

Considerations for women with COVID-19 admitted to hospital

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Abstract

The number of pregnant women being admitted with severe COVID-19 infection and dying has increased with each wave of the pandemic. These women often present unique challenges to the medical and obstetric teams given the changes in physiology that occur in pregnancy, affecting assessment and management, as well as the practical difficulties such as the ideal location of care. Whilst the basis of treatment remains the same, there are nuances to caring for pregnant women that need considerable thought and multidisciplinary collaboration. Obstetricians, neonatologists, midwives, intensivists, anaesthetists and physicians may all be involved at some point, depending on the gestation and severity of illness. Implementing a COVID-19 in pregnancy guideline or checklist for your hospital will help ensure pregnant women are managed in a safe and timely manner. Here described are some key recommendations to help in the management of pregnant women admitted with COVID-19.

Keywords

COVID-19, pregnancy complications

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Introduction

Inpatient care of pregnant women with coronavirus disease 2019 (COVID-19) caused by the SARS-CoV-2 virus, brings a unique set of challenges to obstetric and medical teams.¹ Never before in the UK have such a number of pregnant women required inpatient care simultaneously, requiring the provision of optimal obstetric and medical care when these requirements are usually provided in very different parts of the hospital. Hospital geography and service provision have to be taken into consideration when caring for pregnant women with medical problems and each hospital may have a slightly different pattern of care for this reason. With preparation, planning, and close liaison between the different members of the multidisciplinary team, consistent and good care can be delivered.

This review aims to provide a framework for the care of pregnant women with COVID-19 wherever they are cared for, to cover both medical and obstetric aspects.

Hospital admission

More than two-thirds of pregnant women with SARS-CoV-2 infection remain asymptomatic.² However, severe illness in pregnancy appears to be more common in the third trimester especially with the Delta variant.² If women are admitted to hospital with COVID-19 the chances of requiring intensive care admission, invasive ventilation and use of extra corporeal membrane oxygen treatment is higher compared to age-matched non-pregnant population.² Risk factors for severe disease are similar to those of the non-pregnant population.

The most common symptoms of COVID-19 in pregnancy include cough, sore throat, myalgia and fever.³ For the minority that require hospital admission, maternal outcomes including maternal death and pre-term delivery (primarily iatrogenic), are worse compared to pregnant women without COVID-19, although overall rates of death are extremely low in the UK – the UK maternal mortality rate from COVID-19 is 2.2 per 100,000 maternities.^{3,4}

In accordance with a recent rapid report of MBRRACE-UK it is important to involve senior members of the Maternal Medicine team early in the course of the admission of a pregnant woman and therefore their contact details should be easily accessible to all relevant clinicians who may be meeting these women in the Emergency Department or medical unit.⁵

Medical interventions for SARS-CoV-2

The principles of medical treatment are the same as those in non-pregnant individuals. Thresholds for initiating oxygen therapy, medical treatments including steroids, IL-6 inhibitors, remdesivir and combination neutralising monoclonal antibodies (nMABs) are the same and are described elsewhere in the series.

Intravenous fluid therapy should be given judiciously with close monitoring of fluid balance and regular assessment of the clinical picture, where possible aiming for a neutral fluid balance.³ [See Maternal Monitoring and table 1].

Considerations for pregnant women receiving steroid treatment

All individuals with COVID-19 receiving steroid treatment should be monitored for hyperglycaemia. This is particularly pertinent for pregnant

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Table 1. Suggested initial admission checklist for pregnant women admitted to hospital.

Admission Checklist
Practicalities
Inform Medical team
Inform Maternity team
Emergency Maternity numbers documented
Appropriate location of care agreed
Therapies
Oxygen prescribed if saturations below 94%
If oxygen requirement:
prednisolone 40 mg orally once daily OR
hydrocortisone 80 mg intravenously twice daily (if unable to take oral medication)
MDT discussion and consensus for treatment with:
- Remdesivir
- Ii-6 blockade
- Neutralising antibodies
Antibiotics depending on local guidelines
Thromboprophylaxis as per local guidelines
Maternal monitoring
Observations using local Maternity Early Warning Score system, or documentation of appropriate thresholds to use
Blood glucose monitoring
Blood ketone monitoring
Fluid balance chart
Other medications
Omeprazole 20 mg once daily if steroids prescribed
Folic acid prescribed if required (first trimester or other risk factors for deficiency according to local guidelines)
Vitamin D according to local guidelines
Pain relief prescribed if needed
Anti-emetics prescribed if needed
Fetal monitoring
Plan for monitoring documented
Plan for administration of steroids for fetal lung maturation
Other considerations
Escalation plan documented
Consideration of enrolling in clinical trial

