Original Article

Approach to dyspnoea in pregnancy in the COVID-19 era

A Banerjee, LA Arrandale, S Sankaran, GW Glover & C Nelson-Piercy

Abstract

Importance: *Dyspnoea and hypoxia in pregnant women during the COVID-19 pandemic may be due to causes other than SARS Co-V-2 infection which should not be ignored. Shared decision-making regarding early delivery is paramount.*
Objective: *To highlight and discuss the differential diagnoses of dyspnoea and hypoxia in pregnant women and to discuss the risks versus benefit of delivery for maternal compromise.*
Design, setting and participants: *Case series of two pregnant women who presented with dyspnoea and hypoxia during the COVID-19 pandemic.*
Results: *Two pregnant women presented with dyspnoea and hypoxia. The first case had COVID-19 infection in the 3rd trimester. The second case had an exacerbation of asthma without concurrent COVID-19. Only the first case required intubation and delivery. Both recovered and were discharged home.*
Conclusion and relevance: *Our two cases highlight the importance of making the correct diagnosis and timely decision-making to consider if delivery for maternal compromise is warranted. Whilst COVID-19 is a current healthcare concern other differential diagnoses must still be considered when pregnant women present with dyspnoea and hypoxia.*

Keywords

Pregnancy, hypoxia, dyspnoea, differential diagnosis, COVID-19

Learning points

- There is a broad differential diagnosis for dyspnoea and hypoxia in pregnant patients, and clinicians should continue to consider diseases other than COVID-19
- Maternal compromise requires consideration of delivery of the baby
- Premature delivery is not a straightforward 'cure-all' for maternal illness and the risks/benefits should be weighed and discussed by the multidisciplinary team
- The RCP toolkit is a useful resource for all physicians to use in managing pregnant patients

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Introduction

A state of 'clinical inertia' has been described when managing an unwell pregnant woman - there are two lives: mother and baby.[1,2] With the emergence of the coronavirus SARS-CoV-2 infection (COVID-19), there is a call for a change of mind-set in our current clinical practice when approaching pregnant women with dyspnoea and hypoxia.[3-5] From the current literature, it appears that COVID-19 during pregnancy probably has a similar clinical picture and severity, resembling that in the non-pregnant population.[6-10] During the COVID-19 pandemic, rapid assessment and prompt investigations are crucial; which establishes the correct diagnosis and initiates the right treatment - making a diagnosis not just ruling COVID-19 out. The *availability heuristic* describes the potential distortion in an individual's estimate of the probability of an event (in this case a diagnosis), based on the immediacy or ascribed consequence of the event. In a pandemic scenario, there is a risk that clinicians may neglect their usual diagnostic sieve and ascribe all respiratory symptoms to COVID-19. Both cases were managed along our hospital COVID-suspected and confirmed pathway in terms of cohorting and isolation. The aim of this article is to highlight the importance of considering other non-COVID-19 related causes of dyspnoea and hypoxia in pregnancy, as well as the importance of multidisciplinary decision making regarding early delivery and the risks of preterm delivery for the mother and baby.

Case presentations

Case 1: 40-year-old South American primiparous pregnant woman at 27+6 weeks of gestation was admitted with a ten-day history of a dry cough and

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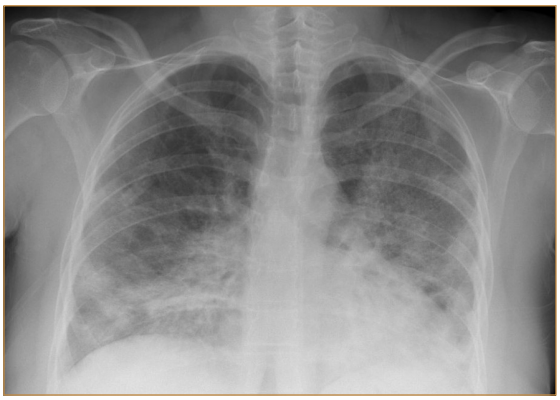

Figure 1a. Further Imaging of Case 1
Legend 1.A Chest X-ray showing bilateral alveolar opacities consistent with COVID-19 infection

