of the respiratory epithelial cells in the host. The predominant pulmonary features are from expression of ACE2 in the type 2 alveolar cells. Elevated blood pressure is known to occur from interaction between the virus and angiotensin converting enzyme 2 (ACE2). [46] This might result in misdirected management towards preeclampsia while the hypertension was a cardiovascular manifestation of COVID-19. Myocardial injury as evidenced by raised troponins is a feature of cytokines storm [47] high concentrations of granulocyte-colony stimulating factors, (GCSF), interferon gamma-induced protein 10 (IP10), monocyte chemoattractant protein-1 (MCP1), macrophage inflammatory protein-1 alpha (MIP1α), and tumor necrosis factor alpha (TNFα). [15] Cytokine storms are known to associated with disease severity and admissions to the ICU. [17, 47]

Morbid manifestations of COVID-19 such as severe pneumonia, ARDS, multi-organ dysfunction syndrome (MODS) require advanced ventilatory and circulatory support.[12] When patients present with hypoxemia, It is important to differentiate between failure of gas exchange in the lungs and cardiogenic causes of pump failure.[43] Pulmonary causes of desaturation from pneumonia, acute lung injury and ARDS are more difficult to manage as they may require prolonged mechanical ventilation.

Pressurized air enriched with oxygen is needed for improving oxygenation in acutely ill patients with respiratory compromise. It can be administered via nasal masks, full face masks, and helmets. Simulator based experiments have shown that continuous positive airway pressure (CPAP) with tight fitting oronasal mask and Non-Invasive ventilation with well-sealed helmets are effective, posing negligible risk of exhaled air dispersion. [48] Similar studies have shown that

exhaled air dispersion distance during application of high flow nasal cannula is shorter than CPAP that tend to be less tightly applied.[49] Hence centers that are experienced and equipped with negative pressure rooms could consider non-invasive ventilation, high flow nasal cannula and CPAP, especially in the face of COVID-19 pandemic when facilities with full mechanical ventilatory support are overwhelmed.

Where the patient's oxygen saturation is refractory to mechanical ventilatory support, extracorporeal membrane oxygenation (ECMO) [50] should be considered. Initiating ECMO in a pregnant patient needs special considerations. While anticoagulation is needed to prevent clotting in the extracorporeal circulation, this complicates hemostasis at the placental site if ECMO is used in the peripartum period. The setting up of ECMO requires multidisciplinary planning and is best done in tertiary institutions. Maternal and child health facilities without cardiac surgical intensive care units might not be able to acquire this service. The transfer of critically ill patients to tertiary institutions needs meticulous planning.

Drugs and evolving therapy for COVID-19

Antiviral treatment

Much of the early information on treating COVID-19 was derived from experience in SARS. Data on the use of antiviral therapy for COVID-19 in pregnancy is limited.[51]In SARS, ribavirin and corticosteroid showed possible harm with inconclusive clinical data, while studies on convalescent plasma, interferon and lopinavir were inconclusive. [52] In the first randomized controlled trial on treating COVID-19, lopinavir-ritonavir 400mg/100mg twice daily was found

to be similar to standard of care in time to clinical improvement, mortality and viral shedding.[53] This may be due to differences in viral proteases between human immunodeficiency virus (HIV) and coronavirus. [54] An invitro study on repurposed drugs for COVID-19 reported effective concentration 50 (EC50) of 0.77 for remdesivir, 1.13 for chloroquine, 61.88 for favipiravir and 109.50 for ribavirin. [55] The EC50 for hydroxychloroquine was significantly higher than chloroquine. [56] In a French non-randomized study,[57] 26 patients received hydroxychloroquine 200mg thrice daily for ten days of whom six also received azithromycin 500mg on day one and 250mg daily for next four days. Compared with 16 patients not treated, there was significant reduction in viral load at day 6 and shorter duration of viral shedding, with additive effect from azithromycin. In a Chinese non-randomized study,[58] 35 patients were treated with favipiravir 1600mg twice daily on day one and 600mg twice daily from day 2-14 and 45 patients were treated with lopinavir-ritonavir; patients in both arms received aerosolized interferon alpha (IFNα) 5 million units twice daily. Compared with control, favipiravir was associated with shorter viral shedding and faster radiological improvement.

The delivery suite and considerations for minimizing cross contamination

Enhanced infection control precautions include restrictions to the number of personnel in the delivery suite. This is to minimize cross contaminations, movements between care locations and the number of external visitors and care providers.[59] The care of the parturient should be specialist-led. When there is a suspicion of, or confirmed case of COVID-19, delivery processes such as water birth, need to be revised to limit the potential spread of infection. In addition, strict adherence to policies for segregations of teams deployed in delivery suite, general ward,

procedure rooms and outpatient units is recommended.[51] The workflow on peripartum management of COVID-19 women is detailed in Appendix.

Labor analgesia can be planned well in advance such that when patients are in early labor, they receive good pain control through initiation of epidural analgesia.[10] This reduces chances of viral disseminations during hyperventilation when the parturient is in pain, thus reducing risks of cross-contamination for staff attending to the patient. [25] Inhaled entonox is not recommended [10] as it could increase the risk of viral dissemination through aerosols, especially when the parturient is not able to achieve tight uninterrupted mask seal throughout the duration of labor. [42, 48, 49]

Care of newborn of COVID-19 mothers

Current evidence shows that there is no vertical transmission during pregnancy.[2, 9] Yet, babies that are born to COVID-19 mothers can acquire the infection post-delivery. Practices such as delayed cord clamping and skin to skin bonding between mothers and newborns are not recommended. The evidence regarding the safety of breast feeding is still limited. [2, 25, 51] Considerations can be made to allow the use of screened donated breast milk from mothers who are free of COVID-19.

The process of segregation is simple when the newborn is healthy. However, when there is perinatal asphyxia or need for ventilatory support, the process is more complicated. Finding an isolation unit for the newborn who requires continuous monitoring is a challenge. Specific care

locations for newborns of COVID-19 mothers have to be designated in advance; care teams need to be trained on the workflow and infection control measures.

