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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

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Title page

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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.

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65 **Short title**

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67 **COVID-19: Peripartum care of the acutely ill parturient**

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70 **Condensation**

71 Stepwise approach for managing acutely ill parturients to improve maternal outcomes and

72 minimizing disease transmission

73

74 **Keywords**

75 COVID-19, Coronavirus disease 2019, SARS-CoV-2, pandemic, coronavirus, virus, MERS,

76 SARS, severe acute respiratory syndrome, ACE2, acute respiratory distress syndrome, ARDS,

77 obstetric management, maternal morbidity, acutely ill, pregnancy, vertical transmission.

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83 **Introduction**

84 Coronavirus Disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome
85 coronavirus 2 (SARS-CoV-2). SARS-CoV-2 are the largest among the ribonucleic acid (RNA)
86 viruses.¹ The World Health Organization (WHO) has now declared COVID-19 a pandemic. The
87 elderly are at greatest risk.² Current evidence suggests that pregnant women are no more at risk
88 of COVID-19 than other adults,³ nor is the condition thought to be more severe in them.⁴ A case
89 series of nine pregnant women at term, and late preterm (36 weeks and above), reported good
90 maternal and fetal outcomes.⁵ However, all these cases had short time-intervals between
91 diagnosis of COVID-19, and cesarean deliveries, and the true impact of the disease on pregnant
92 women should not be extrapolated from this descriptive study. Indeed, when a larger cohort of
93 147 pregnant patients was evaluated (WHO-China Joint Mission Report),⁶ up to 8% of the
94 cohort were either severely ill (tachypnoea ≥ 30 breaths/min, or oxygen saturation $\leq 93\%$ at rest,
95 or $\text{PaO}_2/\text{FiO}_2 < 300$ mmHg) or 1% critically ill (respiratory failure requiring mechanical
96 ventilation, shock, or other organ failure that requires intensive care). This rate of presentation of
97 severe illness in pregnancy was less than that observed from influenza (H1N1) pandemic.⁶ This
98 statistic came from a country that is now recognized globally to be dealing with the COVID-19
99 outbreak admirably, having gained experience from the 2003 severe acute respiratory syndrome
100 (SARS) epidemic. It is uncertain whether other health systems would experience an under-10%
101 severe maternal morbidity, or instead, severe illnesses in pregnant women being closer to 25% as
102 was observed in other coronaviral infections such as the Middle east respiratory syndrome
103 (MERS) and SARS.^{1,7}

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

106 epidemics had significant adverse effects on pregnant women including preterm deliveries,
107 stillbirths, respiratory complications and maternal mortality.¹ Preexisting physiological factors
108 such as basal atelectasis from gravid uterus, lower lung reserves (reduced functional residual
109 capacity), and increased oxygen consumption (30%)⁸ predispose the parturient to poor outcomes
110 during respiratory illnesses, such as coronaviral pneumonias. On the other hand, there is
111 reasonably good evidence to suggest that vertical transmission from the pregnant patient to the
112 fetus is unlikely.^{2,9} Recommendations are in place for managing suspect or confirmed COVID-
113 19 patients who are pregnant, ensuring the safety of their neonates, other parturients in the
114 delivery suite, and healthcare workers caring for them.^{3,10,11}

115 It is known that disease transmission and case fatality rate (2.3%)¹² are lower in health systems
116 that had better systematic pandemic preparedness strategies,¹³ and with experience managing
117 coronaviral outbreaks. As of March 25, 2020, Singapore has hospitalized 631 cases of COVID-
118 19 confirmed by real-time reverse transcriptase–polymerase chain reaction (RT-PCR) of which 3
119 were pregnant. Of these 631 patients, 160 have fully recovered from the infection and have been
120 discharged from hospital. There are have been two mortalities from complications due to
121 COVID-19. One of this was an imported case who was ill before coming to Singapore, and
122 admitted to the intensive care unit (ICU) upon arrival.¹⁴ Singapore was taken by surprise during
123 the 2003 SARS epidemic, but has since build capacity and capability within the country to
124 manage global infectious disease emergencies with protocols in place for non-gravid and
125 pregnant patients.