women, who are more likely to be insulin resistant and develop hyperglycaemia, as well as requiring very tight glucose control if they are found to be hyperglycaemic. A recommended testing regime would be the same as that in women with gestational diabetes, i.e., fasting glucose followed by one hour post-meal (three times a day). The target for fasting capillary glucose in pregnancy is under 5.3 mmol/l and 1 h after each meal is less than 7.8 mmol/l.⁶ Persistent hyperglycaemia should be treated either with metformin or insulin. The duration of steroid treatment can make this more difficult, as the steroid course may end shortly after treatment is instituted. For this reason, some women may require a variable rate insulin infusion, but given the concurrent fluid prescription and risk of significant volumes of fluid received this way, alternatives to this are preferable. The fetal effects of short-term hyperglycaemia are poorly elucidated. In some women, continuation of metformin or insulin may be warranted if hyperglycaemia persists. Review by the diabetes team prior to discharge is recommended.

Concomitant prescription of a proton-pump inhibitor is suggested alongside the steroid treatment, given the risk of gastric irritation, particularly with the co-prescription of aspirin (frequently prescribed in pregnancy for pre-eclampsia prophylaxis) and the frequency of heartburn in pregnancy.

Supplementary vitamins

The need for supplementary vitamins, such as folic acid and vitamin D, should be reviewed in all pregnant women admitted to hospital and based on national guidelines. Folic acid supplementation depends on gestation and the dose is determined by standard antenatal risk assessment tools.

Antibiotics

Antibiotics should only be given when co-existent bacterial infection is suspected and in accordance with local guidelines about the use of antibiotics in patients with COVID-19. Evidence of bacterial infection can include having a productive cough, radiographic evidence of pneumonia or elevated procalcitonin. Procalcitonin is increasingly used to aid decision making about antibiotic use and can be used in a similar way in pregnancy.⁷ Re-assessing for secondary infection and careful consideration about alternative sources of sepsis is also important. Bacteriuria is not uncommon in pregnancy, and chorioamnionitis may not be familiar to clinicians in a non-obstetric setting.³

Symptom control

Symptoms from COVID-19 infection can include cough, fever, breathlessness, chest pain, anxiety and delirium. Simple measures like avoiding lying patients on their backs can reduce a cough, and a trial of codeine linctus may be beneficial, with the expected caveat it can worsen constipation. Fever should be treated with paracetamol and oral hydration. Breathlessness and chest pain should be investigated, and adequate analgesia given to alleviate symptoms.⁸

Venous thromboembolism (VTE) assessment

All women admitted with confirmed or suspected COVID-19 should have their VTE risk assessed using local maternity guidelines or national guidelines, for example the RCOG Green-top Guidelines 37a.^{3,9} COVID-19 is considered a transient risk factor for venous thrombosis, as is immobility as a result of infection.³ Irrespective of COVID-19 status, anyone admitted to hospital with infection should be commenced on low molecular weight heparin (LMWH) unless delivery is expected within 12 h or there is a serious risk of haemorrhage. Many hospitals have different risk assessment tools for pregnant and non-pregnant individuals, so it is important to ensure the correct tool is used.

Latest national guidance has recently been updated (October 2021) and now recommends that all patients, regardless of the severity of their COVID-19 infection, receive standard VTE prophylaxis with LMWH to avoid complications from major bleeding events unless considered very high risk for thrombosis.⁸ The NICE guidance signposts users to the RCOG Coronavirus (COVID-19) infection and pregnancy guidelines where prophylactic LMWH is advised unless a multi-disciplinary team (including obstetrician and clinician with expertise in managing VTE in pregnancy) feels a different dosing regimen of LMWH is more appropriate. Prior to discharge from hospital, all women should have their VTE risk re-assessed and given VTE prophylaxis for 7–14 days (or longer if risk is higher).^{3,8} During admission, persistent hypoxia or tachypnoea, chest pain or failure to improve with treatment, may trigger further investigation for pulmonary thromboembolism. Cross-sectional imaging should be considered to investigate pulmonary embolism (PE) with the secondary benefit that it can provide information about the extent of lung involvement from COVID-19 infection and look for evidence of consolidation suggestive of bacterial infection. Advanced CT scanners now have several techniques to reduce radiation exposure without compromising the image quality and can be used for CT pulmonary angiography knowing that there is a negligible