Maternal collapse and perimortem delivery

In the unfortunate event of maternal collapse, it can be challenging to regulate and adapt all aspects of infection prevention. The delivery suite is overwhelmed when many personnel simultaneously attempt to resuscitate the collapsed patient, perform a peri-mortem cesarean delivery, and resuscitate the newborn. The resuscitation team should don full PPE. The most common occurrence of serious cross infections to healthcare workers during outbreaks were in crisis situations when first responders were not wearing the recommended PPE.[1]

Summary

The number of cases of COVID-19 continue to rise exponentially in many parts of the world. Pregnant women at all gestational ages will count among this increase, and greatest at risk would be the gravida in labor, and the acutely ill parturient. Whether the woman in labor needs an emergency cesarean delivery or the plan is to aim for achieving a vaginal birth, she and the team supporting her face many unique challenges. We present here the best evidence available to address many of these challenges, from making the diagnosis in symptomatic cases, to the debate between nucleic acid testing and chest imaging, to the management of the unwell patient in labor. There is reasonably good evidence that vertical transmission is unlikely, and efforts must be taken to prevent infection of the neonate. Given the limited knowledge about this novel

coronavirus, which has both similarities and differences to SARS and MERS, the management strategies provided here are a general guide based upon current available evidence, and may change as we continue to learn more about the effect of COVID-19 in the pregnant woman.

REFERENCE

1. Schwartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-ncov infecting pregnant women: Lessons from SARS, MERS, and other human coronavirus infections. Viruses 2020;12(2):194.

2. Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.

3. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) and Pregnancy: What obstetricians need to know. Am J Obstet Gynecol 2020; published online February 24.

4. Qiao J. What are the risks of COVID-19 infection in pregnant women? Lancet 2020; published online February 12.

5. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. Lancet 2020; published online February 12.

6. World Health Organisation (WHO). Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Published February 28, 2020. https://www.who.int/docs/default-source/coronaviruse/who-china-joint-mission-on-covid-19-final-report.pdf Accessed March 16.

7. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. Am J Obstet Gynecol 2004;191(1):292-7.

8. Tan EK, Tan EL. Alterations in physiology and anatomy during pregnancy. Best Pract Res Clin Obstet Gynaecol 2013;27(6):791-802

9. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. Transl Pediatr 2020;(1):51.

10. Coronavirus (COVID-19) Infection in Pregnancy. RCOG. Published March 9, 2020, https://www.rcog.org.uk/globalassets/documents/guidelines/coronavirus-covid-19-virus-infection-in-pregnancy-2020-03-09.pdf Accessed March 22, 2020.

11. Poon LC, Yang H, Lee JCS, et al. (in press) ISUOG Interim Guidance on 2019 novel coronavirus infection during pregnancy and puerperium: information for healthcare professionals. Ultrasound Obstet Gynecol 2020.

12. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA 2020; published online February 24.

13. Wong JEL, Leo YS, Tan CC. COVID-19 in Singapore - current experience: critical global issues that require attention and action. JAMA 2020; published online February 20.

14. Ministry of Health. Singapore. Published March 21, 2020. https://www.moh.gov.sg/news-highlights/details/passing-of-two-patients-with-covid-19-infection. Accessed March 23.

15. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020;395:497-506.

16. Liu H, Liu F, Li J, Zhang T, Wang D, Lan W. Clinical and CT imaging features of the covid-19 pneumonia: focus on pregnant women and children. J Infect 2020; published online February 27.

17. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; published online February 28.

18. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus - infected pneumonia in Wuhan, China. JAMA 2020; published online February 7.

19. National University of Singapore. Saw Swee Hock School of Public Health. COVID-19 Science Report: Diagnostics. https://sph.nus.edu.sg/wp-content/uploads/2020/03/COVID-19-Science-Report-Diagnostics-23-Mar.pdf Accessed March 23, 2020.

20. Hosseiny M, Kooraki S, Gholamrezanezhad A, Reddy S, Myers L. Radiology perspective of coronavirus disease 2019 (COVID-19): Lessons from severe acute respiratory syndrome and Middle East respiratory syndrome. AJR Am J Roentgenol 2020; published online February 15.

21. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020; published online February 24.

22. Liu D, Li L, Wu X, et al. Pregnancy and perinatal outcomes of women with coronavirus disease (COVID-19) pneumonia: a preliminary analysis. AJR Am J Roentgenol 2020; published online March 7.

23. Ai T, Yang Z, Hou H, et al. Correlation of chest CT and RT-PCR testing in coronavirus disease 2019 (COVID-19) in China: a report of 1014 cases. Radiology. 2020; published online February 26.

24. American College of Radiology. ACR-SPR practice parameter for imaging pregnant or potentially pregnant adolescents and women with ionizing radiation. Reston, Va: American College of Radiology. 2013.

505 25. Yang H, Wang C, Poon LC. Novel coronavirus infection and pregnancy.
506 Ultrasound Obstet Gynecol 2020; published online March 5.

507 26. Wong KT, Antonio GE, Hui DS, et al. Severe acute respiratory syndrome: radiographic
508 appearances and pattern of progression in 138 patients. Radiology 2003;228(2):401-6.

509 27. Das KM, Lee EY, Jawder SE, et al. Acute Middle East respiratory syndrome coronavirus:
510 temporal lung changes observed on the chest radiographs of 55 patients. AJR Am J
511 Roentgenol 2015;205(3):267-274.

512 28. Miller Jr WT, Mickus TJ, Barbosa Jr E, Mullin C, Van Deerlin VM, Shiley KT. CT of
513 viral lower respiratory tract infections in adults: comparison among viral organisms and
514 between viral and bacterial infections. AJR Am J Roentgenol 2011;197(5):1088-95.