126 **Clinical presentation**

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

133 **Clinical Virology**

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

150

151

152 Diagnosing COVID-19

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

157 Chest imaging

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

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

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

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

184

185 **Differential Diagnoses**

186 COVID-19 is primarily a respiratory illness. As our understanding of the diagnostic imaging
187 features of COVID-19 evolves, significant overlap with other viral and atypical pneumonias are
188 increasingly reported. On CXR, COVID-19 pneumonia often presents with multifocal, bilateral
189 airspace opacification.² This distinguishes it from the more common unifocal involvement noted
190 in SARS,²⁶ but not from MERS.²⁷ When imaged by CT, the distribution seen in COVID-19 is
191 similar to that noted in other viral and coronaviral²⁰ pneumonias, such as influenza,

192 parainfluenza, respiratory syncytial virus, and adenovirus.^{28, 29} Even the multifocal GGO,
193 described in more than 80% of COVID-19 pneumonias³⁰ are common features of atypical (e.g.
194 *Mycoplasma pneumoniae*) and opportunistic (e.g. *Pneumocystis jirovecii*) pneumonias.^{31, 32} As
195 with other viral pneumonias, lymphadenopathy and pleural effusions are uncommon associated
196 findings.³⁰ In the latter stages of COVID-19, confluent consolidation and interstitial thickening
197 become more pronounced, with up to 20% patients developing features of ARDS.^{18, 21} Given the
198 significant overlap of imaging findings with other acute viral respiratory infections, imaging
199 alone is unlikely to supplant the role of RT-PCR for the primary diagnosis of COVID-19.

200

201 **Minimizing disease transmission**

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

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

214

215 Infection control

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

228

229 Managing COVID-19 patients in labor

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

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

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

248

249 **Anesthesia in emergency cesareans for COVID-19 pregnant patients**

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

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

263 When the parturient's oxygen saturation is adequate (94% and above),^{6, 10} regional anesthesia
264 with epidural top up or single shot subarachnoid blockade, needs to be actively considered in
265 place of general anesthesia¹⁰ to minimize aerosolization and cross infection during airway
266 management. Where there is a working epidural catheter in place for ongoing labor analgesia,
267 administering a top up with potent local anesthetics (e.g. 10 to 15ml of 1.5% lignocaine,
268 alkalized with 8.4% sodium bicarbonate) achieves anesthesia plane for surgery with a rapid
269 onset of 3.5 minutes. Rapid sequence spinal anesthesia³⁹ is described for emergency cesarean
270 deliveries, where patients are transferred in a left lateral position with supplemental oxygen, and
271 a single shot subarachnoid blockade is administered by the most experienced anesthetist who is
272 pre-scrubbed. The surgical readiness time is comparable to general anesthesia and neonatal
273 outcomes are better.⁴⁰

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

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

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

286

287 **The acutely ill parturient**

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

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

294

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

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

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

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

320 Cardiovascular causes of desaturation in COVID-19 include systolic failure from viral
321 myocarditis, congestive cardiac failure and pulmonary edema. The SARS-CoV-2 surface
322 glycoprotein interacts with the angiotensin converting enzyme 2 (ACE2) of the respiratory
323 epithelial cells in the host. The predominant pulmonary features are from expression of ACE2 in
324 the type 2 alveolar cells. Elevated blood pressure is known to occur from interaction between the
325 virus and angiotensin converting enzyme 2 (ACE2).⁴⁶ This might result in misdirected
326 management towards preeclampsia while the hypertension was a cardiovascular manifestation of
327 COVID-19. Myocardial injury as evidenced by raised troponins is a feature of cytokines storm⁴⁷
328 high concentrations of granulocyte-colony stimulating factors, (GCSF), interferon gamma-
329 induced protein 10 (IP10), monocyte chemoattractant protein-1 (MCP1), macrophage
330 inflammatory protein-1 alpha (MIP1 α), and tumor necrosis factor alpha (TNF α).¹⁵ Cytokine
331 storms are known to associated with disease severity and admissions to the ICU.^{17,47}