increased cancer risk to maternal breast tissue and that fetal radiation dose is far below the threshold associated with radiation complications.¹⁰ Treatment dose LMWH should be given in the event of a diagnosis of venous thromboembolism, but discussion with the consultant obstetrician and consultant obstetric anaesthetist is essential for delivery plans and counselling the patient about analgesia options during labour.

Maternal monitoring

Early warning scores

The use of specific obstetric early warning systems (EWS) is recommended for all pregnant women, but it has been widely noted that this is challenging when women are in a non-obstetric setting. There are a multitude of reasons for this: a lack of awareness of alternatives to the normal early warning scores in routine use, a lack of training, or a lack of resources (for example there may be no availability of obstetric EWS charts either on paper or electronically depending on the method used locally).

Detailing observation thresholds for referral and having a clear escalation pathway for review should be part of the shared-care decision making for all pregnant women admitted with COVID-19. Importantly,

blood pressure thresholds for scoring differ significantly between non-pregnant and pregnant individuals. If the generic adult EWS is used, the blood pressure for diagnosing severe hypertension in pregnancy (160/110 mmHg) may not even score. A tachycardia is also a difficult area to give clear guidance about; recent MBRRACE-UK reports appropriately advise that a sinus tachycardia should never be ignored, but recent data shows that the upper limit of normal heart rate in pregnancy is above 100 beats per minute.^{11,12} This therefore often makes it challenging to know who to investigate and who to reassure.

RCOG guidelines recommend hourly observations including respiratory rate, heart rate and oxygen saturations, acknowledging that young people can compensate for longer and thus are at risk of acute deterioration.³ Continuous cardiac monitoring should be instituted for all women admitted to high dependency unit or intensive care (level 2 or 3) or where there is a persistent tachycardia. Fluid charts should be used to document hourly fluid balance in women with moderate or severe COVID-19.³ Being vigilant for other obstetric issues such as pre-eclampsia is essential, and not simply the remit of the obstetrician. Daily assessment for symptoms suggestive of pre-eclampsia (oedema, right upper quadrant pain, headache, visual changes such as flashing lights) is advised, as is checking for proteinuria on urine dipstick, perhaps every 2–3 days. A sample for spot protein/creatinine ratio should be sent to the laboratory if there is 1+ of

Inform	
Delivery suite midwife co-ordinator (contact number:)	
Consultant Obstetrician (contact number:)	
Consultant Obstetric Anaesthetist (contact number:)	
Neonatal team (contact number:)	
On call anaesthetist for main theatres (contact number:)	
Scrub nurse coordinator (contact number:)	
Adult intensive care team (contact number:)	
Patient's partner (contact number:)	

To come from Maternity	
Appropriately experienced Midwife	
Consultant Obstetrician	
Consultant Obstetric Anaesthetist	
Maternity scrub nurse (<i>when available</i>)	
Caesarean section pack (in addition to one on ward)	
Maternity WHO checklist	
Consent form	
Uterotonic medication (source:)	

Maternal	
Consent form completed	
Large bore intravenous access x 2	
Up-to-date group and save	
Review of all blood results (including clotting and full blood count)	
Arterial line placement prior to transfer if time available	
Route checked and cleared (corridors and lift lobby doors)	
Confirm with AICU the location patient will be going to after procedure	

Fetal	
Fetal steroids depending on gestation	
Magnesium sulphate depending on gestation	
Location of neonatal resuscitation equipment confirmed	

Figure 1. Sample: Checklist for emergency delivery in COVID-19 positive pregnant woman in a non-maternity setting.

protein or more on the dipstick, the threshold for confirmation of proteinuria in pregnancy being 30 mg/mmol.

A clear maternity escalation plan can help signpost clinicians to seek early and appropriate review from intensive care and obstetric colleagues.³

Ketones

Ketoacidosis has been reported in the setting of COVID-19 infection in non-pregnant individuals, and more recently noticed and reported in pregnant women with COVID-19.^{13,14} Irrespective of Covid infection, pregnant women are more at risk of significant ketosis, particularly in the third trimester, which is usually the result of relatively short periods of reduced oral intake. Importantly, the blood glucose may be low or normal so ketones should be checked even in the absence of hyperglycaemia, if there are any concerns about the woman becoming unwell, but this is of particular importance if tachypnoea or metabolic acidosis develops.