515 29. Marchiori E, Zanetti G, D'Ippolito G, et al. Swine-origin influenza A (H1N1) viral
516 infection: thoracic findings on CT. AJR Am J Roentgenol 2011;196(6):723-8.

517 30. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus Disease 2019
518 (COVID-19): A systematic review of imaging findings in 919 patients. AJR Am J
519 Roentgenol 2020; published online February 29.

520 31. Koo HJ, Lim S, Choe J, Choi SH, Sung H, Do KH. Radiographic and CT features of viral
521 pneumonia. Radiographics 2018;38(3):719-39.

522 32. Franquet T. Imaging of pulmonary viral pneumonia. Radiology 2011;260(1):18-39.

523 33. Chinazzi M, Davis JT, Ajelli M, et al. The effect of travel restrictions on the spread of the
524 2019 novel coronavirus (COVID-19) outbreak. Science 2020; published online March 6.

34. van Doremalen N, Bushmaker T, Morris D, et al. Aerosol and surface stability of HCoV-19 (SARS-CoV-2) compared to SARS-CoV-1. medRxiv 2020; published online January 1.

35. Ong SW, Tan YK, Chia PY, et al. Air, Surface environmental, and personal protective equipment contamination by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from a symptomatic patient. JAMA 2020; published online March 4.

36. Ng K, Poon BH, Puar TH, et al. COVID-19 and the risk to health care workers: a case report. Ann Intern Med 2020; published online March 16.

37. Kilpatrick SJ, Papile LA, Macones GA. Guidelines for perinatal care. Am. Acad. Pediatr 2017.

38. Ti LK, Ang LS, Foong TW, Ng BS. What we do when a COVID-19 patient needs an operation: operating room preparation and guidance. Can J Anaesth 2020; published online March 6.

39. Kinsella SM, Girgirah K, Scrutton MJ. Rapid sequence spinal anesthesia for category□1 urgency caesarean section: a case series. Anesthesia 2010;65(7):664-9.

40. Lim G, Facco FL, Nathan N, Waters JH, Wong CA, Eltzschig HK. A review of the impact of obstetric anesthesia on maternal and neonatal outcomes. Anesthesiology 2018;129(1):192.

41. Wax RS, Christian MD. Practical recommendations for critical care and anesthesiology teams caring for novel coronavirus (2019-nCoV) patients. Can J Anaesth 2020; published online February 6.

42. Chan MT, Chow BK, Lo T, et al. Exhaled air dispersion during bag-mask ventilation and sputum suctioning-Implications for infection control. Scientific reports 2018;8(1):1-8.

43. Dennis AT, Solnordal CB. Acute pulmonary oedema in pregnant women. Anesthesia. 2012;67(6):646-59.

44. Zeserson E, Goodgame B, Hess JD, et al. Correlation of venous blood gas and pulse oximetry with arterial blood gas in the undifferentiated critically ill patient. Intensive Care Med 2018;33(3):176-81.

45. Dennis AT. Transthoracic echocardiography in obstetric anesthesia and obstetric critical illness. Int J Obstet Anest 2011;20(2):160-8.

46. Zheng YY, Ma YT, Zhang JY, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol 2020; published online March 5.

47. Wong CK, Lam CW, Wu AK, et al. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin Exp Immunol 2004 ;136(1):95-103.

48. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during noninvasive ventilation via helmets and a total facemask. Chest 2015;147(5):1336-43.

49. Hui DS, Chow BK, Lo T, et al. Exhaled air dispersion during high-flow nasal cannula therapy versus CPAP via different masks. Eur Respir J 2019;53(4):1802339.

50. MacLaren G, Fisher D, Brodie D. Preparing for the most critically ill patients with COVID-19: The potential role of extracorporeal membrane oxygenation. JAMA 2020; published online February 19.

51. Dashraath P, Wong JLJ, Lim MXK, et al. (accepted) Coronavirus Disease 2019 (COVID-19) Pandemic and Pregnancy. Am J Obstet Gynecol 2020; https://www.ajog.org/ Accessed March 25.

52. Stockman LJ, Bellamy R, Garner P. SARS: systematic review of treatment effects. PLoS med 2006;9.

53. Cao B, Wang Y, Wen D, et al. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. N Engl J Med 2020; published online March 18.

54. Li G, De Clercq E. Therapeutic options for the 2019 novel coronavirus (2019-nCoV). Nat. Rev. Drug Discov 2020;19:149-150.

55. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res 2020;30(3):269-71.

56. Liu J, Cao R, Xu M, et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. Cell Discov 2020;6(1):1-4.

57. Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 2020; published online March 20.

582 58. Cai Q, Yang M, Liu D, et al. Experimental treatment with favipiravir for COVID-19: an
583 open-label control study. Engineering 2020; published online March 18.

584 59. Chua MS, Lee JC, Sulaiman S, Tan HK. From the frontlines of COVID□19 - How
585 prepared are we as obstetricians: a commentary. BJOG. Int. J. Gynecol. Obstet 2020;
586 published online March 4.

587

588

589 **FIGURE LEGEND**

590

591 **Figure 1 Legend:** Imaging of two COVID-19 patients. Contrast enhanced CT of one patient in
592 (1A) the axial plane across the lower lobes of lungs shows patchy GGO in a lobular distribution.
593 Early changes of consolidation are present in the posterior segment of the right lower lobe
594 (arrow).

595 Corresponding (1B) chest radiograph does not reveal significant abnormality other than for a
596 small focus of consolidation in the medial right lower zone (arrow), which would have been
597 easily missed due to projection adjacent to the right cardiophrenic angle and overlapping rib
598 shadow.

599 CT pulmonary angiogram of a different patient with severe pneumonia in the (1C) axial and (1D)
600 coronal planes showing extensive multilobar GGO (arrows) with areas of confluent
601 consolidation (arrowheads) mostly distributed in the posterior and basal regions of the lower

lobes. No pulmonary embolism was detected. These findings are not specific to COVID-19 and may be seen in other viral and atypical pneumonias.