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

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

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

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

356

357 **Drugs and evolving therapy for COVID-19**

358 **Antiviral treatment**

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

364 to be similar to standard of care in time to clinical improvement, mortality and viral shedding.⁵³
365 This may be due to differences in viral proteases between human immunodeficiency virus (HIV)
366 and coronavirus.⁵⁴ An invitro study on repurposed drugs for COVID-19 reported effective
367 concentration 50 (EC50) of 0.77 for remdesivir, 1.13 for chloroquine, 61.88 for favipiravir and
368 109.50 for ribavirin.⁵⁵ The EC50 for hydroxychloroquine was significantly higher than
369 chloroquine.⁵⁶ In a French non-randomized study,⁵⁷ 26 patients received hydroxychloroquine
370 200mg thrice daily for ten days of whom six also received azithromycin 500mg on day one and
371 250mg daily for next four days. Compared with 16 patients not treated, there was significant
372 reduction in viral load at day 6 and shorter duration of viral shedding, with additive effect from
373 azithromycin. In a Chinese non-randomized study,⁵⁸ 35 patients were treated with favipiravir
374 1600mg twice daily on day one and 600mg twice daily from day 2-14 and 45 patients were
375 treated with lopinavir-ritonavir; patients in both arms received aerosolized interferon alpha
376 (IFN α) 5 million units twice daily. Compared with control, favipiravir was associated with
377 shorter viral shedding and faster radiological improvement.

378

379 **The delivery suite and considerations for minimizing cross contamination**

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

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

388 Labor analgesia can be planned well in advance such that when patients are in early labor, they
389 receive good pain control through initiation of epidural analgesia.¹⁰ This reduces chances of viral
390 disseminations during hyperventilation when the parturient is in pain, thus reducing risks of
391 cross-contamination for staff attending to the patient.²⁵ Inhaled entonox is not recommended¹⁰
392 as it could increase the risk of viral dissemination through aerosols, especially when the
393 parturient is not able to achieve tight uninterrupted mask seal throughout the duration of labor.^{42,}
394 48, 49

395

396 **Care of newborn of COVID-19 mothers**

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

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

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

408

409 **Maternal collapse and perimortem delivery**

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

416

417 **Summary**

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

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

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FIGURE LEGEND

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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

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

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

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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. SpO₂: 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.