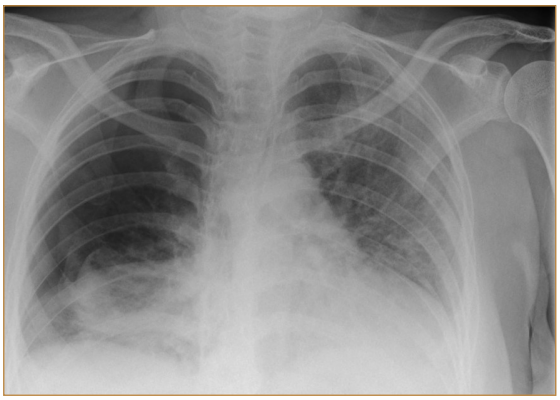

Figure 1b. A Imaging of Case 1.
Legend 1.B Chest X-Ray of a right sided pneumothorax.

pyrexia. Her body mass index (BMI) was 27.9 kg/m^2. Her past medical history included previous Hodgkin's lymphoma, now in remission for 10 years. On admission peripheral oxygen saturations (SaO_2) were 88% on room air, which improved to >94% with a fractional inspired oxygen concentration (FiO_2) of 0.28, heart rate 85 beats per minute (bpm) and respiratory rate 22 breaths per minute. A chest radiograph (CXR) was undertaken (Fig. 1.A). The throat and nasal swab from admission were positive for SARS-CoV-2 RNA using multiplexed-tandem polymerase chain reaction (AusDiagnostics, Mascot, Australia). Legionellla and Pneumococcal screens were negative. The peak values with normal ranges in brackets were: D-dimer 6.62mg/L (0.00-0.55mg/L), ferritin 312µg/L (13-150 µg/L), fibrinogen 10g/L (1.7-3.9g/L), LDH 262U/L (135-214U/L), CRP 244mg/L (0-4mg/L) and a trough lymphocyte count of 0.7 x10^9/L (1.2-3.5 x10^9/L. No liver or renal impairment was observed. In the hours following admission her oxygen requirements and work of breathing increased culminating in SaO_2 93% on 15l/min O_2 with a respiratory rate of 40 breaths per minute. The decision to deliver for maternal reasons was made with the multidisciplinary team the following day when she was 28 weeks of gestation. A single dose of 12 mg betamethasone intramuscularly was administrated for fetal lung maturation, as well as intravenous magnesium sulphate 4g over 20 minutes, followed by maintenance infusion of 1g/hr for 24 hours for fetal neuroprotection. She underwent a Grade I emergency Caesarean-section under general anaesthesia for both respiratory failure and the need to undertake a Caesarean-section. The newborn was a male weighing 1430g, born in moderate condition, intubated, ventilated and was admitted to the neonatal unit. COVID-19 swab of the baby was reported as negative on Day2 and Day4. Post-operatively the mother was transferred to critical care where she improved quickly and was extubated on day 2 and after 5 days stepped down to a medical ward. Six days after delivery she became more hypoxic and was found to have a right-sided simple pneumothorax which was managed with a chest drain insertion and later with blood patching for persistent airleak. (Fig. 1.B).

The key learning point is the timely recognition of maternal respiratory compromise and joint decision-making around risks versus benefits of early delivery in COVID-19 positive women with worsening hypoxia, not responding to high flow Oxygen and requiring mechanical ventilation.

Case 2: 27-year-old Caucasian multiparous P1^{+4} who had suffered from asthma since childhood and stopped smoking in the 1st trimester. Her BMI was 23.2 kg/m^2. In the 2nd trimester she had several exacerbations of asthma; treated with a short courses of steroids at 18 weeks of gestation and 25 weeks of gestation and she had required antibiotics for recurrent urinary tract infections. At 29^{+4}/40 weeks of gestation she presented with increasing dyspnoea and SaO_2 94% breathing on room air. She denied cough or fever but complained of 'tightness' in the chest. A blood gas on air showed pH 7.47, pO_2 8.75 kPa, pCO_2 3.69 kPa and lactate 1.22 mmol/L. There was bilateral wheeze on chest auscultation. She was admitted to the obstetric high dependence unit and treated with 4L/min oxygen, intravenous magnesium sulphate 8mmol (2g), a further course of oral steroids and broad spectrum antibiotics. Three days later she was more hypoxic with widespread wheeze on auscultation. Other differentials were considered at this time and a computed tomography pulmonary angiogram (CTPA) scan excluded a pulmonary embolus (PE) and a repeat throat and nasal swab on two occasions excluded a COVID-19 infection. The scan was more consistent with inflammation of the airways. The Pneumococcal and Legionella antigen screen were negative. The peak D-dimer was 0.9mg/L, fibrinogen was 5.7g/L, CRP was 9mg/L,