Figure 2 Legend: *A suspect case of COVID-19 is one who present with an acute respiratory illness of any degree of severity who, within 14 days before onset of illness had travelled to any listed countries requiring heightened vigilance, or had prolonged close contact with a confirmed COVID-19 patient. ¶ Negative RT-PCR tested twice on consecutive days, and at least 24 hours apart. ** Close monitoring includes social and physical distancing, monitoring of body temperature, and symptoms of acute respiratory illness. RT-PCR: reverse transcriptase polymerized chain reaction. Chest imaging includes chest X-ray, CT chest, and point of care ultrasound (POCUS) of lungs.

621 **Figure 3 Legend:** At all times, maternal and fetal compromise have to be assessed and acted
622 upon as per standard intrapartum obstetric management. *Exclude obstetric contraindication to
623 vaginal delivery. SpO_2: percentage saturation of hemoglobin with oxygen; RA: regional
624 anesthesia; GA: general anesthesia; SVR: systemic vascular resistance; CO: cardiac output
625 measured by non-invasive pulse contour methodology from intra-arterial waveform analysis;
626 LV: left ventricle; RV: right ventricle; ARDS: adult respiratory distress syndrome; AFE:
627 amniotic fluid embolism; ECMO: extracorporeal membrane oxygenation.

628

629

Figure

Figure 1: Chest Imaging in COVID-19 Patients

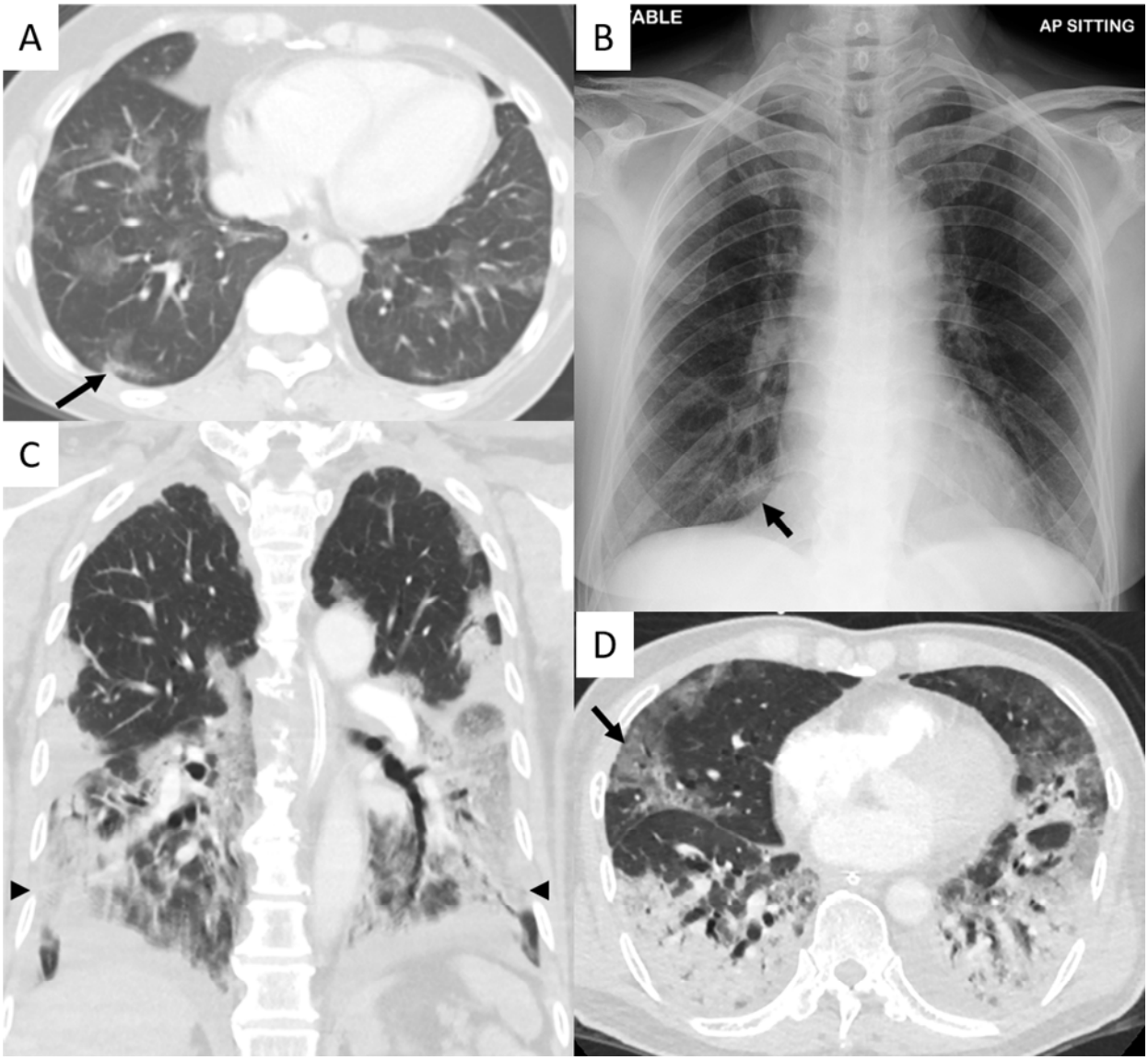

Figure 1 Legend: Imaging of two COVID-19 patients. Contrast enhanced CT of one patient in (1A) the axial plane across the lower lobes of lungs shows patchy GGO in a lobular distribution. Early changes of consolidation are present in the posterior segment of the right lower lobe (arrow).

Corresponding (1B) chest radiograph does not reveal significant abnormality other than for a small focus of consolidation in the medial right lower zone (arrow), which would have been easily missed due to projection adjacent to the right cardiophrenic angle and overlapping rib shadow.

CT pulmonary angiogram of a different patient with severe pneumonia in the (1C) axial and (1D) coronal planes showing extensive multilobar GGO (arrows) with areas of confluent consolidation (arrowheads) mostly distributed in the posterior and basal regions of the lower lobes. No pulmonary embolism was detected. These findings are not specific to COVID-19 and may be seen in other viral and atypical pneumonias.