The treatment of ketosis in the setting of COVID-19 in pregnancy can be challenging. If ketosis does not resolve with glucose alone, consider concurrent insulin. Fixed rate insulin may be required if significant insulin resistance is present. Intravenous dextrose should be carefully administered to reduce the risk of iatrogenic fluid overload, to which pregnant women are particularly vulnerable.

Fetal considerations

Steroids for fetal indications

Corticosteroids (dexamethasone or betamethasone) for fetal lung maturation are advised in any woman deemed to be at significant risk of preterm delivery. They also prevent the development of intraventricular haemorrhage in the preterm infant. The optimal time window for administration is 24–48 h prior to delivery, and less than 7 days. They should only be given after discussion with the obstetric team and are not given prior to 22 weeks and 5 days of gestation. In all individuals with COVID-19 infection the trajectory of the illness is very variable, and difficult to predict on an individual basis. The decision to give fetal steroids for lung maturation is therefore often a challenge but should be reviewed regularly with the multidisciplinary team. If fetal steroids are given (either betamethasone or dexamethasone according to local hospital protocol) then maternal steroids can be omitted on the days these are administered.

Fetal monitoring

The necessity for fetal monitoring depends on the gestational age of the fetus and the maternal condition, and the frequency and type of monitoring (fetal heart auscultation, cardiotography or ultrasound) should be made on an individual basis. The obstetric and midwifery team reviewing the woman can advise on this for each pregnant woman admitted to hospital. Daily monitoring with cardiotocography would be appropriate for women over 26 weeks' gestation.

Delivery

The decision to deliver a pregnant woman with COVID-19 infection is very difficult. Different hospitals have different approaches to the timing of intubation and ventilation, and this therefore means that it is impossible to have 'one rule fits all' for when pregnant women should be delivered. Delivery may not lead to a dramatic improvement in the respiratory status of the patient, but may make caring for her, when very unwell, somewhat easier (for example proning to improve oxygenation if gestation advanced). There is no threshold at which delivery is mandated, and pregnant women of all gestations can receive high flow nasal oxygen, non-invasive respiratory support and ultimately intubation

and ventilation if needed. Crucially, any delivery decision needs to be made in conjunction with senior members of the relevant specialities. Normal obstetric indications for delivery apply irrespective of COVID-19 status, but delivery purely for severe COVID-19 is more difficult.¹⁵

The practical aspects of care of an unwell pregnant woman can also have an impact on delivery decisions, for example the location of the pregnant inpatient and the distance of this from a theatre setting where delivery can safely be performed. If a pregnant individual is an inpatient on a medical ward, geographically distant from maternity theatres, then if emergency delivery is required, it may be more appropriate to do this in a non-maternity theatre setting closer to her location. It is therefore advisable to construct a plan for if an emergency delivery is required, so that all clinicians involved in her care are aware of the practical issues and these can be rapidly addressed irrespective of the time of day or night. [Figure 1: An example of a checklist for delivery in a non-maternity setting].

Research trials

Pregnant women have historically been excluded from clinical trials, and of the 250 registered drug and vaccine trials during the COVID-19 pandemic, 80% excluded pregnant women.¹⁶ However, for women admitted to hospital there are opportunities to enrol in some clinical trials such as RECOVERY and your hospital research team, or research nurse/midwife should have up-to-date information on which trials are open to pregnant women and how to enrol them.

Conclusion

The use of oxygen therapy and thromboprophylaxis alongside fluid resuscitation and antibiotics where indicated, provide the mainstay of treatment for pregnant women with COVID-19. Some women will meet the criteria for additional drug therapies such as il-6 blockade and nMABs and multidisciplinary decision making may be required for treatment consensus and risk/benefit counselling. Careful monitoring and frequent reassessment of the clinical picture will enable proactive decision-making particularly as young women can compensate for longer and clinical deterioration may be sudden. The management of pregnant women with COVID-19 in hospital requires multidisciplinary input from the medical team, obstetricians and midwives, obstetric anaesthetists, intensive care physicians and paediatricians.

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