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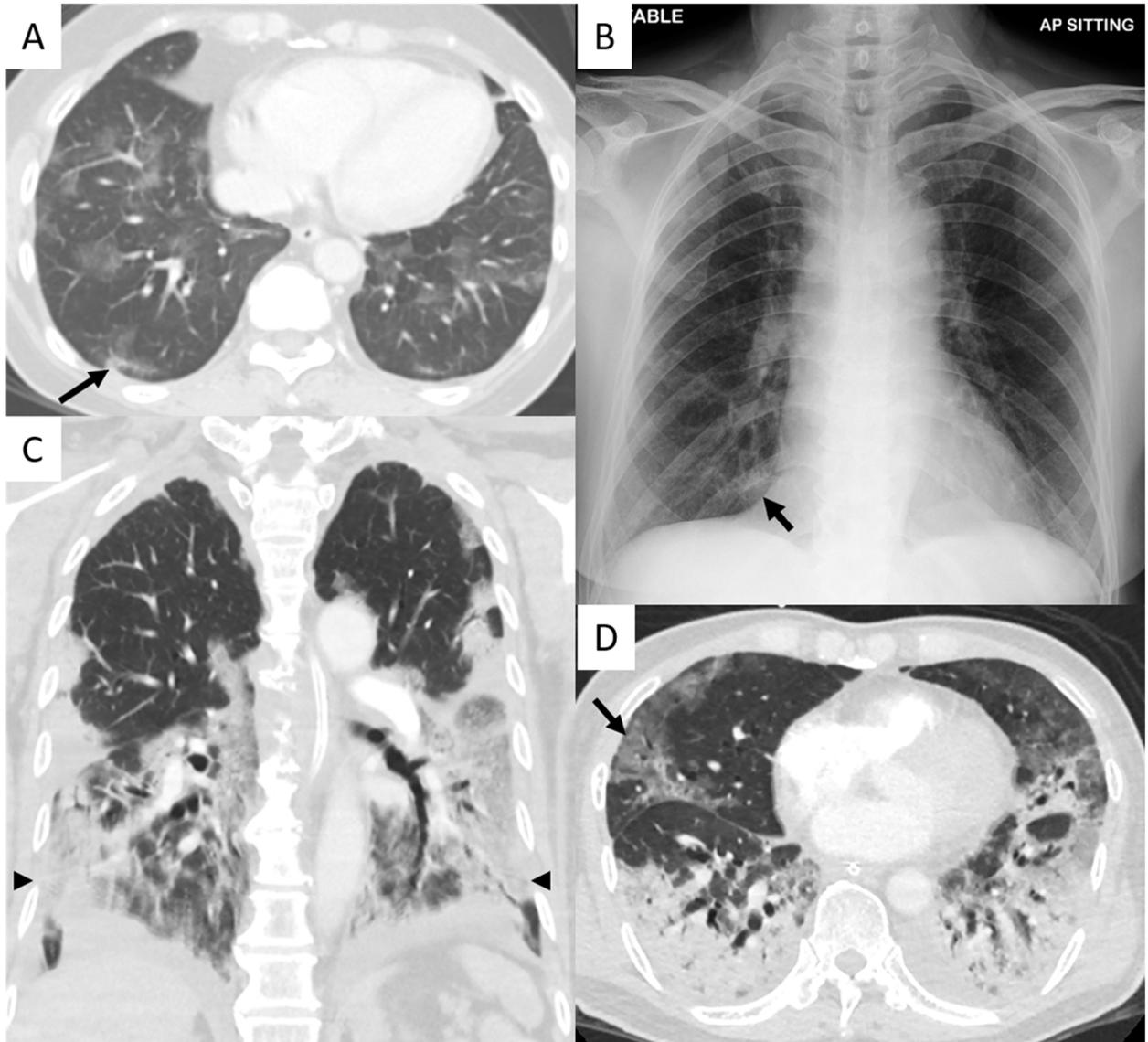
Figure**Figure 1: Chest Imaging in COVID-19 Patients**

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.

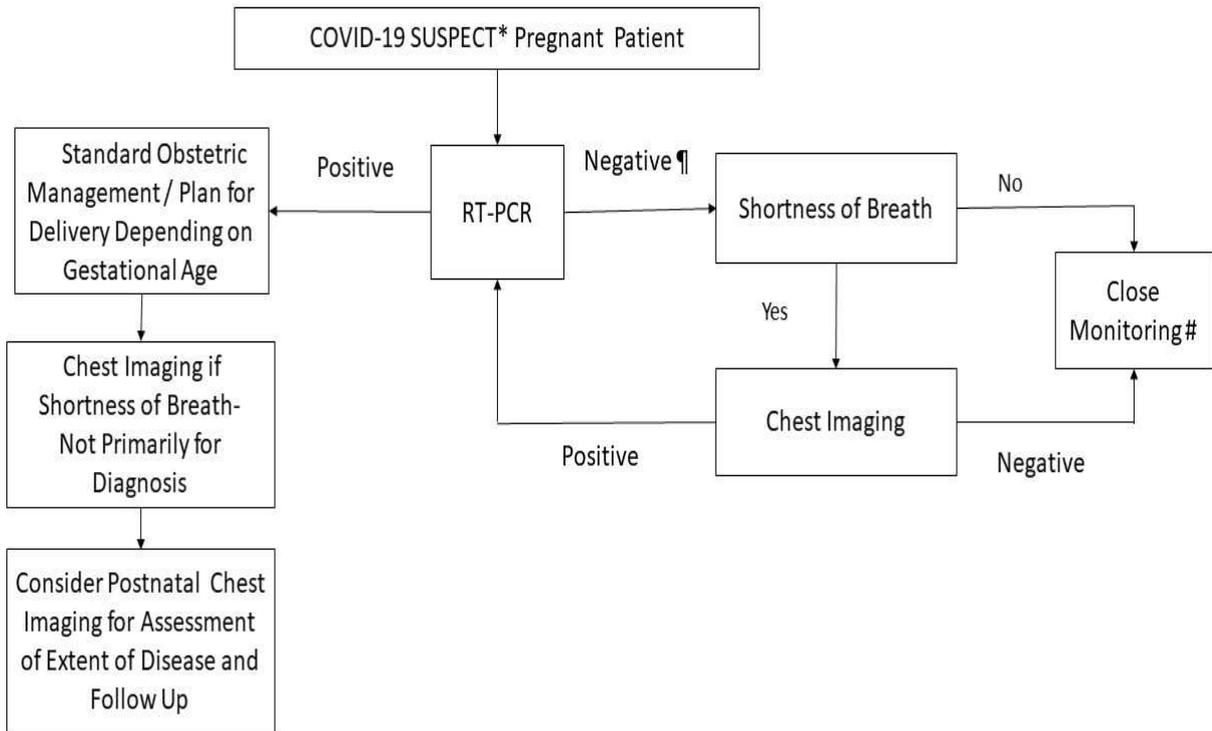
Figure 2: COVID-19 SUSPECT Pregnant Patient Diagnostic Workflow