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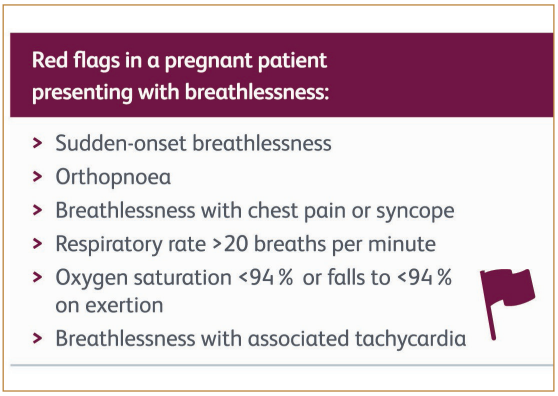

Figure 2a. A Red flags of dyspnoea in pregnancy from the Royal College of Physicians, Acute care toolkit 15: Managing acute medical problems in pregnancy
Legend 2.A These symptoms and signs need to be addressed. A differential diagnosis should be sought.

the trough lymphocyte count was 1.0 x10^9/L and no eosinophilia. Normal liver and renal profile. The clinical picture remained consistent with moderate asthma and her clinical condition improved with the addition of a leukotriene receptor antagonist, montelukast. She had no further hospital admissions for asthma during pregnancy. She had a vaginal delivery, at 38^{+2} weeks of gestation. The newborn was a female weighing 3060g, Post-partum follow-up was arranged with the asthma team for consideration of biologic agents for control of asthma.

The key learning point being, a thorough clinical assessment including auscultation of chest should be undertaken and in the presence of wheeze and hypoxia consider other differentials and treat accordingly.

Discussion

The approach to hypoxia was challenging during the current COVID-19 pandemic as we were dealing with uncertainty and employing tentative clinical knowledge. There is a risk of fixation on COVID-19 diagnosis when a woman presents with symptoms and signs of dyspnoea. The 1st case was a severe case of COVID-19 in pregnancy, conversely the 2nd case was a moderate case of asthma in pregnancy not requiring ventilation. The large cohort study of 427 COVID-19 positive pregnant women hospitalised with confirmed SARS-CoV-2 infection in the UK found approximately 1 in 10 pregnant women admitted required respiratory support in a critical care setting.[11] This national cohort study using the UK Obstetric Surveillance System (UKOSS) found 18 of these women were intubated due to maternal respiratory compromise and 10 were intubated to allow for urgent delivery. These data and others show that this is not common, and most pregnant women have mild SARS-CoV2 infection.

Exacerbation of asthma is one of the most common presentations during pregnancy. Treating an acute exacerbation of asthma is similar in pregnancy and non-pregnancy and no asthma medication should be withheld. During pregnancy, worsening asthma symptoms should be managed aggressively via up-titration of medication as per the British Thoracic Society guidelines.[12] In the last mortality report of respiratory disease in the MBRRACE report, 9 women died from respiratory causes, two from cystic fibrosis, two from asthma, two from other known lung diseases, two from non-specific respiratory failure and one from acute airway obstruction. Five of these women died more than 42 days after the end of pregnancy. Undiagnosed pulmonary hypertension was a feature in some of the women with known lung disease that died. Both of the women in the MBRRACE report who died from asthma were smokers. Our case was a presentation of moderate asthma that was treated accordingly and who did not deteriorate to severe asthma.

Clinical suspicion, accurate history taking and bedside assessment skills are needed more now than ever before. Auscultation of the lungs (as in case 2) is vital as with asthma there will be evidence of polyphonic wheeze; whereas in COVID-19 lungs there is either an absence of added sounds, or the presence of fine inspiratory crackles (case 1). The interpretation of clinical features and investigations is vital, as is the tracking of maternal physiology with regular observation and the use of the MEOWS early warning score. The usual clinical assessment of respiratory failure is potentially confounded by the physiological changes associated with adaptation to pregnancy, such as dyspnoea and tachycardia, and the fact that in a novel disease such as COVID-19, significant tachypnoea, or tachycardia may be very late signs. Therefore, the involvement of a multi-disciplinary team of experienced clinicians when managing the two lives of the mother and the baby is vital. Practical guidance on managing women with acute medical problems in pregnancy has been developed as an acute care toolkit with the Royal College of Physicians, London and the Society of Acute Medicine and launched in October 2019.[2] This provides up-to-date information and a refresher of the physiological changes of pregnancy and the safety profile of radiological investigations and medication in pregnancy. The red flags of dyspnoea in pregnancy are described (Fig. 2.A). The table in Figure 2.B describes the common differential diagnosis at trimester specific times. Referring to this table will enable clinicians to make a diagnosis and not just exclude a diagnosis. Withholding crucial investigations inappropriately, leading to an incomplete or inaccurate diagnosis