Figure 2: COVID-19 SUSPECT Pregnant Patient Diagnostic Workflow

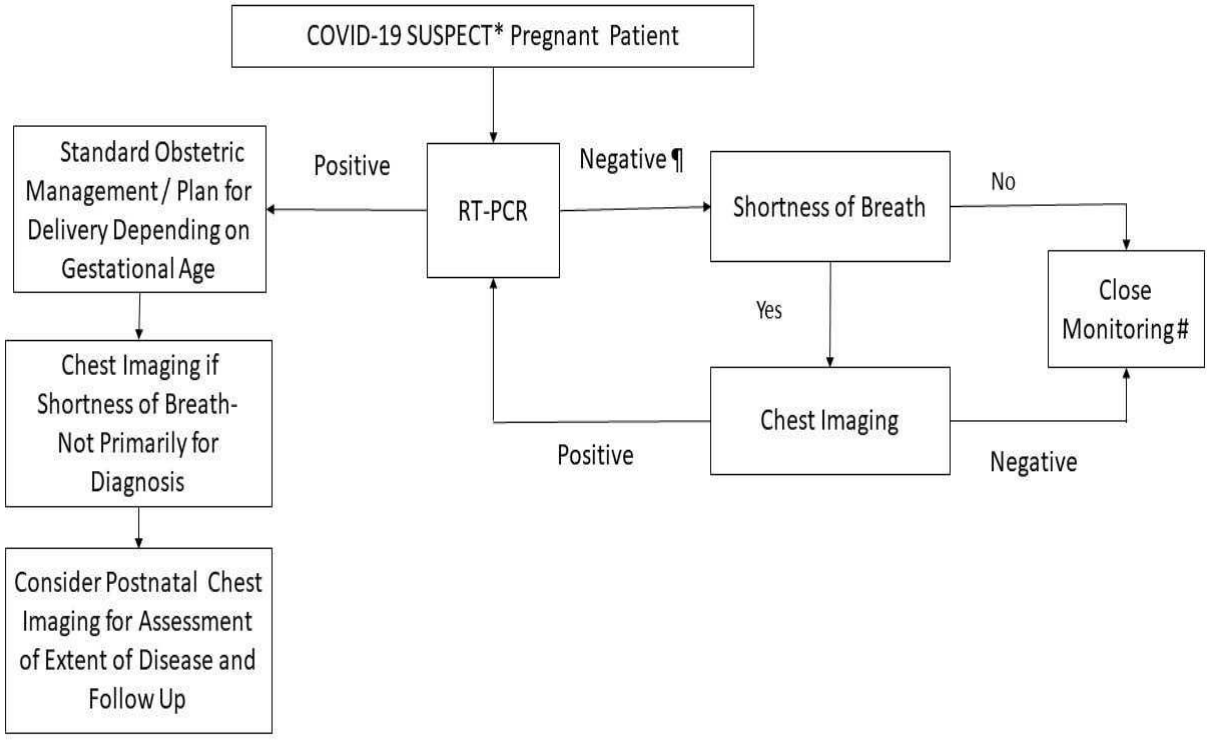

Figure 2 Legend: *A suspect case of COVID-19 is one who present with an acute respiratory illness of any degree of severity who, within 14 days before onset of illness had travelled to any listed countries requiring heightened vigilance, or had prolonged close contact with a confirmed COVID-19 patient. ¶ Negative RT-PCR tested twice on consecutive days, and at least 24 hours apart. ** Close monitoring includes social and physical distancing, monitoring of body temperature, and symptoms of acute respiratory illness. RT-PCR: reverse transcriptase polymerized chain reaction. Chest imaging includes chest X-ray, CT chest, and ultrasound lungs