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

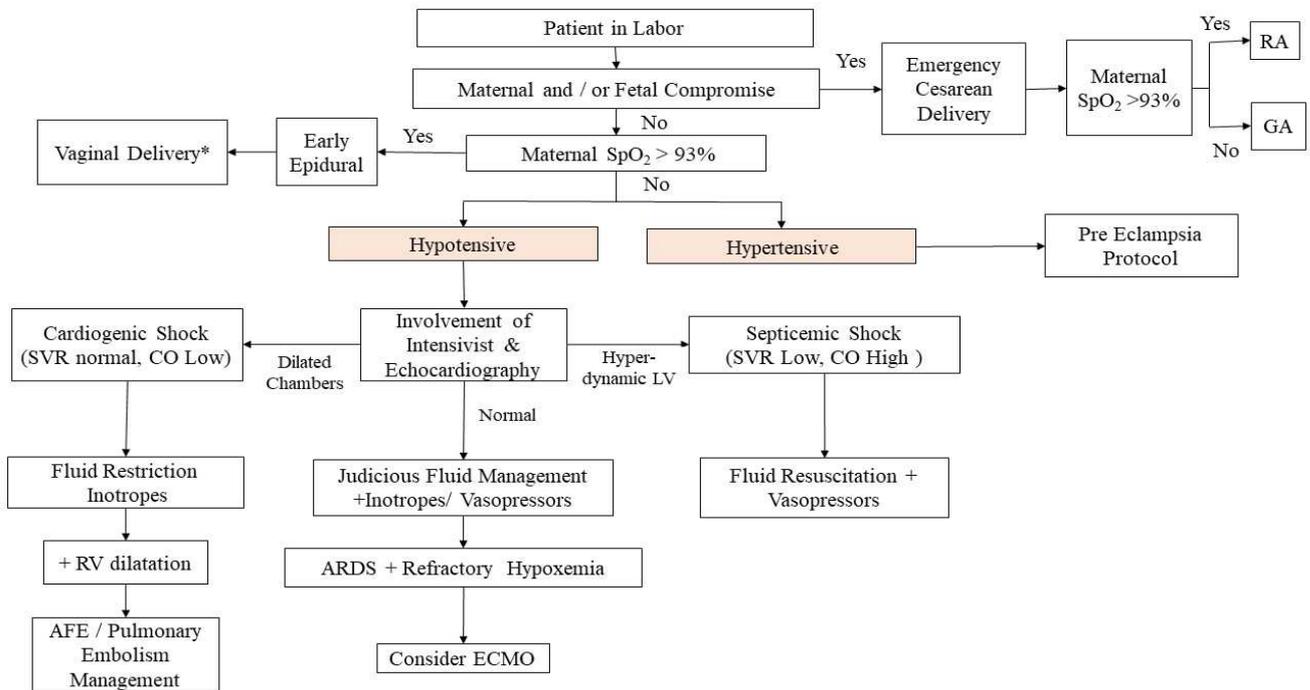
Figure 3: Stepwise Approach to the Care of Acutely Ill Parturient

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. SpO₂: 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.