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	First trimester	Second trimester	Third trimester	Postpartum
Physiological breathlessness of pregnancy	Can occur	Can occur	More common	n/a
Anaemia	Can occur	Can occur	More common	More common
Asthma	Can occur throughout pregnancy and in the postpartum period			
Pulmonary embolism	Can occur throughout pregnancy and is most common in the postpartum period			
Dilated cardiomyopathy (DCM)	Rarely presents	May decompensate	Could be decompensated pre-existing DCM or peripartum cardiomyopathy (PPCM)	Could be decompensated pre-existing DCM or PPCM
Pneumonia	Can occur throughout pregnancy and postpartum			
Pneumothorax	Can occur	Can occur	Can occur	Most common after vaginal delivery
Hyperventilation	Can occur throughout pregnancy and postpartum			

Figure 2b. Table from the Royal College of Physicians, Acute care toolkit 15: Managing acute medical problems in pregnancy of the differential diagnosis of breathlessness in pregnancy and postpartum.
Legend 2.B This provides trimester specific differential diagnosis to be considered in a pregnant woman.

in pregnancy is a recurrent theme that has figured in maternal mortality reports. For example, the D-dimer can increase several fold in the second half of pregnancy, and this was illustrated in case 2.[13] The D-dimer was also markedly raised in case 1, and in this case may have been more consistent with the inflammatory response and pro-coagulant features of COVID-19. Neither patient had a PE as the cause of breathlessness. The most likely contributory factors for the pneumothorax in case 1 may be the degree of underlying lung disease post lymphoma treatment 10 years earlier or else the acute infection and coughing weakened her pleura.

The core principle of management of COVID-19 in pregnancy is a multidisciplinary team approach, which involves obstetricians, midwives, obstetric anaesthetists, maternal-fetal experts, obstetric physicians and intensivists. Whilst management in the early phase of the COVID-19 pandemic was limited to supportive care, there is now emerging evidence for novel therapeutic options. Unfortunately pregnant patients may either be excluded from trials or are represented in small numbers and hence generalisability of the results to this population is challenging. The Recovery trial demonstrating the beneficial effect of steroids in patients requiring oxygen or ventilation did include pregnant women but they received prednisolone instead of dexamethasone.

Preterm delivery is not a straightforward 'cure-all' for maternal illness and the risks/benefits should be weighed and discussed. Preterm delivery is defined as birth before 37 weeks of gestation. It accounts for nearly 8% of all live births in England and Wales and contributes to neonatal and infant morbidity and mortality.[14] Morbidity is inversely correlated to gestational age at birth with the most severe adverse outcomes including neurodevelopmental impairments (e.g. cerebral palsy, sensory and visual problems), together with respiratory and gastrointestinal complications.[15] Each case should be individualised and discussed with the mother and team.

In conclusion we have shown that dyspnoea and hypoxia in pregnant women during the COVID-19 pandemic may be due to other causes which should not be ignored. We must not forget that deaths due to indirect causes (non-obstetric maternal deaths during pregnancy and up to 42 days postpartum) were high even before the current COVID-19 pandemic.[1] We cannot afford to miss other causes of dyspnoea and hypoxia in the current climate.

Conflicts of interest

AB, LA, SS, GWG report no conflict of interest. CNP has received lecturing fees from Sanofi, Jenssen, Warner Chilcott, Falk, Alliance Pharma and UCB. She has received consultancy fees from UCB and Alliance Pharma.

Anita Banerjee conceived the idea of the manuscript. Anita Banerjee, Srividhya Sankaran and Lindsay Arrandale were involved in data collection. The original draft was prepared by Anita Banerjee. Catherine Nelson-Piercy and Guy W Glover validated the work. All authors were involved in writing, reviewing and editing the final manuscript.

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