Figure 3: Stepwise Approach to the Care of Acutely Ill Parturient

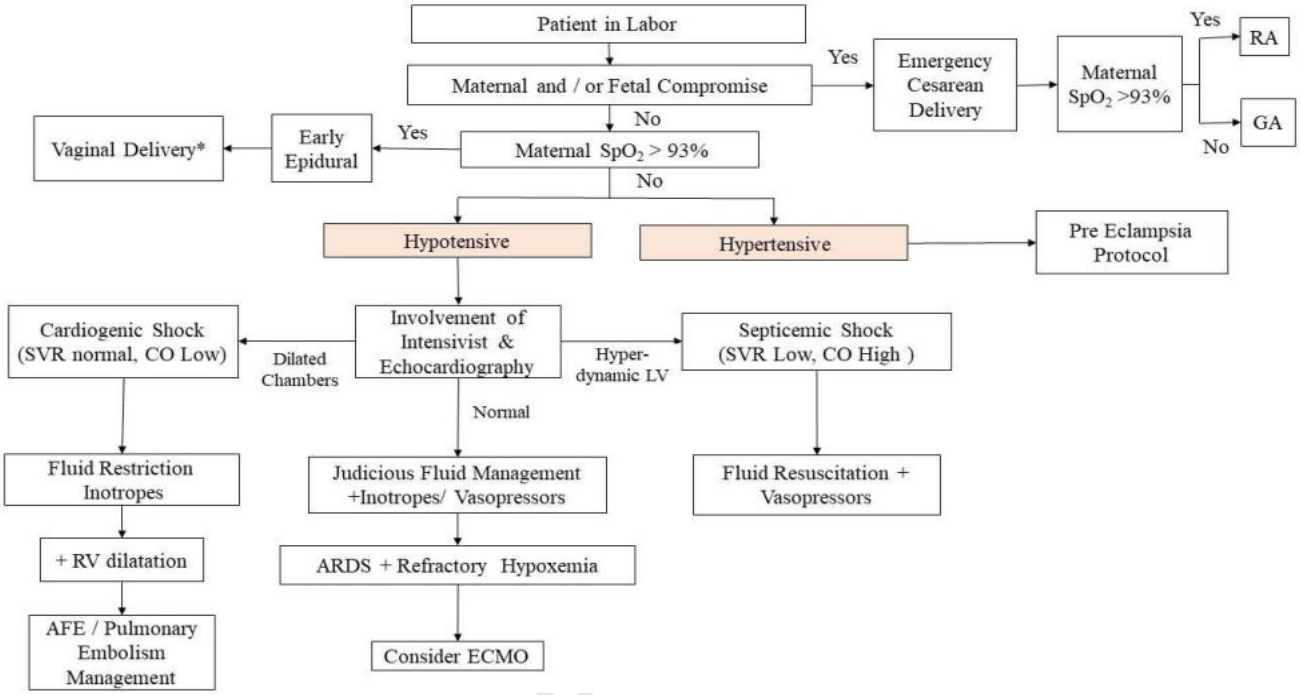

Figure 3 Legend: At all times, maternal and fetal compromise have to be assessed and acted upon as per standard intrapartum obstetric management. *Exclude obstetric contraindication to vaginal delivery. SpO_2: percentage saturation of hemoglobin with oxygen; RA: regional anesthesia; GA: general anesthesia; SVR: systemic vascular resistance; CO: cardiac output measured by non-invasive pulse contour methodology from intra-arterial waveform analysis; LV: left ventricle; RV: right ventricle; ARDS: adult respiratory distress syndrome; AFE: amniotic fluid embolism; ECMO: extracorporeal membrane oxygenation.

Figure 3: Stepwise Approach to the Care of Acutely Ill Parturient

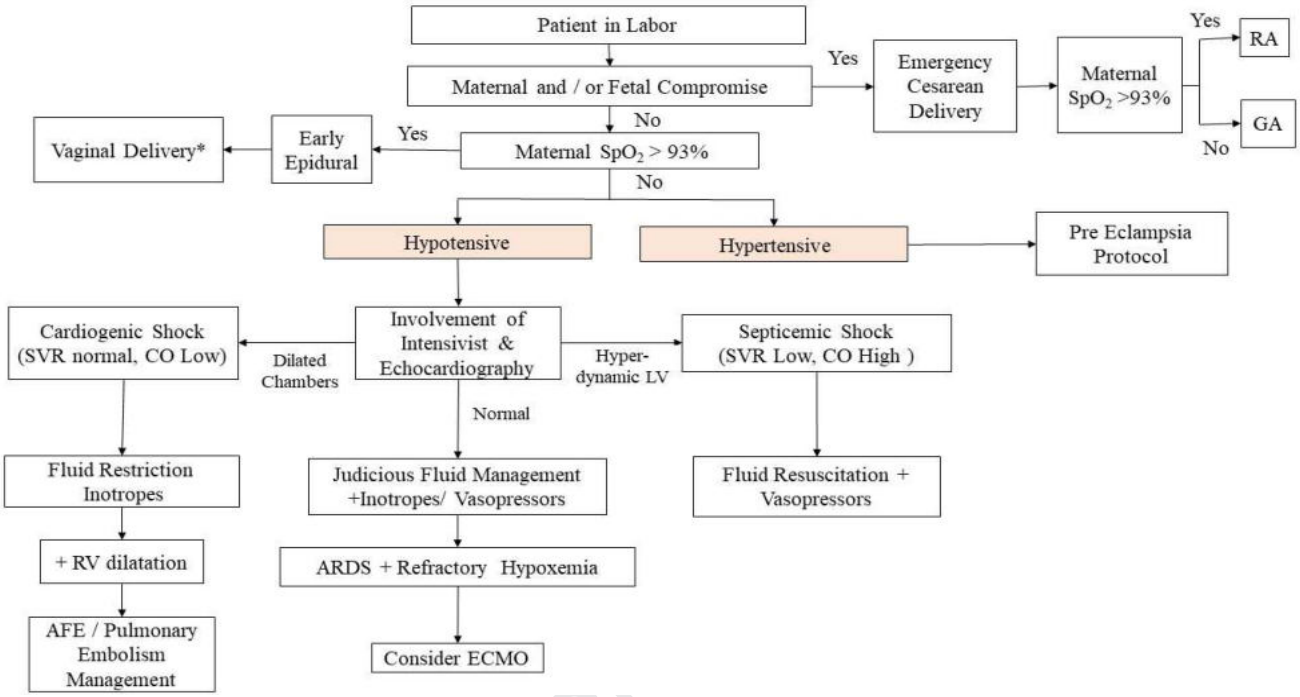

Figure 3 Legend: At all times, maternal and fetal compromise have to be assessed and acted upon as per standard intrapartum obstetric management. *Exclude obstetric contraindication to vaginal delivery. SpO_2: percentage saturation of hemoglobin with oxygen; RA: regional anesthesia; GA: general anesthesia; SVR: systemic vascular resistance; CO: cardiac output measured by non-invasive pulse contour methodology from intra-arterial waveform analysis; LV: left ventricle; RV: right ventricle; ARDS: adult respiratory distress syndrome; AFE: amniotic fluid embolism; ECMO: extracorporeal membrane oxygenation.