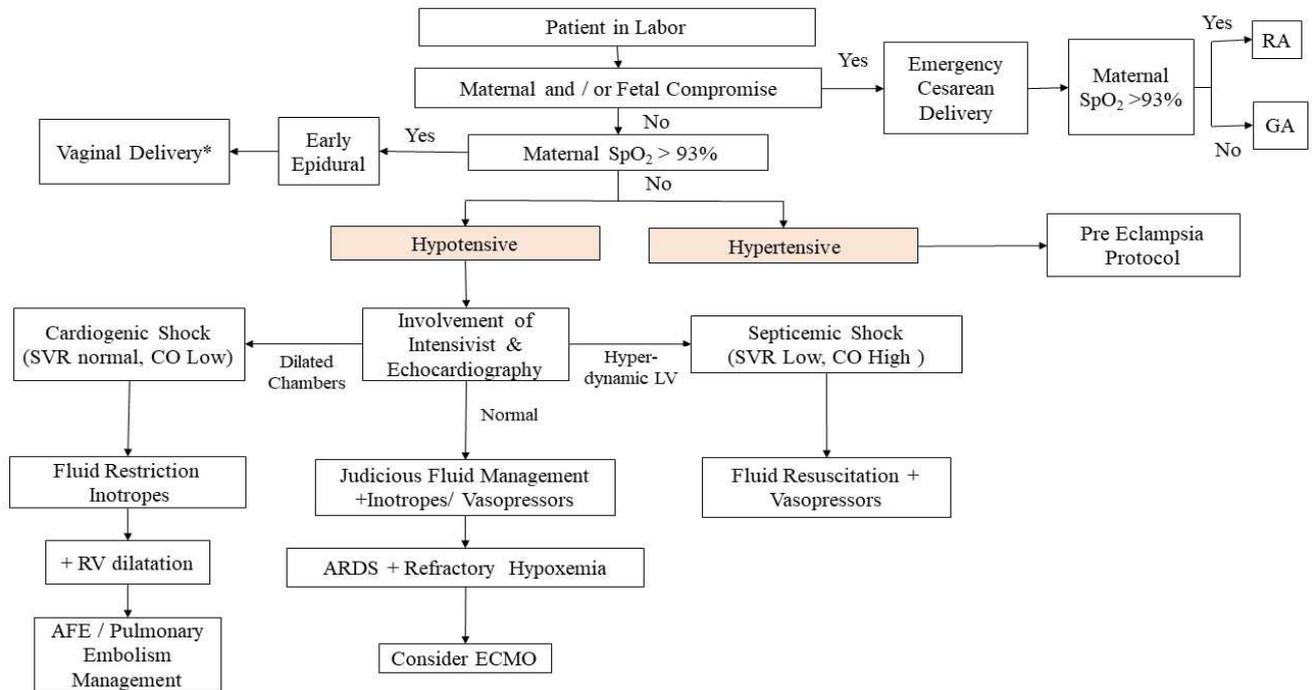
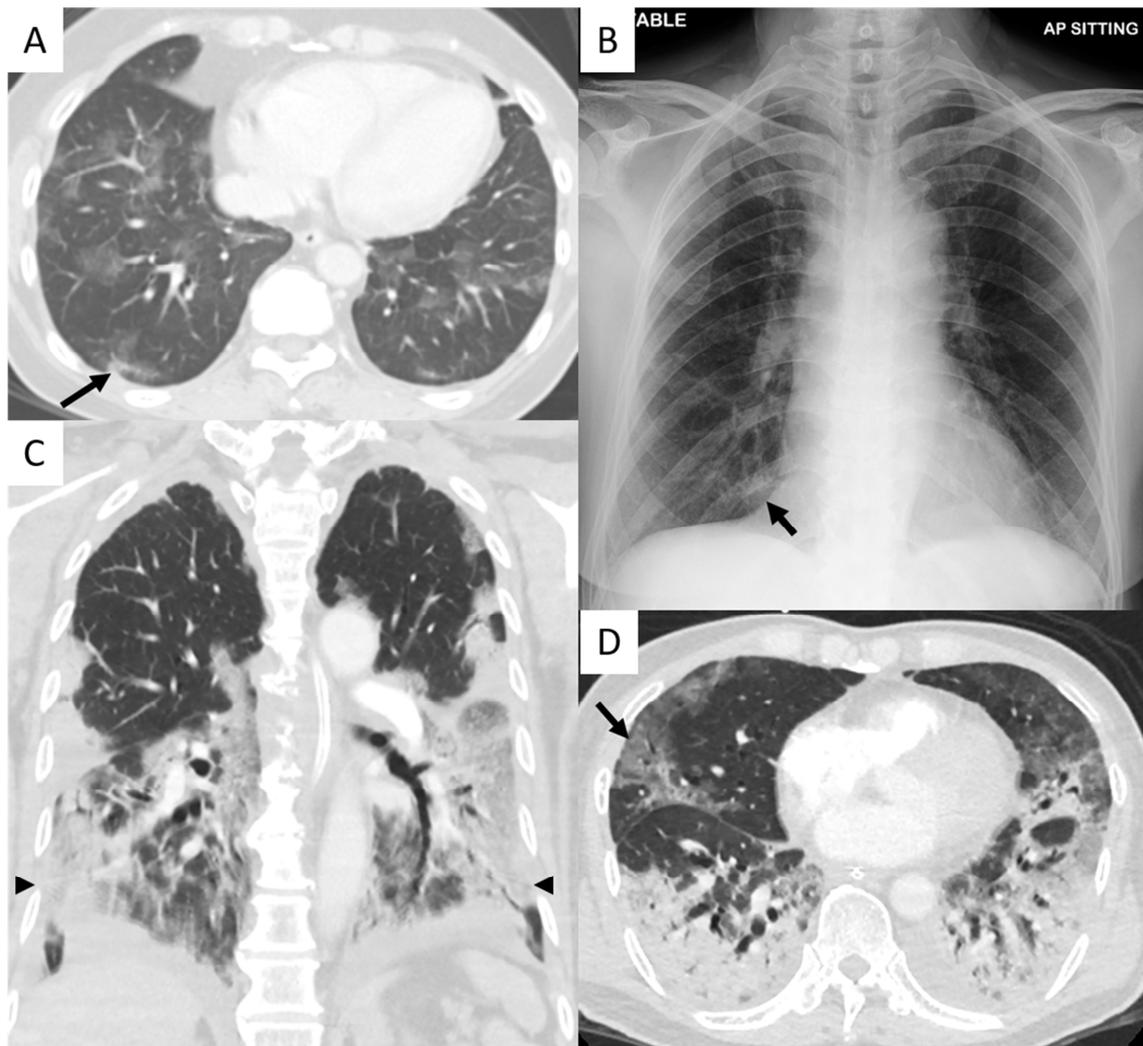
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Figure 1: Chest Imaging in COVID-19 Patients**Figure 1 Legend**

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.

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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

FiO₂: 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

IFN α : Interferon alpha

IP10: Interferon gamma-induced protein 10

IVC: Inferior vena cava

LV: Left ventricle

MCP1: Monocyte chemoattractant protein-1

MIP1 α : 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

PaO₂: Arterial partial pressure of oxygen

PAPR: Powered air-purifying respirator

P-F ratio: Ratio between arterial pressure of oxygen (PaO₂) and fraction of inspired oxygen (FiO₂)

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

SpO₂: 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

TNF α : Tumor necrosis factor alpha

TTE: Transthoracic echocardiography

WHO: World health organization

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