Figure 1: Chest Imaging in COVID-19 Patients

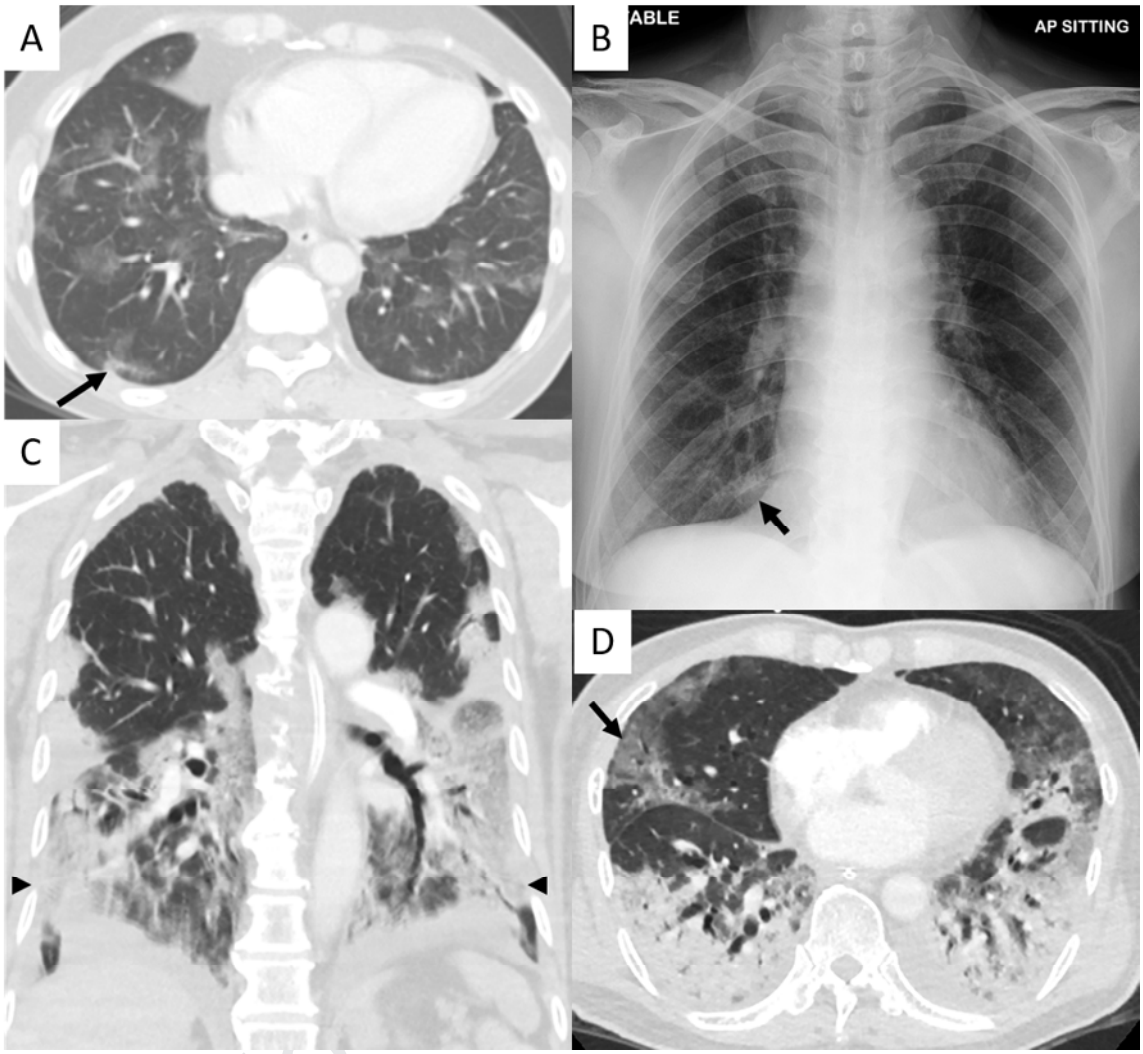

Figure 1 Legend

Imaging of two COVID-19 patients. Contrast enhanced CT of one patient in (1A) the axial plane across the lower lobes of lungs shows patchy GGO in a lobular distribution. Early changes of consolidation are present in the posterior segment of the right lower lobe (arrow).

Corresponding (1B) chest radiograph does not reveal significant abnormality other than for a small focus of consolidation in the medial right lower zone (arrow), which would have been easily missed due to projection adjacent to the right cardiophrenic angle and overlapping rib shadow.

CT pulmonary angiogram of a different patient with severe pneumonia in the (1C) axial and (1D) coronal planes showing extensive multilobar GGO (arrows) with areas of confluent consolidation (arrowheads) mostly distributed in the posterior and basal regions of the lower lobes. No pulmonary embolism was detected. These findings are not specific to COVID-19 and may be seen in other viral and atypical pneumonias.

Highlights

COVID-19 in pregnancy can cause severe maternal morbidity in up to 9% of affected gravidae

Chest imaging is helpful in pregnant women who have a high pretest probability of COVID-19, but are RT-PCR negative

Vertical transmission is unlikely, but active measures are needed to prevent neonatal infection

We present an algorithm of care for the acutely ill parturient

We present a protocol for intrapartum care of the pregnant woman in labor

Peripartum Management of Women with COVID-19

Antenatal Management

Patient will be admitted to the Isolation Ward with Negative Pressure Room

Teams to be activated upon admission to Isolation Ward

❑Primary Physician
❑Maternal-Fetal Medicine Team
❑Neonatology Team and Paediatric Infectious Diseases Team
❑Paediatric Intensive Care Unit Team
❑Anaesthesia Team
❑Infectious Diseases Team
❑Nursing Team
❑Operating Theatre Team
❑Medical Social Worker

If administration of steroids is considered, the decision will be made following joint discussion by Obstetrics, Neonatology and Infectious Disease teams.

Items to be discussed and completed in the antenatal ward:

❑The aim is for normal vaginal delivery

❑Discuss with patient regarding the delivery process and postpartum care

❑To inform patient that baby will be separated immediately after delivery and will be admitted to PICU. COVID-19 testing will be carried out on the baby.
- ❑If the test result is positive for baby, baby will stay with mother.
- ❑If the test result is negative for baby, baby will remain isolated.

❑Consent forms for normal vaginal delivery, assisted vaginal delivery and caesarean delivery to be signed.

❑Strongly recommend early epidural analgesia so as to minimise the need for general anaesthesia in the event of emergency caesarean delivery.

❑Informed consent for labour epidural analgesia to be pre-obtained; consent to be re-verified at time of procedure.

❑Strictly NO use of Entonox due to the risk of aerosolisation.

Intrapartum Management

Once labour starts, patient is to be transferred from Isolation Ward to the Isolation Room in the Delivery Suite. If the Isolation Room in Delivery Suite is not available, the patient will be transferred from Isolation Ward to Medical Intensive Care Unit for delivery.

Teams to activate once patient arrives in Delivery Suite

❑Overall Coordinator
❑Primary Obstetrician
❑Neonatology team – Consultant and Neonatology Registrar on call – who will contact Paediatric Infectious Diseases and Paediatrics Intensive Care Unit teams
❑Anaesthesia - Obstetric Anaesthesia (Epidural Consultant on call)
❑Operating Theatre Nurse in charge
❑Infectious Diseases Team Consultant
❑Coordinator for clinical sample collection

✓Team to wear full PPE / (PAPR-Airway team) during delivery in Isolation Room in Delivery Suite.

✓Designated nurse assigned to the patient. Nurse in Charge / Sister is the second assistant.

✓Medical staff to manage the case will be consultants and / or registrars and not junior residents.

✓Practices of delay cord clamping and skin to skin bonding between mother and newborn is not recommended.

✓Should an emergency caesarean delivery is needed, designated operating room should be used. There are 2 designated operating rooms (Operating room nurse in charge will inform the operating room upon being activated)

✓Please refer to the routes from Delivery Suite or Medical ICU to Operating Theatre.

Clinical Samples to be collected at the time of delivery (perinatal) -Full PPE for collection of samples. This may vary depending on clinical needs and facilities available at each centre.

❑High vaginal swab #1 – PCR
❑High vaginal swab #2 – PCR
❑Amniotic fluid (in specimen bottle) – PCR
❑Maternal blood – 1 x EDTA tube, 1 x plain tube – PCR
❑Umbilical cord blood – *additional* 1-2mL for PCR (EDTA tube)

❑Placenta - fetal surface swab (1 swab) - PCR

❑Placenta - maternal surface swab (1 swab) - PCR

❑Umbilical cord - external surface of the cord (1 swab) - PCR

❑Umbilical cord - intravascular surface (1 swab, from inside UA or UV) - PCR

❑Placenta - full thickness biopsy (include fetal and maternal surfaces - to put stitch in maternal surface) - for histology

❑Umbilical cord at the insertion site - full thickness segment - for histology

Disposal of placenta - placenta is to be placed in triple BIOHAZARD bags before disposal. If Caesarean delivery is performed, placenta is to be disposed in the Operating Theatre.

Postpartum Management

After delivery:

✓Baby will be immediately transferred to Paediatric Intensive Care Unit.

✓Patient will be transferred back to Isolation ward.

✓Transfer will be as for hospital protocol.

✓Upon completion of transfer, medical and nursing staff to shower and change out to new set of scrub uniform for the next case.

✓Book cleaning team to disinfect the room as per infectious control protocol. (turnaround time: up to 3 hours for the next availability of bed.)

Glossary

ACE2: Angiotensin-converting enzyme 2 – the functional receptor of SARS-CoV-2

AFE: Amniotic fluid embolism

ARDS: Acute respiratory distress syndrome

CO: cardiac output measured by non-invasive pulse contour methodology from intra-arterial waveform analysis

COVID-19: Coronavirus Disease 2019 (previously called 2019 novel coronavirus (2019-nCoV)

CT: Computed tomography

CXR: Chest X-ray

ECMO: Extracorporeal membrane oxygenation

EC50: Effective concentration 50 – concentration of a drug that gives half maximal response

Emergency cesarean delivery: Operative delivery that is to be conducted within 30 minutes after the decision is made for the surgery

FiO_2: Fraction of inspired oxygen

Functional residual capacity: Volume of air in the lungs at the end of expiration; it is

the sum of residual volume and end expiratory volume

GA: General anesthesia

GCSF: Granulocyte-colony stimulating factors

GGO: Ground glass opacities

HIV: Human immunodeficiency virus

ICU: Intensive care unit

IFNα: Interferon alpha

IP10: Interferon gamma-induced protein 10

IVC: Inferior vena cava

LV: Left ventricle

MCP1: Monocyte chemoattractant protein-1

MIP1α: Macrophage inflammatory protein-1 alpha

MERS: Middle East respiratory syndrome

MERS-CoV: Middle East respiratory syndrome coronavirus – the virus that causes MERS

MODS: Multi-organ dysfunction syndrome

NAAT: nucleic acid amplification test

Negative pressure room: Room that maintains a lower air pressure inside the treatment area than that of the surrounding environment

NIV: Non-invasive ventilation

N95 mask: Respiratory protective device that removes at least 95% of very small (0.3 micron) test particles; the American equivalent of an FFP2 respirator

PACU: Post anesthesia care unit

PaO_2: Arterial partial pressure of oxygen

PAPR: Powered air-purifying respirator

P-F ratio: Ratio between arterial pressure of oxygen (PaO_2) and fraction of inspired oxygen (FiO_2)

PPE: Personal protective equipment

RA: Regional anesthesia

RNA: Ribonucleic acid

RSI: Rapid sequence induction

RT-PCR: Reverse transcription polymerase chain reaction

RV: Right ventricle

SARS: Severe Acute Respiratory Syndrome

SARS-CoV: Severe acute respiratory syndrome coronavirus – virus that causes SARS

SARS-CoV-2: Severe acute respiratory syndrome coronavirus-2 virus – virus that causes COVID-19

SpO_2: Percentage saturation of hemoglobin with oxygen

Suspect case of COVID-19: A patient who presents with an acute respiratory illness of any degree of severity who, within 14 days before onset of illness had travelled to any listed countries requiring heightened vigilance, or had prolonged close contact with a confirmed COVID-19 patient

SVR: Systemic vascular resistance

TNFα: Tumor necrosis factor alpha

TTE: Transthoracic echocardiography

WHO: World health organization

https://drive.google.com/drive/folders/1IvdxQvaDbiRCV7z0SmgxARXiO7W3PlVf?usp=sharing